

OUTLIVE

THE SCIENCE & ART
OF LONGEVITY

PETER ATTIA, MD

WITH BILL GIFFORD

RETHINKING MEDICINE TO LIVE BETTER LONGER



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HARMONY
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AUTHOR'S NOTE

作者註

Writing about science and medicine for the public requires striking a balance between brevity and nuance, rigor and readability. I've done my best to find the sweet spot on that continuum, getting the substance right while keeping this book accessible to the lay reader. You'll be the judge of whether or not I hit the target.

為大眾撰寫有關科學和醫學的文章需要在簡潔與細微差別、嚴謹與可讀性之間取得平衡。我已盡最大努力在這個連續體中找到最佳點，在保證本書內容適合非專業讀者的同時，保證其內容正確。你將判斷我是否擊中目標。

CONTENTS

內容

Introduction

介紹

Part I

第一部分

CHAPTER 1: The Long Game: From Fast Death to Slow Death

第一章：漫長的遊戲：從快死到慢死

CHAPTER 2: Medicine 3.0: Rethinking Medicine for the Age of Chronic Disease

第 2 章：醫學 3.0：重新思考慢性病時代的醫學

CHAPTER 3: Objective, Strategy, Tactics: A Road Map for Reading This Book

第 3 章：目標、策略、戰術：閱讀本書的路線圖

Part II

第二部分

CHAPTER 4: Centenarians: The Older You Get, the Healthier You Have Been

第四章：百歲老人：年紀越大，越健康

CHAPTER 5: Eat Less, Live Longer: The Science of Hunger and Health

第五章：少吃，長壽：飢餓與健康的科學

CHAPTER 6: The Crisis of Abundance: Can Our Ancient Genes Cope with Our Modern Diet?

第六章：豐富的危機：我們古老的基因能否應付我們的現代飲食？

CHAPTER 7: The Ticker: Confronting—and Preventing—Heart Disease, the Deadliest Killer on the Planet

第 7 章：股票行情：面對並預防心臟病，地球上最致命的殺手

CHAPTER 8: The Runaway Cell: New Ways to Address the Killer That Is Cancer

第 8 章：失控的細胞：解決癌症殺手的新方法

CHAPTER 9: Chasing Memory: Understanding Alzheimer's Disease and Other Neurodegenerative Diseases

第 9 章：追逐記憶：了解阿茲海默症和其他神經退化性疾病

Part III

第三部分

CHAPTER 10: Thinking Tactically: Building a Framework of Principles That Work for You

第 10 章：戰術性思考：建立適合您的原則框架

CHAPTER 11: Exercise: The Most Powerful Longevity Drug

第十一章：運動：最有效的長壽藥

CHAPTER 12: Training 101: How to Prepare for the Centenarian Decathlon

第12章：訓練101：如何為百歲十項全能做準備

CHAPTER 13: The Gospel of Stability: Relearning How to Move to Prevent Injury

第 13 章：穩定的福音：重新學習如何移動以防止受傷

CHAPTER 14: Nutrition 3.0: You Say Potato, I Say “Nutritional Biochemistry”

第14章：營養3.0：你說馬鈴薯，我說“營養生物化學”

CHAPTER 15: Putting Nutritional Biochemistry into Practice: How to Find the Right Eating Pattern for You

第 15 章：將營養生物化學付諸實踐：如何找到適合您的飲食模式

CHAPTER 16: The Awakening: How to Learn to Love Sleep, the Best Medicine for Your Brain

第 16 章：覺醒：如何學習愛睡眠，它是大腦的最佳良藥

CHAPTER 17: Work in Progress: The High Price of Ignoring Emotional Health

第 17 章：正在進行的工作：忽視情緒健康的高昂代價

Epilogue

結語

Acknowledgments

致謝

Notes

筆記

References

參考

Index

指數

INTRODUCTION

介紹

In the dream, I'm trying to catch the falling eggs.

在夢中，我試著接住掉落的雞蛋。

I'm standing on a sidewalk in a big, dirty city that looks a lot like Baltimore, holding a padded basket and looking up. Every few seconds, I spot an egg whizzing down at me from above, and I run to try to catch it in the basket.

我站在一座骯髒的大城市的人行道上，這個城市看起來很像巴爾的摩，手裡拿著一個帶襯墊的籃子，抬起頭來。每隔幾秒鐘，我就會看到一個雞蛋從上面呼嘯而下，我就跑去試圖把它接進籃子裡。

They're coming at me fast, and I'm doing my best to catch them, running all over the place with my basket outstretched like an outfielder's glove. But I can't catch them all. Some of them—many of them—smack on the ground, splattering yellow yolk all over my shoes and medical scrubs. I'm desperate for this to stop.

他們向我快速逼近，我盡全力去追趕他們，我的籃子像外野手的手套一樣伸開，到處跑。但我無法全部捕捉到。其中一些——很多——掉在地上，黃色的蛋黃濺滿了我的鞋子和醫療服。我迫切希望這一切能夠停止。

Where are the eggs coming from? There must be a guy up there on top of the building, or on a balcony, just casually tossing them over the rail. But I can't see him, and I'm so busy I barely even have time to think about him. I'm

just running around trying to catch as many eggs as possible. And I'm failing miserably. Emotion wells up in my body as I realize that no matter how hard I try, I'll never be able to catch all the eggs. I feel overwhelmed, and helpless.

雞蛋從哪裡來？一定有人在樓頂或陽台上，隨意地將它們丟到欄桿上。但我看不到他，而且我太忙了，幾乎沒有時間去想他。我只是到處跑，試圖抓住盡可能多的雞蛋。而我卻一敗塗地。當我意識到無論我如何努力，我永遠無法抓住所有的雞蛋時，我的情緒在我的體內湧動。我感到不知所措，又無助。

And then I wake up, another chance at precious sleep ruined.

然後我就醒了，又一次寶貴的睡眠機會被毀了。

We forget nearly all our dreams, but two decades later, I can't seem to get this one out of my head. It invaded my nights many times when I was a surgical resident at Johns Hopkins Hospital, in training to become a cancer surgeon. It was one of the best periods of my life, even if at times I felt like I was going crazy. It wasn't uncommon for my colleagues and me to work for twenty-four hours straight. I craved sleep. The dream kept ruining it.

我們幾乎忘記了所有的夢想，但二十年後，我似乎無法將這個夢想從我的腦海中抹去。當我在約翰霍普金斯醫院擔任外科住院醫師時，它多次侵入我的夜晚，接受癌症外科醫生的培訓。這是我人生中最美好的時期之一，即使有時我覺得自己快要瘋了。對我和我的同事來說，連續工作二十四小時並不罕見。我渴望睡覺。夢想不斷地毀掉它。

The attending surgeons at Hopkins specialized in serious cases like pancreatic cancer, which meant that very often we were the only people standing between the patient and death. Pancreatic cancer grows silently, without symptoms, and by the time it is discovered, it is often quite advanced. Surgery was an option for only about 20 to 30 percent of patients. We were their last hope.

霍普金斯大學的主治外科醫師專門治療胰臟癌等嚴重病例，這意味著我們常常是唯一站在病人和死亡之間的人。胰臟癌悄無聲息地生長，沒有任何症狀，當被發現時，往往已經是晚期了。只有約 20% 至 30% 的患者可以選擇手術。我們是他們最後的希望。

Our weapon of choice was something called the Whipple Procedure, which involved removing the head of the patient's pancreas and the upper part of the small intestine, called the duodenum. It's a difficult, dangerous operation, and in the early days it was almost always fatal. Yet still surgeons attempted it; that's how desperate pancreatic cancer is. By the time I was in training, more than 99 percent of patients survived for at least thirty days after this surgery. We had gotten pretty good at catching the eggs.

我們選擇的武器是惠普爾手術，其中包括切除患者的胰頭和小腸的上部（稱為十二指腸）。這是一項困難、危險的手術，在早期幾乎總是致命的。然而外科醫生仍然嘗試這樣做。胰臟癌就是這麼絕望。當我接受訓練時，超過 99% 的患者在手術後至少存活了 30 天。我們已經很擅長抓雞蛋了。

At that point in my life, I was determined to become the best cancer surgeon that I could possibly be. I had worked really hard to get where I was; most of my high school teachers, and even my parents, had not expected me to make it to college, much less graduate from Stanford Medical School. But more and more, I found myself torn. On the one hand, I loved the complexity of these surgeries, and I felt elated every time we finished a successful procedure. We had removed the tumor—we had caught the egg, or so we thought.

在我生命中的那個時刻，我決心成為盡可能最好的癌症外科醫生。我非常努力地工作才達到現在的水平。我的大多數高中老師，甚至我的父母，都沒想到我能考上大學，更不用說從史丹佛醫學院畢業了。但我越來越發現自己陷入了困境。一方面，我喜歡這些手術的複雜性，每次成功完成手術時我都感到很高興。我們已經切除了腫瘤——我們已經抓住了雞蛋，至少我們是這麼認為的。

On the other hand, I was beginning to wonder how “success” was defined. The reality was that nearly all these patients would still die within a few years. The egg would inevitably hit the ground. What were we really accomplishing?

另一方面，我開始想知道「成功」是如何定義的。現實情況是，幾乎所有這些患者仍會在幾年內死亡。雞蛋不可避免地會落地。我們真正

實現了什麼？

When I finally recognized the futility of this, I grew so frustrated that I quit medicine for an entirely different career. But then a confluence of events occurred that ended up radically changing the way I thought about health and disease. I made my way back into the medical profession with a fresh approach, and new hope.

當我最終意識到這樣做是徒勞無功的時，我變得非常沮喪，以至於我放棄了醫學，轉而從事完全不同的職業。但隨後發生的一系列事件最終徹底改變了我對健康和疾病的看法。我帶著新的方法和新的希望重返醫學界。

The reason why goes back to my dream about the falling eggs. In short, it had finally dawned on me that the only way to solve the problem was not to get better at catching the eggs. Instead, we needed to try to stop the guy who was throwing them. We had to figure out how to get to the top of the building, find the guy, and take him out.

究其原因，還要追溯到我夢見雞蛋掉下來的事。簡而言之，我終於明白了，解決問題的唯一方法並不是提高抓雞蛋的能力。相反，我們需要嘗試阻止扔東西的人。我們必須弄清楚如何到達建築物的頂部，找到那個人，然後把他幹掉。

I'd have relished that job in real life; as a young boxer, I had a pretty mean left hook. But medicine is obviously a bit more complicated. Ultimately, I realized that we needed to approach the situation—the falling eggs—in an entirely different way, with a different mindset, and using a different set of tools.

在現實生活中我會很喜歡這份工作的。作為一名年輕的拳擊手，我的左勾拳非常厲害。但醫學顯然要複雜一些。最終，我意識到我們需要以一種完全不同的方式、不同的心態、使用不同的工具來處理這種情況——雞蛋掉落。

That, very briefly, is what this book is about.

簡而言之，這就是本書的主題。

PART I

第一部分

CHAPTER 1

第1章

The Long Game

漫長的遊戲

From Fast Death to Slow Death

從快死到慢死

There comes a point where we need to stop just pulling people out of the river. We need to go upstream and find out why they're falling in.

到了某個時候，我們需要停止只是把人們從河裡拉出來。我們需要逆流而上，找出他們掉進去的原因。

—BISHOP DESMOND TUTU

——德斯蒙德·圖圖主教

I'll never forget the first patient whom I ever saw die. It was early in my second year of medical school, and I was spending a Saturday evening volunteering at the hospital, which is something the school encouraged us to do. But we were only supposed to observe, because by that point we knew just enough to be dangerous.

我永遠不會忘記我見過的第一個死去的病人。那是我在醫學院讀二年級的時候，週六晚上我在醫院做志願者，這是學校鼓勵我們做的事情。但我們只應該觀察，因為到那時我們所知道的就夠危險了。

At some point, a woman in her midthirties came into the ER complaining of shortness of breath. She was from East Palo Alto, a pocket of poverty in that very wealthy town. While the nurses snapped a set of EKG leads on her and fitted an oxygen mask over her nose and mouth, I sat by her side, trying to distract her with small talk. *What's your name? Do you have kids? How long have you been feeling this way?*

在某個時候，一名三十多歲的女性因呼吸急促進入急診室。她來自東帕洛阿爾托，那是那個非常富裕的小鎮上的一個貧困地區。當護士為她安裝心電圖導極並在她的鼻子和嘴巴上戴上氧氣面罩時，我坐在她旁邊，試圖透過閒聊分散她的注意力。你叫什麼名字？你有孩子嗎？你有這種感覺多久了？

All of a sudden, her face tightened with fear and she began gasping for breath. Then her eyes rolled back and she lost consciousness.

突然，她的臉因恐懼而繃緊，呼吸開始急促。然後她的眼睛一翻，失去了知覺。

Within seconds, nurses and doctors flooded into the ER bay and began running a "code" on her, snaking a breathing tube down her airway and injecting her full of potent drugs in a last-ditch effort at resuscitation. Meanwhile, one of the residents began doing chest compressions on her prone body. Every couple of minutes, everyone would step back as the attending physician slapped defibrillation paddles on her chest, and her body would twitch with the immense jolt of electricity. Everything was precisely choreographed; they knew the drill.

幾秒鐘之內，護士和醫生湧入急診室，開始對她進行“編碼”，將一根呼吸管插入她的氣道，並向她注射大量強效藥物，為她做最後的復甦努力。同時，一名住院醫生開始對她俯臥的身體進行胸部按壓。每隔幾分鐘，當主治醫生將除顫板拍打在她的胸口時，每個人都會退後一步，她的身體會因巨大的電流而抽搐。一切都經過精心設計；他們知道該怎麼做。

I shrank into a corner, trying to stay out of the way, but the resident doing CPR caught my eye and said, “Hey, man, can you come over here and relieve me? Just pump with the same force and rhythm as I am now, okay?”

我躲到一個角落裡，試圖躲開，但正在做心肺復甦術的住院醫生注意到了我，說：「嘿，夥計，你能過來幫我一下嗎？用和我現在一樣的力量和節奏來泵，好嗎？」

So I began doing compressions for the first time in my life on someone who was not a mannequin. But nothing worked. She died, right there on the table, as I was still pounding on her chest. Just a few minutes earlier, I'd been asking about her family. A nurse pulled the sheet up over her face and everyone scattered as quickly as they had arrived.

所以我開始對一個不是人體模型的人進行我一生中的第一次按壓。但沒有任何效果。當我仍在敲擊她的胸口時，她死了，就在桌子上。就在幾分鐘前，我還在詢問她的家人。一名護士拉起床單蓋住她的臉，大家一到就迅速散開。

This was not a rare occurrence for anyone else in the room, but I was freaked out, horrified. *What the hell just happened?*

對於房間裡的其他人來說，這種情況並不罕見，但我嚇壞了，害怕極了。剛剛到底發生了什麼事？

I would see many other patients die, but that woman's death haunted me for years. I now suspect that she probably died because of a massive pulmonary embolism, but I kept wondering, what was really wrong with her? What was going on before she made her way to the ER? And would things

have turned out differently if she had had better access to medical care? Could her sad fate have been changed?

我會看到許多其他病人死去，但那個女人的死多年來一直困擾著我。我現在懷疑她可能是死於嚴重的肺栓塞，但我一直在想，她到底出了什麼問題？她去急診室之前發生了什麼事？如果她能更好地獲得醫療護理，事情會有所不同嗎？難道她的悲慘命運可以改變嗎？

Later, as a surgical resident at Johns Hopkins, I would learn that death comes at two speeds: fast and slow. In inner-city Baltimore, fast death ruled the streets, meted out by guns, knives, and speeding automobiles. As perverse as it sounds, the violence of the city was a “feature” of the training program. While I chose Hopkins because of its excellence in liver and pancreatic cancer surgery, the fact that it averaged more than ten penetrating trauma cases per day, mostly gunshot or stabbing wounds, meant that my colleagues and I would have ample opportunity to develop our surgical skills repairing bodies that were too often young, poor, Black, and male.

後來，身為約翰霍普金斯大學的外科住院醫生，我了解到死亡有兩種速度：快和慢。在巴爾的摩市中心，快速的死亡統治著街道，槍、刀和飛馳的汽車充斥著死亡。儘管聽起來有些反常，但城市的暴力卻是培訓計畫的「特色」。雖然我選擇霍普金斯大學是因為它在肝癌和胰腺癌手術方面表現出色，但事實上，它平均每天有十多個穿透性創傷病例，其中大部分是槍傷或刺傷，這意味著我和我的同事有足夠的機會發展我們的手術技能修復的身體往往是年輕的、貧窮的、黑人和男性的。

If trauma dominated the nighttime, our days belonged to patients with vascular disease, GI disease, and especially cancer. The difference was that these patients’ “wounds” were caused by slow-growing, long-undetected tumors, and not all of them survived either—not even the wealthy ones, the ones who were on top of the world. Cancer doesn’t care how rich you are. Or who your surgeon is, really. If it wants to find a way to kill you, it will. Ultimately, these slow deaths ended up bothering me even more.

如果創傷在夜間佔據主導地位，那麼我們的日子就屬於患有血管疾病、胃腸道疾病，尤其是癌症的患者。不同的是，這些病人的「傷口」是由生長緩慢、長期未被發現的腫瘤造成的，而且並不是所有人都能活下來——即使是那些富有的人，那些站在世界之巔的人也不能活下來。巨蟹座不在乎你有多富有。或者你的外科醫生是誰，真的。如果它想找到殺死你的方法，它就會的。最終，這些緩慢的死亡最終讓我更加困擾。

But this is not a book about death. Quite the opposite, in fact.

但這不是一本關於死亡的書。事實上恰恰相反。

—

More than twenty-five years after that woman walked into the ER, I'm still practicing medicine, but in a very different way from how I had imagined. I no longer perform cancer surgeries, or any other kind of surgery. If you come to see me with a rash or a broken arm, I probably won't be of very much help.

那個女人走進急診室已經二十五年多了，我仍在行醫，但方式與我想像的非常不同。我不再進行癌症手術或任何其他類型的手術。如果你帶著皮疹或手臂骨折來找我，我可能幫不上忙。

So, what *do* I do?

那麼，我該怎麼辦？

Good question. If you were to ask me that at a party, I would do my best to duck out of the conversation. Or I would lie and say I'm a race car driver, which is what I really want to be when I grow up. (Plan B: shepherd.)

好問題。如果你在聚會上問我這個問題，我會盡力迴避談話。或者我會撒謊說我是賽車手，這是我長大後真正想成為的人。（B 計劃：牧羊人。）

My focus as a physician is on longevity. The problem is that I kind of hate the word *longevity*. It has been hopelessly tainted by a centuries-long parade of quacks and charlatans who have claimed to possess the secret elixir to a longer

life. I don't want to be associated with those people, and I'm not arrogant enough to think that I myself have some sort of easy answer to this problem, which has puzzled humankind for millennia. If longevity were simple, then there might not be a need for this book.

身為醫生，我關注的焦點是長壽。問題是我有點討厭長壽這個詞。它已經被長達幾個世紀的庸醫和江湖騙子無可救藥地玷污了，他們聲稱擁有長壽的秘密靈丹妙藥。我不想和那些人有任何联系，我也沒有傲慢到認為我自己對這個困擾人類數千年的問題有某種簡單的答案。如果長壽很簡單，那麼可能就不需要這本書了。

I'll start with what longevity isn't. Longevity does not mean living forever. Or even to age 120, or 150, which some self-proclaimed experts are now routinely promising to their followers. Barring some major breakthrough that, somehow, somehow, reverses two billion years of evolutionary history and frees us from time's arrow, everyone and everything that is alive today will inevitably die. It's a one-way street.

我將從長壽不是什麼開始。長壽並不意味著永遠活著。甚至可以活到 120 歲或 150 歲，一些自稱專家的人現在經常向他們的追隨者許諾。除非出現重大突破，以某種方式逆轉 20 億年的進化歷史，並將我們從時間之箭中解放出來，否則今天活著的每個人和所有事物都將不可避免地死亡。這是一條單行道。

Nor does longevity mean merely notching more and more birthdays as we slowly wither away. This is what happened to a hapless mythical Greek named Tithonus, who asked the gods for eternal life. To his joy, the gods granted his wish. But because he forgot to ask for eternal youth as well, his body continued to decay. Oops.

長壽也不意味著僅僅隨著我們慢慢老化而度過越來越多的生日。這就是發生在一個名叫提托努斯的不幸的希臘神話人物身上的事，他向眾神祈求永生。令他高興的是，諸神滿足了他的願望。但由於他也忘了祈求永保青春，他的身體不斷腐爛。哎呀。

Most of my patients instinctively get this. When they first come to see me, they generally insist that they *don't* want to live longer, if doing so means

lingering on in a state of ever-declining health. Many of them have watched their parents or grandparents endure such a fate, still alive but crippled by physical frailty or dementia. They have no desire to reenact their elders' suffering. Here's where I stop them. Just because your parents endured a painful old age, or died younger than they should have, I say, does not mean that you must do the same. The past need not dictate the future. Your longevity is more malleable than you think.

我的病人大多本能地明白這一點。當他們第一次來見我時，他們通常堅持說他們不想活得更長，如果這樣做意味著健康狀況不斷惡化。他們中的許多人親眼目睹自己的父母或祖父母遭受這樣的命運，他們仍然活著，但因身體虛弱或癡呆而癱瘓。他們不想重演長輩的痛苦。這就是我阻止他們的地方。我說，僅僅因為你的父母經歷了痛苦的晚年，或比他們應有的年齡更早去世，並不意味著你也必須這樣做。過去不一定決定未來。你的壽命比你想像的更有延展性。

In 1900, life expectancy hovered somewhere south of age fifty, and most people were likely to die from “fast” causes: accidents, injuries, and infectious diseases of various kinds. Since then, slow death has supplanted fast death. The majority of people reading this book can expect to die somewhere in their seventies or eighties, give or take, and almost all from “slow” causes. Assuming that you're not someone who engages in ultrarisky behaviors like BASE jumping, motorcycle racing, or texting and driving, the odds are overwhelming that you will die as a result of one of the chronic diseases of aging that I call the Four Horsemen: heart disease, cancer, neurodegenerative disease, or type 2 diabetes and related metabolic dysfunction. To achieve longevity—to live longer and live better for longer—we must understand and confront these causes of slow death.

1900 年，預期壽命徘徊在 50 歲左右，大多數人可能死於「快速」原因：意外、傷害和各種傳染病。從那時起，慢死取代了快死。大多數讀這本書的人預計會在七十歲或八十歲的時候死去，無論是給予還是接受，而且幾乎都是死於「緩慢」的原因。假設您不從事定點跳傘、摩托車比賽或發短信和駕駛等高風險行為，那麼您死於我稱之為“四騎士”的慢性衰老疾病之一的可能性是巨大的：心臟病、癌症、神經退化

性疾病或2 型糖尿病以及相關的代謝功能障礙。為了實現長壽——活得更長、活得更好、活得更久——我們必須理解並面對這些緩慢死亡的原因。

Longevity has two components. The first is how *long* you live, your chronological lifespan, but the second and equally important part is how *well* you live—the quality of your years. This is called *healthspan*, and it is what Tithonus forgot to ask for. Healthspan is typically defined as the period of life when we are free from disability or disease, but I find this too simplistic. I'm as free from “disability and disease” as when I was a twenty-five-year-old medical student, but my twenty-something self could run circles around fifty-year-old me, both physically and mentally. That's just a fact. Thus the second part of our plan for longevity is to maintain and improve our physical and mental function.

長壽有兩個組成部分。第一個是你的壽命，也就是按時間順序排列的壽命，但第二個也是同樣重要的部分是你的生活質量，也就是你的生活品質。這就是所謂的健康壽命，而這正是提托努斯忘記要求的。健康壽命通常被定義為我們在生命中沒有殘疾或疾病的時期，但我發現這太簡單了。我就像二十五歲的醫學生一樣沒有“殘疾和疾病”，但二十多歲的我可以在身體和精神上繞著五十歲的我轉。這只是事實。因此，我們長壽計劃的第二部分是維持和改善我們的身心功能。

The key question is, Where am I headed from here? What's my future trajectory? Already, in midlife, the warning signs abound. I've been to funerals for friends from high school, reflecting the steep rise in mortality risk that begins in middle age. At the same time, many of us in our thirties, forties, and fifties are watching our parents disappear down the road to physical disability, dementia, or long-term disease. This is always sad to see, and it reinforces one of my core principles, which is that the only way to create a better future for yourself—to set yourself on a better trajectory—is to start thinking about it and taking action *now*.

關鍵問題是，我要從這裡走向何方？我未來的軌跡是什麼？人到中年，警訊已經比比皆是。我參加過高中朋友的葬禮，反映出從中年開始的死亡風險急劇上升。與此同時，我們中的許多三十幾歲、四十歲

和五十歲的人正在看著我們的父母在身體殘疾、癡呆或長期疾病的道路上消失。看到這種情況總是令人難過，它強化了我的核心原則之一，那就是為自己創造更美好未來的唯一方法——讓自己走上更好的軌道——就是現在就開始思考並採取行動。

One of the main obstacles in anyone's quest for longevity is the fact that the skills that my colleagues and I acquired during our medical training have proved to be far more effective against fast death than slow death. We learned to fix broken bones, wipe out infections with powerful antibiotics, support and even replace damaged organs, and decompress serious spine or brain injuries. We had an amazing ability to save lives and restore full function to broken bodies, even reviving patients who were nearly dead. But we were markedly less successful at helping our patients with chronic conditions, such as cancer, cardiovascular disease, or neurological disease, evade slow death. We could relieve their symptoms, and often delay the end slightly, but it didn't seem as if we could reset the clock the way we could with acute problems. We had become better at catching the eggs, but we had little ability to stop them from falling off the building in the first place.

任何人追求長壽的主要障礙之一是，事實證明，我和我的同事在醫學訓練中獲得的技能對於防止快速死亡比緩慢死亡更有效。我們學會了修復骨折、用強效抗生素消除感染、支持甚至取代受損器官，以及緩解嚴重的脊椎或腦損傷。我們擁有驚人的能力來拯救生命，使破碎的身體恢復全部功能，甚至使瀕臨死亡的病人復活。但我們在幫助癌症、心血管疾病或神經系統疾病等慢性病患者避免緩慢死亡方面顯然不太成功。我們可以緩解他們的症狀，通常會稍微推遲結束時間，但似乎我們無法像解決嚴重問題那樣重置時鐘。我們已經更擅長捕捉雞蛋了，但我們一開始就沒有能力阻止它們從建築物上掉下來。

The problem was that we approached both sets of patients—trauma victims and chronic disease sufferers—with the same basic script. Our job was to *stop the patient from dying*, no matter what. I remember one case in

particular, a fourteen-year-old boy who was brought into our ER one night, barely alive. He had been a passenger in a Honda that was T-boned by a driver who ran a red light at murderous speed. His vital signs were weak and his pupils were fixed and dilated, suggesting severe head trauma. He was close to death. As trauma chief, I immediately ran a code to try to revive him, but just as with the woman in the Stanford ER, nothing worked. My colleagues wanted me to call it, yet I stubbornly refused to declare him dead. Instead, I kept coding him, pouring bag after bag of blood and epinephrine into his lifeless body, because I couldn't accept the fact that an innocent young boy's life could end like this. Afterwards, I sobbed in the stairwell, wishing I could have saved him. But by the time he got to me, his fate was sealed.

問題在於，我們用相同的基本腳本來接觸兩組患者——創傷受害者和慢性病患者。無論如何，我們的工作就是阻止病人死亡。我特別記得一個案例，一個十四歲的男孩有一天晚上被送進我們的急診室，當時已經奄奄一息。他曾是一輛本田車的乘客，這輛本田車被一名以致命的速度闖紅燈的司機撞到了。他的生命徵象微弱，瞳孔固定且散大，顯示頭部受到嚴重外傷。他已經快要死了。作為創傷科主任，我立即運行了一個代碼試圖讓他甦醒，但就像史丹佛急診室的那位女士一樣，沒有任何作用。我的同事們想讓我宣布他的死亡，但我固執地拒絕宣布他死亡。相反，我不斷地對他進行編碼，將一袋又一袋的血液和腎上腺素倒入他毫無生氣的身體中，因為我無法接受一個無辜的小男孩的生命就這樣結束的事實。之後，我在樓梯間哭泣，希望我能救他。但當他找到我時，他的命運就已經註定了。

This ethos is ingrained in anyone who goes into medicine: nobody dies on my watch. We approached our cancer patients in the same way. But very often it was clear that we were coming in too late, when the disease had already progressed to the point where death was almost inevitable. Nevertheless, just as with the boy in the car crash, we did everything possible to prolong their lives, deploying toxic and often painful treatments right up until the very end, buying a few more weeks or months of life at best.

這種精神在任何從事醫學的人身上根深蒂固：在我的監督下沒有人死去。我們以同樣的方式對待癌症患者。但很多時候，很明顯我們來得

太晚了，當時疾病已經發展到死亡幾乎不可避免的地步。然而，就像車禍中的男孩一樣，我們盡一切可能延長他們的生命，直到生命的最後一刻，我們都採用有毒且常常痛苦的治療方法，最多可以多爭取幾週或幾個月生命。

The problem is not that we aren't trying. Modern medicine has thrown an unbelievable amount of effort and resources at each of these diseases. But our progress has been less than stellar, with the possible exception of cardiovascular disease, where we have cut mortality rates by two-thirds in the industrialized world in about sixty years (although there's more yet to do, as we will see). Death rates from cancer, on the other hand, have hardly budged in the more than fifty years since the War on Cancer was declared, despite hundreds of billions of dollars' worth of public and private spending on research. Type 2 diabetes remains a raging public health crisis, showing no sign of abating, and Alzheimer's disease and related neurodegenerative diseases stalk our growing elderly population, with virtually no effective treatments on the horizon.

問題不在於我們沒有嘗試。現代醫學對每種疾病投入了令人難以置信的努力和資源。但我們的進展並不那麼出色，心血管疾病可能是個例外，在大約六十年的時間裡，我們已將工業化世界的死亡率降低了三分之二（儘管我們將看到，還有更多工作要做）。另一方面，儘管公共和私人在研究方面投入了數千億美元，但自向癌症宣戰以來的五十多年來，癌症死亡率幾乎沒有改變。2型糖尿病仍然是一場嚴重的公共衛生危機，沒有任何減弱的跡象，阿茲海默症和相關的神經退化性疾病困擾著我們不斷增長的老年人口，幾乎沒有有效的治療方法。

But in every case, we are intervening at the wrong point in time, well after the disease has taken hold, and often when it's already too late—when the eggs are already dropping. It gutted me every time I had to tell someone suffering from cancer that she had six months to live, knowing that the disease had likely taken up residence in her body several years before it was ever detectable. We had wasted a lot of time. While the prevalence of each of the Horsemen diseases increases sharply with age, they typically begin much earlier than we recognize, and they generally take a very long time to kill you.

Even when someone dies “suddenly” of a heart attack, the disease had likely been progressing in their coronary arteries for two decades. Slow death moves even more slowly than we realize.

但在每種情況下，我們都在錯誤的時間點進行幹預，在疾病發生很久之後，而且往往已經為時已晚——當雞蛋已經掉落時。每當我必須告訴患有癌症的人她還有六個月的生命時，我都感到非常沮喪，因為我知道這種疾病很可能在被發現之前幾年就已經在她的體內紮根了。我們浪費了很多時間。雖然每種騎士疾病的盛行率隨著年齡的增長而急劇增加，但它們通常比我們意識到的要早得多，而且通常需要很長時間才能殺死你。即使有人因心臟病「突然」死亡，這種疾病也可能已經在他們的冠狀動脈中發展了二十年。緩慢的死亡比我們意識到的還要慢。

The logical conclusion is that we need to step in sooner to try to stop the Horsemen in their tracks—or better yet, prevent them altogether. None of our treatments for late-stage lung cancer has reduced mortality by nearly as much as the worldwide reduction in smoking that has occurred over the last two decades, thanks in part to widespread smoking bans. This simple preventive measure (not smoking) has saved more lives than any late-stage intervention that medicine has devised. Yet mainstream medicine still insists on waiting until the point of diagnosis before we intervene.

合乎邏輯的結論是，我們需要儘早介入，試圖阻止天啟騎士的腳步——或者更好的是，完全阻止他們。我們對晚期肺癌的治療方法所降低的死亡率幾乎無法與過去二十年來全球範圍內吸煙人數的減少相比，這在一定程度上要歸功於廣泛的禁煙令。這種簡單的預防措施（不吸煙）比醫學設計的任何後期幹預措施挽救了更多的生命。然而主流醫學仍然堅持等到診斷後才進行幹預。

Type 2 diabetes offers a perfect example of this. The standard-of-care treatment guidelines of the American Diabetes Association specify that a patient can be diagnosed with diabetes mellitus when they return a hemoglobin A1c (HbA1c) test result^[*1] of 6.5 percent or higher, corresponding to an average blood glucose level of 140 mg/dL (normal is more like 100 mg/dL, or an HbA1c of 5.1 percent). These patients are given

extensive treatment, including drugs that help the body produce more insulin, drugs that reduce the amount of glucose the body produces, and eventually the hormone insulin itself, to ram glucose into their highly insulin-resistant tissues.

2 型糖尿病就是一個完美的例子。美國糖尿病協會的護理標準治療指南規定，當患者返回的糖化血紅蛋白 (HbA1c) 測試結果 [*1] 為 6.5% 或更高（相當於平均血糖）時，即可診斷患有糖尿病水平為 140 mg/dL（正常值更像是 100 mg/dL，或 HbA1c 為 5.1%）。這些患者接受廣泛的治療，包括幫助身體產生更多胰島素的藥物、減少身體產生的葡萄糖量的藥物，以及最終的胰島素激素本身，以將葡萄糖注入高度胰島素抗性的組織。

But if their HbA1c test comes back at 6.4 percent, implying an average blood glucose of 137 mg/dL—just three points lower—they technically don't have type 2 diabetes at all. Instead, they have a condition called prediabetes, where the standard-of-care guidelines recommend mild amounts of exercise, vaguely defined dietary changes, possible use of a glucose control medication called metformin, and “annual monitoring”—basically, to wait and see if the patient actually develops diabetes before treating it as an urgent problem.

但如果他們的 HbA1c 測試結果為 6.4%，這意味著平均血糖為 137 mg/dL（僅低三個百分點），從技術上講，他們根本沒有患有 2 型糖尿病。相反，他們患有一種稱為前驅糖尿病的疾病，標準治療指南建議進行適度的運動、模糊定義的飲食改變、可能使用稱為二甲雙胍的血糖控制藥物以及「年度監測」——基本上是觀望。如果患者在將其視為緊急問題之前確實患有糖尿病。

I would argue that this is almost the exact wrong way to approach type 2 diabetes. As we will see in chapter 6, type 2 diabetes belongs to a spectrum of metabolic dysfunction that begins long before someone crosses that magical diagnostic threshold on a blood test. Type 2 diabetes is merely the last stop on the line. The time to intervene is well before the patient gets anywhere near that zone; even prediabetes is very late in the game. It is absurd and harmful to treat this disease like a cold or a broken bone, where you either have it or you don't; it's not binary. Yet too often, the point of clinical diagnosis is where our interventions begin. Why is this okay?

我認為這幾乎是治療第 2 型糖尿病的完全錯誤的方法。正如我們將在第 6 章中看到的，2 型糖尿病屬於一系列代謝功能障礙，這種功能障礙早在某人跨過血液檢查中神奇的診斷閾值之前就開始了。2 型糖尿病只是這條線上的最後一站。幹預時間早於患者接近該區域之前；即使是糖尿病前期也已進入晚期。把這種疾病當作感冒或骨折來治療是荒謬和有害的，無論你是否患有這種疾病。它不是二進制的。然而，很多時候，臨床診斷就是我們介入措施的起點。為什麼這樣可以呢？

I believe that our goal should be to act as early as possible, to try to *prevent* people from developing type 2 diabetes and all the other Horsemen. We should be proactive instead of reactive in our approach. Changing that mindset must be our first step in attacking slow death. We want to delay or prevent these conditions so that we can live longer *without* disease, rather than lingering *with* disease. That means that the best time to intervene is before the eggs start falling—as I discovered in my own life.

我相信我們的目標應該是儘早採取行動，努力防止人們患上第 2 型糖尿病和所有其他騎士病。我們的方法應該是積極主動的，而不是被動的。改變這種心態必須是我們對抗緩慢死亡的第一步。我們想要延遲或預防這些情況，這樣我們就可以在沒有疾病的情況下活得更久，而不是在疾病中徘徊。這意味著最好的干預時間是在雞蛋開始掉落之前——正如我在自己的生活中發現的那樣。

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On September 8, 2009, a day I will never forget, I was standing on a beach on Catalina Island when my wife, Jill, turned to me and said, “Peter, I think you should work on being a little less not thin.”

2009 年 9 月 8 日，我永遠不會忘記的一天，我站在卡塔利娜島的海灘上，我的妻子吉爾轉向我說：“彼得，我認為你應該努力變得不那麼瘦。”

I was so shocked that I nearly dropped my cheeseburger. “Less not thin?” My sweet wife said *that*?

我太震驚了，我的起司漢堡差點掉了。“少了不瘦了？”我可愛的妻子這麼說？

I was pretty sure that I'd earned the burger, as well as the Coke in my other hand, having just swum to this island from Los Angeles, across twenty-one miles of open ocean—a journey that had taken me fourteen hours, with a current in my face for much of the way. A minute earlier, I'd been thrilled to have finished this bucket-list long-distance swim.^[*2] Now I was Not-Thin Peter.

我非常確定自己贏得了漢堡，另一隻手也贏得了可樂，因為我剛從洛杉磯遊過二十一英里的公海來到這座島嶼——這段旅程花了我十四個小時，一路上大部分時間我臉上都有電流。一分鐘前，我很高興完成了這次願望清單上的長距離游泳。[*2] 現在我是不瘦的彼得了。

Nevertheless, I instantly knew that Jill was right. Without even realizing it, I had ballooned up to 210 pounds, a solid 50 more than my fighting weight as a teenage boxer. Like a lot of middle-aged guys, I still thought of myself as an “athlete,” even as I squeezed my sausage-like body into size 36 pants. Photographs from around that time remind me that my stomach looked just like Jill's when she was six months pregnant. I had become the proud owner of a full-fledged dad bod, and I had not even hit forty.

儘管如此，我立刻就知道吉爾是對的。我甚至沒有意識到，我的體重已經飆升至 210 磅，比我作為青少年拳擊手的戰鬥體重足足多了 50 磅。和許多中年男子一樣，我仍然認為自己是一名“運動員”，儘管我把香腸般的身體擠進了 36 碼的褲子裡。當時的照片讓我想起，我的肚子看起來就像吉爾懷孕六個月時的一樣。我自豪地擁有了成熟的爸爸身材，而我還不到四十歲。

Blood tests revealed worse problems than the ones I could see in the mirror. Despite the fact that I exercised fanatically and ate what I believed to be a healthy diet (notwithstanding the odd post-swim cheeseburger), I had somehow become insulin resistant, one of the first steps down the road to type 2 diabetes and many other bad things. My testosterone levels were below the 5th percentile for a man my age. It's not an exaggeration to say that my life

was in danger—not imminently, but certainly over the long term. I knew exactly where this road could lead. I had amputated the feet of people who, twenty years earlier, had been a lot like me. Closer to home, my own family tree was full of men who had died in their forties from cardiovascular disease.

驗血顯示出的問題比我在鏡子中看到的更嚴重。儘管事實上我狂熱地鍛煉並吃著我認為健康的飲食（儘管游泳後吃了奇怪的芝士漢堡），但我不知何故變得胰島素抵抗，這是通往2型糖尿病和許多其他不良疾病道路上的第一步之一事物。我的羥固酮水平低於同齡男性的第五個百分點。毫不誇張地說，我的生命處於危險之中——不是迫在眉睫，但從長遠來看肯定是這樣。我清楚地知道這條路會通往哪裡。我截掉了二十年前和我很像的人的腳。言歸正傳，我的家譜裡充滿了四十多歲時死於心血管疾病的男性。

That moment on the beach marked the beginning of my interest in—that word again—longevity. I was thirty-six years old, and I was on the precipice. I had just become a father with the birth of our first child, Olivia. From the moment I first held her, wrapped in her white swaddling blanket, I fell in love—and knew my life had changed forever. But I would also soon learn that my various risk factors and my genetics likely pointed toward an early death from cardiovascular disease. What I didn't yet realize was that my situation was entirely fixable.

在海灘上的那一刻標誌著我對——又是這個詞——長壽的興趣的開始。我當時三十六歲，正處於懸崖邊。隨著我們的第一個孩子奧利維亞的出生，我剛剛成為父親。從我第一次抱著她，裹著她白色的襁褓毯的那一刻起，我就墜入愛河了——並且知道我的生活已經永遠改變了。但我也很快就會了解到，我的各種危險因子和我的基因很可能導致我因心血管疾病而早逝。我還沒有意識到我的情況是完全可以解決的。

As I delved into the scientific literature, I quickly became as obsessed with understanding nutrition and metabolism as I had once been with learning cancer surgery. Because I am an insatiably curious person by nature, I reached out to the leading experts in these fields and persuaded them to mentor me on my quest for knowledge. I wanted to understand how I'd gotten myself into

that state and what it meant for my future. And I needed to figure out how to get myself back on track.

當我深入研究科學文獻時，我很快就像以前學習癌症手術一樣著迷於了解營養和新陳代謝。因為我本質上是一個永不滿足的好奇心，所以我聯繫了這些領域的頂尖專家，並說服他們指導我對知識的追求。我想了解我是如何讓自己陷入這種狀態的，以及它對我的未來意味著什麼。我需要弄清楚如何讓自己回到正軌。

My next task was to try to understand the true nature and causes of atherosclerosis, or heart disease, which stalks the men in my dad's family. Two of his brothers had died from heart attacks before age fifty, and a third had succumbed in his sixties. From there it was a short leap over to cancer, which has always fascinated me, and then to neurodegenerative diseases like Alzheimer's disease. Finally, I began to study the fast-moving field of gerontology—the effort to understand what drives the aging process itself and how it might be slowed.

我的下一個任務是嘗試了解動脈粥狀硬化或心臟病的真正本質和原因，這種疾病困擾著我父親的家人。他的兩個兄弟在五十歲之前死於心臟病，第三個兄弟在六十多歲時去世。從那時起，它短暫地跨越了一直讓我著迷的癌症，然後又轉向了阿茲海默症等神經退化性疾病。最後，我開始研究快速發展的老年學領域——努力了解老化過程本身的驅動因素以及如何減緩老化過程。

Perhaps my biggest takeaway was that modern medicine does not really have a handle on when and how to treat the chronic diseases of aging that will likely kill most of us. This is in part because each of the Horsemen is intricately complex, more of a disease *process* than an acute illness like a common cold. The surprise is that this is actually good news for us, in a way. Each one of the Horsemen is cumulative, the product of multiple risk factors adding up and compounding over time. Many of these same individual risk factors, it turns out, are relatively easy to reduce or even eliminate. Even better, they share certain features or drivers in common that make them vulnerable to some of the same tactics and behavioral changes we will discuss in this book.

也許我最大的收穫是，現代醫學並沒有真正掌握何時以及如何治療可能殺死我們大多數人的慢性老化疾病。部分原因是每位天啟騎士都錯綜複雜，更像是一種疾病過程，而不是像普通感冒這樣的急性疾病。令人驚訝的是，在某種程度上，這對我們來說其實是個好消息。每位天啟騎士都是累積的，是多種風險因素隨著時間的推移而累積和複合的產物。事實證明，許多相同的個人風險因素相對容易減少甚至消除。更好的是，它們具有某些共同的功能或驅動因素，這使得它們很容易受到我們將在本書中討論的一些相同策略和行為變化的影響。

Medicine's biggest failing is in attempting to treat all these conditions at the wrong end of the timescale—after they are entrenched—rather than before they take root. As a result, we ignore important warning signs and miss opportunities to intervene at a point where we still have a chance to beat back these diseases, improve health, and potentially extend lifespan.

醫學最大的失敗在於試圖在錯誤的時間尺度上治療所有這些疾病——在它們根深蒂固之後——而不是在它們紮根之前。結果，我們忽略了重要的警訊，錯過了在我們仍有機會擊退這些疾病、改善健康並有可能延長壽命的時候進行幹預的機會。

Just to pick a few examples:

僅舉幾個例子：

- Despite throwing billions of dollars in research funding at the Horsemen, mainstream medicine has gotten crucial things dead wrong about their root causes. We will examine some promising new theories about the origin and causes of each, and possible strategies for prevention.

儘管在天啟騎士身上投入了數十億美元的研究經費，但主流醫學對其根本原因的認知卻是完全錯誤的。我們將研究一些關於每種現象的起源和原因的有前景的新理論，以及可能的預防策略。

- The typical cholesterol panel that you receive and discuss at your annual physical, along with many of the underlying assumptions behind it (e.g., “good” and “bad” cholesterol), is misleading and oversimplified to the

point of uselessness. It doesn't tell us nearly enough about your actual risk of dying from heart disease—and we don't do nearly enough to stop this killer.

您在年度體檢中收到和討論的典型膽固醇面板，以及其背後的許多基本假設（例如“好”和“壞”膽固醇），具有誤導性，並且過於簡單化，以至於毫無用處。它並沒有足夠地告訴我們您死於心臟病的實際風險，而且我們也沒有採取足夠的措施來阻止這個殺手。

- Millions of people are suffering from a little-known and underdiagnosed liver condition that is a potential precursor to type 2 diabetes. Yet people at the early stages of this metabolic derangement will often return blood test results in the “normal” range. Unfortunately, in today's unhealthy society, “normal” or “average” is not the same as “optimal.”

數百萬人患有一種鮮為人知且診斷不足的肝臟疾病，這種疾病是第2型糖尿病的潛在先兆。然而，處於這種代謝紊亂早期階段的人通常會返回「正常」範圍內的血液檢查結果。不幸的是，在當今不健康的社會中，「正常」或「平均」並不等於「最佳」。

- The metabolic derangement that leads to type 2 diabetes also helps foster and promote heart disease, cancer, *and* Alzheimer's disease. Addressing our metabolic health can lower the risk of each of the Horsemen.

導致第2型糖尿病的代謝紊亂也有助於促進和促進心臟病、癌症和阿茲海默症。解決我們的代謝健康問題可以降低每位騎士的風險。

- Almost all “diets” are similar: they may help some people but prove useless for most. Instead of arguing about diets, we will focus on *nutritional biochemistry*—how the combinations of nutrients that you eat affect your own metabolism and physiology, and how to use data and technology to come up with the best eating pattern for you.

幾乎所有「飲食」都是相似的：它們可能對某些人有幫助，但對大多數人來說毫無用處。我們不會爭論飲食，而是專注於營養生

物化學——您所吃的營養素組合如何影響您自己的新陳代謝和生理機能，以及如何使用數據和技術為您提出最佳的飲食模式。

- One macronutrient, in particular, demands more of our attention than most people realize: not carbs, not fat, but *protein* becomes critically important as we age.

尤其是一種常量營養素，比大多數人意識到的更需要我們的關注：隨著年齡的增長，蛋白質變得至關重要，不是碳水化合物，不是脂肪，而是蛋白質。

- Exercise is by far the most potent longevity “drug.” No other intervention does nearly as much to prolong our lifespan and preserve our cognitive and physical function. But most people don’t do nearly enough—and exercising the wrong way can do as much harm as good.

運動是迄今為止最有效的長壽「藥物」。沒有其他幹預措施能夠如此有效地延長我們的壽命並保護我們的認知和身體功能。但大多數人做得還不夠，而且運動方式錯誤可能弊大於利。

- Finally, as I learned the hard way, striving for physical health and longevity is meaningless if we ignore our emotional health. Emotional suffering can decimate our health on all fronts, and it must be addressed.

最後，我透過慘痛的教訓體認到，如果我們忽視情緒健康，那麼追求身體健康和長壽就沒有意義。情緒上的痛苦會從各方面損害我們的健康，必須加以解決。

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Why does the world need another book about longevity? I’ve asked myself that question often over the last few years. Most writers in this space fall into certain categories. There are the true believers, who insist that if you follow their specific diet (the more restrictive the better), or practice meditation a certain way, or eat a particular type of superfood, or maintain your “energy”

properly, then you will be able to avoid death and live forever. What they often lack in scientific rigor they make up for with passion.

為什麼世界需要另一本關於長壽的書？過去幾年我常問自己這個問題。這個領域的大多數作家都屬於某些類別。有些真正的信徒堅持認為，如果你遵循他們特定的飲食（限制越多越好），或者以某種方式練習冥想，或者吃某種特定類型的超級食物，或者正確地保持你的“能量”，那麼你就會能夠避免死亡並永生。他們常常缺乏科學嚴謹性，但他們卻用熱情來彌補。

On the other end of the spectrum are those who are convinced that science will soon figure out how to unplug the aging process itself, by tweaking some obscure cellular pathway, or lengthening our telomeres, or “reprogramming” our cells so that we no longer need to age at all. This seems highly unlikely in our lifetime, although it is certainly true that science is making huge leaps in our understanding of aging and of the Horsemen diseases. We are learning so much, but the tricky part is knowing how to apply this new knowledge to real people outside the lab—or at a minimum, how to hedge our bets in case this highfalutin science somehow fails to put longevity into a pill.

另一方面，那些相信科學很快就會找出如何消除老化過程本身的方法，透過調整一些模糊的細胞途徑，或延長我們的端粒，或「重新編程」我們的細胞，使我們不再需要完全變老。在我們的有生之年，這似乎不太可能，儘管科學確實在我們對衰老和騎士疾病的理解方面取得了巨大飛躍。我們學到了很多東西，但棘手的部分是知道如何將這些新知識應用到實驗室外的真人身上，或者至少，如何對沖我們的賭注，以防這種華而不實的科學不知何故無法將長壽變成藥丸。

This is how I see my role: I am not a laboratory scientist or clinical researcher but more of a translator, helping you understand and apply these insights. This requires a thorough understanding of the science but also a bit of art, just as if we were translating a poem by Shakespeare into another language. We have to get the meaning of the words exactly right (the science), while also capturing the tone, the nuance, the feeling, and the rhythm (the art). Similarly, my approach to longevity is firmly rooted in science, but there is also a good deal of art in figuring out how and when to apply our knowledge

to you, the patient, with your specific genes, your history and habits, and your goals.

這就是我對自己角色的看法：我不是實驗室科學家或臨床研究人員，而是更多的翻譯者，幫助您理解和應用這些見解。這需要對科學有透徹的理解，但也需要一點藝術，就像我們將莎士比亞的一首詩翻譯成另一種語言一樣。我們必須準確地理解單字的意思（科學），同時也要捕捉語氣、細微差別、感覺和節奏（藝術）。同樣，我的長壽方法牢固地植根於科學，但在弄清楚如何以及何時將我們的知識應用到您（患者）身上，以及您的特定基因、您的歷史和習慣以及您的目標方面，也有很多藝術。。

I believe that we already know more than enough to bend the curve. That is why this book is called *Outlive*. I mean it in both senses of the word: live longer and live better. Unlike Tithonus, you can outlive your life expectancy *and* enjoy better health, getting more out of your life.

我相信我們已經知道足夠的資訊來扭轉曲線。這就是為什麼這本書被稱為“Outlive”。我的意思是這個字的兩個意思：活得更長，活得更好。與 Tithonus 不同，您可以比預期壽命更長，享受更好的健康，從生活中獲得更多。

My goal is to create an actionable operating manual for the *practice* of longevity. A guide that will help you Outlive. I hope to convince you that with enough time and effort, you can potentially extend your lifespan by a decade and your healthspan possibly by two, meaning you might hope to function like someone twenty years younger than you.

我的目標是為長壽實踐創建一本可操作的操作手冊。一本可以幫助您生存的指南。我希望讓您相信，只要有足夠的時間和努力，您就有可能將壽命延長十年，健康壽命可能延長兩年，這意味著您可能希望像比您年輕二十歲的人一樣生活。

But my intent here is not to tell you exactly *what to do*; it's to help you learn *how to think* about doing these things. For me, that has been the journey, an obsessive process of study and iteration that began that day on the rocky shore of Catalina Island.

但我在這裡的目的不是告訴你到底要做什麼；而是告訴你該做什麼。這是為了幫助您學習如何思考做這些事情。對我來說，這就是一段旅程，一個痴迷的研究和迭代過程，從那天在卡塔利娜島的岩石海岸開始。

More broadly, longevity demands a paradigm-shifting approach to medicine, one that directs our efforts toward preventing chronic diseases and improving our healthspan—and doing it now, rather than waiting until disease has taken hold or until our cognitive and physical function has already declined. It's not “preventive” medicine; it's *proactive* medicine, and I believe it has the potential not only to change the lives of individuals but also to relieve vast amounts of suffering in our society as a whole. This change is not coming from the medical establishment, either; it will happen only if and when patients and physicians demand it.

更廣泛地說，長壽需要一種範式轉變的醫學方法，這種方法引導我們努力預防慢性疾病和改善我們的健康壽命，並且現在就做，而不是等到疾病發生或我們的認知和身體功能已經下降。這不是「預防」醫學；而是「預防」醫學。這是積極主動的醫學，我相信它不僅有可能改變個人的生活，而且有可能減輕整個社會的巨大痛苦。這種改變也不是來自醫療機構；而是來自醫療機構。只有當患者和醫生要求時，它才會發生。

Only by altering our approach to medicine itself can we get to the rooftop and stop the eggs from falling. None of us should be satisfied racing around at the bottom to try to catch them.

只有改變我們對醫學本身的態度，我們才能到達屋頂並阻止雞蛋掉下來。我們誰都不應該滿足於在水底跑來跑去試圖抓住它們。

[SKIP NOTES](#)

[跳過註釋](#)

^{*1} HbA1c measures the amount of glycosylated hemoglobin in the blood, which allows us to estimate the patient's average level of blood glucose over the past ninety days or so.

*1 HbA1c 測量血液中糖化血紅蛋白的量，這使我們能夠估計患者在過去 90 天左右的平均血糖值。

*2 This was actually my second time making this crossing. I'd swum from Catalina to LA a few years earlier, but the reverse direction took four hours longer, because of the current.

*2 這其實是我第二次穿越。幾年前，我從卡塔利娜游到了洛杉磯，但由於水流的原因，反向遊的時間多了四個小時。

CHAPTER 2

第2章

Medicine 3.0

醫學3.0

Rethinking Medicine for the Age of Chronic
Disease

重新思考慢性病時代的醫學

The time to repair the roof is when the sun is shining.

修屋頂的時間是在陽光明媚的時候。

—JOHN F. KENNEDY

——約翰·F·甘迺迪

I don't remember what the last straw was in my growing frustration with medical training, but I do know that the beginning of the end came

courtesy of a drug called gentamicin. Late in my second year of residency, I had a patient in the ICU with severe sepsis. He was basically being kept alive by this drug, which is a powerful IV antibiotic. The tricky thing about gentamicin is that it has a very narrow therapeutic window. If you give a patient too little, it won't do anything, but if you give him too much it could destroy his kidneys and hearing. The dosing is based on the patient's weight and the expected half-life of the drug in the body, and because I am a bit of a math geek (actually, more than a bit), one evening I came up with a mathematical model that predicted the precise time when this patient would need his next dose: 4:30 a.m.

我不記得壓垮我對醫學訓練日益沮喪的最後一根稻草是什麼，但我確實知道，終結的開始是由一種叫做慶大霉素的藥物帶來的。在我住院醫師實習的第二年末，我在加護病房接診了一位患有嚴重敗血症的病人。他基本上是靠這種藥物維持生命的，這是一種強效的靜脈注射抗生素。慶大霉素的棘手之處在於它的治療窗非常窄。如果你給病人太少，它不會有任何作用，但如果你給他太多，可能會破壞他的腎臟和聽力。劑量是根據患者的體重和藥物在體內的預期半衰期而定的，因為我是一個數學極客（實際上，不止一點），一天晚上我想出了一個數學模型預測了該患者需要下一次劑量的準確時間：凌晨4:30。

Sure enough, when 4:30 rolled around we tested the patient and found that his blood levels of gentamicin had dropped to exactly the point where he needed another dose. I asked his nurse to give him the medication but found myself at odds with the ICU fellow, a trainee who was one level above us residents in the hospital pecking order. I wouldn't do that, she said. Just have them give it at seven, when the next nursing shift comes on. This puzzled me, because we knew that the patient would have to go for more than two hours basically unprotected from a massive infection that could kill him. Why wait? When the fellow left, I had the nurse give the medicine anyway.

果然，當下午 4 點 30 分左右時，我們對患者進行了檢測，發現他血液中慶大霉素的濃度已降至需要再次注射的水平。我要求他的護士給他開藥，但發現自己與重症監護病房的同事意見不合，這位實習生在醫院的地位比我們住院醫生高一級。我不會那樣做，她說。只要讓他們

在七點鐘，也就是下一個護理班次開始的時候，就可以了。這讓我很困惑，因為我們知道病人必須在沒有任何保護的情況下度過兩個多小時，才能免受可能致命的大規模感染。為什麼要等？當那傢伙離開後，我還是讓護士給了藥。

Later that morning at rounds, I presented the patient to the attending physician and explained what I had done, and why. I thought she would appreciate my attention to patient care—getting the drug dosed just right—but instead, she turned and gave me a tongue-lashing like I'd never experienced. I'd been awake for more than twenty-four hours at this point, but I wasn't hallucinating. I was getting screamed at, even threatened with being fired, for trying to improve the way we delivered medication to a very sick patient. True, I had disregarded the suggestion (not a direct order) from the fellow, my immediate superior, and that was wrong, but the attending's tirade stunned me. Shouldn't we *always* be looking for better ways to do things?

那天早上在查房時，我將病人介紹給主治醫生，並解釋了我所做的事情以及原因。我以為她會感激我對病人照護的關注——讓藥物劑量恰到好處——但相反，她轉過身來對我進行了嚴厲的斥責，這是我從未經歷過的。此時我已經清醒了超過二十四小時，但我並不是出現幻覺。因為我試圖改進我們為重症患者提供藥物的方式，我遭到了尖叫，甚至被威脅要被解僱。確實，我無視了那位同事、我的頂頭上司的建議（不是直接命令），這是錯的，但主治醫生的長篇大論令我震驚。我們不應該一直尋找更好的做事方法嗎？

Ultimately, I put my pride in check and apologized for my disobedience, but this was just one incident of many. As my residency progressed, my doubts about my chosen profession only mounted. Time and again, my colleagues and I found ourselves coming into conflict with a culture of resistance to change and innovation. There are some good reasons why medicine is conservative in nature, of course. But at times it seemed as if the whole edifice of modern medicine was so firmly rooted in its traditions that it was unable to change even slightly, even in ways that would potentially save the lives of people for whom we were supposed to be caring.

最終，我抑制住了自己的驕傲，並為自己的不服從行為道歉，但這只

是眾多事件中的一件事。隨著住院醫師實習的進展，我對自己選擇的職業的懷疑有增無減。我和我的同事一次又一次地發現自己與抵制變革和創新的文化發生衝突。當然，醫學本質上是保守的，有一些充分的理由。但有時，現代醫學的整個大廈似乎如此牢固地植根於其傳統，以至於它無法做出哪怕是輕微的改變，即使是以可能挽救我們本應照顧的人們生命的方式。

By my fifth year, tormented by doubts and frustration, I informed my superiors that I would be leaving that June. My colleagues and mentors thought I was insane; almost nobody leaves residency, certainly not at Hopkins with only two years to go. But there was no dissuading me. Throwing nine years of medical training out the window, or so it seemed, I took a job with McKinsey & Company, the well-known management consulting firm. My wife and I moved across the country to the posh playground of Palo Alto and San Francisco, where I had loved living while at Stanford. It was about as far away from medicine (and Baltimore) as it was possible to get, and I was glad. I felt as if I had wasted a decade of my life. But in the end, this seeming detour ended up reshaping the way I look at medicine—and more importantly, each of my patients.

到了第五年，我在懷疑和沮喪的折磨下，通知我的上級我將於那年六月離開。我的同事和導師都認為我瘋了；幾乎沒有人離開住院醫師實習期，尤其是在霍普金斯大學，只剩下兩年了。但沒有人阻止我。我拋棄了九年的醫學培訓，至少看起來是這樣，我在著名的管理顧問公司麥肯錫公司找到了一份工作。我和我的妻子搬到了全國各地的帕洛阿爾托和舊金山的豪華遊樂場，我在史丹佛大學期間很喜歡住在那裡。它距離醫學（和巴爾的摩）盡可能遠，我很高興。我感覺自己好像浪費了十年的生命。但最終，這種看似迂迴的做法最終重塑了我看待醫學的方式，更重要的是，重塑了我對每位病人的看法。

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The key word, it turned out, was *risk*.

事實證明，關鍵字是風險。

McKinsey originally hired me into their healthcare practice, but because of my quantitative background (I had studied applied math and mechanical engineering in college, planning to pursue a PhD in aerospace engineering), they moved me over to credit risk. This was in 2006, during the runup to the global financial crisis, but before almost anyone besides the folks featured in Michael Lewis's *The Big Short* understood the magnitude of what was about to happen.

麥肯錫最初聘請我從事他們的醫療保健實踐，但由於我的定量背景（我在大學學習應用數學和機械工程，計劃攻讀航空航天工程博士學位），他們將我調到信用風險領域。那是 2006 年，全球金融危機爆發前夕，但在此之前，除了邁克爾·劉易斯 (Michael Lewis) 的《大空頭》中的人物之外，幾乎所有人都了解即將發生的事情的嚴重性。

Our job was to help US banks comply with a new set of rules that required them to maintain enough reserves to cover their unexpected losses. The banks had done a good job of estimating their *expected* losses, but nobody really knew how to deal with the *unexpected* losses, which by definition were much more difficult to predict. Our task was to analyze the banks' internal data and come up with mathematical models to try to predict these unexpected losses on the basis of correlations among asset classes—which was just as tricky as it sounds, like a crapshoot on top of a crapshoot.

我們的工作是幫助美國銀行遵守一套新規則，要求它們保持足夠的準備金以彌補意外損失。銀行在估計預期損失方面做得很好，但沒有人真正知道如何應對意外損失，從定義上來說，意外損失更難以預測。我們的任務是分析銀行的內部數據，並提出數學模型，試圖根據資產類別之間的相關性來預測這些意外損失——這就像聽起來一樣棘手，就像是一次又一次的冒險。

What started out as an exercise to help the biggest banks in the United States jump through some regulatory hoops uncovered a brewing disaster in what was considered to be one of their least risky, most stable portfolios: prime mortgages. By the late summer of 2007, we had arrived at the horrifying but inescapable conclusion that the big banks were about to lose

more money on mortgages in the next two years than they had made in the previous decade.

最初是為了幫助美國最大的銀行跨越一些監管障礙而進行的一項行動，結果卻發現了一場正在醞釀的災難，而這些災難被認為是它們風險最小、最穩定的投資組合之一：優質抵押貸款。到 2007 年夏末，我們得出了一個令人震驚但不可避免的結論：未來兩年內，大銀行在抵押貸款上的損失將比過去十年還要多。

In late 2007, after six months of round-the-clock work, we had a big meeting with the top brass of our client, a major US bank. Normally, my boss, as the senior partner on the project, would have handled the presentation. But instead he picked me. “Based on your previous career choice,” he said, “I suspect you are better prepared to deliver truly horrible news to people.”

2007 年底，經過六個月的全天候工作，我們與我們的客戶（美國大型銀行）的高層舉行了一次大型會議。通常情況下，我的老闆作為該專案的高級合夥人，會處理演示。但他卻選擇了我。“根據你之前的職業選擇，”他說，“我懷疑你已經做好了更好的準備，向人們傳達真正可怕的消息。”

This was not unlike delivering a terminal diagnosis. I stood up in a high-floor conference room and walked the bank’s management team through the numbers that foretold their doom. As I went through my presentation, I watched the five stages of grief described by Elisabeth Kübler-Ross in her classic book *On Death and Dying*—denial, anger, bargaining, sadness, and acceptance—flash across the executives’ faces. I had never seen that happen before outside of a hospital room.

這與做出最終診斷沒有什麼不同。我站在高層會議室，向銀行的管理團隊介紹了預示他們厄運的數字。當我進行演講時，我看到伊麗莎白·庫伯勒-羅斯在她的經典著作《論死亡與臨終》中描述的悲傷的五個階段——否認、憤怒、討價還價、悲傷和接受——在高管們的臉上閃過。我以前從未在病房外見過這種情況。

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My detour into the world of consulting came to an end, but it opened my eyes to a huge blind spot in medicine, and that is the understanding of risk. In finance and banking, understanding risk is key to survival. Great investors do not take on risk blindly; they do so with a thorough knowledge of both risk and reward. The study of credit risk is a science, albeit an imperfect one, as I learned with the banks. While risk is obviously also important in medicine, the medical profession often approaches risk more emotionally than analytically.

我的諮商世界繞道結束了，但它讓我看到了醫學上一個巨大的盲點，那就是對風險的理解。在金融和銀行業，了解風險是生存的關鍵。偉大的投資者不會盲目承擔風險；他們這樣做時對風險和回報都有透徹的了解。正如我在銀行學到的那樣，信用風險研究是一門科學，儘管並不完美。雖然風險在醫學中顯然也很重要，但醫學界往往更以情感而非分析的方式對待風險。

The trouble began with Hippocrates. Most people are familiar with the ancient Greek's famous dictum: "First, do no harm." It succinctly states the physician's primary responsibility, which is to not kill our patients or do anything that might make their condition worse instead of better. Makes sense. There are only three problems with this: (a) Hippocrates never actually said these words,^[*1] (b) it's sanctimonious bullshit, and (c) it's unhelpful on multiple levels.

麻煩始於希波克拉底。大多數人都熟悉古希臘的著名格言：“首先，不要傷害。”它簡潔地說明了醫生的主要責任，即不殺死我們的病人或做任何可能使他們的病情變得更糟而不是更好的事情。說得通。這只有三個問題：（a）希波克拉底從未真正說過這些話，[*1]（b）這是道貌岸然的廢話，（c）它在多個層面上都沒有幫助。

“Do no harm”? Seriously? Many of the treatments deployed by our medical forebears, from Hippocrates's time well into the twentieth century, were if anything *more* likely to do harm than to heal. Did your head hurt? You'd be a candidate for trepanation, or having a hole drilled in your skull. Strange sores on your private parts? Try not to scream while the Doktor of Physik dabs some toxic mercury on your genitals. And then, of course, there

was the millennia-old standby of bloodletting, which was generally the very last thing that a sick or wounded person needed.

“不要傷害”？嚴重地？從希波克拉底時代到二十世紀，我們的醫學前輩所採用的許多治療方法，弊大於利。你的頭受傷了嗎？您可能需要進行環鑽術，或在頭骨上鑽一個洞。你的私處有奇怪的瘡嗎？當物理學博士在您的生殖器上塗抹有毒汞時，盡量不要尖叫。當然，還有幾千年歷史的放血療法，這通常是病人或受傷的人最不需要的東西。

What bothers me most about “First, do no harm,” though, is its implication that the best treatment option is always the one with the least immediate downside risk—and, very often, doing nothing at all. Every doctor worth their diploma has a story to disprove this nonsense. Here’s one of mine: During one of the last trauma calls I took as a resident, a seventeen-year-old kid came in with a single stab wound in his upper abdomen, just below his xiphoid process, the little piece of cartilage at the bottom end of his sternum. He seemed to be stable when he rolled in, but then he started acting odd, becoming very anxious. A quick ultrasound suggested he might have some fluid in his pericardium, the tough fibrous sac around the heart. This was now a full-blown emergency, because if enough fluid collected in there, it would stop his heart and kill him within a minute or two.

然而，「首先，不要造成傷害」最讓我困擾的是，它暗示著最好的治療選擇始終是直接負面風險最小的選擇，而且通常什麼也不做。每個值得獲得文憑的醫生都有一個故事來反駁這種胡言亂語。這是我的一個經歷：在我作為住院醫生最後一次接聽外傷電話時，一名17歲的孩子進來了，他的上腹部有一處刺傷，就在劍突下方，劍突處的一小塊軟骨。他的胸骨下端。當他滾進來時，他看起來很穩定，但隨後他的行為就開始變得奇怪，變得非常焦慮。快速超音波檢查顯示他的心包膜（心臟周圍堅硬的纖維囊）中可能有一些液體。現在這是一個全面的緊急情況，因為如果那裡積聚了足夠的液體，他的心臟就會停止跳動，在一兩分鐘內就會殺死他。

There was no time to take him up to the OR; he could easily die on the elevator ride. As he lost consciousness, I had to make a split-second decision to cut into his chest right then and there and slice open his pericardium to

relieve the pressure on his heart. It was stressful and bloody, but it worked, and his vital signs soon stabilized. No doubt the procedure was hugely risky and caused him great short-term harm, but had I not done it, he might have died waiting for a safer and more sterile procedure in the operating room. Fast death waits for no one.

沒有時間帶他去手術室；他很容易死在電梯裡。當他失去知覺時，我不得不當場做出決定，當場切開他的胸腔，切開他的心包，以減輕他心臟的壓力。雖然壓力大、血腥，但很有效，他的生命體徵很快就穩定下來。毫無疑問，這個手術風險極大，給他帶來了巨大的短期傷害，但如果我不這麼做，他可能會在手術室等待更安全、更無菌的手術時死去。快速的死亡不會等待任何人。

The reason I had to act so dramatically in the moment was that the risk was so asymmetric: doing nothing—avoiding “harm”—would likely have resulted in his death. Conversely, even if I was wrong in my diagnosis, the hasty chest surgery we performed was quite survivable, though obviously not how one might wish to spend a Wednesday night. After we got him out of imminent danger, it became clear that the tip of the knife had just barely punctured his pulmonary artery, a simple wound that took two stitches to fix once he was stabilized and in the OR. He went home four nights later.

我當時必須採取如此戲劇性的行動的原因是風險是如此不對稱：什麼都不做——避免「傷害」——很可能會導致他的死亡。相反，即使我的診斷是錯誤的，我們進行的倉促胸部手術也是可以存活的，儘管顯然不是人們希望如何度過週三晚上。當我們把他從迫在眉睫的危險中救出來後，我們發現刀尖剛剛刺破了他的肺動脈，這是一個簡單的傷口，一旦他穩定下來並進入手術室，就需要縫兩針才能修復。四晚後他回家了。

Risk is not something to be avoided at all costs; rather, it's something we need to understand, analyze, and work with. Every single thing we do, in medicine and in life, is based on some calculation of risk versus reward. Did you eat a salad from Whole Foods for lunch? There's a small chance there could have been *E. coli* on the greens. Did you drive to Whole Foods to get it?

Also risky. But on balance, that salad is probably good for you (or at least less bad than some other things you could eat).

風險不是要不惜一切代價避免的；相反，它是我們需要理解、分析和處理的東西。我們在醫學和生活中所做的每一件事都是基於風險與回報的計算。你午餐吃了全食超市的沙拉嗎？果嶺上存在大腸桿菌的可能性很小。你開車去全食超市買嗎？也有風險。但總的來說，這種沙拉可能對你有好處（或至少比你可以吃的其他東西沒那麼糟）。

Sometimes, as in the case of my seventeen-year-old stab victim, you have to take the leap. In other, less rushed situations, you might have to choose more carefully between subjecting a patient to a colonoscopy, with its slight but real risk of injury, versus not doing the examination and potentially missing a cancer diagnosis. My point is that a physician who has never done *any* harm, or at least confronted the risk of harm, has probably never done much of anything to help a patient either. And as in the case of my teenage stabbing victim, sometimes doing nothing is the riskiest choice of all.

有時，就像我十七歲的刺傷受害者的情況一樣，你必須踏出一步。在其他不那麼匆忙的情況下，您可能必須更謹慎地選擇是對患者進行大腸鏡檢查（雖然有輕微但真實的受傷風險），還是不進行檢查並可能錯過癌症診斷。我的觀點是，一位從未造成任何傷害或至少面臨過傷害風險的醫生，也可能從未做過任何事情來幫助病人。就像我十幾歲的刺傷受害者的例子一樣，有時什麼都不做是最危險的選擇。

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I actually kind of wish Hippocrates had been around to witness that operation on the kid who was stabbed—or any procedure in a modern hospital setting, really. He would have been blown away by all of it, from the precision steel instruments to the antibiotics and anesthesia, to the bright electric lights.

事實上，我有點希望希波克拉底能夠親眼目睹對被刺傷的孩子進行的手術——或者現代醫院環境中的任何手術，真的。從精密的鋼製儀器到抗生素和麻醉劑，再到明亮的電燈，這一切都會讓他震驚。

While it is true that we owe a lot to the ancients—such as the twenty thousand new words that medical school injected into my vocabulary, most derived from Greek or Latin—the notion of a continuous march of progress from Hippocrates’s era to the present is a complete fiction. It seems to me that there have been two distinct eras in medical history, and that we may now be on the verge of a third.

雖然我們確實欠古人很多——比如醫學院在我的詞彙中註入了兩萬個新單詞，其中大部分源自希臘語或拉丁語——但從希波克拉底時代到現在不斷進步的概念是一部完整的小說。在我看來，醫學史上有兩個截然不同的時代，而我們現在可能正處於第三個時代的邊緣。

The first era, exemplified by Hippocrates but lasting almost two thousand years after his death, is what I call *Medicine 1.0*. Its conclusions were based on direct observation and abetted more or less by pure guesswork, some of which was on target and some not so much. Hippocrates advocated walking for exercise, for example, and opined that “in food excellent medicine can be found; in food bad medicine can be found,” which still holds up. But much of *Medicine 1.0* missed the mark entirely, such as the notion of bodily “humors,” to cite just one example of many. Hippocrates’s major contribution was the insight that diseases are caused by nature and not by actions of the gods, as had previously been believed. That alone represented a huge step in the right direction. So it’s hard to be too critical of him and his contemporaries. They did the best they could without an understanding of science or the scientific method. You can’t use a tool that has not yet been invented.

第一個時代，以希波克拉底為代表，在他死後持續了近兩千多年，我稱之為醫學 1.0。它的結論是基於直接觀察，並或多或少受到純粹猜測的影響，其中一些是正確的，而另一些則不太準確。例如，希波克拉底提倡步行鍛鍊身體，並認為「食物中可以找到良藥；食物中可以找到良藥；食物中可以找到很好的藥物」。食中可見劣藥”，這句話至今仍然成立。但醫學 1.0 的大部分內容完全沒有達到目標，例如身體「幽默」的概念（僅舉眾多例子之一）。希波克拉底的主要貢獻是認識到疾病是由自然引起的，而不是像以前所認為的那樣是由神的行為引起的。僅此一點就代表朝著正確方向邁出了一大步。因此，很難對

他和他的同時代人過於批評。他們在不了解科學或科學方法的情況下盡了最大努力。你不能使用尚未發明的工具。

Medicine 2.0 arrived in the mid-nineteenth century with the advent of the germ theory of disease, which supplanted the idea that most illness was spread by “miasmas,” or bad air. This led to improved sanitary practices by physicians and ultimately the development of antibiotics. But it was far from a clean transition; it’s not as though one day Louis Pasteur, Joseph Lister, and Robert Koch simply published their groundbreaking studies,^[*2] and the rest of the medical profession fell into line and changed the way they did everything overnight. In fact, the shift from Medicine 1.0 to Medicine 2.0 was a long, bloody slog that took centuries, meeting trench-warfare resistance from the establishment at many points along the way.

十九世紀中葉，隨著疾病細菌理論的出現，醫學 2.0 時代到來，該理論取代了大多數疾病是透過「瘴氣」或不良空氣傳播的觀點。這導致了醫生衛生習慣的改善，並最終導致了抗生素的開發。但這遠非乾淨俐落的轉變。路易斯·巴斯德、約瑟夫·李斯特和羅伯特·科赫並不是有一天簡單地發表了他們的開創性研究，[*2]而醫學界的其他人也紛紛效仿，一夜之間改變了他們做一切事情的方式。事實上，從醫學 1.0 到醫學 2.0 的轉變是一個漫長而血腥的過程，持續了幾個世紀，在此過程中的許多地方都遇到了來自當權派的陣地戰阻力。

Consider the case of poor Ignaz Semmelweis, a Viennese obstetrician who was troubled by the fact that so many new mothers were dying in the hospital where he worked. He concluded that their strange “childbed fever” might somehow be linked to the autopsies that he and his colleagues performed in the mornings, before delivering babies in the afternoons—without washing their hands in between. The existence of germs had not yet been discovered, but Semmelweis nonetheless believed that the doctors were transmitting *something* to these women that caused their illness. His observations were most unwelcome. His colleagues ostracized him, and Semmelweis died in an insane asylum in 1865.

想想可憐的伊格納茲·塞梅爾維斯（Ignaz Semmelweis）的例子，他是一位維也納產科醫生，他對自己工作的醫院裡有這麼多新媽媽死去感

到困擾。他得出的結論是，他們奇怪的「產床熱」可能與他和他的同事在下午分娩之前早上進行的屍檢有關，而中間沒有洗手。細菌的存在尚未被發現，但塞梅爾維斯仍然相信醫生正在向這些婦女傳播某種導致她們生病的東西。他的意見是最不受歡迎的。他的同事們排斥他，塞梅爾維斯於 1865 年在瘋人院去世。

That very same year, Joseph Lister first successfully demonstrated the principle of antiseptic surgery, using sterile techniques to operate on a young boy in a hospital in Glasgow. It was the first application of the germ theory of disease. Semmelweis had been right all along.

同年，約瑟夫·李斯特（Joseph Lister）首次成功展示了消毒手術的原理，他在格拉斯哥的一家醫院使用無菌技術對一名小男孩進行了手術。這是疾病細菌理論的首次應用。塞梅爾維斯一直都是對的。

The shift from Medicine 1.0 to Medicine 2.0 was prompted in part by new technologies such as the microscope, but it was more about a *new way of thinking*. The foundation was laid back in 1628, when Sir Francis Bacon first articulated what we now know as the scientific method. This represented a major philosophical shift, from observing and guessing to observing, and then forming a hypothesis, which as Richard Feynman pointed out is basically a fancy word for a guess.

從醫學1.0到醫學2.0的轉變部分是由顯微鏡等新技術推動的，但更多的是一種新的思考方式。1628年，弗朗西斯·培根爵士首次闡明了我們現在所知的科學方法，奠定了基礎。這代表了一個重大的哲學轉變，從觀察和猜測到觀察，然後形成假設，正如理查德·費曼指出的那樣，這基本上是猜測的一個花哨的詞。

The next step is crucial: rigorously testing that hypothesis/guess to determine whether it is correct, also known as experimenting. Instead of using treatments that they *believed* might work, often despite ample anecdotal evidence to the contrary, scientists and physicians could systematically test and evaluate potential cures, then choose the ones that had performed best in experiments. Yet three centuries elapsed between Bacon's essay and the discovery of penicillin, the true game-changer of Medicine 2.0.

下一步至關重要：嚴格測試該假設/猜測以確定其是否正確，也稱為實驗。科學家和醫生可以系統地測試和評估潛在的治療方法，然後選擇在實驗中表現最好的治療方法，而不是使用他們認為可能有效的治療方法，儘管有大量相反的軼事證據。然而，從培根的論文發表到青黴素（醫學 2.0 真正的遊戲規則改變者）的發現，已經過去了三個世紀。

Medicine 2.0 was transformational. It is a defining feature of our civilization, a scientific war machine that has eradicated deadly diseases such as polio and smallpox. Its successes continued with the containment of HIV and AIDS in the 1990s and 2000s, turning what had seemed like a plague that threatened all humanity into a manageable chronic disease. I'd put the recent cure of hepatitis C right up there as well. I remember being told in medical school that hepatitis C was an unstoppable epidemic that was going to completely overwhelm the liver transplant infrastructure in the United States within twenty-five years. Today, most cases can be cured by a short course of drugs (albeit very expensive ones).

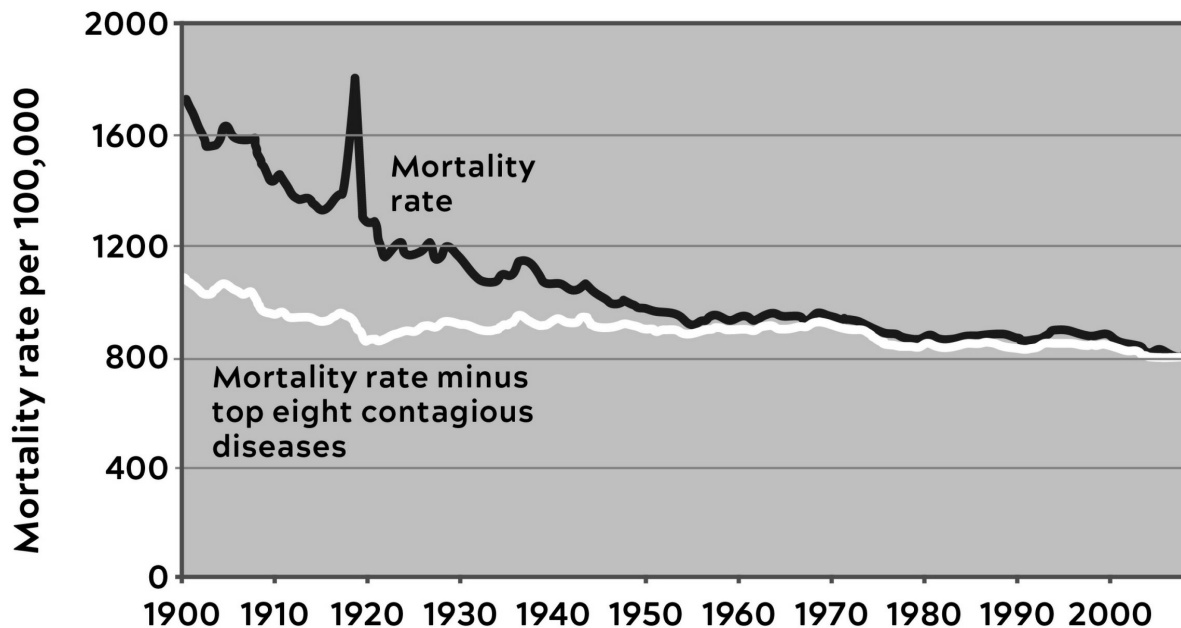
醫學 2.0 具有變革性。它是我們文明的決定性特徵，是一個科學的戰爭機器，已經根除了小兒麻痺和天花等致命疾病。1990 年代和 2000 年代，它繼續取得成功，遏制了愛滋病毒和愛滋病，將威脅全人類的瘟疫變成了可控制的慢性疾病。我也把最近治療 C 型肝炎的方法也放在那裡。我記得在醫學院時有人告訴我，C 型肝炎是一種不可阻擋的流行病，將在二十五年內完全壓垮美國的肝臟移植基礎設施。如今，大多數病例可以透過短期藥物治癒（儘管非常昂貴）。

Perhaps even more amazing was the rapid development of not just one but several effective vaccines against COVID-19, not even a year after the pandemic took hold in early 2020. The virus genome was sequenced within weeks of the first deaths, allowing the speedy formulation of vaccines that specifically target its surface proteins. Progress with COVID treatments has also been remarkable, yielding multiple types of antiviral drugs within less than two years. This represents Medicine 2.0 at its absolute finest.

也許更令人驚訝的是，在2020年初大流行爆發不到一年後，針對COVID-19的有效疫苗不僅是一種，而且是幾種的快速開發。病毒基因組在第一例死亡後的幾週內就被定序，從而可以快速配製專門針對其表面蛋白的疫苗。新冠治療的進展也非常顯著，在不到兩年的時間內就產生了多種類型的抗病毒藥物。這代表了醫學 2.0 的絕對最佳狀態。

Yet Medicine 2.0 has proved far less successful against long-term diseases such as cancer. While books like this always trumpet the fact that lifespans have nearly doubled since the late 1800s, the lion's share of that progress may have resulted entirely from antibiotics and improved sanitation, as Steven Johnson points out in his book *Extra Life*. The Northwestern University economist Robert J. Gordon analyzed mortality data going back to 1900 (see figure 1) and found that if you subtract out deaths from the eight top infectious diseases, which were largely brought under control by the advent of antibiotics in the 1930s, overall mortality rates declined relatively little over the course of the twentieth century. That means that Medicine 2.0 has made scant progress against the Horsemen.

然而事實證明，醫學 2.0 在對抗癌症等長期疾病方面遠沒有那麼成功。雖然這類書籍總是宣揚這樣一個事實：自1800年代末以來，人類的壽命幾乎翻了一番，但正如史蒂文·約翰遜(Steven Johnson)在他的《額外生命》一書中指出的那樣，這項進步的大部分可能完全歸功於抗生素和衛生條件的改善。西北大學經濟學家羅伯特·戈登(Robert J. Gordon)分析了1900年以來的死亡率數據（見圖1），發現如果減去8種主要傳染病的死亡人數（這些疾病在20世紀30年代因抗生素的出現而在很大程度上得到了控制），二十世紀期間，整體死亡率下降幅度相對較小。這意味著Medicine 2.0在對抗天啟騎士方面進展甚微。

Figure 1. Change in Mortality Rates Since 1900

Source: Gordon (2016).

資料來源：戈登（2016）。

This graph shows how *little* real mortality rates have improved since 1900, once you remove the top eight contagious/infectious diseases, which were largely controlled by the advent of antibiotics in the early twentieth century.

該圖顯示，自 1900 年以來，如果剔除排名前八的傳染性疾病，實際死亡率幾乎沒有改善，而這些疾病在很大程度上是由二十世紀初期抗生素的出現所控制的。

Toward Medicine 3.0

邁向醫學3.0

During my stint away from medicine, I realized that my colleagues and I had been trained to solve the problems of an earlier era: the acute illnesses and injuries that Medicine 2.0 had evolved to treat. Those problems had a much shorter event horizon; for our cancer patients, time itself was the enemy. And we were always coming in too late.

在離開醫學界期間，我意識到我和我的同事們接受的訓練是為了解決早期時代的問題：醫學 2.0 已經發展到可以治療的急性疾病和傷害。這些問題的事件視界要短得多。對我們的癌症患者來說，時間本身就是敵人。而且我們總是來得太晚。

This actually wasn't so obvious until I'd spent my little sabbatical immersed in the worlds of mathematics and finance, thinking every day about the nature of risk. The banks' problem was not all that different from the situation faced by some of my patients: their seemingly minor risk factors had, over time, compounded into an unstoppable, asymmetric catastrophe. Chronic diseases work in a similar fashion, building over years and decades—and once they become entrenched, it's hard to make them go away. Atherosclerosis, for example, begins many decades before the person has a coronary "event" that could result in their death. But that event, often a heart attack, too often marks the point where treatment begins.

事實上，直到我花了一點假期沉浸在數學和金融的世界中，每天思考風險的本質之前，這一點並不那麼明顯。銀行的問題與我的一些患者面臨的情況並沒有什麼不同：隨著時間的推移，它們看似微不足道的風險因素已經複雜化為一場不可阻擋的、不對稱的災難。慢性病的發病機轉與此類似，會持續數年甚至數十年，一旦變得根深蒂固，就很難消除。例如，動脈粥狀硬化在一個人發生可能導致死亡的冠狀動脈「事件」之前幾十年就開始了。但這種事件（通常是心臟病發作）往往標誌著治療的開始。

This is why I believe we need a new way of thinking about chronic diseases, their treatment, and how to maintain long-term health. The goal of this new medicine—which I call *Medicine 3.0*—is not to patch people up and get them out the door, removing their tumors and hoping for the best, but rather to prevent the tumors from appearing and spreading in the first place. Or to avoid that first heart attack. Or to divert someone from the path to Alzheimer's disease. Our treatments, and our prevention and detection strategies, need to change to fit the nature of these diseases, with their long, slow prologues.

這就是為什麼我認為我們需要一種新的方式來思考慢性病、其治療以及如何保持長期健康。這種新藥物（我稱之為醫學 3.0）的目標不是讓人們包紮傷口，讓他們走出家門，切除腫瘤並希望得到最好的結果，而是從一開始就防止腫瘤的出現和擴散。或避免第一次心臟病發作。或讓某人遠離患阿茲海默症的道路。我們的治療、預防和檢測策略需要改變，以適應這些疾病的本質，以及它們漫長而緩慢的序幕。

It is already obvious that medicine is changing rapidly in our era. Many pundits have been predicting a glorious new era of “personalized” or “precision” medicine, where our care will be tailored to our exact needs, down to our very genes. This is, obviously, a worthy goal; it is clear that no two patients are exactly alike, even when they are presenting with what appears to be an identical upper-respiratory illness. A treatment that works for one patient may prove useless in the other, either because her immune system is reacting differently or because her infection is viral rather than bacterial. Even now, it remains extremely difficult to tell the difference, resulting in millions of useless antibiotic prescriptions.

很明顯，我們這個時代的醫學正在迅速改變。許多專家一直預測「個人化」或「精準」醫學的輝煌新時代將會到來，我們的照護將根據我們的具體需求量身定制，甚至深入到我們的基因。顯然，這是一個有價值的目標。顯然，沒有兩個患者是完全相同的，即使他們患有看似相同的上呼吸道疾病。對一名患者有效的治療方法可能對另一名患者無效，要么是因為她的免疫系統反應不同，要么是因為她的感染是病毒性而非細菌性的。即使現在，區分兩者仍然極其困難，導致數百萬張無用的抗生素處方。

Many thinkers in this space believe that this new era will be driven by advances in technology, and they are likely right; at the same time, however, technology has (so far) been largely a limiting factor. Let me explain. On the one hand, improved technology enables us to collect much more data on patients than ever before, and patients themselves are better able to monitor their own biomarkers. This is good. Even better, artificial intelligence and machine learning are being harnessed to try to digest this massive profusion of data and come up with more definitive assessments of our risk of, say, heart

disease than the rather simple risk factor-based calculators we have now. Others point to the possibilities of nanotechnology, which could enable doctors to diagnose and treat disease by means of microscopic bioactive particles injected into the bloodstream. But the nanobots aren't here yet, and barring a major public or private research push, it could be a while before they become reality.

該領域的許多思想家認為，這個新時代將由技術進步推動，他們可能是對的。但同時，技術（迄今為止）在很大程度上一直是一個限制因素。讓我解釋。一方面，改進的技術使我們能夠收集比以往更多的患者數據，並且患者本身能夠更好地監測自己的生物標記。這很好。更好的是，人工智慧和機器學習正在被用來消化大量的數據，並對我們患心臟病的風險做出更明確的評估，而不是我們現在擁有的相當簡單的基於風險因素的計算器。其他人指出了奈米技術的可能性，它可以使醫生透過注入血液中的微觀生物活性顆粒來診斷和治療疾病。但奈米機器人還沒有出現，除非有重大的公共或私人研究推動，否則它們可能還需要一段時間才能成為現實。

The problem is that our *idea* of personalized or precision medicine remains some distance ahead of the technology necessary to realize its full promise. It's a bit like the concept of the self-driving car, which has been talked about for almost as long as automobiles have been crashing into each other and killing and injuring people. Clearly, removing human error from the equation as much as possible would be a good thing. But our technology is only today catching up to a vision we've held for decades.

問題在於，我們的個人化或精準醫療理念距離實現其全部承諾所需的技術仍有一定距離。這有點像自動駕駛汽車的概念，自從汽車相互碰撞並造成人員傷亡以來，人們一直在談論這個概念。顯然，盡可能消除人為錯誤將是一件好事。但我們的技術直到今天才趕上我們幾十年來的願景。

If you had wanted to create a "self-driving" car in the 1950s, your best option might have been to strap a brick to the accelerator. Yes, the vehicle would have been able to move forward on its own, but it could not slow down, stop, or turn to avoid obstacles. Obviously not ideal. But does that mean the

entire concept of the self-driving car is not worth pursuing? No, it only means that at the time we did not yet have the tools we now possess to help enable vehicles to operate both autonomously and safely: computers, sensors, artificial intelligence, machine learning, and so on. This once-distant dream now seems within our reach.

如果你想在 20 世紀 50 年代製造一輛「自動駕駛」汽車，你最好的選擇可能就是在加速器上綁一塊磚頭。是的，車輛本來能夠自行前進，但它無法減速、停止或轉彎以避開障礙物。顯然並不理想。但這是否意味著自動駕駛汽車的整個概念不值得追求？不，這只意味著當時我們還沒有現在擁有的工具來幫助車輛自動安全地運行：電腦、感測器、人工智慧、機器學習等等。這個曾經遙不可及的夢想，如今似乎觸手可及。

It is much the same story in medicine. Two decades ago, we were still taping bricks to gas pedals, metaphorically speaking. Today, we are approaching the point where we can begin to bring some appropriate technology to bear in ways that advance our understanding of patients as unique individuals. For example, doctors have traditionally relied on two tests to gauge their patients' metabolic health: a fasting glucose test, typically given once a year; or the HbA1c test we mentioned earlier, which gives us an estimate of their average blood glucose over the last 90 days. But those tests are of limited use because they are static and backward-looking. So instead, many of my patients have worn a device that monitors their blood glucose levels in real time, which allows me to talk to them about nutrition in a specific, nuanced, feedback-driven way that was not even possible a decade ago. This technology, known as continuous glucose monitoring (CGM), lets me observe how *their individual metabolism* responds to a certain eating pattern and make changes to their diet quickly. In time, we will have many more sensors like this that will allow us to tailor our therapies and interventions far more quickly and precisely. The self-driving car will do a better job of following the twists and turns of the road, staying out of the ditch.

醫學上的情況也大致相同。打個比方，二十年前，我們還在用磚塊貼在油門踏板上。今天，我們即將開始應用一些適當的技術，以增進我們對患者作為獨特個體的理解。例如，醫生傳統上依靠兩項測試來衡量患者的代謝健康狀況：空腹血糖測試，通常每年進行一次；或者我們之前提到的 HbA1c 測試，它可以讓我們估計他們過去 90 天的平均血糖。但這些測試的用途有限，因為它們是靜態的和向後看的。因此，我的許多患者都佩戴了一種即時監測血糖水平的設備，這使我能夠以一種特定的、細緻入微的、反饋驅動的方式與他們談論營養問題，這在十年前甚至是不可能的。這項技術被稱為連續血糖監測

（CGM），讓我可以觀察他們的個體新陳代謝如何對某種飲食模式做出反應，並快速改變他們的飲食。隨著時間的推移，我們將擁有更多這樣的感測器，這將使我們能夠更快、更精確地調整我們的治療和介入措施。自動駕駛汽車將更好地沿著曲折的道路行駛，遠離溝渠。

But Medicine 3.0, in my opinion, is not really about technology; rather, it requires an evolution in our mindset, a shift in the way in which we approach medicine. I've broken it down into four main points.

但在我看來，醫學 3.0 並不是真正的技術，而是技術。相反，它需要我們思維方式的轉變，以及我們對待醫學的方式的轉變。我把它分成四個要點。

First, *Medicine 3.0 places a far greater emphasis on prevention than treatment.* When did Noah build the ark? Long before it began to rain. Medicine 2.0 tries to figure out how to get dry after it starts raining. Medicine 3.0 studies meteorology and tries to determine whether we need to build a better roof, or a boat.

首先，醫學3.0更強調預防而非治療。諾亞方舟是什麼時候建造的？早在開始下雨之前。Medicine 2.0 試著找出下雨後如何保持乾燥的方法。醫學 3.0 研究氣象學並試圖確定我們是否需要建造更好的屋頂或船。

Second, *Medicine 3.0 considers the patient as a unique individual.* Medicine 2.0 treats everyone as basically the same, obeying the findings of the clinical trials that underlie evidence-based medicine. These trials take heterogeneous

inputs (the people in the study or studies) and come up with homogeneous results (the average result across all those people). Evidence-based medicine then insists that we apply those average findings back to individuals. The problem is that no patient is strictly average. Medicine 3.0 takes the findings of evidence-based medicine and goes one step further, looking more deeply into the data to determine how our patient is similar or different from the “average” subject in the study, and how its findings might or might not be applicable to them. Think of it as “evidence-informed” medicine.

其次，醫學3.0將患者視為獨特的個體。醫學2.0對每個人都一視同仁，遵循實證醫學基礎的臨床試驗結果。這些試驗採用異質輸入（一項或多項研究中的人員）並得出同質結果（所有這些人的平均結果）。實證醫學堅持我們將這些平均結果應用到個人身上。問題是沒有一個病人是嚴格意義上的平均水準。醫學 3.0 採用實證醫學的發現，並更進一步，更深入地研究數據，以確定我們的患者與研究中的「平均」受試者有何相似或不同，以及其發現可能或可能不一樣。適用於他們。將其視為「循證」醫學。

The third philosophical shift has to do with our attitude toward risk. *In Medicine 3.0, our starting point is the honest assessment, and acceptance, of risk—including the risk of doing nothing.*

第三個哲學轉變與我們對風險的態度有關。在醫學 3.0 中，我們的出發點是誠實地評估和接受風險——包括不採取任何行動的風險。

There are many examples of how Medicine 2.0 gets risk wrong, but one of the most egregious has to do with hormone replacement therapy (HRT) for postmenopausal women, long entrenched as standard practice before the results of the Women’s Health Initiative Study (WHI) were published in 2002. This large clinical trial, involving thousands of older women, compared a multitude of health outcomes in women taking HRT versus those who did not take it. The study reported a 24 percent relative increase in the risk of breast cancer among a subset of women taking HRT, and headlines all over the world condemned HRT as a dangerous, cancer-causing therapy. All of a sudden, on the basis of this one study, hormone replacement treatment became virtually taboo.

醫學2.0 錯誤風險的例子有很多，但最令人震驚的例子之一與停經後女性的激素替代療法(HRT) 有關，在婦女健康倡議研究(WHI) 結果公佈之前，該療法長期以來一直被視為標準做法。發表於 2002 年。這項大型臨床試驗涉及數千名老年女性，比較了接受 HRT 的女性與未接受 HRT 的女性的多種健康結果。研究報告稱，部分接受 HRT 的女性罹患乳癌的風險相對增加了 24%，世界各地的頭條新聞都譴責 HRT 是一種危險的致癌療法。突然之間，根據這項研究，荷爾蒙替代治療幾乎成為禁忌。

This reported 24 percent risk increase sounded scary indeed. But nobody seemed to care that the *absolute* risk increase of breast cancer for women in the study remained minuscule. Roughly five out of every one thousand women in the HRT group developed breast cancer, versus four out of every one thousand in the control group, who received no hormones. The absolute risk increase was just 0.1 percentage point. HRT was linked to, potentially, one additional case of breast cancer in every thousand patients. Yet this tiny increase in absolute risk was deemed to outweigh any benefits, meaning menopausal women would potentially be subject to hot flashes and night sweats, as well as loss of bone density and muscle mass, and other unpleasant symptoms of menopause—not to mention a potentially increased risk of Alzheimer's disease, as we'll see in chapter 9.

所報告的 24% 的風險增加聽起來確實很可怕。但似乎沒有人關心研究中女性罹患乳癌的絕對風險增加仍然很小。HRT 組中約每 1000 名女性中有 5 名罹患乳癌，而未接受荷爾蒙治療的對照組中每 1000 名女性中有 4 名罹患乳癌。絕對風險僅增加0.1個百分點。HRT 可能與每 1000 名患者中增加 1 例乳癌有關。然而，這種絕對風險的微小增加被認為超過了任何好處，這意味著更年期女性可能會出現潮熱和盜汗、骨密度和肌肉質量下降以及其他令人不快的更年期症狀，更不用說患有阿爾茨海默氏症的風險可能會增加，我們將在第9 章中看到。

Medicine 2.0 would rather throw out this therapy entirely, on the basis of one clinical trial, than try to understand and address the nuances involved. Medicine 3.0 would take this study into account, while recognizing its inevitable limitations and built-in biases. The key question that Medicine 3.0

asks is whether this intervention, hormone replacement therapy, with its relatively small increase in *average* risk in a large group of women older than sixty-five, might still be net beneficial for our *individual* patient, with her own unique mix of symptoms and risk factors. How is she similar to or different from the population in the study? One huge difference: none of the women selected for the study were actually symptomatic, and most were many years out of menopause. So how applicable are the findings of this study to women who are in or just entering menopause (and are presumably younger)? Finally, is there some other possible explanation for the slight observed increase in risk with this specific HRT protocol?[*3]

醫學 2.0 寧願在一項臨床試驗的基礎上完全拋棄這種療法，也不願嘗試理解和解決其中的細微差別。醫學 3.0 將考慮這項研究，同時認識到其不可避免的局限性和內在偏見。醫學3.0 提出的關鍵問題是，這種幹預措施，即激素替代療法，在一大群65 歲以上女性中平均風險增加相對較小，是否仍然對我們的個別患者產生淨有益，因為她有自己獨特的特徵。症狀和危險因子的混合。她與研究中的族群有何相似或不同？一個巨大的差異是：被選中參加這項研究的女性中沒有一位真正出現症狀，而且大多數都已經脫離更年期很多年了。那麼這項研究的結果對於處於或剛進入更年期的女性（並且可能更年輕）有多大的適用性呢？最後，對於這種特定 HRT 方案觀察到的風險輕微增加是否有其他可能的解釋？ [*3]

My broader point is that at the level of the individual patient, we should be willing to ask deeper questions of risk versus reward versus cost for this therapy—and for almost anything else we might do.

我更廣泛的觀點是，在個別患者的層面上，我們應該願意就這種療法以及我們可能做的幾乎任何其他事情提出更深層次的問題，即風險、回報和成本。

The fourth and perhaps largest shift is that where Medicine 2.0 focuses largely on lifespan, and is almost entirely geared toward staving off death, *Medicine 3.0 pays far more attention to maintaining healthspan, the quality of life.*

第四個也許是最大的轉變是，醫學 2.0 主要關注壽命，並且幾乎完全旨在避免死亡，而醫學 3.0 則更加關注維持健康壽命和生活品質。

Healthspan was a concept that barely even existed when I went to medical school. My professors said little to nothing about how to help our patients maintain their physical and cognitive capacity as they aged. The word *exercise* was almost never uttered. Sleep was totally ignored, both in class and in residency, as we routinely worked twenty-four hours at a stretch. Our instruction in nutrition was also minimal to nonexistent.

當我上醫學院時，健康壽命這個概念幾乎不存在。我的教授幾乎沒有提及如何幫助我們的患者隨著年齡的增長保持身體和認知能力。「鍛煉」這個詞幾乎從未被提及。無論是在課堂上還是在實習中，睡眠都被完全忽視了，因為我們通常會連續工作二十四小時。我們的營養指導也很少甚至根本不存在。

Today, Medicine 2.0 at least acknowledges the importance of healthspan, but the standard definition—the period of life free of disease or disability—is totally insufficient, in my view. We want more out of life than simply the absence of sickness or disability. We want to be thriving, in every way, throughout the latter half of our lives.

今天，醫學2.0至少承認健康壽命的重要性，但在我看來，標準定義——沒有疾病或殘疾的生命週期——是完全不夠的。我們想要的生活不僅僅是沒有疾病或殘疾。我們希望在後半生中在各方面都蓬勃發展。

Another, related issue is that longevity itself, and healthspan in particular, doesn't really fit into the business model of our current healthcare system. There are few insurance reimbursement codes for most of the largely preventive interventions that I believe are necessary to extend lifespan and healthspan. Health insurance companies won't pay a doctor very much to tell a patient to change the way he eats, or to monitor his blood glucose levels in order to help prevent him from developing type 2 diabetes. Yet insurance will pay for this same patient's (very expensive) insulin *after* he has been diagnosed. Similarly, there's no billing code for putting a patient on a

comprehensive exercise program designed to maintain her muscle mass and sense of balance while building her resistance to injury. But if she falls and breaks her hip, then her surgery and physical therapy will be covered. Nearly all the money flows to treatment rather than prevention—and when I say “prevention,” I mean *prevention of human suffering*. Continuing to ignore healthspan, as we’ve been doing, not only condemns people to a sick and miserable older age but is guaranteed to bankrupt us eventually.

另一個相關問題是，長壽本身，尤其是健康壽命，並不真正適合我們目前醫療保健系統的商業模式。我認為大多數預防性幹預措施對於延長壽命和健康壽命是必要的，但幾乎沒有保險報銷代碼。健康保險公司不會付醫生很多錢來告訴病人改變飲食方式，或監測他的血糖值以幫助預防他罹患第 2 型糖尿病。然而，在這位患者被診斷後，保險將支付他的（非常昂貴的）胰島素費用。同樣，也沒有計費代碼可以讓患者接受旨在保持肌肉質量和平衡感同時增強對傷害的抵抗力的綜合鍛煉計劃。但如果她摔倒並摔斷臀部，那麼她的手術和物理治療將得到承保。幾乎所有的錢都流向了治療而不是預防——當我說「預防」時，我的意思是預防人類痛苦。正如我們一直在做的那樣，繼續忽視健康壽命，不僅會導致人們生病、悲慘地度過老年，而且最終肯定會讓我們破產。

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When I introduce my patients to this approach, I often talk about icebergs—specifically, the ones that ended the first and final voyage of the *Titanic*. At 9:30 p.m. on the fatal night, the massive steamship received an urgent message from another vessel that it was headed into an icefield. The message was ignored. More than an hour later, another ship telegraphed a warning of icebergs in the ship’s path. The *Titanic*’s wireless operator, busy trying to communicate with Newfoundland over crowded airwaves, replied (via Morse code): “Keep out; shut up.”

當我向我的患者介紹這種方法時，我經常談論冰山，特別是那些結束泰坦尼克號第一次和最後一次航行的冰山。晚上 9:30 在那個致命的夜

晚，這艘巨大的輪船收到了另一艘船發出的緊急訊息，稱它正駛入冰原。該訊息被忽略。一個多小時後，另一艘船發出電報警告，稱該船航線上有冰山。泰坦尼克號的無線電操作員正忙於透過擁擠的電波與紐芬蘭進行通信，他回覆（透過莫爾斯電碼）：「請勿進入；住口。」

There were other problems. The ship was traveling at too fast a speed for a foggy night with poor visibility. The water was unusually calm, giving the crew a false sense of security. And although there was a set of binoculars on board, they were locked away and no one had a key, meaning the ship's lookout was relying on his naked eyes alone. Forty-five minutes after that last radio call, the lookout spotted the fatal iceberg just five hundred yards ahead. Everyone knows how that ended.

還有其他問題。對於能見度很低的大霧之夜來說，這艘船的行駛速度太快了。水面異常平靜，給船員一種虛假的安全感。而且船上雖然有望遠鏡，但都鎖著，沒有人帶鑰匙，這意味著船上的瞭望只能靠肉眼。最後一次無線電呼叫四十五分鐘後，瞭望員在前方五百碼處發現了致命的冰山。大家都知道事情是如何結束的。

But what if the *Titanic* had had radar and sonar (which were not developed until World War II, more than fifteen years later)? Or better yet, GPS and satellite imaging? Rather than trying to dodge through the maze of deadly icebergs, hoping for the best, the captain could have made a slight course correction a day or two before and steered clear of the entire mess. This is exactly what ship captains do now, thanks to improved technology that has made *Titanic*-style sinkings largely a thing of the past, relegated to sappy, nostalgic movies with overwrought soundtracks.

但是，如果泰坦尼克號配備了雷達和聲納（直到第二次世界大戰，即十五年多後才開發出來）呢？或者更好的是 GPS 和衛星成像？船長與其試圖躲避致命冰山的迷宮，希望得到最好的結果，不如在一兩天前稍微修正航線，避開整個混亂的地方。這正是船長們現在所做的事情，由於科技的進步，泰坦尼克式的沉沒基本上已經成為過去，成為配樂過度的多愁善感、懷舊的電影。

The problem is that in medicine our tools do not allow us to see very far over the horizon. Our “radar,” if you will, is not powerful enough. The longest randomized clinical trials of statin drugs for primary prevention of heart disease, for example, might last five to seven years. Our longest risk prediction time frame is ten years. But cardiovascular disease can take decades to develop.

問題在於，在醫學領域，我們的工具不允許我們看得更遠。如果你願意的話，我們的「雷達」還不夠強大。例如，用於心臟病一級預防的他汀類藥物最長的隨機臨床試驗可能會持續五到七年。我們最長的風險預測期限是十年。但心血管疾病可能需要數十年的時間才能形成。

Medicine 3.0 looks at the situation through a longer lens. A forty-year-old should be concerned with her thirty- or forty-year cardiovascular risk profile, not merely her ten-year risk. We therefore need tools with a much longer reach than relatively brief clinical trials. We need long-range radar and GPS, and satellite imaging, and all the rest. Not just a snapshot.

醫學3.0以更長遠的視角來看這種情況。四十歲的人應該關心她三、四十年的心血管風險狀況，而不僅僅是她十年的風險。因此，我們需要比相對簡短的臨床試驗具有更廣泛影響範圍的工具。我們需要遠端雷達、全球定位系統、衛星成像，等等。不僅僅是快照。

As I tell my patients, I'd like to be the navigator of your ship. My job, as I see it, is to steer you through the icefield. I'm on iceberg duty, 24-7. How many icebergs are out there? Which ones are closest? If we steer away from those, will that bring us into the path of other hazards? Are there bigger, more dangerous icebergs lurking over the horizon, out of sight?

正如我告訴我的病人，我想成為你們這艘船的領航員。在我看來，我的工作就是引導你穿越冰原。我正在執行冰山值班，每天 24 小時、每週 7 小時。那裡有多少座冰山？哪些最接近？如果我們避開這些，是否會導致我們陷入其他危險的情況？是否還有更大、更危險的冰山潛伏在地平線上、看不見的地方？

Which brings us to perhaps the most important difference between Medicine 2.0 and Medicine 3.0. In Medicine 2.0, you are a passenger on the

ship, being carried along somewhat passively. Medicine 3.0 demands much more from you, the patient: You must be well informed, medically literate to a reasonable degree, clear-eyed about your goals, and cognizant of the true nature of risk. You must be willing to change ingrained habits, accept new challenges, and venture outside of your comfort zone if necessary. You are always participating, never passive. You confront problems, even uncomfortable or scary ones, rather than ignoring them until it's too late. You have skin in the game, in a very literal sense. And you make important decisions.

這或許為我們帶來了醫學 2.0 和醫學 3.0 之間最重要的差異。在醫學 2.0 中，你是船上的乘客，有點被動地被運送著。醫學 3.0 對您（病人）的要求更高：您必須消息靈通，具有一定程度的醫學素養，對自己的目標有清晰的認識，並認識到風險的真正本質。您必須願意改變根深蒂固的習慣，接受新的挑戰，並在必要時冒險走出舒適圈。你總是參與其中，從不被動。你要面對問題，甚至是不舒服或可怕的問題，而不是忽視它們，直到為時已晚。從字面意義上講，你是利益相關者。你會做出重要的決定。

Because in this scenario, you are no longer a passenger on the ship; you are its captain.

因為在這種場景下，你不再是船上的乘客；你是它的船長。

[SKIP NOTES](#)

[跳過註釋](#)

[*1](#) The words “First, do no harm” do not appear in Hippocrates’s actual writings. He urged physicians to “practice two things in your dealings with disease: either help or do not harm the patient.” This was changed to “First, do no harm” by an aristocratic nineteenth-century British surgeon named Thomas Inman, whose other claim to fame was, well, nothing. Somehow it became the sacred motto of the medical profession for all of eternity.

*1 「首先，不要傷害」這句話並沒有出現在希波克拉底的實際著作中。他敦促醫生“在處理疾病時要注意兩件事：要么幫助病人，要么不傷害病人。”一位名叫托馬斯·英曼 (Thomas Inman) 的 19 世紀英國貴族外科醫生將這句話改為“首先，不要傷害”，而他的其他名聲其實沒什麼。不知何故，它成為了醫學界永恆的神聖座右銘。

*2 Pasteur discovered the existence of airborne pathogens and bacteria that caused food to rot; Lister developed antiseptic surgical techniques; and Koch identified the germs that caused tuberculosis and cholera.

*2 巴斯德發現空氣中存在導致食物腐爛的病原體和細菌；李斯特發展了消毒外科技術；科赫確定了引起結核病和霍亂的細菌。

*3 A deeper dive into the data suggests that the tiny increase in breast cancer risk was quite possibly due to the type of synthetic progesterone used in the study, and not the estrogen; the devil is always in the details.

*3 深入研究數據表明，乳癌風險的微小增加很可能是由於研究中使用的合成黃體酮類型所致，而不是雌激素所致；魔鬼總是在細節中。

CHAPTER 3

第3章

Objective, Strategy, Tactics

目標、戰略、戰術

A Road Map for Reading This Book

閱讀本書的路線圖

Strategy without tactics is the slowest route to victory.

Tactics without strategy is the noise before defeat.

沒有戰術的戰略是通往勝利最慢的道路。沒有戰略的戰術是失敗前的喧囂。

—SUN TZU

——孫子

Several years ago, I flew to San Francisco to attend the funeral of the mother of a good friend from college, whom I'll call Becky. Because Becky's parents lived near Palo Alto, where I went to medical school, they invited me to dinner many times. We often ate in their garden, which had been beautifully planned and meticulously maintained by Becky's mother, whose name was Sophie.

幾年前，我飛往舊金山參加一位大學好友（我稱之為貝琪）母親的葬禮。因為貝琪的父母住在我就讀醫學院的帕洛阿爾托附近，所以他們多次邀請我吃飯。我們經常在他們的花園裡吃飯，花園是貝琪的母親蘇菲精心規劃和維護的。

I remembered Sophie as a vibrant, athletic woman who had seemed ageless. But I hadn't seen her since my wedding nearly fifteen years earlier. Becky filled me in on what I had missed. Beginning in her early seventies, Sophie had undergone a steep physical decline that began when she slipped and fell while gardening, tearing a muscle in her shoulder. That soon escalated into back and neck pain so severe that she could no longer work in the garden or play golf at all, her two primary passions in retirement. She simply sat around the house, feeling depressed. This was followed by a descent into dementia in the last couple of years of her life, before she died of a respiratory infection at age eighty-three.

在我的記憶中，蘇菲是一位充滿活力、運動能力強的女性，看起來似乎不老。但自從大約十五年前我結婚以來，我就沒有見過她了。貝琪告訴我我錯過了什麼。從七十歲出頭開始，蘇菲的身體狀況急劇惡化，始於她在園藝時滑倒，撕裂了肩膀的肌肉。這種情況很快就升級為嚴重的背部和頸部疼痛，以至於她根本無法再在花園工作或打高爾夫球，而這是她退休後的兩大主要愛好。她只是坐在房子周圍，感到沮喪。隨後，她在生命的最後幾年陷入了癡呆症，直到八十三歲時死於呼吸道感染。

At her memorial service, everyone agreed that it was a "blessing" that Sophie hadn't had to linger in that demented state for very long, but as I sat in the pew, I reflected on the fact that she had spent the last decade of her life

being unable to participate in any of the activities that had given her pleasure. Instead, she had been in considerable pain. Nobody mentioned that. We were gathered to mourn Sophie's biological death, but it saddened me even more deeply that she had been robbed of the joy of her final years.

在她的追悼會上，每個人都認為蘇菲不必在那種瘋狂的狀態中徘徊太久，這是一種“祝福”，但當我坐在長椅上時，我反思了這樣一個事實：她在過去的十年裡度過了她一生中無法參加任何帶給她快樂的活動。相反，她一直承受著極大的痛苦。沒有人提到這一點。我們聚集在一起哀悼蘇菲的生理死亡，但令我更加難過的是，她被剝奪了晚年的歡樂。

I often talk about Sophie with my patients, not because her tale is unusual but because it is so sadly typical. We have all watched our parents, grandparents, spouses, or friends undergo similar ordeals. The sad thing is that we almost expect this to happen to our elders; and even with this knowledge, relatively few of us take measures that might help ourselves avoid that fate. Even for Becky, who had cared for her mother during her difficult final years, the idea that she might end up in the same condition was probably the furthest thing from her mind. The future, for most of us, remains a hazy abstraction.

我經常和我的病人談論蘇菲，不是因為她的故事不同尋常，而是因為它是如此典型，令人悲傷。我們都目睹過我們的父母、祖父母、配偶或朋友經歷類似的磨難。可悲的是，我們幾乎預料到這種事會發生在我們的長輩身上；即使了解了這一點，我們很少有人採取措施來幫助自己避免這種命運。即使對於在母親艱難的最後幾年裡一直照顧她的貝琪來說，她可能也最不可能想到自己可能會陷入同樣的境地。對我們大多數人來說，未來仍然是一個模糊的抽象概念。

I tell Sophie's story to help illustrate a fundamental concept in my approach to longevity, which is the need to think about and plan for the later decades of our lives—our seventies, eighties, nineties, or beyond. For many people, like Sophie, the last ten years of life are not a particularly happy time. They typically suffer from one or more of the Horsemen diseases and the effects of the requisite treatments. Their cognitive and physical abilities may be weakening or gone. Generally, they are unable to participate in the

activities they once loved, whether that means gardening, or playing chess, or riding a bicycle, or whatever else in their life gave them joy. I call this the Marginal Decade, and for many, if not most, it is a period of diminishment and limitation.

我講述索菲的故事是為了幫助說明我的長壽方法中的一個基本概念，即需要思考和規劃我們生命的後幾十年——七十歲、八十歲、九十歲或更久。對許多像蘇菲這樣的人來說，生命的最後十年並不是特別幸福的時光。他們通常患有一種或多種騎士疾病並受到必要治療的影響。他們的認知和身體能力可能正在減弱或消失。一般來說，他們無法參加他們曾經喜歡的活動，無論是園藝、下棋、騎自行車，或是生活中任何其他帶給他們快樂的活動。我將其稱為“邊緣十年”，對於許多人（如果不是大多數）來說，這是一個衰退和限制的時期。

I ask all my patients to sketch out an alternative future for themselves. What do you *want* to be doing in your later decades? What is your plan for the rest of your life?

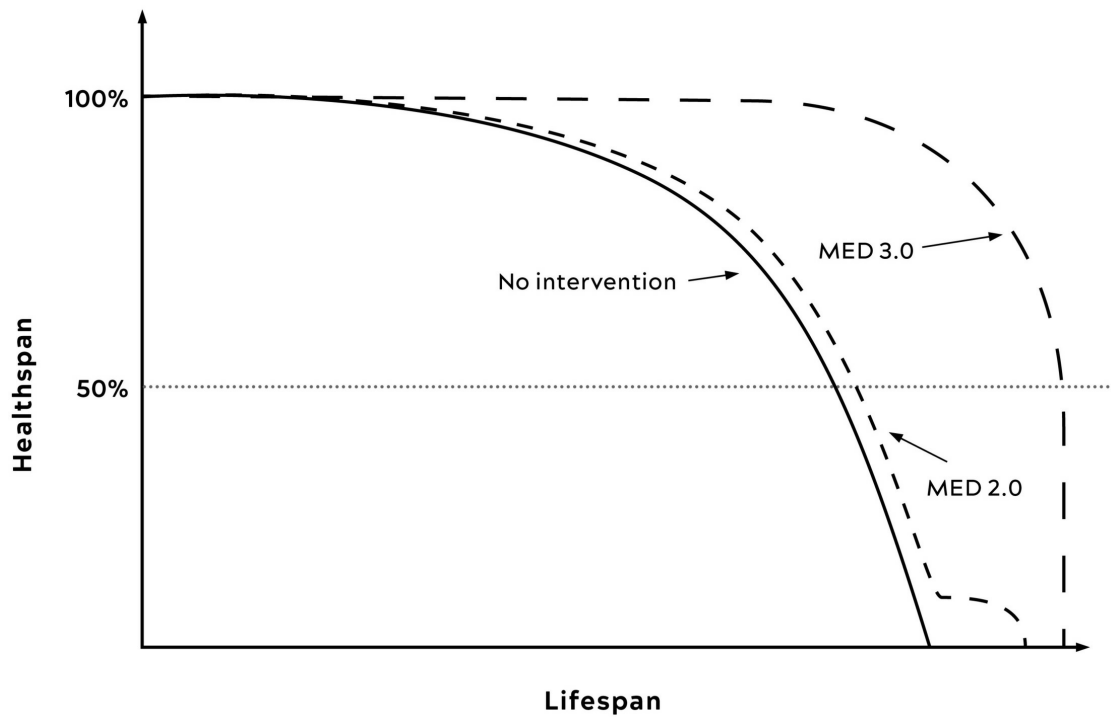
我要求所有的病人為自己勾勒出一個替代的未來。在晚年的幾十年你想做什麼？你的餘生有什麼計劃？

Everyone has a slightly different answer—they might want to travel, or continue playing golf or hiking in nature, or simply be able to play with their grandkids and great-grandkids (top of my own list). The point of this exercise is twofold. First, it forces people to focus on their own endgame, which most of us might prefer to avoid thinking about. Economists call this “hyperbolic discounting,” the natural tendency for people to choose immediate gratification over potential future gains, especially if those gains entail hard work. Second, it drives home the importance of healthspan. If Becky wants to enjoy a healthy, rewarding life in her later years, and not repeat her mother’s fate, she will have to maintain and hopefully improve her physical and cognitive function every decade between now and then. Otherwise, the gravitational pull of aging will do its thing, and she will decline, just as her mother did.

每個人的答案都略有不同 - 他們可能想要旅行，或者繼續打高爾夫球或在大自然中徒步旅行，或者只是能夠與他們的孫子和曾孫一起玩耍（我自己的清單中的頂部）。這項練習的意義是雙重的。首先，它迫使人們專注於自己的結局，而我們大多數人可能寧願避免思考這一點。經濟學家稱之為“雙曲線折現”，即人們選擇眼前的滿足而不是潛在的未來收益的自然傾向，特別是如果這些收益需要努力工作的話。其次，它讓人們認識到健康壽命的重要性。如果貝琪想在晚年享受健康、有意義的生活，而不是重蹈母親的覆轍，那麼從現在到那時，她必須每十年保持並希望改善自己的身體和認知功能。否則，衰老的引力就會起作用，她就會衰弱，就像她母親一樣。

Because I am a math guy, I like to visualize lifespan and healthspan in terms of a mathematical function, as in figure 2 on the following page—one of many graphs that I draw for my patients. The horizontal or x-axis of the graph represents your lifespan, how long you will live, while the vertical or y-axis represents a kind of sum total of your physical and cognitive function, the two age-dependent dimensions of healthspan. (Obviously, healthspan is not really quantifiable, but bear with my oversimplification.)

因為我是數學專家，所以我喜歡用數學函數來形象化壽命和健康壽命，如下頁圖 2 所示，這是我為患者繪製的眾多圖表之一。圖表的水平軸或 x 軸代表您的壽命，即您的壽命，而垂直軸或 y 軸代表您的身體和認知功能的總和，這是健康壽命的兩個與年齡相關的維度。（顯然，健康壽命並不能真正量化，但請忍受我的過於簡化。）

Figure 2. Lifespan vs. Healthspan in Medicine 2.0 vs. Medicine 3.0

The black line represents the natural trajectory of your life: You are born at time zero, and for purposes of our diagram, we'll say your physical and cognitive health start out at 100 percent. You remain relatively robust until about the fifth decade of life, at which point your cognitive and physical health will likely begin a gradual but steady decline, until you die (healthspan = zero) sometime in your sixties or early seventies. This would have been a not untypical lifespan for someone born into a hunter-gatherer or primitive agrarian tribe, provided they managed to avoid early death thanks to infectious disease or another calamity.

黑線代表你生命的自然軌跡：你出生在零時間，出於我們的圖表的目的，我們會說你的身體和認知健康狀況從 100% 開始。在生命的大約五十歲之前，您仍然保持相對強健，此時您的認知和身體健康可能會開始逐漸但穩定的下降，直到您在六十歲或七十歲出頭的某個時候去世（健康壽命=零）。對於出生於狩獵採集者或原始農業部落的人來說，如果他們能夠避免因傳染病或其他災難而早逝，那麼這將是一個不尋常的壽命。

Now look at the typical modern life course, represented by the short-dashed line on the graph, marked “Med 2.0.” You will live a bit longer, thanks to the relative comfort and safety of our lives. But in midlife, you will gradually begin to feel some changes. You will lose a bit of your youthful strength and stamina. You might notice that you occasionally forget passwords, or the names of people you meet, or the names of actors in movies you watched long ago. Your friends and peers will begin to be diagnosed with cancer, cardiovascular disease and related conditions like high blood pressure, and diabetes or prediabetes. You will attend memorial services for friends from school.

現在看看典型的現代生命歷程，由圖表上的短虛線表示，標記為「Med 2.0」。由於我們的生活相對舒適和安全，您會活得更久一些。但到了中年，你會逐漸開始感受到一些改變。你會失去一些年輕的力量和耐力。您可能會注意到，您偶爾會忘記密碼，或您遇到的人的名字，或您很久以前看過的電影中的演員的名字。您的朋友和同事將開始被診斷出罹患癌症、心血管疾病以及高血壓、糖尿病或糖尿病前期等相關疾病。您將參加學校朋友的追悼會。

At a certain point, the decline begins to steepen. Eventually, sometime around age seventy or seventy-five, give or take, your cognitive and physical capacities will diminish to roughly their halfway point (represented by the horizontal dotted line), which I sort of arbitrarily define as the point below which you are no longer able to do the things that you want to do with ease. You're constrained, and bad stuff starts to happen more frequently and with greater consequence. It's one thing to break your femur in a skiing accident when you're forty and still strong and resilient; it's quite another to break it falling off a curb when you're seventy-five and functioning at 25 percent of your capacity. At the same time, your own risk of chronic disease is rising exponentially.

在某一點上，下降開始加劇。最終，在七十歲或七十五歲左右的某個時候，無論給予或接受，你的認知和身體能力將減弱到大約中間點（由水平虛線表示），我有點武斷地定義為低於這個點你就不能夠更輕鬆地做自己想做的事情。你受到限制，壞事開始更頻繁地發生，

後果也更嚴重。當你四十歲仍然強壯有彈性時，在一次滑雪事故中摔斷股骨是一回事；當你七十五歲時，身體還只發揮出你能力的 25% 時，從路邊摔下來就完全是另一回事了。同時，您自己罹患慢性病的風險正在呈指數級上升。

This is where Medicine 2.0 steps in. We treat your heart disease, or cancer, or whatever else afflicts you, prolonging your life by a few months, or years if you're lucky. This is when the lifespan/healthspan curve flattens out horizontally to the right, representing this postponement of death. But now look at *where* this occurs: when your healthspan is already compromised. This means that we have delayed your death without significantly improving your quality of life—something at which Medicine 2.0 is quite adept. This is the Marginal Decade that most of us can expect, in our current system.

這就是醫學 2.0 發揮作用的地方。我們治療您的心臟病、癌症或其他任何困擾您的疾病，如果幸運的話，可以延長您的生命幾個月或幾年。此時壽命/健康曲線向右水平變平，代表死亡的延遲。但現在看看這種情況發生在哪裡：當您的健康壽命已經受到損害時。這意味著我們推遲了您的死亡，但沒有顯著改善您的生活品質——醫學 2.0 非常擅長做到這一點。在我們目前的體系中，這是我們大多數人可以預期的邊緣十年。

Now look at the long-dashed line on the graph. This represents your ideal trajectory. This is what you want. Instead of beginning a slow decline in midlife, your overall healthspan stays the same *or even improves* into your fifties and beyond. You will be fitter and healthier at fifty-five and even sixty-five than you were at forty-five and will remain physically fit and cognitively sharp well into your seventies and eighties, and possibly beyond. You will seem like someone a decade younger than the age on your passport, or possibly two. There is much more space under this curve, and all that space represents your longer, better life: more time being with your family, pursuing your passions, traveling, or continuing to do meaningful work. Moreover, when you do begin to decline, the descent is steep but relatively brief. This is called squaring the longevity curve.

現在看看圖表上的長虛線。這代表了你的理想軌跡。這就是你想要

的。您的整體健康壽命不會在中年開始緩慢衰退，而是會保持不變，甚至會在五十多歲時有所改善。與四十五歲時相比，五十五歲甚至六十五歲時你會更加健康，並且在七十歲、八十歲甚至更久的時候仍能保持身體健康和認知敏銳。您看起來會比護照上的年齡年輕十歲，甚至可能年輕兩歲。這條曲線下有更多的空間，所有這些空間都代表著你更長、更好的生活：有更多的時間與家人在一起、追求你的熱情、旅行或繼續做有意義的工作。此外，當你開始下降時，下降雖然陡峭但相對較短。這稱為壽命曲線的平方。

In this scenario, we live longer, and we live better for longer. We outlive our life expectancy, and we also exceed society's expectations of what our later life is supposed to look like. Instead of a lousy Marginal Decade, we get to enjoy what feels more like a "Bonus Decade"—or decades—when we are thriving in every dimension. This is our objective: to delay death, and to get the most out of our extra years. The rest of our lives becomes a time to relish rather than to dread.

在這種情況下，我們會活得更久，而且活得更好。我們的壽命超過了預期壽命，也超越了社會對晚年生活的期望。當我們在各個方面都蓬勃發展時，我們不再是糟糕的邊緣十年，而是享受更像是「獎金十年」或幾十年的感覺。這就是我們的目標：延遲死亡，並充分利用我們的額外歲月。我們的餘生將成為享受而不是恐懼的時光。

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The next obvious question is: How do we accomplish this? How do we lengthen our lifespan while simultaneously extending our healthspan? How do we stave off death via the Horsemen while slowing or even reversing physical, cognitive, and emotional decline?

下一個明顯的問題是：我們如何實現這個目標？我們如何在延長壽命的同時延長健康壽命？我們如何透過天啟騎士避免死亡，同時減緩甚至扭轉身體、認知和情緒的衰退？

What's our plan?

我們的計劃是什麼？

This is where most people make a wrong turn. They want to take a shortcut, right to the tactics: *this* is what to eat (and not eat), *that* is how you should exercise, *these* are the supplements or medications you need, and so on. There are warehouses full of books that purport to have the answers, but the one you are reading now is not one of them. Instead, I believe this is exactly where we need to hit pause and take a step back, lest we skip the most important step in the process: the strategy.

這是大多數人走錯方向的地方。他們想走捷徑，採取正確的策略：這是吃什麼（而不是吃什麼），這是你應該如何鍛煉，這些是你需要的補充劑或藥物，等等。有些倉庫裡裝滿了聲稱能找到答案的書籍，但你現在正在閱讀的那本書並不是其中之一。相反，我認為這正是我們需要暫停並後退一步的地方，以免我們跳過這個過程中最重要的一步：戰略。

Take another look at the Sun Tzu quote that opens this chapter: “Tactics without strategy is the noise before defeat.” He was talking about war, but it applies here as well. To achieve our objectives, we first need to have a *strategy*: an overall approach, a conceptual scaffolding or mental model that is informed by science, is tailored to our goals, and gives us options. Our specific tactics flow from our strategy, and the strategy derives from our objective. We know what the objective is by now, but the strategy is the key to victory.

再看看本章開頭的孫子名言：“沒有戰略的戰術是失敗前的噪音。”他談論的是戰爭，但這也適用於這裡。為了實現我們的目標，我們首先需要製定一個策略：一個整體方法、一個以科學為依據的概念支架或心理模型，根據我們的目標量身定制，並為我們提供選擇。我們的具體戰術源自於我們的戰略，而戰略又源自於我們的目標。現在我們知道目標是什麼，但策略才是勝利的關鍵。

The big mistake people often make is to conflate strategy and tactics, thinking they are the same. They are not. I like to explain this distinction using one of the more memorable boxing matches of all time: Muhammad Ali

versus George Foreman, the famed “Rumble in the Jungle” that took place in Kinshasa, Zaire, in 1974. Ali’s *objective*, obviously, was to win the match against Foreman and regain his heavyweight title. The problem Ali faced was that Foreman was younger, stronger, meaner, and favored to win in devastating fashion. It’s hard to reconcile with the jovial guy who sells countertop grills now, but back in the day George Foreman was considered the meanest SOB who ever laced on boxing gloves. He was viewed as literally invincible. The pundits all agreed that colorful and beloved as he was, Ali didn’t stand a chance—which is why he needed a strategy.

人們常犯的一個大錯誤就是將戰略和戰術混為一談，認為它們是相同的。他們不是。我喜歡用有史以來最令人難忘的拳擊比賽之一來解釋這一區別：穆罕默德·阿里(Muhammad Ali) 對陣喬治·福爾曼(George Foreman)，這是1974 年在扎伊爾金沙薩舉行的著名「叢林之戰」。阿里的目標顯然是贏得與福爾曼的比賽並重新獲得重量級冠軍。阿里面臨的問題是福爾曼更年輕、更強壯、更刻薄，而且更喜歡以毀滅性的方式獲勝。現在很難與那個賣檯面烤架的快樂傢伙調和起來，但在當時，喬治·福爾曼被認為是有史以來戴過拳擊手套的最卑鄙的混蛋。他被認為是真正無敵的。專家們一致認為，儘管阿里才華橫溢、深受喜愛，但他沒有機會——這就是為什麼他需要一個策略。

Ali knew he had certain slight advantages over Foreman in that he was faster, more experienced, and mentally tougher. He also knew that Foreman was hotheaded and prone to anger. Rather than try to counter Foreman punch for punch, Ali decided that he would attempt to induce the younger, less seasoned fighter to wear himself out, leaving him frustrated and tired, and thus vulnerable. If he could accomplish that, he knew it would be a more even match. This was his strategy: make Foreman angry, and then let him flail away until he had exhausted himself and Ali could mount an offensive.

阿里知道他比福爾曼有一些輕微的優勢，因為他更快、更有經驗、意志更堅強。他也知道福爾曼性子急躁，容易發怒。阿里沒有試圖以拳法反擊福爾曼，而是決定嘗試誘導這位年輕、經驗不足的拳擊手耗盡自己的精力，讓他感到沮喪和疲憊，從而變得脆弱。如果他能做到這一點，他知道這將是一場更加勢均力敵的比賽。這就是他的策略：讓

福爾曼生氣，然後讓他胡亂揮舞，直到他筋疲力盡，阿里才能發動攻擊。

From this strategy flowed the tactics that are now legendary: first, come at Foreman with a series of lead straight rights, an obvious, even disrespectful punch that was guaranteed to make Foreman mad. Nobody hits the heavyweight champion of the world like that. Ali then let an enraged Foreman chase him around the ring and press him up against the ropes, wasting energy, while he concentrated on trying to minimize the damage he absorbed—the famous “rope-a-dope.”

從這個策略中衍生出了現在傳奇般的戰術：首先，用一系列的直拳攻擊福爾曼，這是一個明顯的、甚至是不尊重的拳頭，這肯定會讓福爾曼生氣。沒有人能像這樣擊中世界重量級冠軍。然後，阿里讓憤怒的福爾曼在拳擊場周圍追趕他，把他按在繩子上，浪費了能量，而他則集中精力盡量減少他所受到的傷害——著名的“繩子與毒品”。

For the first few rounds, everyone thought Foreman was absolutely crushing Ali, including Foreman. But because Ali's strategy was to try to outlast Foreman, he had trained himself to endure the abuse. By about the fifth round, you can almost see Foreman realizing, *Damn, I'm already gassed*. Meanwhile, Ali's superior physical conditioning meant he had much more left in the tank. He went on to win the match via a knockout in the eighth round.

前幾輪，所有人都認為福爾曼絕對碾壓阿里，包括福爾曼。但由於阿里的策略是試圖比福爾曼活得更久，他已經訓練自己忍受虐待。到了第五輪左右，你幾乎可以看到福爾曼意識到，該死，我已經氣死了。同時，阿里出色的身體素質意味著他還有更多的精力。他在第八輪通過淘汰賽贏得了比賽。

The point is that the tactics are what you do when you are actually in the ring. The strategy is the harder part, because it requires careful study of one's opponent, identifying his strengths and weaknesses, and figuring out how to use both to your advantage, well before actually stepping in the ring. In this book, we will apply this three-part approach to longevity: **objective** → **strategy** → **tactics**.

重點是，戰術就是你真正在擂台上時所做的事情。策略是更難的部分，因為它需要在實際踏上擂台之前仔細研究對手，識別他的優勢和劣勢，並找出如何利用這兩種優勢來發揮自己的優勢。在本書中，我們將應用這種由三個部分組成的長壽方法：目標→戰略→戰術。

Our Strategy

我們的策略

Going into the fight with Foreman, Ali knew that time was on his side. The longer he could keep his opponent riled up and wasting energy, while avoiding getting knocked out himself, the better his chances of winning in the long run. Unfortunately for us, time is definitely not on our side. Every moment we are alive, our risk of disease and death is tugging at us, the way gravity pulls a long jumper toward earth.

在與福爾曼的戰鬥中，阿里知道時間站在他這邊。他能讓對手激怒並浪費精力的時間越長，同時避免自己被擊倒，從長遠來看，他獲勝的機會就越大。不幸的是，對我們來說，時間絕對不在我們這邊。我們活著的每一刻，疾病和死亡的風險都在牽引我們，就像重力將跳遠運動員拉向地球一樣。

Of course, not every problem you face requires a strategy. In fact, many don't. You don't need a strategy if your objective is, say, to avoid getting a sunburn. Your straightforward tactical options are to put on sunblock, long sleeves and pants, and perhaps a big hat, or to stay out of the sun altogether. But we need a strategy in order to live longer and better, because longevity is a far more complex problem than sunburn.^[*1]

當然，並非您遇到的每個問題都需要策略。事實上，很多人都沒有。如果您的目標是避免曬傷，那麼您就不需要製定策略。您直接的策略選擇是塗上防曬霜、穿長袖衣服和長褲，也許還可以戴一頂大帽子，或者乾脆遠離陽光。但我們需要一種策略來活得更長、更好，因為長壽是比曬傷複雜得多的問題。[*1]

Living longer means delaying death from *all four* of the Horsemen. The Horsemen do have one powerful risk factor in common, and that is age. As you grow older, the risk grows exponentially that one or more of these diseases has begun to take hold in your body. Unfortunately, there's not much we can do about our chronological age—but what do we mean by “aging,” exactly? It's not merely the passage of time, but what is happening inside us, beneath the surface, in our organs and our cells, as time passes. Entropy is working on us every single day.

活得更久意味著推遲所有四位天啟騎士的死亡。天啟騎士確實有一個強大的共同風險因素，那就是年齡。隨著年齡的增長，其中一種或多種疾病開始在您體內發病的風險呈指數級增長。不幸的是，我們對我們的實際年齡無能為力——但我們所說的「老化」到底是什麼意思呢？這不僅僅是時間的流逝，而是隨著時間的流逝，我們體內、表面之下、我們的器官和細胞中正在發生的事情。熵每天都在影響我們。

“Aging is characterized by a progressive loss of physiological integrity, leading to impaired function and increased vulnerability to death,” wrote the authors of an influential 2013 paper describing what they termed the “hallmarks of aging.” They continued: “This deterioration is the primary risk factor for major human pathologies, including cancer, diabetes, cardiovascular disorders, and neurodegenerative diseases.”

「老化的特徵是生理完整性逐漸喪失，從而導致功能受損和死亡風險增加，」2013 年一篇頗具影響力的論文的作者在描述他們所謂的「衰老標誌」時寫道。他們繼續說：“這種惡化是主要人類疾病的主要危險因素，包括癌症、糖尿病、心血管疾病和神經退化性疾病。”

The very process of aging itself is what makes us vulnerable to these diseases, while also affecting our healthspan. Someone who drops dead of a heart attack did not just get sick an hour earlier. The disease was working inside them, silently and invisibly, for decades. As they grew older, their own internal defense mechanisms weakened, and disease gained the upper hand. We saw something similar in the COVID-19 pandemic. The virus infected people across all age groups, but it killed older people in vastly disproportionate numbers, precisely because it exposed and exploited their

existing vulnerability to disease and death: their weakened immune systems, their cardiovascular and respiratory issues, and so on. Thus, our strategy must account for the effects of aging, just as Ali took his own advancing years into account as he searched for a way to defeat Foreman. Without the right strategy, Ali would have almost certainly lost the fight.

老化過程本身使我們容易患上這些疾病，同時也會影響我們的健康壽命。死於心臟病的人並不是一小時前就生病了。幾十年來，這種疾病在他們體內悄無聲息、無形地發揮作用。隨著年齡的增長，他們自身的內在防禦機制減弱，疾病佔了上風。我們在 COVID-19 大流行中看到了類似的情況。該病毒感染了所有年齡層的人，但它殺死了絕大多數老年人，正是因為它暴露並利用了他們現有的疾病和死亡脆弱性：他們脆弱的免疫系統，他們的心血管和呼吸系統問題等等。因此，我們的策略必須考慮到衰老的影響，就像阿里在尋找擊敗福爾曼的方法時考慮到了自己的年歲增長一樣。如果沒有正確的策略，阿里幾乎肯定會輸掉這場戰鬥。

This is why we can't just skip ahead to the tactics, where I tell you what to do. If you are tempted, my advice is to pause, take a breath, and settle in. Without an understanding of the strategy, and the science that informs it, our tactics will not mean much, and you'll forever ride the merry-go-round of fad diets and trendy workouts and miracle supplements. You'll be stuck in a Medicine 2.0 mentality, seeking a quick fix to your problems. The only way to become an adroit tactician is to shift your mindset to Medicine 3.0, which requires becoming a master strategist first.

這就是為什麼我們不能直接跳到戰術部分，我會告訴你該怎麼做。如果你受了誘惑，我的建議是停下來，喘口氣，然後安定下來。如果不了解策略及其背後的科學依據，我們的策略就沒有多大意義，你將永遠在旋轉木馬上-一輪時尚飲食、流行運動和神奇補充劑。您將陷入醫學 2.0 心態，尋求快速解決問題的方法。成為熟練的戰術家的唯一方法就是將你的思維方式轉向醫學3.0，這需要先成為戰略大師。

In the chapters to come, we will be taking a deep dive into some of the mechanisms underlying the aging process, and we will also be taking a very close look at the inner workings of each of the Horsemen diseases. How and

when do they begin? What forces drive them—internal and external? How are they sustained? Most importantly, how can they be delayed or even prevented entirely? As we'll see in the next chapter, this is how the centenarians achieve their extraordinarily long lifespans: they delay or prevent the onset of chronic disease, by decades compared to the average.

在接下來的章節中，我們將深入探討老化過程背後的一些機制，我們也將仔細研究每種騎士疾病的內部運作機制。它們如何以及何時開始？是什麼力量在驅動它們——內在的還是外在的？它們是如何維持的？最重要的是，如何才能延遲甚至完全阻止它們？正如我們將在下一章中看到的，這就是百歲老人如何實現超長壽命的：與平均水平相比，他們推遲或預防慢性疾病的發作數十年。

We will also be taking a more detailed look at healthspan—another one of those overused buzzwords that has lost all meaning. The standard definition, as the period of life when we are free from disease and disability, sets far too low of a bar. If we're not sick and housebound, then we're "healthy"? I prefer to use more pointed language—so pointed that it often makes my patients uncomfortable.

我們也將更詳細地研究健康壽命——另一個被過度使用但失去意義的流行詞彙。標準定義，即我們在生命中沒有疾病和殘疾的時期，設定的標準太低了。如果我們沒有生病、足不出戶，那我們就是「健康」的嗎？我更喜歡使用更尖銳的語言——尖銳到常常讓我的病人感到不舒服。

Here's another way to think of it. Lifespan deals with death, which is binary: you're alive, and then you're dead. It's final. But before that happens, sometimes long before, most people suffer through a period of decline that, I would argue, is like dying in slow motion. Certainly, that was the case for Sophie, Becky's mom. This can happen quickly, such as after a bad accident, but usually it goes so slowly that we barely perceive the change.

這是另一種思考方式。壽命涉及死亡，這是二元的：你活著，然後你就死了。這是最終的。但在此之前，有時甚至是很久以前，大多數人都會經歷一段衰退期，我認為，這就像慢動作中的死亡。當然，貝琪

的媽媽索菲就是這種情況。這種情況可能發生得很快，例如在發生嚴重事故後，但通常發生得非常緩慢，以至於我們幾乎察覺不到這種變化。

I think about healthspan and its deterioration in terms of three categories, or vectors. The first vector of deterioration is cognitive decline. Our processing speed slows down. We can't solve complex problems with the quickness and ease that we once did. Our memory begins to fade. Our executive function is less reliable. Our personality changes, and if it goes on for long enough, even our sentient self is lost. Fortunately, most people don't progress all the way to frank dementia, but many people experience some decline in their cognitive capacity as they age. Our objective is to minimize this.

我從三個類別或向量的角度來思考健康壽命及其惡化。惡化的第一個向量是認知能力下降。我們的處理速度變慢了。我們無法像以前那樣快速輕鬆地解決複雜的問題。我們的記憶開始衰退。我們的執行功能較不可靠。我們的性格會發生變化，如果這種情況持續足夠長的時間，甚至我們有知覺的自我也會消失。幸運的是，大多數人不會一路發展到明顯的癡呆症，但隨著年齡的增長，許多人的認知能力會下降。我們的目標是盡量減少這種情況。

The second vector of deterioration is the decline and eventual loss of function of our physical body. This may precede or follow cognitive decline; there is no predetermined order. But as we grow older, frailty stalks us. We lose muscle mass and strength, along with bone density, stamina, stability, and balance, until it becomes almost impossible to carry a bag of groceries into the house. Chronic pains prevent us from doing things we once did with ease. At the same time, the inexorable progression of atherosclerotic disease might leave us gasping for breath when we walk to the end of the driveway to fetch the newspaper (if newspapers still exist when we are old). Or we could be living a relatively active and healthy life until we fall or suffer some unexpected injury, as Sophie did, that tips us into a downward spiral from which we never recover.

惡化的第二個向量是我們身體功能的衰退和最終喪失。這可能發生在

認知能力下降之前或之後；沒有預定的順序。但隨著年齡的增長，身體的虛弱也隨之而來。我們失去了肌肉質量和力量，以及骨密度、耐力、穩定性和平衡性，直到幾乎不可能將一袋雜貨帶進屋。慢性疼痛使我們無法做以前輕鬆做的事情。同時，當我們走到車道盡頭去拿報紙時，動脈粥狀硬化疾病的不可避免的進展可能會讓我們氣喘吁籲（如果我們老了報紙仍然存在的話）。或者，我們可能過著相對積極和健康的生活，直到我們跌倒或遭受一些意外傷害，就像蘇菲一樣，這使我們陷入螺旋式下降，永遠無法恢復。

My patients rarely expect this decline to affect *them*. I ask them to be very specific about their ideal future. What do they want to be doing when they are older? It's striking how rosy their predictions tend to be. They feel supremely confident that they will still be snowboarding or kickboxing, or whatever else it is they enjoy doing now, when they're in their seventies and eighties.

我的病人很少預料到這種衰退會影響他們。我要求他們非常具體地闡述自己的理想未來。當他們老了的時候想做什麼？令人驚訝的是，他們的預測往往如此樂觀。他們非常有信心，當他們七、八十歲的時候，他們仍然會滑雪或跆拳道，或任何他們現在喜歡做的事情。

Then I stop them and explain: Look, in order to do that, you will need to have a certain level of muscular strength and aerobic fitness at that age. But even right now, at age fifty-two (for example), your strength and your maximum volume of oxygen uptake (VO_2 max) are already barely sufficient to do those things, and they are virtually certain to decline from here. So your choices are (a) surrender to the decline, or (b) come up with a plan, starting *now*.

然後我阻止他們並解釋：聽著，為了做到這一點，你需要在那個年齡有一定程度的肌肉力量和有氧運動。但即使是現在，以五十二歲為例，您的力量和最大攝氧量 (VO_2 max) 已經不足以完成這些事情，幾乎肯定會從這裡開始衰落。所以你的選擇是（a）屈服於衰退，或（b）從現在開始製定一個計劃。

No matter how ambitious your goals are for your later years, I suggest that you familiarize yourself with something called the “activities of daily living,”

a checklist used to assess the health and functionality of elderly people. The list includes such basic tasks as preparing a meal for oneself, walking without assistance, bathing and grooming, using a phone, going to the grocery store, handling personal finances, and so on. Now imagine living your life without the ability to feed or bathe yourself or walk a few blocks to meet friends for coffee. We take these for granted now, but to continue to live actively as we age, retaining even these minimal abilities, requires us to begin building a foundation of fitness and to maintain it diligently.

無論您晚年的目標有多麼雄心勃勃，我建議您熟悉所謂的“日常生活活動”，這是一份用於評估老年人健康和功能的清單。清單包括為自己準備餐點、無需幫忙行走、洗澡和梳洗、使用電話、去雜貨店、處理個人財務等基本任務。現在想像一下您的生活，無法自己吃飯或洗澡，也無法步行幾個街區去見朋友喝咖啡。我們現在認為這些是理所當然的，但隨著年齡的增長，要繼續積極地生活，甚至保留這些最低限度的能力，就需要我們開始建立健康的基礎並努力保持它。

The third and final category of deterioration, I believe, has to do with emotional health. Unlike the others, this one is largely independent of age; it can afflict outwardly healthy young people in their twenties, or it can creep up on you in middle age, as it did with me. Or it can descend later in life. Surveys show that happiness tends to reach its nadir in our forties (age forty-seven, to be exact), but as I learned through painful experience, middle-aged distress often has its roots much earlier, in adolescence or childhood. And we may not recognize that we are in danger until we reach a crisis point, as I did. How we deal with it has a huge bearing on our physical health, our happiness, and our very survival.

我認為，第三類也是最後一類惡化與情緒健康有關。與其他人不同的是，這一人在很大程度上與年齡無關。它可能會折磨二十幾歲外表健康的年輕人，也可能會在中年時悄悄降臨到你身上，就像我一樣。或者它可能會在以後的生活中下降。調查顯示，幸福感往往在四十多歲（準確地說是四十七歲）達到最低點，但正如我從痛苦的經歷中了解到的那樣，中年的痛苦往往根源於更早的時期，即青春期或童年時期。在達到危機點之前，我們可能不會意識到我們正處於危險之中，

正如我所做的那樣。我們如何應對它對我們的身體健康、幸福和生存有著巨大的影響。

To me, longevity as a concept is really only meaningful to the extent that we are defying or avoiding *all* these vectors of decline, simultaneously. And none of these individual components of longevity is worth much without all the others. To live to the age of one hundred without our mind *and* our body intact is not something that anyone would willingly choose. Similarly, to have the greatest quality of life, only to have it cut short at a young age, is also undesirable. And to retain good health as we age, but without love and friendship and purpose, is a purgatory I would not wish on my worst enemy.

對我來說，長壽作為一個概念只有在我們同時反抗或避免所有這些衰退向量的情況下才有意義。如果沒有其他因素的幫助，長壽的這些單獨因素就沒有太大價值。活到一百歲，心智和身體都完好無損，這不是任何人願意選擇的。同樣，想要擁有最好的生活質量，卻在年輕時就結束了，這也是不可取的。隨著年齡的增長，保持身體健康，但沒有愛、友誼和目標，我不希望我最大的敵人陷入煉獄。

The important distinction here is that while actual death is inevitable, this deterioration that we're talking about is less so. Not everyone who dies in their eighties or nineties passes through the valleys of cognitive, physical, or emotional destruction on the way there. They are preventable—and I believe that they are largely optional, despite their ever-increasing gravitational pull over time. As we will see in later chapters, cognitive, physical, and even emotional deterioration can all be slowed and even reversed in some cases with the application of the proper tactics.

這裡重要的區別是，雖然實際的死亡是不可避免的，但我們所談論的惡化卻沒有那麼嚴重。並不是每個八九十歲去世的人都會經歷認知、身體或情感毀滅的低潮。它們是可以預防的——而且我相信它們在很大程度上是可選的，儘管它們的引力隨著時間的推移而不斷增加。正如我們將在後面的章節中看到的那樣，透過應用適當的策略，認知、身體甚至情緒的惡化在某些情況下都可以減緩甚至逆轉。

The other key point is that lifespan and healthspan are not independent variables; they are tightly intertwined. If you increase your muscle strength and improve your cardiorespiratory fitness, you have also reduced your risk of dying from all causes by a far greater magnitude than you could achieve by taking any cocktail of medications. The same goes for better cognitive and emotional health. The actions we take to improve our healthspan will almost always result in a longer lifespan. This is why our tactics are largely aimed at improving healthspan first; the lifespan benefits will follow.

另一個關鍵點是壽命和健康期不是自變數；它們緊密地交織在一起。如果您增加肌肉力量並改善心肺健康，那麼您因各種原因死亡的風險也將大大降低，其程度遠高於服用任何混合藥物所能達到的效果。更好的認知和情緒健康也是如此。我們為改善健康而採取的行動幾乎總是會導致更長的壽命。這就是為什麼我們的策略很大程度上首先是為了提高健康壽命；終生效益將隨之而來。

Tactics

策略

The key difference between Medicine 2.0 and Medicine 3.0 has to do with how and *when* we apply our tactics. Typically, Medicine 2.0 steps in only when something is acutely wrong, like an infection or a broken bone, with short-term fixes for the immediate problem. In Medicine 3.0, our tactics must become interwoven into our daily lives. We eat, breathe, and sleep them—literally.

醫學 2.0 和醫學 3.0 之間的主要區別在於我們如何以及何時應用我們的策略。通常，醫學 2.0 僅在出現嚴重問題（例如感染或骨折）時才會介入，並對眼前的問題進行短期修復。在醫學 3.0 中，我們的策略必須融入我們的日常生活。毫不誇張地說，我們吃它們、呼吸它們、睡它們。

Medicine 2.0 relies on two types of tactics, broadly speaking: procedures (e.g., surgery) and medications. Our tactics in Medicine 3.0 fall into five broad domains: exercise, nutrition, sleep, emotional health, and exogenous molecules, meaning drugs, hormones, or supplements. I will not be talking much about molecules, because that would make this book twice as long as it already is, but one thing that I will say is that I do not shy away from pharmaceutical drugs because they are not “natural.” I consider many drugs and supplements, including lipid-lowering medications, to be essential items in our longevity tool kit, and I hope that in the not-too-distant future we will have many even more effective tools at our disposal.

廣義而言，醫學 2.0 依賴兩種策略：手術（例如手術）和藥物。我們在醫學 3.0 的策略分為五個廣泛的領域：運動、營養、睡眠、情緒健康和外源性分子，即藥物、荷爾蒙或補充劑。我不會過多談論分子，因為這將使這本書的篇幅增加一倍，但我要說的一件事是，我不會因為藥物不是「天然的」而迴避它們。我認為許多藥物和補充劑，包括降血脂藥物，是我們長壽工具包中的必備物品，我希望在不久的將來，我們將擁有更多更有效的工具可供使用。

Drugs and supplements aside, our first tactical domain is exercise. Like “healthspan,” exercise is another one of those overly broad blanket terms that annoy me, because it can encompass everything from a walk in the park to a hard bike ride up a mountain pass, a set of tennis, or a session in the gym lifting heavy weights. These all count as “exercise,” but they obviously have very different effects (and risks, by the way). So we will break down this thing called exercise into its most important components: strength, stability, aerobic efficiency, and peak aerobic capacity. Increasing your limits in each of these areas is necessary if you are hoping to reach your limit of lifespan and healthspan. Again, my goal is not to tell you how to lose weight fast or improve the aesthetic quality of your midsection. We want to maintain physical strength, stamina, stability across a broad range of movements, while remaining free from pain and disability.

除了藥物和補充劑之外，我們的第一個戰術領域是鍛鍊。就像「健康壽命」一樣，運動也是一個讓我惱火的過於寬泛的籠統術語，因為它

可以涵蓋一切，從在公園散步到騎自行車上山口、打網球或在戶外鍛煉。健身房舉重。這些都算作“鍛煉”，但它們顯然具有非常不同的效果（順便說一下，還有風險）。因此，我們將把運動分解為最重要的組成部分：力量、穩定性、有氧效率和峰值有氧能力。如果您希望達到壽命和健康壽命的極限，則有必要增加這些領域的極限。再次強調，我的目標不是告訴您如何快速減肥或改善腹部的美觀。我們希望在各種運動中保持體力、耐力和穩定性，同時避免疼痛和殘疾。

This is another area where my thinking has changed over time. I used to prioritize nutrition over everything else, but I now consider exercise to be the most potent longevity “drug” in our arsenal, in terms of lifespan and healthspan. The data are unambiguous: exercise not only delays actual death but also prevents both cognitive and physical decline, better than any other intervention. We also tend to feel better when we exercise, so it probably has some harder-to-measure effect on emotional health as well. My hope is that you will understand not only the *how* but the *why* of various types of exercise, so you will be able to formulate a program that fits your own personal goals.

這是我的想法隨著時間的推移而改變的另一個領域。我曾經把營養放在第一位，但現在我認為，就壽命和健康而言，運動是我們武器庫中最有效的長壽「藥物」。數據明確無誤：運動不僅可以延緩實際死亡，還可以防止認知能力和身體素質下降，比任何其他幹預措施都更好。當我們運動時，我們往往會感覺更好，因此它可能對情緒健康也有一些難以衡量的影響。我希望您不僅能了解各種運動的方式，還能了解原因，這樣您就能夠制定適合您個人目標的計畫。

Our second domain is nutrition. I won't be telling you to eat this, not that, or prescribing a specific diet that everyone should follow, and I'm definitely not taking sides in the pointless, never-ending diet wars pitting low carb versus paleo versus vegan, and so on. We will avoid such religious discussions in favor of biochemical evidence. The best science out there says that what you eat matters, but the first-order term is how *much* you eat: how many calories you take into your body.

我們的第二個領域是營養。我不會告訴你要吃這個，而不是那個，或規定每個人都應該遵循的特定飲食，而且我絕對不會在低碳水化合

物、舊石器時代和純素食之間毫無意義、永無止境的飲食戰爭中選邊站，很快。我們將避免此類宗教討論，轉而支持生化證據。最好的科學表明，你吃什麼很重要，但首要條件是你吃了多少：你攝取了多少卡路里到你的身體。

How you go about achieving the Goldilocks zone here—not too much, not too little, but just right—will vary depending on numerous factors. My goal is to enable you to determine the best eating pattern for yourself. But please keep in mind that none of the tactics we will discuss are set in stone; we seek feedback from as many sources as possible to try to determine what works and what doesn't. A good strategy allows us to adopt new tactics and discard old ones in service of our objectives.

您如何實現金髮姑娘區（不要太多，也不要太少，但恰到好處）將取決於許多因素。我的目標是讓您能夠確定適合自己的最佳飲食模式。但請記住，我們將要討論的策略都不是一成不變的。我們從盡可能多的來源尋求回饋，以確定哪些有效，哪些無效。良好的策略使我們能夠採用新策略並放棄舊策略來實現我們的目標。

Next is sleep, which I and many others had ignored for far too long. Fortunately, over the past decade or so sleep has finally received the attention it deserves. Today, we have a far better understanding of its importance, and what goes wrong in the short and long term when our sleep is compromised (spoiler: a lot). There is not much that can compare to the feeling of waking up from a great night of sleep, feeling completely refreshed and totally primed for the day. Good sleep is critical to our innate physiological repair processes, especially in the brain, while poor sleep triggers a cascade of negative downstream consequences, from insulin resistance to cognitive decline, as well as mental health issues. I too used to be one of those people who enjoyed pulling all-nighters and thought sleep was for people who had nothing better to do. Long story short, I found out how wrong I was in very dramatic fashion. I am now convinced that Not-Thin Peter's biggest problem was less what he ate than how little he slept.

接下來是睡眠，我和其他許多人已經忽視它太久了。幸運的是，在過去十年左右的時間裡，睡眠終於得到了應有的重視。今天，我們對睡

眠的重要性以及當我們的睡眠受到損害時短期和長期會出現什麼問題有了更好的理解（劇透：很多）。沒有什麼比從一夜好眠中醒來、感覺神清氣爽、為新的一天做好準備的感覺更好的了。良好的睡眠對於我們先天的生理修復過程至關重要，尤其是在大腦中，而睡眠不足會引發一系列負面的下游後果，從胰島素阻抗到認知能力下降，以及心理健康問題。我也曾經是那些喜歡通宵達旦的人之一，並認為睡眠是為那些無事可做的人準備的。長話短說，我以戲劇性的方式發現自己錯得多離譜。我現在確信，不瘦的彼得最大的問題不是他吃什麼，而是他睡得少。

Finally, we will explore the importance of emotional health, which I believe is every bit as important a component of healthspan as the others. This is an area in which I have very little professional expertise but a great deal of personal experience. So while I do not have much hard experimental data and studies to point to, as in the other chapters, I will be sharing my own very long and painful journey to come to terms with things that happened to me in the past and to correct my own behavior and heal the relationships that I have damaged. If nothing else, it may serve as a cautionary tale—and a prod to get you to consider the state of your own emotional house, if warranted.

最後，我們將探討情緒健康的重要性，我相信情緒健康與其他因素一樣是健康壽命的重要部分。在這個領域，我的專業知識很少，但個人經驗豐富。因此，雖然我沒有太多的實驗數據和研究可以指出，就像在其他章節中一樣，我將分享我自己漫長而痛苦的旅程，以接受過去發生在我身上的事情並糾正我的錯誤。自己的行為並治癒我所破壞的關係。如果不出意外的話，它可能會成為一個警示故事，並在有必要的情況下促使你考慮自己的情感宮的狀態。

I will discuss my journey in much more detail in chapter 17, but one phrase from that period has stuck with me, almost like a mantra. It is something that one of my therapists, Esther Perel, said to me early in our work together.

我將在第 17 章中更詳細地討論我的旅程，但那個時期的一句話一直困擾著我，幾乎就像一句咒語。這是我的一位治療師埃絲特·佩雷爾（Esther Perel）在我們一起工作的早期對我說的話。

“Isn’t it ironic that your entire professional life is predicated around trying to make people live longer,” she mused, “yet you’re putting *no* energy into being less miserable, into suffering less emotionally?”

“你的整個職業生涯都是為了讓人們活得更長久，”她若有所思地說，“但你卻沒有花精力去減少痛苦，減少情感上的痛苦，這不是很諷刺嗎？”

She continued: “Why would you want to live longer if you’re so unhappy?” 她繼續說：“如果你如此不快樂，為什麼還想活得更久？”

Her logic was undeniable, and it changed my whole approach to longevity. 她的邏輯是不可否認的，它改變了我對長壽的整個看法。

From Evidence Based to Evidence Informed

從基於證據到實證告知

It’s important, obviously, that our strategy be based on evidence. Unfortunately, the pursuit of longevity is where the most powerful tool of Medicine 2.0, the randomized clinical trial in humans, runs into a brick wall. Randomized controlled trials are used to determine cause and effect in relatively simple, short-term situations. It’s fairly easy, for example, to run a study showing that sunscreen prevents sunburn. But such studies are of limited use in our quest for longevity.

顯然，我們的策略必須以證據為基礎，這一點很重要。不幸的是，對長壽的追求是醫學2.0最強大的工具——人體隨機臨床試驗——遇到障礙的地方。隨機對照試驗用於確定相對簡單、短期情況下的因果關係。例如，進行一項研究表明防曬霜可以防止曬傷，這是相當容易的。但此類研究對於我們追求長壽的作用有限。

This is where my approach may ruffle some people's feathers. The purists of evidence-based medicine demand data from randomized controlled trials (RCTs) before doing *anything*. Those trials are the gold standard of medical evidence, yet they also reinforce some major limitations of Medicine 2.0, beginning with its short time horizon. In general, the types of clinical questions that are best resolved by RCTs are those involving simple interventions such as a vaccine, or a medication to lower cholesterol. We give this treatment over a relatively short period, from six months up to maybe five or six years at the longest and look for its effect on a specified outcome. Does the vaccine reduce the rate of serious illness and death? Does this drug lower cholesterol and prevent cardiac death, or at least heart attacks, in highly susceptible individuals?

這就是我的方法可能會激怒某些人的地方。實證醫學的純粹主義者在做任何事情之前都需要來自隨機對照試驗（RCT）的數據。這些試驗是醫學證據的黃金標準，但它們也強化了醫學 2.0 的一些主要局限性，首先是其時間範圍較短。一般來說，最好透過隨機對照試驗解決的臨床問題類型是那些涉及簡單幹預措施的問題，例如疫苗或降低膽固醇的藥物。我們在相對較短的時間內（從六個月到最長五、六年）進行這種治療，並尋找其對特定結果的影響。疫苗能否降低嚴重疾病和死亡率？對於高度易感人群，這種藥物是否可以降低膽固醇並預防心臟死亡，或至少預防心臟病發作？

This type of study is the foundation of evidence-based medicine. But if our goal is longevity, the situation becomes more complicated. A one-year clinical trial, or even a five-year study, will not tell us everything we need to know about disease processes that take decades to unfold. There will never be a clinical trial to guide a cardiovascular prevention strategy for a healthy forty-year-old. It would simply take too long to do the study. Furthermore, outside of pharmacology, the interventions are very complex, particularly if they involve exercise, nutrition, and sleep. Studying longevity itself in this way is almost impossible—unless we could somehow take a hundred thousand babies, randomize them to four or five different interventions, and follow them throughout their lifetimes. That would (hopefully) yield a rock-solid,

evidence-based prescription for maximizing lifespan and healthspan. But the obstacles to doing this are insurmountable, not least because it would require a century to complete.

此類研究是實證醫學的基礎。但如果我們的目標是長壽，情況就變得更複雜。為期一年的臨床試驗，甚至為期五年的研究，都無法告訴我們需要了解的有關需要數十年才能展開的疾病過程的所有資訊。永遠不會有臨床試驗來指導健康的四十歲老年人的心血管預防策略。做這項研究需要太長時間。此外，在藥理學之外，幹預措施非常複雜，特別是當它們涉及運動、營養和睡眠時。以這種方式研究長壽本身幾乎是不可能的——除非我們能以某種方式選取十萬名嬰兒，將他們隨機分配到四到五種不同的干預措施，並追蹤他們的一生。這將（希望）產生一個堅如磐石、基於證據的處方，以最大限度地延長壽命和健康壽命。但實現這一目標的障礙是無法克服的，尤其是因為它需要一個世紀才能完成。

Option B is to look at the different types of data that we do have and then develop a strategy that triangulates between them. This might not *definitively* solve the problem, but it can at least point us in the right direction. Our Option B strategy is based on combining insights from five different sources of data that, viewed separately, probably aren't strong enough to act on. When taken together, however, they can provide a solid foundation for our tactics. But our supporting framework must shift, from exclusively evidence-based to evidence-informed, risk-adjusted precision medicine.

選項 B 是查看我們擁有的不同類型的數據，然後制定一個在它們之間進行三角測量的策略。這可能不能徹底解決問題，但至少可以為我們指明正確的方向。我們的選項 B 策略是基於結合來自五個不同資料來源的見解，如果單獨查看這些數據，這些數據可能不足以採取行動。然而，當它們結合在一起時，可以為我們的戰術提供堅實的基礎。但我們的支持框架必須從完全基於證據轉向以證據為依據、風險調整的精準醫學。

Our first source of data comes from studies of centenarians, people who have lived to the age of one hundred and beyond, often in good health. These are the extreme outliers, the tiny sliver of the population who have outlived

our usual life expectancy by two decades or more. By and large, they have delayed or evaded the diseases that kill most of the rest of us, and many of them have remained in fairly good shape. We would like to know how they accomplished this feat. What do centenarians have in common? What genes do they share that might give them an advantage over noncentenarians? What explains their survival and their apparently slower rate of aging? And most of all, what can the rest of us do to emulate their good fortune?

我們的第一個資料來源來自對百歲老人的研究，這些人活到了一百歲甚至更長，而且通常身體健康。這些人是極端的異常值，是極少數比我們通常的預期壽命多活了二十年或更長時間的人。總的來說，他們推遲或避免了那些導致我們大多數人死亡的疾病，而且他們中的許多人仍然保持相當好的狀態。我們想知道他們是如何完成這項壯舉的。百歲老人有什麼共同點？他們共有哪些基因可能使他們比非百歲老人更有優勢？如何解釋他們的生存和明顯較慢的衰老速度？最重要的是，我們其他人可以做些什麼來效仿他們的好運呢？

This evidence is made stronger by the fact that centenarians represent our “species of interest”—that is, they are human. Unfortunately, centenarian data are almost entirely observational rather than experimental, so we can’t truly infer cause and effect. Centenarians’ life histories and habits tend to be idiosyncratic, to say the least, and the fact that their numbers are relatively small means that it can be difficult to draw firm conclusions at all. (We will discuss centenarians in more detail in the next chapter.)

百歲老人代表了我們的「感興趣的物種」——也就是說，他們是人類，這一事實使這一證據更加有力。不幸的是，百歲數據幾乎完全是觀察性的而不是實驗性的，因此我們無法真正推論因果關係。至少可以說，百歲老人的生活史和習慣往往很特殊，而且他們的數量相對較少，這意味著很難得出確切的結論。（我們將在下一章更詳細地討論百歲老人。）

Next, we turn to lifespan data from animal “models,” such as laboratory mice. It is obviously much easier, ethically and logistically, to test lifespan-altering tactics in mice, which typically only live about two or three years, than in humans. We have a huge amount of data about how different sorts of

interventions, both dietary and in the form of exogenous molecules, affect mouse lifespan. The limitation, obviously, is that mice are not human; many drugs have succeeded in mice only to fail spectacularly in human studies. There are other types of animal models, including a tiny species of nematode worm called *C. elegans* that is often used in research, as well as fruit flies, dogs, primates, and even lowly yeast cells. All of these have strengths and weaknesses. My rule of thumb is that if a given intervention can be shown to extend lifespan or healthspan in multiple species spanning a billion years of evolution, for example, from worms to monkeys, then I am inclined to take it seriously.

接下來，我們轉向動物「模型」（例如實驗室小鼠）的壽命數據。從倫理和邏輯上來說，在老鼠身上測試改變壽命的策略顯然比在人類身上要容易得多，老鼠通常只能活兩三年左右。我們擁有大量關於不同類型的干預措施（包括飲食干預措施和外源性分子形式的干預措施）如何影響小鼠壽命的數據。顯然，其限制在於老鼠不是人類。許多藥物在小鼠身上取得了成功，但在人體研究中卻慘遭失敗。還有其他類型的動物模型，包括一種經常用於研究的線蟲，稱為線蟲，以及果蠅、狗、靈長類動物，甚至低級酵母細胞。所有這些都有優點和缺點。我的經驗法則是，如果一項特定的干預措施能夠被證明可以延長跨越十億年進化的多個物種的壽命或健康壽命，例如從蠕蟲到猴子，那麼我傾向於認真對待它。

A third and important source of information to support our strategy comes from human studies of the Horsemen: cardiovascular and cerebrovascular disease, cancer, Alzheimer's disease and related neurodegenerative conditions, and type 2 diabetes and related metabolic dysfunction. How do these diseases begin? How do they progress? What risk factors help to cause them, or fuel them? What underlying factors do they share? What are the cutting-edge treatment modalities for those with "advanced" disease—and what do they tell us about developing a strategy for prevention? We want to know each of these diseases inside and out, understanding their weaknesses and vulnerabilities, just as Ali scrutinized Foreman before their match.

支持我們策略的第三個重要資訊來源來自對天啟騎士的人體研究：心血管和腦血管疾病、癌症、阿茲海默症和相關的神經退化性疾病，以及2型糖尿病和相關的代謝功能障礙。這些疾病是如何開始的？他們進展如何？哪些風險因素會導致或助長這些風險？他們有哪些共同的根本因素？對於患有「晚期」疾病的人來說，最先進的治療方式是什麼？它們告訴我們如何制定預防策略？我們想徹底了解這些疾病，了解它們的弱點和弱點，就像阿里在比賽前仔細審視福爾曼一樣。

Fourth, we consider the molecular and mechanistic insights derived from the study of aging in both humans and animal models. We have learned an enormous amount about the cellular changes that occur during the aging process and in specific diseases. From this, we also have developed some ideas for how to manipulate these changes, via exogenous molecules (e.g., drugs) or behavioral changes (e.g., exercise).

第四，我們考慮從人類和動物模型老化研究中得出的分子和機制見解。我們已經了解了大量關於老化過程和特定疾病中發生的細胞變化的知識。由此，我們也提出了一些關於如何透過外源性分子（例如藥物）或行為改變（例如運動）來操縱這些變化的想法。

Our final source of insights is a very clever method of analysis called Mendelian randomization, or MR for short. MR helps bridge the gap between randomized controlled trials, which can establish causality, and pure epidemiology, which often cannot. We'll talk about epidemiology in more detail later, but while it has proved useful in certain situations, such as determining the link between smoking and lung cancer, it has been less useful in more complex scenarios. Mendelian randomization helps tease out causal relationships between modifiable risk factors (e.g., LDL cholesterol) and an outcome of interest (e.g., cancer) in situations where actual randomized experiments cannot easily be done. It accomplishes this by letting nature do the randomization.^[*2] By considering the random variation in relevant genes and comparing them against the observed results, it eliminates many of the biases and confounders that limit the usefulness of pure epidemiology.

我們最終的見解來源是一種非常聰明的分析方法，稱為孟德爾隨機化，簡稱 MR。MR 有助於彌合隨機對照試驗（可以確定因果關係）與純粹流行病學（通常無法確定）之間的差距。我們稍後將更詳細地討論流行病學，但雖然它在某些情況下被證明是有用的，例如確定吸煙和肺癌之間的聯繫，但在更複雜的情況下它的用處不大。在實際隨機實驗不易完成的情況下，孟德爾隨機化有助於梳理可改變的風險因子（例如 LDL 膽固醇）與感興趣的結果（例如癌症）之間的因果關係。它透過讓自然進行隨機化來實現這一點。[*2] 透過考慮相關基因的隨機變異並將其與觀察到的結果進行比較，它消除了許多限制純粹流行病學有用性的偏差和混雜因素。

For example, some epidemiologic studies have suggested an inverse relationship between LDL cholesterol and cancer risk. That is, people with lower LDL cholesterol appear to have a higher risk of cancer. But is the relationship *causal*? That's a tricky but important question. If true, it would imply that lowering LDL cholesterol, such as with statins, increases the risk of cancer, which would obviously be bad news. Epidemiology does not tell us the direction of causality, so we turn to MR.

例如，一些流行病學研究顯示低密度脂蛋白膽固醇與癌症風險之間存在反比關係。也就是說，低密度脂蛋白膽固醇較低的人罹患癌症的風險似乎較高。但這種關係是因果關係嗎？這是一個棘手但重要的問題。如果屬實，則意味著降低低密度脂蛋白膽固醇（例如使用他汀類藥物）會增加罹患癌症的風險，這顯然是個壞消息。流行病學並不能告訴我們因果關係的方向，所以我們轉向 MR。

With MR, we can look at genetic variations that result in low, medium, and high levels of LDL cholesterol. These genes are randomly occurring, so they serve as a proxy for a randomized natural experiment. By examining the relationship between the resulting LDL cholesterol levels and cancer incidence, we can answer the question without the usual confounders that plague traditional epidemiology. And lo and behold, it turns out that low LDL cholesterol does not cause cancer or increase its risk. If we use the same technique to look at the effect of LDL levels on cardiovascular disease (our

dependent variable), it turns out that higher LDL cholesterol *is* causally linked to the development of cardiovascular disease (as we'll discuss in chapter 7).

透過 MR，我們可以觀察到導致低、中、高 LDL 膽固醇水平的遺傳變異。這些基因是隨機發生的，因此它們可以作為隨機自然實驗的代理。透過檢查由此產生的低密度脂蛋白膽固醇水平與癌症發生率之間的關係，我們可以回答這個問題，而不會遇到困擾傳統流行病學的常見混雜因素。你瞧，事實證明，低 LDL 膽固醇不會導致癌症或增加癌症風險。如果我們使用相同的技術來觀察 LDL 水平對心血管疾病（我們的因變數）的影響，就會發現較高的 LDL 膽固醇與心血管疾病的發展存在因果關係（正如我們將在第 7 章中討論的）。

An astute reader will notice that one concept has been conspicuously absent from this chapter so far: absolute certainty. This took me a little while to grasp when I transitioned from mathematics to medicine, but in biology we can rarely “prove” anything definitively the way we can in mathematics. Living systems are messy, and confounding, and complex, and our understanding of even fairly simple things is constantly evolving. The best we can hope for is reducing our uncertainty. A good experiment in biology only increases or decreases our confidence in the probability that our hypothesis is true or false. (Although we can feel fairly certain about some things, such as the evidence supporting the idea that your doctor should wash her hands and put on sterile gloves before operating on you.)

精明的讀者會注意到，到目前為止，本章明顯缺少一個概念：絕對確定性。當我從數學轉向醫學時，我花了一些時間才理解這一點，但在生物學中，我們很少能像數學中那樣明確地「證明」任何東西。生命系統是混亂、混亂和複雜的，我們對即使是相當簡單的事物的理解也在不斷發展。我們所能期望的最好的結果就是減少我們的不確定性。一次好的生物學實驗只會增加或減少我們對假設正確或錯誤的機率的信心。（儘管我們對某些事情可以相當確定，例如有證據支持您的醫生在對您進行手術之前應該洗手並戴上無菌手套的想法。）

In the absence of multiple, repeated, decades-long randomized clinical trials that might answer our questions with certainty, we are forced to think in terms of probabilities and risk. In a sense it's a bit like charting an investment

strategy: we are seeking the tactics that are likeliest, based on what we know now, to deliver a better-than-average return on our capital, while operating within our own individual tolerance for risk. On Wall Street, gaining an advantage like this is called alpha, and we're going to borrow the idea and apply it to health. I propose that with some unorthodox but very reasonable lifestyle changes, you can minimize the most serious threats to your lifespan and healthspan and achieve your own measure of longevity alpha.

由於缺乏多次、重複、長達數十年的隨機臨床試驗可以肯定地回答我們的問題，我們被迫從機率和風險的角度來思考。從某種意義上說，這有點像是製定投資策略：根據我們目前所知，我們正在尋找最有可能實現高於平均水平的資本回報率的策略，同時在我們個人的風險承受能力範圍內運作。在華爾街，獲得這樣的優勢被稱為阿爾法，我們將借鑒這個想法並將其應用於健康領域。我建議，透過一些非正統但非常合理的生活方式改變，您可以最大限度地減少對您的壽命和健康壽命的最嚴重威脅，並實現您自己的長壽阿爾法測量。

My aim here is to equip you with a set of tools that you can apply to your own specific situation—whether you need to pay attention to your glucose regulation, your weight, your physical condition, your Alzheimer's disease risk, and so on. Your personal tactics should never be static, but will evolve as needed, as you journey through life with all its uncertainties—and as we learn more about the science of aging and the workings of diseases like cancer. As your own situation changes, your tactics can (and must) change, because as the great philosopher Mike Tyson once put it, “Everyone has a plan until they get punched in the mouth.”

我的目的是為您提供一套工具，您可以將其應用於您自己的具體情況——無論您是否需要關注您的血糖調節、體重、身體狀況、阿茲海默症風險等等。你的個人策略永遠不應該是一成不變的，而是會隨著你經歷充滿不確定性的人生旅程，以及隨著我們更多地了解衰老科學和癌症等疾病的運作原理，而根據需要而變化。隨著你自己的情況發生變化，你的策略可以（而且必須）改變，因為正如偉大的哲學家邁克泰森曾經說過的那樣，「每個人都有一個計劃，直到他們被打在嘴上。」

Advice George Foreman could have used.

喬治·福爾曼本來可以採納建議。

[SKIP NOTES](#)

[跳過註釋](#)

[*1](#) Although avoiding sunburn, which contributes to the aged appearance of skin, not to mention melanoma risk, is unquestionably a good idea.

*1 雖然避免曬傷無疑是一個好主意，因為曬傷會導致皮膚老化，更不用說黑色素瘤風險了。

[*2](#) For MR to work properly, certain conditions must be met. First, the genetic variant(s) being considered must associate with the risk factor of interest (this is called the relevance assumption); second, the genetic variant does not share a common cause with the outcome (this is called the independence assumption); and third, the genetic variant does not affect the outcome except through the risk factor (this is called the exclusion restriction assumption).

*2 為了使 MR 正常運作，必須滿足某些條件。首先，所考慮的遺傳變異必須與感興趣的風險因素相關（這稱為相關性假設）；其次，遺傳變異與結果沒有共同原因（稱為獨立性假設）；第三，遺傳變異不會影響結果，除非透過風險因素（稱為排除限制假設）。

PART II

第二部分

CHAPTER 4

第 4 章

Centenarians

百歲老人

The Older You Get, the Healthier You Have Been

你年紀越大，你就越健康

Whiskey's a good medicine. It keeps your muscles
tender.

威士忌是一劑良藥。它可以讓你的肌肉保持柔
嫩。

—RICHARD OVERTON, 1906–2018

——理查·歐佛頓，1906–2018

In his later years, Richard Overton liked to take the edge off his days with a shot of bourbon and a few puffs of a Tampa Sweet cigar, lit directly from the gas stove in his home in Austin, Texas. He insisted that he never inhaled—word to the wise. Mr. Overton, as he was known, was born during the Theodore Roosevelt administration and died in late 2018 at the age of 112.

在晚年，理查德·奧弗頓(Richard Overton) 喜歡喝一杯波本威士忌，抽幾口坦帕甜雪茄，從他位於德克薩斯州奧斯汀的家中的煤氣灶上直接點燃，以此來打發日子。他堅稱自己從未吸入過——智者的話。眾所周知，奧弗頓先生出生於西奧多·羅斯福執政期間，於 2018 年底去世，享年 112 歲。

Not to be outdone, British World War I veteran Henry Allingham attributed his own 113-year lifespan to “cigarettes, whiskey, and wild, wild women.” It’s a shame he never met the adventurous Frenchwoman Jeanne Calment, who once joked, “I’ve only ever had one wrinkle, and I’m sitting on it.” She rode her bicycle until she was 100 and kept smoking until the age of 117. Perhaps she shouldn’t have quit, because she died five years later at 122, making her the oldest person ever to have lived.

英國一戰老兵亨利·阿林厄姆也不甘示弱，將自己 113 歲的壽命歸功於「香菸、威士忌和狂野的女人」。遺憾的是他從未見過富有冒險精神的法國女性珍妮·卡爾芒(Jeanne Calment)，她曾開玩笑說：“我只有一條皺紋，而我就坐在它上面。”她騎自行車直到 100 歲，一直抽煙直到 117 歲。也許她不應該戒菸，因為五年後她去世，享年 122 歲，成為有史以來最長壽的人。

Mildred Bowers, at a comparatively youthful 106, preferred beer, cracking open a cold one every day at 4 p.m. sharp—it’s five o’clock somewhere, right? Theresa Rowley of Grand Rapids, Michigan, credited her daily Diet Coke for helping her live to the age of 104, while Ruth Benjamin of Illinois said the key to reaching her 109th birthday was her daily dose of bacon. “And potatoes, some way,” she added. They were all youngsters compared with Emma Morano of Italy, who consumed three eggs a day, two of them raw, up until her death at age 117.

106 歲的米爾德里德鮑爾斯 (Mildred Bowers) 相對年輕，她更喜歡啤酒，每天下午 4 點都會打開一瓶冰鎮啤酒。很準——現在是五點鐘，對吧？密西根州大急流域的特蕾莎·羅利(Theresa Rowley) 認為，每天喝健怡可樂幫助她活到了104 歲，而伊利諾伊州的露絲·本傑明(Ruth Benjamin) 則表示，她能活到109歲生日的關鍵是每天服用培根。“某種程度上還有土豆，”她補充道。與義大利的艾瑪·莫拉諾 (Emma Morano) 相比，他們都是年輕人，她每天吃三個雞蛋，其中兩個生雞蛋，直到她 117 歲去世。

If we were epidemiologists from Saturn and all we had to go on was articles about centenarians in publications like *USA Today* and *Good Housekeeping*, we might conclude that the secret to extreme longevity is the breakfast special at Denny's, washed down with Jim Beam and a good cigar. And perhaps this is so. Another possibility is that these celebrity centenarians are messing with the rest of us. We cannot be certain, because the relevant experiment cannot be done, as much as I'd like to open *JAMA* and see the title "Do Cream-Filled Chocolate Doughnuts Extend Lifespan? A Randomized Clinical Trial."

如果我們是來自土星的流行病學家，而我們所要做的只是閱讀《今日美國》和《好管家》等出版物上有關百歲老人的文章，我們可能會得出這樣的結論：超長壽的秘訣是丹尼餐廳的特色早餐，用吉姆賓和美味的早餐一起衝下。雪茄。也許確實如此。另一種可能性是，這些名人百歲老人正在擾亂我們其他人。我們不能確定，因為相關實驗無法做，儘管我很想打開JAMA，看到標題“奶油巧克力甜甜圈能延長壽命嗎？”一項隨機臨床試驗。”

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We yearn for there to be some sort of “secret” to living a longer, healthier, happier life. That desire drives our obsession with knowing the special habits and rituals of those who live longest. We are fascinated by people like Madame Calment, who seem to have escaped the gravitational pull of mortality, despite having smoked or done other naughty things throughout

their lives. Was it the bike riding that saved her? Or was it something else, such as the pound of chocolate that she purportedly consumed each week?

我們渴望有某種「秘訣」來過更長壽、更健康、更幸福的生活。這種渴望驅使我們沉迷於了解長壽者的特殊習慣和儀式。我們對像卡爾門特夫人這樣的人著迷，儘管她們一生都抽煙或做過其他頑皮的事情，但她似乎擺脫了死亡的引力。是騎腳踏車救了她嗎？還是其他什麼，例如據稱她每週消耗的一磅巧克力？

More broadly, it's worth asking: What do healthy centenarians actually have in common? And, more importantly, what can we learn from them—if anything? Do they really live longer because of their idiosyncratic behaviors, like drinking whiskey, or despite them? Is there some other common factor that explains their extreme longevity, or is it simply luck?

更廣泛地說，值得問的是：健康的百歲老人其實有什麼共同點？更重要的是，我們可以從他們身上學到什麼——如果有的話？他們的壽命延長真的是因為他們的特殊行為，例如喝威士忌，還是儘管如此？是否還有其他共同因素可以解釋它們的長壽，或者只是運氣？

More rigorous research into large groups of centenarians has cast (further) doubt on the notion that “healthy” behaviors, which I can't resist putting into scare quotes, are required to attain extreme longevity. According to results from a large study of Ashkenazi Jewish centenarians, run by Nir Barzilai at the Albert Einstein College of Medicine in the Bronx, centenarians are no more health-conscious than the rest of us. They may actually be worse: a large proportion of the nearly five hundred subjects in the Einstein study drank alcohol and smoked, in some cases for decades. If anything, the centenarian males in the study were *less* likely to have exercised regularly at age seventy than age-matched controls. And many were overweight. So much for healthy lifestyles.

對大量百歲老人進行更嚴格的研究，對這樣一種觀念產生了（進一步）懷疑，即“健康”行為是獲得超長壽命所必需的，我忍不住要引用這些嚇人的話。布朗克斯阿爾伯特愛因斯坦醫學院的尼爾巴齊萊(Nir Barzilai) 對德系猶太百歲老人進行的一項大型研究結果顯示，百歲老

人並不比我們其他人更有健康意識。事實上，情況可能更糟：愛因斯坦研究中的近五百名受試者中，很大一部分人酗酒和吸煙，有些人甚至長達數十年。如果有什麼不同的話，那就是研究中的百歲男性在七十歲時定期運動的可能性低於年齡匹配的對照組。許多人超重。健康的生活方式就這麼多。

Could the centenarians merely be lucky? Certainly, their age alone makes them extreme statistical outliers. As of 2021, there were just under 100,000 centenarians in the United States, according to the Census Bureau. And although their number has increased by nearly 50 percent in just two decades, the over-one-hundred age group still represents only about 0.03 percent of the population, or about 1 out of every 3,333 of us.

百歲老人只是幸運嗎？當然，僅憑他們的年齡就使他們成為極端的統計異常值。根據人口普查局的數據，截至 2021 年，美國百歲老人接近 10 萬人。儘管這一數字在短短 20 年內增加了近 50%，但 100 歲以上的年齡組仍然只佔總人口的 0.03% 左右，即每 3,333 人中約有 1 人。

After ten decades of age, the air gets pretty thin, pretty quickly. Those who live to their 110th birthday qualify for the ultra-elite cadre of “supercentenarians,” the world’s smallest age group, with only about three hundred members worldwide at any given time (although the number fluctuates). Just to give you a sense of how exclusive this club is, for every supercentenarian in the world at this writing, there are about nine billionaires.

十歲之後，空氣很快就會變得非常稀薄。那些活到110 歲生日的人有資格成為「超級百歲老人」的超級精英幹部，這是最小的年齡組，在任何特定時間全球範圍內只有約300 名成員（儘管數量有所波動）。只是為了讓您感受到這個俱樂部的獨特性，在撰寫本文時，世界上每一位超級百歲老人中大約有九位億萬富翁。

Yet nobody has come close to Madame Calment’s record. The next-longest-lived person ever recorded, Pennsylvania native Sarah Knauss, was a mere 119 when she died in 1999. Since then, the world’s oldest person has rarely exceeded the age of 117, and she is almost always female. While some individuals have claimed extremely lengthy lifespans, of 140 years or more,

Calment remains the only person ever to be verified as having lived past 120, leading some researchers to speculate that that may represent the upper limit of human lifespan, programmed into our genes.

然而，還沒有人能接近卡爾門特夫人的記錄。有史以來最長壽的人是賓夕法尼亞州人莎拉·諾斯(Sarah Knauss)，她於1999 年去世時年僅119 歲。從那時起，世界上最長壽的人很少超過117 歲，而且她幾乎都是女性。雖然有些人聲稱自己的壽命非常長，達到140 歲甚至更長，但卡爾門特仍然是唯一被證實活過120 歲的人，這導致一些研究人員推測，這可能代表了人類壽命的上限，並被編程到我們的基因。

We are interested in a slightly different question: Why are some people able to just blow past the eighty-year mark, which represents the finish line for most of the rest of us? Could their exceptional longevity—and exceptional healthspan—be primarily a function of their genes?

我們對一個稍微不同的問題感興趣：為什麼有些人能夠輕鬆跨越八十歲的大關，這代表著我們大多數人的終點線？他們非凡的長壽和非凡的健康壽命主要是基因的作用嗎？

Studies of Scandinavian twins have found that genes may be responsible for only about 20 to 30 percent of the overall variation in human lifespan. The catch is that the older you get, the more genes start to matter. For centenarians, they seem to matter a lot. Being the sister of a centenarian makes you eight times more likely to reach that age yourself, while brothers of centenarians are seventeen times as likely to celebrate their hundredth birthday, according to data from the one-thousand-subject New England Centenarian Study, which has been tracking extremely long-lived individuals since 1995 (although because these subjects grew up in the same families, with presumably similar lifestyles and habits, this finding could be due to some environmental factors as well). If you don't happen to have centenarian siblings, the next best option is to choose long-lived parents.

一項針對斯堪的納維亞雙胞胎的研究發現，基因可能只對人類壽命整體變異的 20% 至 30% 負責。問題是，年紀越大，基因開始變得越重要。對百歲老人來說，他們似乎很重要。新英格蘭百歲老人研究的數

據顯示，身為百歲老人的妹妹，您達到百歲老人年齡的可能性會增加八倍，而百歲老人的兄弟慶祝百歲生日的可能性會增加十七倍。自 1995 年以來一直在追蹤極其長壽的個體（儘管因為這些受試者在同一家庭長大，生活方式和習慣可能相似，這一發現也可能是由於一些環境因素造成的）。如果你碰巧沒有百歲的兄弟姐妹，那麼下一個最好的選擇就是選擇長壽的父母。

This is part of why I place so much importance on taking a detailed family history from my patients: I need to know when your relatives died and why. What are your likely “icebergs,” genetically speaking? And if you do happen to have centenarians in your family tree, let me offer my congratulations. Such genes are, after all, a form of inherited luck. But in my family, you were doing well if you made it to retirement age. So if you’re like me, and most people reading this book, your genes aren’t likely to take you very far. Why should we even bother with this line of inquiry?

這就是為什麼我如此重視從病人那裡獲取詳細的家族史的部分原因：我需要知道你的親戚何時死亡以及原因。從基因角度來說，你可能的「冰山」是什麼？如果您的家譜中確實有百歲老人，請讓我表示祝賀。畢竟，這樣的基因是遺傳運氣的一種形式。但在我的家庭，如果你到了退休年齡，你就過得很好。因此，如果你像我和大多數讀這本書的人一樣，你的基因不太可能帶你走得太遠。我們為什麼要費心去進行這種探究呢？

Because we are probing a more relevant question: Can we, through our behaviors, somehow reap the same benefits that centenarians get for “free” via their genes? Or to put it more technically, can we mimic the centenarians’ *phenotype*, the physical traits that enable them to resist disease and survive for so long, even if we lack their *genotype*? Is it possible to outlive our own life expectancy if we are smart and strategic and deliberate about it?

因為我們正在探討一個更相關的問題：我們能否透過我們的行為，以某種方式獲得與百歲老人透過基因「免費」獲得的同樣的好處？或者更專業地說，我們是否可以模仿百歲老人的表型，即即使我們缺乏他們的基因型，也使他們能夠抵抗疾病並存活很長時間的身體特徵？如

果我們聰明、有策略、深思熟慮，是否有可能比我們自己的預期壽命更長？

If the answer to this question is yes, as I believe it is, then understanding the inner workings of these actuarial lottery winners—how they achieve their extreme longevity—is a worthwhile endeavor that can inform our strategy.

如果這個問題的答案是肯定的，正如我所相信的那樣，那麼了解這些精算彩票中獎者的內部運作方式——他們如何實現超長壽命——是一項值得努力的工作，可以為我們的策略提供資訊。

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When I first became interested in longevity, my greatest fear was that we would somehow figure out how to delay death without also extending the healthy period of people's lives, à la Tithonus (and à la Medicine 2.0). My mistake was to assume that this was *already* the fate of the very long-lived, and that all of them are essentially condemned to spend their extra years in a nursing home or under other long-term care.

當我第一次對長壽感興趣時，我最大的恐懼是我們會以某種方式弄清楚如何推遲死亡而不同時延長人們生命的健康期，就像提托努斯（和醫學2.0）一樣。我的錯誤是認為這已經是非常長壽的人的命運，而且他們所有人本質上都注定要在療養院或其他長期護理機構中度過餘生。

A deeper look at the data from multiple large centenarian studies worldwide reveals a more hopeful picture. It's true that many centenarians exist in a somewhat fragile state: The overall mortality rate for Americans ages 100 and older is a staggering 36 percent, meaning that if Grandma is 101, she has about a one-in-three chance of dying in the next twelve months. Death is knocking at her door. Digging further, we find that many of the oldest old die from pneumonia and other opportunistic infections, and that a few centenarians, such as Madame Calment, really do die of what used to be called old age. But the vast majority still succumb to diseases of aging—the Horsemen—just like the rest of us.

更深入研究全球多項大型百歲老人研究的數據，揭示了一幅更有希望的畫面。確實，許多百歲老人都處於一種脆弱的狀態：100 歲及以上的美國人的總體死亡率高達36%，這意味著如果奶奶已經101歲了，她有三分之一的機會在接下來的歲月裡死去。十二個月。死亡正在敲她的門。進一步挖掘，我們發現許多最年長的老人死於肺炎和其他機會性感染，而一些百歲老人，例如卡爾門特夫人，確實死於過去所謂的老年。但絕大多數人仍然像我們其他人一樣死於衰老疾病——天啟騎士。

The crucial distinction, the essential distinction, is that they tend to develop these diseases *much later in life* than the rest of us—if they develop them at all. We're not talking about two or three or even five years later; we're talking decades. According to research by Thomas Perls of Boston University and his colleagues, who run the New England Centenarian Study, one in five people in the general population will have received some type of cancer diagnosis by age seventy-two. Among centenarians, that one-in-five threshold is not reached until age one hundred, nearly *three decades* later. Similarly, one-quarter of the general population will have been diagnosed with clinically apparent cardiovascular disease by age seventy-five; among centenarians, that prevalence is reached only at age ninety-two. The same pattern holds for bone loss, or osteoporosis, which strikes centenarians sixteen years later than average, as well as for stroke, dementia, and hypertension: centenarians succumb to these conditions much later, if at all.

關鍵的區別，本質的區別是，他們患這些疾病的時間往往比我們其他人晚得多——如果他們真的患上這些疾病的話。我們不是在談論兩年、三年甚至五年後；而是在談論什麼。我們正在談論幾十年。根據波士頓大學的托馬斯·珀爾斯 (Thomas Perls) 及其負責新英格蘭百歲老人研究的同事的研究，普通人群中五分之一的人在 72 歲時會被診斷出某種類型的癌症。在百歲老人中，這一五分之一的門檻要到一百歲（近三十年後）才達到。同樣，四分之一的一般人群在七十五歲時被診斷出患有臨床明顯的心血管疾病；在百歲老人中，這一比例只有在九十二歲時才達到。同樣的模式也適用於骨質流失或骨質疏鬆症（百

歲老人比平均晚十六年發病），以及中風、失智症和高血壓：百歲老人患這些疾病的時間要晚得多（如果有的話）。

Their longevity is not merely a function of delaying disease. These people also often defy the stereotype of old age as a period of misery and decline. Perls, Barzilai, and other researchers have observed that centenarians tend to be in pretty good health overall—which, again, is not what most people expect. This doesn't mean that everyone who lives that long will be playing golf and jumping out of airplanes, but Perls's ninety-five-and-older study subjects scored very well on standard assessments of cognitive function and ability to perform those tasks of daily living we mentioned in chapter 3, such as cooking meals and clipping their own toenails, a seemingly simple job that becomes monumentally challenging in older age.

它們的長壽不僅僅是延緩疾病的功能。這些人也常打破人們對老年的刻板印象，認為老年是一段痛苦和衰退的時期。珀爾斯、巴爾齊萊和其他研究人員觀察到，百歲老人的整體健康狀況往往相當好——這又不是大多數人所期望的。這並不意味著每個長壽的人都會打高爾夫球和跳出飛機，但珀爾斯的九十五歲及以上的研究對象在認知功能和執行日常生活任務的能力的標準評估中得分很高我們在第三章中提到過，例如做飯和剪腳趾甲，看似簡單的工作，到了老年卻變得極具挑戰性。

Curiously, despite the fact that female centenarians outnumber males by at least four to one, the men generally scored higher on both cognitive and functional tests. This might seem paradoxical at first, since women clearly live longer than men, on average. Perls believes there is a kind of selection process at work, because men are more susceptible to heart attacks and strokes beginning in middle age, while women delay their vulnerability by a decade or two and die less often from these conditions.

奇怪的是，儘管女性百歲老人的數量至少是男性的四比一，但男性在認知和功能測試中的得分普遍更高。乍一看，這似乎很矛盾，因為平均而言，女性的壽命顯然比男性長。珀爾斯認為，有一種選擇過程在起作用，因為男性從中年開始更容易患心臟病和中風，而女性則將其脆弱性延遲了一兩年，並且死於這些疾病的頻率也較低。

This tends to weed the frailer individuals out of the male population, so that *only* those men who are in relatively robust health even make it to their hundredth birthday, while women tend to be able to survive for longer *with* age-related disease and disability. Perls describes this as “a double-edged sword,” in that women live longer but tend to be in poorer health. “The men tend to be in better shape,” he has said. (The authors didn’t measure this, but my hunch is that it may have something to do with men having more muscle mass, on average, which is highly correlated to longer lifespan and better function, as we’ll discuss further in the chapters on exercise.)

這往往會將較虛弱的個體從男性人口中剔除，因此只有那些健康狀況相對較好的男性才能活到百歲生日，而女性往往能夠在患有與年齡相關的疾病和殘疾的情況下存活更長時間。珀爾斯將其描述為“一把雙刃劍”，因為女性壽命更長，但健康狀況往往較差。「男性的體形往往更好，」他說。（作者沒有測量這一點，但我的預感是，這可能與男性平均擁有更多的肌肉質量有關，這與更長的壽命和更好的功能高度相關，我們將在各章中進一步討論鍛煉時。）

But even if they are not in such great shape in their eleventh decade, these individuals have already enjoyed many extra years of healthy life compared with the rest of the population. Their healthspan, as well as their lifespan, has been extraordinarily long. What’s even more surprising is that Perls’s group has also found that the supercentenarians and the “semisupercentenarians” (ages 105 to 109) actually tend to be in even *better* health than garden-variety hundred-year-olds. These are the super survivors, and at those advanced ages, lifespan and healthspan are pretty much the same. As Perls and his colleagues put it in a paper title, “The Older You Get, the Healthier You Have Been.”

但即使他們在十一個十年的時候身體狀況不那麼好，與其他人相比，這些人已經享受了很多年的健康生活。他們的健康壽命和壽命都非常長。更令人驚訝的是，Perls 的研究小組還發現，超級百歲老人和「半超級百歲老人」（105 歲至 109 歲）實際上比普通百歲老人的健康狀況還要好。他們是超級倖存者，在高齡時，壽命和健康壽命幾乎相同。正如珀爾斯和他的同事在一篇論文標題中所說的那樣，“你年紀越大，你就越健康。”

In mathematical terms, the centenarians' genes have bought them a *phase shift* in time—that is, their entire lifespan and healthspan curve has been shifted a decade or two (or three!) to the right. Not only do they live longer, but these are people who have been healthier than their peers, and biologically younger than them, for virtually their entire lives. When they were sixty, their coronary arteries were as healthy as those of thirty-five-year-olds. At eighty-five, they likely looked and felt and functioned as if they were in their sixties. They seemed like people a generation younger than the age on their driver's license. *This* is the effect that we are seeking to mimic.

用數學術語來說，百歲老人的基因為他們帶來了時間上的相移，也就是說，他們的整個壽命和健康壽命曲線向右移動了一兩年（或三年！）。他們不僅壽命更長，而且幾乎一生都比同齡人更健康，生理上也比同齡人年輕。當他們六十歲的時候，他們的冠狀動脈和三十五歲的人一樣健康。八十五歲時，他們的外表、感覺和行為很可能就像六十多歲一樣。他們看起來比駕駛執照上的年齡年輕一代。這就是我們正在尋求模仿的效果。

Think back to the notion of the Marginal Decade and Bonus Decade that we introduced in chapter 3, and the graph of lifespan versus healthspan. Because Medicine 2.0 often drags out lifespan in the context of low healthspan, it *lengthens* the window of morbidity, the period of disease and disability at the end of life. People are sicker for longer before they die. Their Marginal Decade is spent largely as a patient. When centenarians die, in contrast, they have generally (though not always) been sick and/or disabled for a much shorter period of time than people who die two or three decades earlier. This is called *compression of morbidity*, and it basically means shrinking or shortening the period of decline at the end of life and lengthening the period of healthy life, or healthspan.

回想一下我們在第三章中介紹的邊際十年和獎金十年的概念，以及壽命與健康壽命的圖表。由於醫學2.0常常在健康壽命較低的情況下延長壽命，因此它延長了發病窗口、疾病時期和生命末期的殘疾。人們在死前病情會持續更久。他們的邊緣十年主要是作為病人度過的。相較之下，當百歲老人去世時，他們通常（儘管並非總是）患病和/或殘疾

的時間比兩三十年前去世的人要短得多。這就是所謂的壓縮發生率，基本上意味著縮小或縮短生命末期的衰退期，延長健康壽命或健康壽命。

One goal of Medicine 3.0 is to help people live a life course more like the centenarians—only better. The centenarians not only live longer but live longer in a healthier state, meaning many of them get to enjoy one, or two, or even three Bonus Decades. They are often healthier at ninety than the average person in their sixties. And when they do decline, their decline is typically brief. This is what we want for ourselves: to live longer with good function and without chronic disease, and with a briefer period of morbidity at the end of our lives.

醫學 3.0 的目標之一是幫助人們過著像百歲老人一樣的生活，甚至更好。百歲老人不僅壽命更長，而且在更健康的狀態下壽命更長，這意味著他們中的許多人可以享受一、兩個、甚至三個「紅利十年」。他們九十歲時往往比六十多歲的普通人更健康。當它們確實衰退時，它們的衰退通常是短暫的。這就是我們對自己的期望：活得更長，身體機能良好，沒有慢性疾病，在生命結束時發病期更短。

The difference is that while most centenarians seem to get their longevity and good health almost accidentally, thanks to genes and/or good luck, the rest of us must try to achieve this intentionally. Which brings us to our next two questions: *How* do centenarians delay or avoid chronic disease? And how can we do the same?

不同之處在於，雖然大多數百歲老人似乎幾乎是偶然地獲得了長壽和健康，但由於基因和/或好運，我們其他人必須努力有意地實現這一目標。這給我們帶來了接下來的兩個問題：百歲老人如何延緩或避免慢性病？我們怎樣才能做到同樣的事情呢？

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This is where the genes likely come in—the longevity genes that most of us don't have because we failed to pick the right parents. But if we can identify

specific genes that give centenarians their edge, perhaps we can reverse-engineer their phenotype, their effect.

這就是基因可能發揮作用的地方——我們大多數人沒有長壽基因，因為我們沒有選擇合適的父母。但如果我們能夠識別出賦予百歲老人優勢的特定基因，也許我們可以對他們的表型及其影響進行逆向工程。

This would seem to be a relatively straightforward task: sequence the genomes of a few thousand centenarians and see which individual genes or gene variants stand out as being more prevalent among this population than in the general population. Those would be your candidate genes. But when researchers did this, examining thousands of individuals via genome-wide association studies, they came up almost empty-handed. These individuals appeared to have very little in common with one another genetically. And their longevity may be due to dumb luck after all.

這似乎是一項相對簡單的任務：對數千名百歲老人的基因組進行定序，看看哪些個體基因或基因變異在該族群中比在一般人群中更普遍。這些將會是你的候選基因。但當研究人員透過全基因組關聯研究對數千人進行檢查時，他們幾乎空手而歸。這些人在基因上似乎彼此沒有什麼共通點。畢竟，他們的長壽可能是因為運氣不好。

Why are longevity genes so elusive? And why are centenarians so rare in the first place? It comes down to natural selection.

為什麼長壽基因如此難以捉摸？為什麼百歲老人如此罕見？這歸結為自然選擇。

Hold on a second, you might be saying. We've been taught all our lives that evolution and natural selection have relentlessly optimized us for a billion years, favoring beneficial genes and eliminating harmful ones—survival of the fittest, and all that. So why don't we *all* share these pro-longevity centenarian genes, whatever they are? Why aren't we all “fit” enough to live to be one hundred?

等一下，你可能會說。我們一生都被告知，十億年來，進化和自然選擇無情地優化了我們，有利於有益基因並消除有害基因——適者生

存，等等。那麼，為什麼我們不都擁有這些長壽的百歲基因，無論它們是什麼？為什麼我們都「健康」到不能活到一百歲？

The short answer is that evolution doesn't really care if we live that long. Natural selection has endowed us with genes that work beautifully to help us develop, reproduce, and then raise our offspring, and perhaps help raise our offspring's offspring. Thus, most of us can coast into our fifth decade in relatively good shape. After that, however, things start to go sideways. The evolutionary reason for this is that after the age of reproduction, natural selection loses much of its force. Genes that prove unfavorable or even harmful in midlife and beyond are not weeded out because they have already been passed on. To pick one obvious example: the gene (or genes) responsible for male pattern baldness. When we are young, our hair is full and glorious, helping us attract mates. But natural selection does not really care whether a man in his fifties (or a woman, for that matter) has a full head of hair.

簡而言之，演化並不真正關心我們是否能活那麼久。自然選擇賦予了我們很好的基因，可以幫助我們發育、繁殖，然後養育我們的後代，或許還可以幫助養育我們後代的後代。因此，我們大多數人都能以相對良好的狀態度過第五個十年。然而，在那之後，事情開始出現問題。造成這種情況的進化原因是，在繁殖時代之後，自然選擇失去了大部分力量。那些在中年及以後被證明不利甚至有害的基因並沒有被淘汰，因為它們已經被遺傳了。舉一個明顯的例子：導致雄性禿的基因。當我們年輕時，我們的頭髮濃密而光彩，有助於我們吸引異性。但自然選擇並不真正關心五十多歲的男人（或女人）是否有一頭完整的頭髮。

Hair loss is not terribly relevant to longevity, luckily for me. But this general phenomenon also explains why genes that might predispose someone to Alzheimer's disease or some other illness, later in life, have not vanished from our gene pool. In short, natural selection doesn't care if we develop Alzheimer's disease (or baldness) in old age. It doesn't affect our reproductive fitness. By the time dementia would appear, we have likely already handed down our genes. The same is true of genes that would accelerate our risk of heart disease or cancer in midlife. Most of us still carry these lousy genes—

including some centenarians, by the way. Indeed, there is a chance that those same genes may have conferred some sort of advantage earlier in life, a phenomenon known as “antagonistic pleiotropy.”

幸運的是，脫髮與長壽並沒有太大關係。但這種普遍現象也解釋了為什麼在以後的生活中可能使人容易罹患阿茲海默症或其他疾病的基因並沒有從我們的基因庫中消失。簡而言之，自然選擇並不關心我們是否在老年時患上阿茲海默症（或禿頭）。它不會影響我們的生殖健康。當癡呆症出現時，我們的基因很可能已經遺傳了。對於會增加我們中年心臟病或癌症風險的基因也是如此。我們大多數人仍然攜帶著這些糟糕的基因——順便說一句，包括一些百歲老人。事實上，這些相同的基因有可能在生命早期賦予某種優勢，這種現象稱為「拮抗性多效性」。

One plausible theory holds that centenarians live so long because they also possess certain other genes that protect them from the flaws in our typical genome, by preventing or delaying cardiovascular disease and cancer and maintaining their cognitive function decades after others lose it. But even as natural selection allows harmful genes to flourish in older age, it does almost nothing to promote these more helpful longevity-promoting genes, for the reasons discussed above. Thus it appears that no two centenarians follow the exact same genetic path to reaching extreme old age. There are many ways to achieve longevity; not just one or two.

一個看似合理的理論認為，百歲老人之所以能長壽，是因為他們還擁有某些其他基因，這些基因可以保護他們免受典型基因組缺陷的影響，預防或延緩心血管疾病和癌症，並在其他人喪失認知功能幾十年後仍能維持其認知功能。但由於上述原因，即使自然選擇允許有害基因在老年時大量繁殖，它對促進這些更有用的長壽基因幾乎沒有任何作用。因此，似乎沒有兩個百歲老人遵循完全相同的基因路徑到達高齡。實現長壽的方法有很多；不只是一兩個。

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That said, a handful of potential longevity genes have emerged in various studies, and it turns out that some of them are possibly relevant to our strategy. One of the most potent individual genes yet discovered is related to cholesterol metabolism, glucose metabolism—and Alzheimer’s disease risk.

也就是說，各種研究中已經出現了一些潛在的長壽基因，事實證明其中一些可能與我們的策略有關。迄今為止發現的最有效的個別基因之一與膽固醇代謝、葡萄糖代謝和阿茲海默症風險有關。

You may have heard of this gene, which is called *APOE*, because of its known effect on Alzheimer’s disease risk. It codes for a protein called APOE (apolipoprotein E) that is involved in cholesterol transport and processing, and it has three variants: *e2*, *e3*, and *e4*. Of these, *e3* is the most common by far, but having one or two copies of the *e4* variant seems to multiply one’s risk of developing Alzheimer’s disease by a factor of between two and twelve. This is why I test all my patients for their *APOE* genotype, as we’ll discuss in chapter 9.

您可能聽說過這種基因，稱為 APOE，因為它對阿茲海默症風險有已知影響。它編碼一種稱為 APOE（載脂蛋白 E）的蛋白質，該蛋白質參與膽固醇轉運和加工，具有三種變體：e2、e3 和 e4。其中，e3 是迄今為止最常見的，但擁有一到兩個 e4 變異副本似乎會使人患阿茲海默症的風險增加 2 到 12 倍。這就是為什麼我測試所有患者的 APOE 基因型，我們將在第 9 章中討論。

The *e2* variant of *APOE*, on the other hand, seems to protect its carriers against dementia—and it also turns out to be very highly associated with longevity. According to a large 2019 meta-analysis of seven separate longevity studies, with a total of nearly thirty thousand participants, people who carried at least one copy of *APOE e2* (and no *e4*) were about 30 percent more likely to reach extreme old age (defined as ninety-seven for men, one hundred for women) than people with the standard *e3/e3* combination. Meanwhile, those with two copies of *e4*, one from each parent, were 81 percent *less* likely to live that long, according to the analysis. That’s a pretty big swing.

另一方面，APOE 的 e2 變異似乎可以保護其攜帶者免受癡呆症的侵害，而且它也與長壽密切相關。根據2019 年對七項獨立長壽研究（總共有近三萬名參與者）進行的大型薈萃分析，攜帶至少一份APOE e2（而不攜帶e4）的人達到極端老年的可能性大約高出30%（定義為（男性 97 歲，女性 100 歲）比標準 e3/e3 組合的人高。同時，根據分析，那些擁有兩份 e4 拷貝（父母各一份）的人活那麼久的可能性要低 81%。這是一個相當大的波動。

We will explore the function of APOE in more detail in chapter 9, but it is likely relevant to our strategy on multiple levels. First and most obviously, it appears to play a role in delaying (or not delaying) the onset of Alzheimer's disease, depending on the variant. This is likely not a coincidence, because as we'll see, APOE plays an important role in shuttling cholesterol around the body, particularly in the brain; one's *APOE* variant also has a large influence on glucose metabolism. Its potent correlation with longevity suggests that we should focus our efforts on cognitive health and pay special attention to issues around cholesterol and lipoproteins (the particles that carry cholesterol, which we'll discuss in chapter 7), as well as glucose metabolism (chapter 6).

我們將在第 9 章中更詳細地探討 APOE 的功能，但它可能與我們的多個層面的策略相關。首先也是最明顯的是，它似乎在延遲（或不延遲）阿茲海默症的發作方面發揮了作用，具體取決於變異。這可能不是巧合，因為正如我們將看到的，APOE 在體內膽固醇運輸中發揮著重要作用，尤其是在大腦中。一個人的 APOE 變異對葡萄糖代謝也有很大影響。它與長壽的密切相關性表明，我們應該把精力集中在認知健康上，並特別關注膽固醇和脂蛋白（攜帶膽固醇的顆粒，我們將在第7章中討論）以及葡萄糖代謝（第6章）相關的問題。）。

Researchers have identified two other cholesterol-related genes, known as *CETP* and *APOC3*, that are also correlated with extreme longevity (and may explain why centenarians rarely die from heart disease). But one individual gene, or even three dozen genes, is unlikely to be responsible for centenarians' extreme longevity and healthspan. Broader genetic studies suggest that hundreds, if not thousands, of genes could be involved, each making its own

small contribution—and that there is no such thing as a “perfect” centenarian genome.

研究人員還發現了另外兩個與膽固醇相關的基因，即 CETP 和 APOC3，它們也與超長壽命有關（並且可以解釋為什麼百歲老人很少死於心臟病）。但一個單獨的基因，甚至三打基因，不太可能導致百歲老人的極端長壽和健康壽命。更廣泛的遺傳學研究表明，可能涉及數百個甚至數千個基因，每個基因都做出自己的微小貢獻，而且不存在「完美」的百歲老人基因組。

This is actually good news for those of us without centenarians in our family tree, because it suggests that even on this genetic level there may be no magic bullet; even for centenarians, longevity may be a game of inches, where relatively small interventions, with cumulative effect, could help us replicate the centenarians’ longer lifespan and healthspan. Put another way, if we want to outlive our life expectancy and live better longer, we will have to work hard to earn it—through small, incremental changes.

對於我們這些家譜中沒有百歲老人的人來說，這實際上是個好消息，因為它表明即使在這個基因層面上也可能沒有靈丹妙藥。即使對於百歲老人來說，長壽也可能是一場英寸遊戲，相對較小的干預措施具有累積效應，可以幫助我們複製百歲老人的更長壽命和健康壽命。換句話說，如果我們想活得比預期壽命長，活得更好、活得更久，我們就必須努力工作——透過微小的、漸進的改變來實現這一目標。

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One other possible longevity gene that has emerged, in multiple studies of centenarians worldwide, also provides some possible clues to inform our strategy. These are variants in a particular gene called *FOXO3* that seem to be directly relevant to human longevity.

在對世界各地百歲老人的多項研究中出現的另一種可能的長壽基因也為我們的策略提供了一些可能的線索。這些是 FOXO3 特定基因的變體，似乎與人類壽命直接相關。

In 2008, Bradley Willcox of the University of Hawaii and colleagues reported that a genetic analysis of participants in a long-running study of health and longevity in Hawaiian men of Japanese ancestry had identified three SNPs (or variants) in *FOXO3* that were strongly associated with healthy aging and longevity. Since then, several other studies have found that various other long-lived populations also appear to have *FOXO3* mutations, including Californians, New Englanders, Danes, Germans, Italians, French, Chinese, and American Ashkenazi Jews—making *FOXO3* one of the very few longevity-related genes to be found across multiple different ethnic groups and geographical locations.

2008 年，夏威夷大學的 Bradley Willcox 及其同事報告說，一項針對日本血統的夏威夷男性健康和長壽的長期研究參與者的基因分析發現，FOXO3 中的三個 SNP（或變異體）與健康老齡化和長壽。此後，其他幾項研究發現，其他各種長壽人群似乎也有 FOXO3 突變，包括加州人、新英格蘭人、丹麥人、德國人、義大利人、法國人、中國人和美國德系猶太人，這使得 FOXO3 成為極少數的長壽人群之一。在多個不同種族和地理位置中都可以找到與長壽相關的基因。

FOXO3 belongs to a family of “transcription factors,” which regulate how other genes are expressed—meaning whether they are activated or “silenced.” I think of it as rather like the cellular maintenance department. Its responsibilities are vast, encompassing a variety of cellular repair tasks, regulating metabolism, caring for stem cells, and various other kinds of housekeeping, including helping with disposal of cellular waste or junk. But it doesn’t do the heavy lifting itself, like the mopping, the scrubbing, the minor drywall repairs, and so on. Rather, it delegates the work to other, more specialized genes—its subcontractors, if you will. When *FOXO3* is activated, it in turn activates genes that generally keep our cells healthier. It seems to play an important role in preventing cells from becoming cancerous as well.

FOXO3 屬於「轉錄因子」家族，它調節其他基因的表達方式，即它們是被激活還是「沉默」。我認為它很像蜂窩維護部門。它的職責非常廣泛，涵蓋各種細胞修復任務、調節新陳代謝、護理幹細胞以及各種其他類型的內務管理，包括幫助處理細胞廢物或垃圾。但它本身並不

承擔繁重的工作，例如拖地、擦洗、小型乾牆維修等。相反，它將工作委託給其他更專業的基因——它的分包商，如果你願意的話。當 FOXO3 被活化時，它會激活通常使我們的細胞更健康的基因。它似乎在防止細胞癌變方面也發揮著重要作用。

Here's where we start to see some hope, because *FOXO3* can be activated or suppressed by our own behaviors. For example, when we are slightly deprived of nutrients, or when we are exercising, *FOXO3* tends to be more activated, which is what we want.

從這裡我們開始看到一些希望，因為 FOXO3 可以被我們自己的行為活化或抑制。例如，當我們稍微缺乏營養時，或者當我們運動時，FOXO3 往往會更加激活，這正是我們想要的。

Beyond *FOXO3*, gene expression itself seems to play an important but still poorly understood role in longevity. A genetic analysis of Spanish centenarians found that they displayed extremely youthful patterns of gene expression, more closely resembling a control group of people in their twenties than an older control group of octogenarians. Precisely how these centenarians achieved this is not clear, but it may have something to do with *FOXO3*—or some other, as yet unknown, governor of gene expression.

除了 FOXO3 之外，基因表現本身似乎在長壽中也發揮著重要但仍知之甚少的作用。對西班牙百歲老人的基因分析發現，他們表現出極為年輕的基因表現模式，與二十多歲的對照組相比，更接近二十多歲的對照組。這些百歲老人究竟是如何實現這一目標的尚不清楚，但這可能與 FOXO3 或其他一些尚未為人所知的基因表現調節因子有關。

We still have more questions than answers when it comes to the genetics behind extreme longevity, but this at least points in a more hopeful direction. While your *genome* is immutable, at least for the near future, *gene expression* can be influenced by your environment and your behaviors. For example, a 2007 study found that older people who were put on a regular exercise program shifted to a more youthful pattern of gene expression after six months. This suggests that genetics *and* environment both play a role in

longevity and that it may be possible to implement interventions that replicate at least some of the centenarians' good genetic luck.

當談到極端長壽背後的遺傳學時，我們的問題仍然多於答案，但這至少指出了一個更有希望的方向。雖然您的基因組是不可變的，至少在不久的將來是這樣，但基因表現可能會受到您的環境和行為的影響。例如，2007 年的一項研究發現，定期運動的長者在六個月後基因表現模式轉變為更年輕的模式。這表明遺傳和環境都對長壽產生影響，並且有可能實施幹預措施來複製至少部分百歲老人的良好遺傳運氣。

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I find it useful to think of centenarians as the results of a natural experiment that tells us something important about living longer and living better. Only in this case, Darwin and Mendel, the Russian geneticist, are the scientists. The experiment entails taking a random collection of human genomes and exposing them to a variety of environments and behaviors. The centenarians possess the correct combination of genome X required to survive in environment Y (perhaps with help from behaviors Z). The experiment is not simple; there are likely many pathways to longevity, genetic and otherwise.

我發現將百歲老人視為自然實驗的結果是有用的，它告訴我們一些關於活得更長和生活得更好的重要資訊。只有在這種情況下，達爾文和俄羅斯遺傳學家孟德爾才是科學家。該實驗需要隨機收集人類基因組並將其暴露於各種環境和行為中。百歲老人擁有在環境 Y 中生存所需的基因組 X 的正確組合（也許需要行為 Z 的幫助）。這個實驗並不簡單；長壽可能有很多途徑，包括遺傳途徑和其他途徑。

Most of us, obviously, cannot expect to get away with some of the centenarians' naughty behaviors, such as smoking and drinking for decades. But even if we don't (and in many cases, shouldn't) imitate their "tactics," the centenarians can nevertheless help inform our strategy. Their superpower is their ability to resist or delay the onset of chronic disease by one or two or even three decades, while also maintaining relatively good healthspan.

顯然，我們大多數人不能指望百歲老人的一些頑皮行為能夠逃脫懲罰，例如幾十年來抽煙和喝酒。但即使我們不（而且在許多情況下，不應該）模仿他們的“策略”，百歲老人仍然可以幫助我們制定策略。他們的超能力是能夠抵抗或延遲慢性病的發作一兩年甚至三十年，同時也能維持相對較好的健康壽命。

It's this phase shift that we want to emulate. But Medicine 2.0, which is almost solely focused on helping us live longer *with* disease, is not going to get us there. Its interventions almost always come too late, when disease is already established. We have to look at the other end of the time line, trying to slow or stop diseases before they start. We must focus on delaying the *onset* rather than extending the *duration* of disease—and not just one disease but *all* chronic diseases. Our goal is to live longer *without* disease.

我們想要模擬的就是這種相移。但醫學 2.0 幾乎完全專注於幫助我們在疾病中延長壽命，但它不會讓我們實現這一目標。當疾病已經形成時，它的干預措施幾乎總是來得太晚。我們必須著眼於時間線的另一端，試圖在疾病發生之前減緩或阻止它們。我們必須集中精力延遲疾病的發作，而不是延長疾病的持續時間——不僅是一種疾病，而是所有慢性疾病。我們的目標是在沒有疾病的情況下活得更久。

This points to another flaw of Medicine 2.0, which is that it generally looks at these diseases as entirely separate from one another. We treat diabetes as if it were unrelated to cancer and Alzheimer's, for example, even though it is a major risk factor for both. This disease-by-disease approach is reflected in the “silo” structure of the National Institutes of Health, with separate institutions dedicated to cancer, heart disease, and so on. We treat them as distinct when we should be looking for their commonalities.

這指出了醫學 2.0 的另一個缺陷，即它通常將這些疾病視為完全獨立的疾病。例如，我們對待糖尿病就好像它與癌症和阿茲海默症無關一樣，儘管它是兩者的主要危險因子。這種針對疾病的方法體現在美國國立衛生研究院的「筒倉」結構中，該機構設有專門研究癌症、心臟病等疾病的獨立機構。當我們應該尋找它們的共通點時，我們卻將它們視為獨特的。

“We’re trying to attack heart disease, cancer, stroke, and Alzheimer’s one disease at a time, as if somehow these diseases are all unrelated to each other,” says S. Jay Olshansky, who studies the demography of aging at the University of Illinois–Chicago, “when in fact the underlying risk factor for almost everything that goes wrong with us as we grow older, both in terms of diseases we experience, and of the frailty and disability associated with it, is related to the underlying biological process of aging.”

「我們試圖一次只治療一種疾病，如心臟病、癌症、中風和阿茲海默症，就好像這些疾病在某種程度上彼此無關一樣，」在該大學研究老化人口統計學的S. Jay Olshansky 說。伊利諾伊州芝加哥分校的博士說，「事實上，隨著年齡的增長，我們幾乎所有問題的潛在風險因素，無論是我們經歷的疾病，還是與之相關的虛弱和殘疾，都與潛在的生物因素有關。老化的過程。」

In the next chapter, we will look at one particular intervention, a drug that likely slows or delays that underlying biological process of aging at a mechanistic level. It may become relevant to our strategy as well, but for now this means pursuing two approaches in parallel. We need to think about very early *disease-specific* prevention, which we will explore in detail in the next few chapters dedicated to the Horsemen diseases. And we need to think about very early *general* prevention, targeting all the Horsemen at once, via common drivers and risk factors.

在下一章中，我們將研究一種特定的干預措施，一種可能在機械層面上減緩或延遲老化的潛在生物過程的藥物。它也可能與我們的策略相關，但目前這意味著並行採用兩種方法。我們需要考慮非常早期的疾病特異性預防，我們將在接下來專門討論騎士疾病的章節中詳細探討這一點。我們需要考慮儘早進行全面預防，透過共同的驅動因素和風險因素，同時針對所有騎士。

These approaches overlap, as we’ll see: reducing cardiovascular risk by targeting specific lipoproteins (cholesterol) may also reduce Alzheimer’s disease risk, for example, though not cancer. The steps we take to improve metabolic health and prevent type 2 diabetes almost certainly reduce the risk of cardiovascular disease, cancer, and Alzheimer’s simultaneously. Some types

of exercise reduce risk for all chronic diseases, while others help maintain the physical and cognitive resilience that centenarians largely get via their genes. This level of prevention and intervention may seem excessive by the standards of Medicine 2.0, but I would argue that it is necessary.

正如我們將看到的，這些方法是重疊的：透過針對特定脂蛋白（膽固醇）來降低心血管風險也可能降低阿茲海默症的風險，但不能降低癌症的風險。我們為改善代謝健康和預防第 2 型糖尿病所採取的措施幾乎肯定會同時降低心血管疾病、癌症和阿茲海默症的風險。某些類型的運動可以降低所有慢性疾病的風險，而另一些運動則有助於維持百歲老人主要透過基因獲得的身體和認知能力。以醫學2.0的標準來看，這種程度的預防和介入似乎有些過度，但我認為這是必要的。

In the end, I think that the centenarians' secret comes down to one word: *resilience*. They are able to resist and avoid cancer and cardiovascular disease, even when they have smoked for decades. They are able to maintain ideal metabolic health, often despite a lousy diet. And they resist cognitive and physical decline long after their peers succumb. It is this resilience that we want to cultivate, just as Ali prepared himself to withstand and ultimately outlast Foreman. He prepared intelligently and thoroughly, he trained for a long time before the match, and he deployed his tactics from the opening bell. He could not have lasted forever, but he made it through enough rounds that he was able to fulfill his objective and win the fight.

最後，我認為百歲老人的秘訣可以歸結為一個詞：韌性。他們能夠抵抗和避免癌症和心血管疾病，即使他們已經吸煙了幾十年。儘管飲食很糟糕，他們仍然能夠保持理想的代謝健康。在同儕屈服之後很久，他們仍能抵抗認知和身體衰退。我們想要培養的正是這種韌性，就像阿里準備好承受並最終超越福爾曼一樣。他的準備聰明而徹底，賽前進行了長時間的訓練，從開場就部署了戰術。他不可能永遠堅持下去，但他堅持了足夠的回合，從而實現了他的目標並贏得了戰鬥。

CHAPTER 5

第 5 章

Eat Less, Live Longer?

吃得少，活得更久？

The Science of Hunger and Health

飢餓與健康的科學

Scientists who play by someone else's rules don't have
much chance of making discoveries.

按照別人的規則行事的科學家沒有太多機會做出
發現。

—JACK HORNER

——傑克·霍納

In the fall of 2016, I met three friends at George Bush Intercontinental Airport in Houston to embark on a somewhat unusual vacation. We flew eleven hours overnight to Santiago, Chile, where we drank coffee and ate breakfast before boarding another plane to fly six more hours to the west, across 2,500 miles of open ocean, to Easter Island, the world's most isolated body of land that is inhabited by humans. We were all men in our forties, but this was not your typical guys' weekend.

2016年秋天，我在休士頓喬治布希洲際機場遇到了三個朋友，開始了一個有點不尋常的假期。我們連夜飛行11 個小時抵達智利聖地牙哥，在那裡喝了咖啡、吃了早餐，然後登上另一架飛機，再向西飛行6 個小時，跨越2,500 英里的公海，抵達復活節島，這是世界上最偏僻的陸地。有人類居住。我們都是四十多歲的男人，但這不是典型的男人週末。

Most people know about Easter Island because of the thousand or so mysterious giant stone heads, called *moai*, dotting its shoreline, but there's a lot more to it. The island was named by European explorers who landed there on Easter Sunday in 1722, but the natives call it Rapa Nui. It is an extreme, isolated, spectacular place. The triangle-shaped island of roughly sixty-three square miles is what's left of a trio of ancient volcanoes that surged up more than two miles from the seabed millions of years ago. One end of the island is ringed by very high cliffs that plunge down into the gorgeous blue ocean. The nearest human settlement is more than one thousand miles away.

大多數人了解復活節島是因為其海岸線上點綴著數千個左右神秘的巨型石像，稱為摩艾石像，但它的魅力遠不止於此。該島因 1722 年復活節週日登陸該島的歐洲探險家而得名，但當地人稱之為拉帕努伊 (Rapa Nui)。這是一個極端、孤立、壯觀的地方。這座面積約六十三平方英里的三角形島嶼是三座古老火山的遺跡，這些火山在數百萬年前從海底湧出兩英里多。島嶼的一端被非常高的懸崖環繞，懸崖直插到美麗的藍色海洋。最近的人類居住區距離這裡有一千多英里。

We were not there as tourists. We were on a pilgrimage to the source of one of the most intriguing molecules in all of medicine, one that most people

have never even heard of. The story of how this molecule was discovered, and how it revolutionized the study of longevity, is one of the most incredible sagas in biology. This molecule, which came to be known as rapamycin, had also transformed transplant medicine, giving millions of patients a second chance at life. But that was not why we had traveled ten thousand miles to this remote spot. We had come because rapamycin had been demonstrated to do something that no other drug had ever done before: extend maximum lifespan in a mammal.

我們不是作為遊客在那裡的。我們正在朝整個醫學中最有趣的分子之一的來源朝聖，而大多數人甚至從未聽說過這種分子。這種分子是如何被發現的，以及它如何徹底改變長壽研究的故事，是生物學中最令人難以置信的傳奇故事之一。這種後來被稱為雷帕黴素的分子也改變了移植醫學，為數百萬患者提供了第二次生命的機會。但這不是我們長途跋涉萬裡來到這個偏僻地方的原因。我們來是因為雷帕黴素已被證明具有其他藥物從未做過的作用：延長哺乳動物的最大壽命。

This discovery came about at least in part thanks to the work of one member of our group, David Sabatini, who was then a professor of biology at MIT's Whitehead Institute. David had helped discover the key cellular pathway that rapamycin acts upon. Also on the trip was another biologist named Navdeep Chandel (Nav to his friends), a friend of David's who studies metabolism and mitochondria, the little organelles that produce power (and do much more) in our cells, at Northwestern University. Completing our foursome was my close friend Tim Ferriss. Tim is an entrepreneur and author, not a scientist, but he has a knack for asking the right questions and bringing a fresh perspective to something. Plus, I knew that he would be willing to swim in the ocean with me every day, reducing my chances of being eaten by a shark by approximately 50 percent.

這項發現至少部分歸功於我們小組的一名成員戴維·薩巴蒂尼（David Sabatini）的工作，他當時是麻省理工學院懷特海德研究所的生物學教授。大衛幫助發現了雷帕黴素作用的關鍵細胞途徑。與此同行的還有另一位生物學家，名叫納夫迪普·錢德爾（Navdeep Chandel）（他的朋友們稱為納夫），他是大衛的朋友，在西北大學研究新陳代謝和粒線

體，粒線體是我們細胞中產生能量（並做更多事情）的小細胞器。我的好朋友 Tim Ferriss 是我們四人組的最後一位。蒂姆是一位企業家和作家，而不是科學家，但他有提出正確問題並為某些事情帶來新鮮視角的技巧。另外，我知道他會願意每天和我一起在海裡游泳，這樣我被鯊魚吃掉的機會就會減少約 50%。

One purpose of our trip was to scout out the location for a scientific conference that would be entirely devoted to research about this amazing substance. But mostly, we wanted to make a pilgrimage to the place where this extraordinary molecule had come from and to pay homage to its almost accidental discovery.

我們此行的目的之一是尋找舉辦科學會議的地點，該會議將完全致力於研究這種神奇的物質。但最重要的是，我們想去朝聖這種非凡分子的來源地，並向它幾乎是偶然的發現致敬。

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After we dropped off our luggage at our thirty-room tourist hotel, our first stop was Rano Kau, the one-thousand-foot-tall extinct volcano that dominates the southwest corner of the island. Our destination was the center of the crater, where there is a large swampy lake, nearly a mile across, that had a certain mystique among the locals. According to a local legend that we had heard, when people were feeling sick or unwell, they would make their way down into the crater, perhaps spending a night in the belly of the volcano, which was believed to have special healing powers.

在我們擁有三十間客房的旅遊酒店放下行李後，我們的第一站是拉諾考，這座一千英尺高的死火山佔據了島嶼的西南角。我們的目的地是火山口的中心，那裡有一個大沼澤湖，寬近一英里，對當地人來說有一定的神秘感。根據我們聽到的當地傳說，當人們感到生病或不適時，他們會進入火山口，也許會在火山腹地過夜，人們相信火山具有特殊的治癒能力。

This is where the story of rapamycin begins. In late 1964, a Canadian scientific and medical expedition arrived on Easter Island, having sailed all the

way from Halifax aboard a naval vessel. They spent several weeks conducting research and dispensing much-needed medical care to the local inhabitants, and they brought home numerous specimens of the island's unusual flora and fauna, including soil samples from the area of the crater. The scientists might have heard the same legend about its healing properties that we did.

這就是雷帕黴素的故事開始的地方。1964年底，一支加拿大科學和醫療考察隊乘坐海軍艦艇從哈利法克斯一路航行抵達復活節島。他們花了幾週的時間進行研究，並向當地居民提供急需的醫療服務，並帶回了島上不尋常動植物的大量標本，包括來自火山口地區的土壤樣本。科學家可能和我們聽過關於它的治療功效的相同傳說。

A few years later, a jar of Easter Island dirt ended up on the lab bench of a biochemist in Montreal named Suren Sehgal, who worked for a Canadian pharmaceutical company then called Ayerst. Sehgal found that this soil sample was saturated with a strange and potent antifungal agent that was seemingly produced by a soil bacterium called *Streptomyces hygroscopicus*. Curious, Sehgal isolated the bacterium and grew it in culture, then began testing this mysterious compound in his lab. He named it rapamycin, after Rapa Nui, the native name for Easter Island (*mycin* is the suffix typically applied to antimicrobial agents). But then Ayerst abruptly closed its Montreal lab, and Sehgal's bosses ordered him to destroy all the compounds he was researching.

幾年後，一罐復活節島的泥土出現在蒙特利爾一位名叫蘇倫·塞加爾 (Suren Sehgal) 的生物化學家的實驗室工作台上，他曾在一家當時名為 Ayerst 的加拿大製藥公司工作。塞加爾發現，這種土壤樣本中充滿了一種奇怪而有效的抗真菌劑，這種抗真菌劑似乎是由一種名為吸水鏈黴菌的土壤細菌產生的。出於好奇，塞加爾分離出了這種細菌，並將其培養在培養物中，然後開始在他的實驗室中測試這種神秘的化合物。他將其命名為雷帕黴素 (rapamycin)，以復活節島的原住民名稱拉帕努伊 (Rapa Nui) 命名 (黴素是通常用於抗菌藥物的後綴)。但隨後艾耶斯特突然關閉了蒙特婁實驗室，塞格爾的老闆命令他銷毀他正在研究的所有化合物。

Sehgal disobeyed the order. One day, he smuggled a jar of rapamycin home from work. His son Ajai, who was originally supposed to be the fifth

member of our pilgrimage, remembers opening the family freezer to get ice cream when he was a kid and seeing a well-wrapped container in there marked DO NOT EAT. The jar survived the family's move to Princeton, New Jersey, where Sehgal was ultimately transferred, and when the pharmaceutical giant Wyeth acquired Ayerst in 1987, his new bosses asked Sehgal if he had any interesting projects he'd like to pursue. He pulled the jar of rapamycin out of the freezer and went back to work.

塞格爾違反了命令。有一天，他下班後偷偷帶了一罐雷帕黴素回家。他的兒子阿賈伊原本應該是我們朝聖之旅的第五位成員，他記得小時候打開家裡的冰箱去買冰淇淋，看到裡面有一個包裝完好的容器，上面寫著「請勿食用」。這個罐子在全家搬到新澤西州普林斯頓後倖存下來，Sehgal 最終被轉移到那裡。1987 年製藥巨頭惠氏 (Wyeth) 收購了 Ayerst 時，他的新老闆問 Sehgal 是否有任何感興趣的項目想要從事。他從冰箱裡拿出那罐雷帕黴素，然後繼續工作。

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Sehgal believed he had found a cure for athlete's foot, which would have been a big enough deal. At one point, his son Ajai recalls, he prepared a homemade ointment containing rapamycin for a neighbor who had developed some sort of weird body rash; her rash cleared up almost immediately. But rapamycin turned out to be so much more than the next Dr. Scholl's foot spray. It proved to have powerful effects on the immune system, and in 1999 it was approved by the US Food and Drug Administration (FDA) to help transplant patients accept their new organs. As a surgical resident, I used to give it out like Tic Tacs to kidney and liver transplant patients. Sometimes referred to as sirolimus, rapamycin is also used as a coating on arterial stents because it prevents the stented blood vessels from reoccluding. The hits kept coming, even after Sehgal died in 2003: In 2007, a rapamycin analog^[*1] called everolimus was approved for use against a type of kidney cancer.

塞加爾相信他已經找到了治療腳氣的方法，這已經是一件了不起的事了。他的兒子阿賈伊回憶道，有一次，他為一位出現了某種奇怪的皮

疹的鄰居準備了一種含有雷帕黴素的自製藥膏；她的皮疹幾乎立刻就消失了。但事實證明，雷帕黴素比肖爾醫生的下一個足部噴霧劑強大得多。事實證明它對免疫系統具有強大的作用，並於1999年獲得美國食品和藥物管理局（FDA）批准用於幫助移植患者接受新器官。作為一名外科住院醫師，我曾經像 Tic Tacs 一樣向腎臟移植和肝臟移植患者分發它。雷帕黴素有時被稱為西羅莫司，也用作動脈支架的塗層，因為它可以防止支架內的血管再阻塞。即使在 Sehgal 於 2003 年去世後，熱門藥物仍不斷湧現：2007 年，一種名為依維莫司的雷帕黴素類似物 [*1] 被批准用於治療一種腎癌。

The compound was deemed so important that in the early 2000s Wyeth-Ayerst placed a plaque on Easter Island, not far from the volcano crater, honoring the place where rapamycin had been discovered. But when we went looking for the plaque, we found to our dismay that it had been stolen.

這種化合物被認為非常重要，以至於在 2000 年代初，Wyeth-Ayerst 在距離火山口不遠的復活節島上放置了一塊牌匾，以紀念雷帕黴素的發現地。但當我們去尋找牌匾時，我們沮喪地發現它被偷了。

The reason rapamycin has so many diverse applications is thanks to a property that Sehgal had observed, but never explored, which is that it tends to slow down the process of cellular growth and division. David Sabatini was one of a handful of scientists who picked up the baton from Sehgal, seeking to explain this phenomenon. Understanding rapamycin became his life's work. Beginning when he was a graduate student, working from a sheaf of papers that Sehgal himself had photocopied, Sabatini helped to elucidate how this unique compound worked on the cell. Ultimately, he and others discovered that rapamycin acted directly on a very important intracellular protein complex called mTOR (pronounced "em-tor"), for "mechanistic target of rapamycin." [*2]

雷帕黴素具有如此多種應用的原因是塞加爾觀察到但從未探索過的特性，即它往往會減慢細胞生長和分裂的過程。大衛·薩巴蒂尼（David Sabatini）是少數從塞格爾手中接過接力棒、試圖解釋這一現象的科學家之一。了解雷帕黴素成為他一生的工作。從他還是研究生開始，薩巴蒂尼就根據塞加爾本人複印的一疊論文開始研究，幫助闡明了這種

獨特的化合物如何作用於細胞。最終，他和其他人發現雷帕黴素直接作用於一種非常重要的細胞內蛋白質複合物，稱為 mTOR（發音為「em-tor」），是「雷帕黴素的機械標靶」。[*2]

Why do we care about mTOR? Because this mechanism turns out to be one of the most important mediators of longevity at the cellular level. Not only that, but it is highly “conserved,” meaning it is found in virtually all forms of life, ranging from yeast to flies to worms and right on up to us humans. In biology, “conserved” means that something has been passed on via natural selection, across multiple species and classes of organisms—a sign that evolution has deemed it to be very important.

我們為什麼關心 mTOR？因為這種機制被證明是細胞層面長壽最重要的介質之一。不僅如此，它還高度“保守”，這意味著它幾乎存在於所有生命形式中，從酵母到蒼蠅到蠕蟲，一直到我們人類。在生物學中，「保守」意味著某些東西透過自然選擇在多個物種和生物類別中傳遞——這表明進化認為它非常重要。

It was uncanny: this exotic molecule, found only on an isolated scrap of land in the middle of the ocean, acts almost like a switch that inhibits a very specific cellular mechanism that exists in nearly everything that lives. It was a perfect fit, and this fact still blows my mind every time I think about it.

這是不可思議的：這種奇特的分子只在海洋中央的一塊孤立的土地上發現，它的作用幾乎就像一個開關，抑制幾乎所有生物中都存在的非常特殊的細胞機制。這是一個完美的契合，每次想起這個事實仍然讓我心潮澎湃。

The job of mTOR is basically to balance an organism’s need to grow and reproduce against the availability of nutrients. When food is plentiful, mTOR is activated and the cell (or the organism) goes into growth mode, producing new proteins and undergoing cell division, as with the ultimate goal of reproduction. When nutrients are scarce, mTOR is suppressed and cells go into a kind of “recycling” mode, breaking down cellular components and generally cleaning house. Cell division and growth slow down or stop, and reproduction is put on hold to allow the organism to conserve energy.

mTOR 的工作基本上是平衡生物體生長和繁殖的需要與營養物質的可用性。當食物充足時，mTOR 被激活，細胞（或有機體）進入生長模式，產生新的蛋白質並進行細胞分裂，最終目標是繁殖。當營養素匱乏時，mTOR 會受到抑制，細胞會進入一種「回收」模式，分解細胞成分並通常進行清理工作。細胞分裂和生長減慢或停止，繁殖被擱置，以使有機體保存能量。

“To some extent, mTOR is like the general contractor for the cell,” Sabatini explains. It lies at the nexus of a long and complicated chain of upstream and downstream pathways that basically work together to regulate metabolism. It senses the presence of nutrients, especially certain amino acids, and it helps assemble proteins, the essential cellular building blocks. As he put it, “mTOR basically has a finger in every major process in the cell.”

「在某種程度上，mTOR 就像細胞的總承包商，」Sabatini 解釋道。它位於一條長而複雜的上游和下游途徑鏈的紐帶上，這些途徑基本上共同作用來調節新陳代謝。它感知營養物質的存在，尤其是某些氨基酸，並幫助組裝蛋白質，這是重要的細胞構建模組。正如他所說，“mTOR 基本上參與了細胞的每個主要過程。”

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On July 9, 2009, a brief but important science story appeared in *The New York Times*: “Antibiotic Delayed Aging in Experiments with Mice,” the headline read. Yawn. The “antibiotic” was rapamycin (which is not really an antibiotic), and according to the study, mice that had been given the drug lived significantly longer on average than controls: 13 percent longer for females, 9 percent for males.

2009 年 7 月 9 日，《紐約時報》刊登了一篇簡短但重要的科學故事：“小鼠實驗中的抗生素延遲衰老”，標題是這樣的。打哈欠。這種「抗生素」是雷帕黴素（它不是真正的抗生素），根據這項研究，服用該藥物的小鼠的平均壽命明顯長於對照組：雌性小鼠壽命延長 13%，雄性小鼠壽命延長 9%。

The story was buried on page A20, but it was a stunning result. Even though the drug had been given late in life, when the mice were already “old” (six hundred days, roughly the equivalent of humans in their sixties), it had still boosted the animals’ remaining life expectancy by 28 percent for males and 38 percent for females. It was the equivalent of a pill that could make a sixty-year-old woman live to the age of ninety-five. The authors of the study, published in *Nature*, speculated that rapamycin might extend lifespan “by postponing death from cancer, by retarding mechanisms of aging, or both.” The real headline here, however, was that no other molecule had been shown to extend lifespan in a mammal. Ever.

這個故事被埋在了 A20 頁，但結果卻令人震驚。儘管這種藥物是在晚年給藥的，即小鼠已經「老」了（六百年，大致相當於人類六十多歲的時候），但它仍然使雄性小鼠和小鼠的剩餘預期壽命延長了28%。女性佔 38%。相當於一顆藥丸，可以讓六十歲的女人活到九十五歲。這項發表在《自然》雜誌上的研究的作者推測，雷帕黴素可能「透過推遲癌症死亡、延緩老化機製或兩者兼而有之」來延長壽命。然而，這裡真正的標題是，沒有其他分子被證明可以延長哺乳動物的壽命。曾經。

The results were especially convincing because the experiment had been run by three different teams of researchers in three separate labs, using a total of 1,901 genetically diverse animals, and the results had been consistent across the board. Even better, other labs quickly and readily reproduced these results, which is a relative rarity, even with much-ballyhooed findings.

結果尤其令人信服，因為該實驗是由三個不同的研究團隊在三個不同的實驗室進行的，總共使用了 1,901 只基因多樣化的動物，結果全面一致。更好的是，其他實驗室很快、很容易地複製了這些結果，這相對罕見，即使有大肆宣傳的發現。

You might find this surprising, but many of the most headline-grabbing studies, the ones you read about in the newspaper or see reported on the news, are never repeated. Case in point: the well-publicized finding from 2006 that a substance found in the skins of grapes (and in red wine), resveratrol, extended lifespan in overweight mice. This generated countless news articles and even a

long segment on *60 Minutes* about the benefits of this amazing molecule (and, by extension, red wine). Resveratrol supplement sales shot through the roof. But other labs could not reproduce the initial findings. When resveratrol was subjected to the same sort of rigorous testing as rapamycin, as part of a National Institute on Aging program to test potential antiaging interventions, it did *not* extend lifespan in a similar diverse population of normal mice.

您可能會發現這令人驚訝，但許多最引人注目的研究，您在報紙上讀到的或在新聞報道中看到的研究，從未被重複過。典型的例子是：2006 年廣為人知的發現是，在葡萄皮（和紅酒）中發現的一種物質白藜蘆醇可以延長超重小鼠的壽命。這產生了無數的新聞文章，甚至在 60 分鐘節目中有一長段內容講述了這種神奇分子（進而延伸到紅酒）的好處。白藜蘆醇補充劑的銷量猛增。但其他實驗室無法重現最初的發現。作為國家老化研究所測試潛在抗衰老幹預措施的一部分，當白藜蘆醇接受與雷帕黴素相同的嚴格測試時，它並沒有延長類似的不同正常小鼠群體的壽命。

The same is true of other well-hyped supplements such as nicotinamide riboside, or NR: it, too, failed to extend lifespan consistently in mice. Of course, there are no data showing that any of these supplements lengthen life or improve health in humans. But study after study since 2009 has confirmed that rapamycin can extend mouse lifespans pretty reliably. It has also been shown to do so in yeast and fruit flies, sometimes alongside genetic manipulations that reduced mTOR activity. Thus, a reasonable person could conclude that there was something good about turning down mTOR, at least temporarily—and that rapamycin may have potential as a longevity-enhancing drug.

其他大肆宣傳的補充劑（如菸鹼醯胺核苷或 NR）也是如此：它也未能持續延長小鼠的壽命。當然，沒有數據顯示這些補充劑可以延長人類的壽命或改善健康。但自 2009 年以來的一項又一項研究已經證實，雷帕黴素可以相當可靠地延長小鼠的壽命。它也被證明在酵母和果蠅中也有這種作用，有時伴隨著降低 mTOR 活性的基因操作。因此，一個理智的人可能會得出這樣的結論：關閉 mTOR 是有好處的，至少是暫時的，並且雷帕黴素可能具有作為延長壽命藥物的潛力。

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To scientists who study aging, the life-extending effect of rapamycin was hugely exciting, but it also wasn't exactly a surprise. It appeared to represent the culmination of decades, if not centuries, of observations that how much food we eat correlates somehow with how long we live. This idea goes all the way back to Hippocrates, but more modern experiments have demonstrated, over and over, that reducing the food intake of lab animals could lengthen their lives.

對於研究老化的科學家來說，雷帕黴素的延長壽命效果非常令人興奮，但這並不令人意外。這似乎代表了數十年甚至數百年觀察的頂峰，即我們吃的食物量與我們的壽命有某種關聯。這個想法可以追溯到希波克拉底，但更現代的實驗已經一遍又一遍地證明，減少實驗動物的食物攝取量可以延長它們的壽命。

The first person to really put the idea of *eating less* into practice, in a rigorous, documented way, was not an ancient Greek or a modern scientist but a sixteenth-century Italian businessman named Alvise Cornaro. A self-made real estate developer who had become tremendously wealthy by draining swamps and turning them into productive farmland, Cornaro (whose friends called him “Luigi”) had a beautiful young wife and a villa outside Venice with its own theater. He loved to throw parties. But as he neared forty, he found himself suffering from “a train of infirmities,” as he put it—stomach pains, weight gain, and continual thirst, a classic symptom of incipient diabetes.

第一個以嚴格、有據可查的方式真正將少吃的想法付諸實踐的人不是古希臘人或現代科學家，而是十六世紀的意大利商人阿爾維斯·科爾納羅(Alvise Cornaro)。科納羅（他的朋友們稱他為“路易吉”）是一位白手起家的房地產開發商，通過排幹沼澤並將其變成肥沃的農田而變得非常富有，他有一位年輕漂亮的妻子，在威尼斯郊外有一棟帶自己劇院的別墅。他喜歡舉辦派對。但當他年近四十時，他發現自己患有“一系列虛弱症狀”，正如他所說的那樣——胃痛、體重增加和持續口渴，這是早期糖尿病的典型症狀。

The cause was obvious: too much feasting. The cure was also obvious: knock off the huge meals and parties, his doctors advised him. Not-Thin Luigi balked. He didn't want to give up his lavish lifestyle. But as his symptoms became more and more unbearable, he realized that he had to make a hard course correction or he would never get to see his young daughter grow up. Summoning all his willpower, he cut himself back to a Spartan diet that consisted of about twelve ounces of food per day, typically in the form of some sort of chicken-based stew. It was nourishing, but not overly filling. "[I] constantly rise from the table with a disposition to eat and drink still more," he wrote later.

原因很明顯：吃太飽了。治療方法也很明顯：醫生建議他停止大餐和聚會。不瘦的路易吉猶豫了。他不想放棄自己奢華的生活方式。但隨著他的症狀變得越來越難以忍受，他意識到他必須做出艱難的調整，否則他將永遠無法看到他的小女兒長大。他用盡全力，恢復了斯巴達式的飲食習慣，每天攝取約十二盎司的食物，通常是某種以雞肉為主的燉菜。它很有營養，但又不過分飽足。「[我]不斷地從餐桌上站起來，想要吃得更多、喝得更多，」他後來寫道。

After a year on this regimen, Cornaro's health had improved dramatically. As he put it, "I found myself...entirely freed from all my complaints." He stuck to the diet, and by the time he reached his eighties he was so thrilled to have lived so long in such good health that he felt compelled to share his secret with the world. He penned an autobiographical tract that he called "Discourses on the Sober Life," although it was emphatically not a teetotaler's screed, for he washed down his longevity stew with two generous glasses of wine each day.

在採用這種療法一年後，科納羅的健康狀況有了顯著改善。正如他所說，“我發現自己……完全擺脫了所有的抱怨。”他堅持節食，當他八十多歲的時候，他為自己能健康地活了這麼久而感到非常興奮，以至於他覺得有必要與世界分享他的秘密。他寫了一本自傳小冊子，他稱之為《清醒生活的論述》，儘管這顯然不是滴酒不沾的長篇大論，因為他每天都會用兩杯慷慨的葡萄酒來喝下他的長壽燉菜。

Cornaro's prescriptions lived on long after he died in 1565. His book was

reprinted in several languages over the next few centuries, lauded by Benjamin Franklin, Thomas Edison, and other luminaries, making it perhaps the first bestselling diet book in history. But it was not until the mid-twentieth century that scientists would begin rigorously testing Cornaro's notion that eating less can lengthen one's life (or at least, the lives of laboratory animals).

科納羅的處方在他於1565 年去世後很長一段時間內一直存在。在接下來的幾個世紀裡，他的書以多種語言重印，受到本傑明·富蘭克林、托馬斯·愛迪生和其他名人的稱讚，這使得它可能成為歷史上第一本暢銷的飲食書。但直到二十世紀中葉，科學家才開始嚴格檢驗科納羅的觀點，即少吃可以延長人類的壽命（或至少是實驗動物的壽命）。

We're not talking about simply putting animals on Weight Watchers. Caloric restriction without malnutrition, commonly abbreviated as CR, is a precise experimental method where one group of animals (the controls) are fed *ad libitum*, meaning they eat as much as they want, while the experimental group or groups are given a similar diet containing all the necessary nutrients but 25 or 30 percent fewer total calories (more or less). The restricted animals are then compared against the controls.

我們不是在談論簡單地將動物放在慧儷輕體上。無營養不良的熱量限制，通常縮寫為CR，是一種精確的實驗方法，其中一組動物（對照組）隨意餵養，這意味著它們想吃多少就吃多少，而實驗組或實驗組則給予類似的飲食，其中包含所有必要的營養素，但總熱量減少 25% 或 30%（或多或少）。然後將限制動物與對照動物進行比較。

The results have been remarkably consistent. Studies dating back to the 1930s have found that limiting caloric intake can lengthen the lifespan of a mouse or a rat by anywhere from 15 to 45 percent, depending on the age of onset and degree of restriction. Not only that, but the underfed animals also seem to be markedly healthier for their age, developing fewer spontaneous tumors than normally fed mice. CR seems to improve their healthspan in addition to their lifespan. You'd think that hunger might be unhealthy, but the scientists have actually found that the less they feed the animals, the longer they live. Its effects seem to be dose dependent, up to a point, almost like a drug.

結果非常一致。追溯到 20 世紀 30 年代的研究發現，限制熱量攝取可以將小鼠或大鼠的壽命延長 15% 至 45%，具體取決於發病年齡和限制程度。不僅如此，與正常餵食的小鼠相比，餵食不足的小鼠似乎也明顯更健康，自發性腫瘤的發生率也更低。CR 似乎除了延長壽命之外還可以改善他們的健康狀況。你可能會認為飢餓可能不健康，但科學家實際上發現，餵食動物越少，它們的壽命就越長。它的作用似乎是劑量依賴性的，在某種程度上，幾乎就像藥物一樣。

The life-extending effect of CR seems to be almost universal. Numerous labs have found that restricting caloric intake lengthens lifespan not only in rats and mice (usually) but also in yeast, worms, flies, fish, hamsters, dogs, and even, weirdly, spiders. It has been found to extend lifespan in just about every model organism on which it has been tried, with the odd exception of houseflies. It seems that, across the board, hungry animals become more resilient and better able to survive, at least inside a well-controlled, germ-free laboratory.

CR 的延長壽命效果似乎幾乎是普遍的。許多實驗室發現，限制熱量攝取不僅可以延長大鼠和小鼠的壽命（通常），還可以延長酵母、蠕蟲、蒼蠅、魚、倉鼠、狗，甚至奇怪的是蜘蛛的壽命。人們發現，幾乎所有嘗試過它的模型生物都可以延長其壽命，但家蠅除外。總的來說，飢餓的動物似乎變得更有彈性，更有能力生存，至少在控制良好的無菌實驗室內是如此。

That doesn't mean that I will be recommending this kind of radical caloric restriction as a tactic for my patients, however. For one, CR's usefulness remains doubtful outside of the lab; very lean animals may be more susceptible to death from infection or cold temperatures. And while eating a bit less worked for Luigi Cornaro, as well as for some of my own patients, long-term severe caloric restriction is difficult if not impossible for most humans to sustain. Furthermore, there is no evidence that extreme CR would truly maximize the longevity function in an organism as complex as we humans, who live in a more variable environment than the animals described above. While it seems likely that it would reduce the risk of succumbing to at

least some of the Horsemen, it seems equally likely that the uptick in mortality due to infections, trauma, and frailty might offset those gains.

然而，這並不意味著我會推薦這種徹底的熱量限製作為我的患者的策略。其一，CR 的實用性在實驗室之外仍值得懷疑；非常瘦的動物可能更容易因感染或寒冷而死亡。雖然少吃一點對路易吉·科納羅（Luigi Cornaro）以及我自己的一些患者來說是有效的，但對大多數人來說，長期嚴格的熱量限制即使不是不可能，也是很困難的。此外，沒有證據表明極端 CR 能夠真正最大限度地提高像我們人類這樣複雜的有機體的長壽功能，因為我們人類生活在比上述動物更加多變的環境中。雖然這似乎可能會降低至少部分天啟騎士的死亡風險，但由於感染、創傷和虛弱導致死亡率的上升也可能抵消這些益處。

The real value of caloric restriction research lies in the insights it has contributed to our understanding of the aging process itself. CR studies have helped to uncover critical cellular mechanisms related to nutrients and longevity. Reducing the amount of nutrients available to a cell seems to trigger a group of innate pathways that enhance the cell's stress resistance and metabolic efficiency—all of them related, in some way, to mTOR.

熱量限制研究的真正價值在於它有助於我們理解老化過程本身。CR 研究有助於揭示與營養和壽命相關的關鍵細胞機制。減少細胞可用的營養物質似乎會觸發一組增強細胞抗應激能力和代謝效率的先天途徑——所有這些途徑在某種程度上都與 mTOR 有關。

The first of these is an enzyme called AMP-activated protein kinase, or AMPK for short. AMPK is like the low-fuel light on the dashboard of your car: when it senses low levels of nutrients (fuel), it activates, triggering a cascade of actions. While this typically happens as a response to lack of nutrients, AMPK is also activated when we exercise, responding to the transient drop in nutrient levels. Just as you would change your itinerary if your fuel light came on, heading for the nearest gas station rather than Grandma's house, AMPK prompts the cell to conserve and seek alternative sources of energy.

第一種是一種稱為 AMP 活化蛋白激酶（AMP 活化蛋白激酶）的酶，簡稱 AMPK。AMPK 就像汽車儀表板上的低燃油燈：當它檢測到營養物質（燃油）水平較低時，它就會激活，引發一系列操作。雖然這通常是對營養缺乏的反應，但當我們運動時，AMPK 也會被激活，對營養水平的短暫下降做出反應。就像如果你的燃油燈亮起你會改變你的行程，前往最近的加油站而不是奶奶家一樣，AMPK 會提示細胞節約並尋找替代能源。

It does this first by stimulating the production of new mitochondria, the tiny organelles that produce energy in the cell, via a process called mitochondrial biogenesis. Over time—or with disuse—our mitochondria become vulnerable to oxidative stress and genomic damage, leading to dysfunction and failure. Restricting the amount of nutrients that are available, via dietary restriction or exercise, triggers the production of newer, more efficient mitochondria to replace old and damaged ones. These fresh mitochondria help the cell produce more ATP, the cellular energy currency, with the fuel it does have. AMPK also prompts the body to provide more fuel for these new mitochondria, by producing glucose in the liver (which we'll talk about in the next chapter) and releasing energy stored in fat cells.

它首先透過刺激新粒線體的產生來實現這一點，粒線體是細胞中產生能量的微小細胞器，透過稱為粒線體生物發生的過程。隨著時間的推移或廢棄，我們的粒線體變得容易受到氧化壓力和基因組損傷的影響，從而導致功能障礙和失敗。透過飲食限制或運動來限制可用營養物質的量，會引發更新、更有效的粒線體的產生，以取代舊的和受損的粒線體。這些新鮮的粒線體幫助細胞利用其現有的燃料產生更多的 ATP（細胞能量貨幣）。AMPK 也透過在肝臟中產生葡萄糖（我們將在下一章中討論）並釋放脂肪細胞中儲存的能量，促使身體為這些新粒線體提供更多燃料。

More importantly, AMPK works to inhibit the activity of mTOR, the cellular growth regulator. Specifically, it seems to be a drop in amino acids that induces mTOR to shut down, and with it all the anabolic (growth) processes that mTOR controls. Instead of making new proteins and undergoing cell division, the cell goes into a more fuel-efficient and stress-

resistant mode, activating an important cellular recycling process called *autophagy*, which means “self-eating” (or better yet, “self-devouring”).

更重要的是，AMPK 可以抑制細胞生長調節劑 mTOR 的活性。具體來說，似乎是氨基酸的減少導致 mTOR 關閉，以及 mTOR 控制的所有合成代謝（生長）過程。細胞不再製造新的蛋白質並進行細胞分裂，而是進入一種更省油、更抗壓的模式，激活一種重要的細胞回收過程，稱為自噬，這意味著「自我吞噬」（或更好的是「自我吞噬」）」）。

Autophagy represents the catabolic side of metabolism, when the cell stops producing new proteins and instead begins to break down old proteins and other cellular structures into their amino acid components, using the scavenged materials to build new ones. It's a form of cellular recycling, cleaning out the accumulated junk in the cell and repurposing it or disposing of it. Instead of going to Home Depot to buy more lumber and drywall and screws, the cellular “contractor” scavenges through the debris from the house he just tore down for spare materials that he can reuse, either to build and repair the cell or to burn to produce energy.

自噬作用代表新陳代謝的分解代謝方面，即細胞停止產生新蛋白質，而是開始將舊蛋白質和其他細胞結構分解為其氨基酸成分，並使用清除的材料構建新蛋白質。這是細胞回收的一種形式，清除細胞中積累的垃圾並重新利用或處理掉它。蜂巢「承包商」沒有去家得寶購買更多的木材、乾牆和螺絲，而是從他剛剛拆毀的房子的廢墟中尋找可以重複使用的備用材料，要么用於建造和修復細胞，要么燃燒成燃料。產生能量。

Autophagy is essential to life. If it shuts down completely, the organism dies. Imagine if you stopped taking out the garbage (or the recycling); your house would soon become uninhabitable. Except instead of trash bags, this cellular cleanup is carried out by specialized organelles called lysosomes, which package up the old proteins and other detritus, including pathogens, and grind them down (via enzymes) for reuse. In addition, the lysosomes also break up and destroy things called aggregates, which are clumps of damaged proteins that accumulate over time. Protein aggregates have been implicated

in diseases such as Parkinson's and Alzheimer's disease, so getting rid of them is good; impaired autophagy has been linked to Alzheimer's disease-related pathology and also to amyotrophic lateral sclerosis (ALS), Parkinson's disease, and other neurodegenerative disorders. Mice who lack one specific autophagy gene succumb to neurodegeneration within two to three months.

自噬對於生命至關重要。如果它完全關閉，生物體就會死亡。想像一下，如果您停止倒垃圾（或回收）；你的房子很快就會變得無法居住。除了不是垃圾袋之外，這種細胞清理是由稱為溶酶體的特殊細胞器進行的，它包裝舊的蛋白質和其他碎屑，包括病原體，並將它們磨碎（通過酶）以供再利用。此外，溶小體還會分解和破壞稱為聚集體的物質，這些聚集體是隨著時間的推移而累積的受損蛋白質團塊。蛋白質聚集體與帕金森氏症和阿茲海默症等疾病有關，因此擺脫它們是有好處的。自噬受損與阿茲海默症相關的病理學以及肌萎縮側索硬化症（ALS）、帕金森氏症和其他神經退化性疾病有關。缺乏一種特定自噬基因的小鼠會在兩到三個月內死於神經退化。

By cleansing our cells of damaged proteins and other cellular junk, autophagy allows cells to run more cleanly and efficiently and helps make them more resistant to stress. But as we get older, autophagy declines. Impaired autophagy is thought to be an important driver of numerous aging-related phenotypes and ailments, such as neurodegeneration and osteoarthritis. Thus, I find it fascinating that this very important cellular mechanism can be triggered by certain kinds of interventions, such as a temporary reduction in nutrients (as when we are exercising or fasting)—and the drug rapamycin. (The Nobel Committee shares this fascination, having awarded the 2016 Nobel Prize in Physiology or Medicine to Japanese scientist Yoshinori Ohsumi for his work in elucidating the genetic regulation of autophagy.)

透過清除細胞中受損的蛋白質和其他細胞廢棄物，自噬作用使細胞能夠更清潔、更有效率地運行，並有助於增強它們對壓力的抵抗力。但隨著年齡的增長，自噬能力會下降。自噬受損被認為是許多與老化相關的表型和疾病（例如神經退化和骨關節炎）的重要驅動因素。因此，我覺得很有趣的是，這種非常重要的細胞機制可以透過某些類型的干預措施來觸發，例如暫時減少營養物質（如我們運動或禁食時）

以及藥物雷帕黴素。（諾貝爾委員會也同樣著迷，將 2016 年諾貝爾生理學或醫學獎授予日本科學家大隅良典，以表彰他在闡明白噬基因調控方面的工作。）

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Yet its autophagy-promoting effect is only one reason why rapamycin may have a future as a longevity drug, according to Matt Kaeberlein, a researcher at the University of Washington. Kaeberlein, who has been studying rapamycin and mTOR for a couple of decades, believes that the drug's benefits are much more wide-ranging and that rapamycin and its derivatives have huge potential for use in humans, for the purpose of extending lifespan and healthspan.

然而，華盛頓大學研究員 Matt Kaeberlein 表示，其促進自噬作用的作用只是雷帕黴素可能成為長壽藥物的原因之一。Kaeberlein 幾十年來一直在研究雷帕黴素和 mTOR，他認為該藥物的益處更為廣泛，並且雷帕黴素及其衍生物在人類中具有巨大的應用潛力，可延長壽命和健康壽命。

Even though rapamycin is already approved for use in humans for multiple indications, there are formidable obstacles to launching a clinical trial to look at its possible impact on human aging—mainly, its potential side effects in healthy people, most notably the risk of immunosuppression.

儘管雷帕黴素已被批准用於人類的多種適應症，但啟動臨床試驗來研究其對人類老化可能產生的影響仍然存在巨大的障礙，主要是其對健康人的潛在副作用，最明顯的是免疫抑制的風險。

Historically, rapamycin was approved to treat patients indefinitely following organ transplantation, as part of a cocktail of three or four drugs meant to suppress the part of their immune system that would otherwise attack and destroy their new organ. This immune-suppressing effect explains why there has been some reluctance to consider using (or even studying) rapamycin in the context of delaying aging in healthy people, despite ample animal data suggesting that it might lengthen lifespan and healthspan. Its purported

immune-suppressing effects just seemed to be too daunting to overcome. Thus, it has seemed unlikely that rapamycin could ever realize its promise as a longevity-promoting drug for humans.

從歷史上看，雷帕黴素被批准用於在器官移植後無限期地治療患者，作為三到四種藥物的混合物的一部分，旨在抑制免疫系統的一部分，否則會攻擊和破壞他們的新器官。這種免疫抑製作用解釋了為什麼人們不願意考慮使用（甚至研究）雷帕黴素來延緩健康人的衰老，儘管大量的動物數據表明它可能會延長壽命和健康壽命。它所謂的免疫抑製作用似乎難以克服。因此，雷帕黴素似乎不太可能實現其作為人類長壽藥物的承諾。

But all that started to change in late December 2014 with the publication of a study showing that the rapamycin analog everolimus actually *enhanced* the adaptive immune response to a vaccine in a group of older patients. In the study, led by scientists Joan Mannick and Lloyd Klickstein, who then worked at Novartis, the group of patients on a moderate weekly dose of everolimus seemed to have the best response to the flu vaccine, with the fewest reported side effects. This study suggested that rapamycin (and its derivatives) might actually be more of an immune *modulator* than an “immunosuppressor,” as it had almost always been described before this study: that is, under some dosing regimens it can enhance immunity, while under completely different dosing regimens it may inhibit immunity.

但這一切在 2014 年 12 月下旬開始發生變化，一項研究的發表表明，雷帕黴素類似物依維莫司實際上增強了一組老年患者對疫苗的適應性免疫反應。在這項由當時在諾華工作的科學家瓊·曼尼克(Joan Mannick)和勞埃德·克里克斯坦(Lloyd Klickstein)領導的研究中，每週服用適量依維莫司的患者組似乎對流感疫苗反應最好，報告的副作用也最少。這項研究表明，雷帕黴素（及其衍生物）實際上可能更像是一種免疫調節劑，而不是“免疫抑製劑”，因為在這項研究之前幾乎總是描述它：也就是說，在某些給藥方案下，它可以增強免疫力，而在完全給藥方案下，它可以增強免疫力。不同的給藥方案可能會抑制免疫力。

Until this study appeared, I (like many others) had largely given up on the possibility that rapamycin could ever be used as a preventive therapy in

healthy people. I had assumed that its apparent immunosuppressive effects were too serious. But this very well-done and well-controlled study actually suggested the opposite. It appeared that the immune suppression resulted from daily use of rapamycin at low to moderate doses. The study subjects had been given moderate to high doses followed by a rest period, and this cyclical administration had had an opposite, immune-enhancing effect.

在這項研究出現之前，我（和許多其他人一樣）基本上放棄了雷帕黴素可以用作健康人預防性治療的可能性。我原以為它明顯的免疫抑制作用太嚴重了。但這項非常出色且控制良好的研究實際上顯示了相反的結果。看來免疫抑制是因為每天使用低至中等劑量的雷帕黴素所造成的。研究對象接受了中等到高劑量的治療，然後休息一段時間，這種週期性給藥產生了相反的免疫增強作用。

It seems odd that giving different doses of the same drug could have such disparate effects, but it makes sense if you understand the structure of mTOR, which is actually composed of two separate complexes, called mTOR complex 1 (mTORC1) and mTOR complex 2 (mTORC2). The two complexes have different jobs, but (at risk of oversimplifying) the longevity-related benefits seem to result from inhibiting complex 1. Giving the drug daily, as is typically done with transplant patients, appears to inhibit both complexes, while dosing the drug briefly or cyclically inhibits mainly mTORC1, unlocking its longevity-related benefits, with fewer unwanted side effects. (A rapamycin analog or “rapalog” that selectively inhibited mTORC1 but not mTORC2 would thus be more ideal for longevity purposes, but no one has successfully developed one yet.)

給予不同劑量的同一種藥物可能會產生如此不同的效果，這似乎很奇怪，但如果您了解mTOR 的結構，那就有意義了，它實際上由兩個獨立的複合物組成，稱為mTOR 複合物1 (mTORC1) 和mTOR 複合物2 (mTORC2)。這兩種複合物有不同的作用，但（有過於簡單化的風險）與長壽相關的益處似乎是抑制複合物1 的結果。每天給藥（就像通常對移植患者所做的那樣）似乎可以抑制這兩種複合物，同時給藥主要短暫或週期性地抑制 mTORC1，釋放其與長壽相關的益處，同時減少不良副作用。（因此，選擇性抑制 mTORC1 但不抑制 mTORC2

的雷帕黴素類似物或「雷帕黴素類似物」對於延長壽命而言更為理想，但目前尚未成功開發出這種藥物。）

As it is, its known side effects remain an obstacle to any clinical trial of rapamycin for geroprotection (delaying aging) in healthy people. To get around these objections, Kaeberlein is doing a large clinical trial of rapamycin in companion (pet) dogs, which are not a bad proxy for humans—they're large, they're mammals, they share our environment, and they age in ways similar to us. In a preliminary phase of this study, which he calls the Dog Aging Project, Kaeberlein found that rapamycin actually seemed to improve cardiac function in older animals. "One thing that's been surprising to me," he says, "is the different ways that rapamycin not only seems to delay the decline but seems to make things better. There clearly seems to be, at least in some organs, a rejuvenating function."

事實上，其已知的副作用仍然是雷帕黴素對健康人進行老年保護（延緩衰老）的任何臨床試驗的障礙。為了解決這些反對意見，Kaeberlein 正在伴侶（寵物）狗身上進行雷帕黴素的大型臨床試驗，這些狗對人類來說並不是一個壞的代表——它們體型龐大，是哺乳動物，與我們共享環境，並且在方式與我們相似。在這項被他稱為「狗老化計畫」的研究的初步階段，Kaeberlein 發現雷帕黴素實際上似乎可以改善老年動物的心臟功能。「令我驚訝的一件事是，」他說，「雷帕黴素不僅可以以不同的方式延緩衰退，而且似乎可以使情況變得更好。至少在某些器官中，顯然似乎具有恢復活力的功能。」

Kaeberlein has also observed that rapamycin seems to reduce systemic inflammation, perhaps by tamping down the activity of so-called senescent cells, which are "older" cells that have stopped dividing but have not died; these cells secrete a toxic cocktail of inflammatory cytokines, chemicals that can harm surrounding cells. Rapamycin seems to reduce these inflammatory cytokines. It also improves cancer surveillance, the ways in which our body, most likely the immune system, detects and eliminates cancer cells. In another recent study, Kaeberlein's group found that rapamycin appeared to improve periodontal (gum) health in older dogs.

Kaeberlein 也觀察到，雷帕黴素似乎可以減少全身炎症，這可能是透過

抑制所謂的衰老細胞的活性來實現的，這些細胞是已經停止分裂但尚未死亡的「較老」細胞。這些細胞會分泌一種有毒的發炎細胞激素混合物，這些化學物質會傷害周圍的細胞。雷帕黴素似乎可以減少這些發炎細胞激素。它還改善了癌症監測，即我們的身體（很可能是免疫系統）檢測和消除癌細胞的方式。在最近的另一項研究中，Kaeberlein的研究團隊發現雷帕黴素似乎可以改善老年犬的牙周（牙齦）健康。

The main phase of the Dog Aging Project, involving some 600 pet dogs, is now under way; results from this larger clinical trial are expected in 2026. (Disclosure: I am a partial funder of this research.) The dogs in this study are also following a weekly, cyclical dosing schedule with rapamycin, similar to the protocol in the 2014 immune study in humans. If the results are positive, it would not surprise me if the use of rapamycin for longevity purposes becomes more common. A small but growing number of people, including me and a handful of my patients, already take rapamycin off-label for its potential geroprotective benefits. I can't speak for everyone, but taking it cyclically does appear to reduce unwanted side effects, in my experience.

涉及約600隻寵物狗的狗老化計畫的主要階段目前正在進行中；這項更大規模的臨床試驗預計將於2026 年得出結果。（披露：我是這項研究的部分資助者。）這項研究中的狗也遵循每週、週期性的雷帕黴素給藥物方案，類似2014 年免疫研究中的方案在人類。如果結果是正面的，那麼如果雷帕黴素用於長壽目的變得更加普遍，我不會感到驚訝。包括我和我的幾位患者在內的一小部分人（包括我和我的少數患者）已經因為雷帕黴素潛在的老年保護功效而在標籤外服用雷帕黴素。我不能代表所有人，但根據我的經驗，週期性服用似乎確實可以減少不必要的副作用。

Even so, the hurdles it would have to clear to gain approval for broader human use remain daunting. The vast majority of people who currently take rapamycin comprise transplant patients who already have serious health issues and multiple comorbidities. In populations like this, rapamycin's side effects seem less significant than they might in healthier people.

即便如此，要獲得更廣泛的人類用途的批准，它必須克服的障礙仍然令人畏懼。目前服用雷帕黴素的絕大多數人都是已經有嚴重健康問題

和多種合併症的移植患者。在這樣的族群中，雷帕黴素的副作用似乎沒有在健康族群中那麼顯著。

“There is a very low tolerance for side effects, by the public and by regulatory agencies, if you’re talking about treating a healthy person,” says Kaeberlein. “The intent is to slow aging in people before they get sick, to keep them healthy longer, so in many ways it is the opposite of the traditional biomedical approach, where normally we wait until people are sick and then we try to cure their diseases.”

「如果你談論的是治療健康人，公眾和監管機構對副作用的容忍度非常低，」Kaeberlein 說。「其目的是在人們生病之前減緩衰老，讓他們保持更長時間的健康，所以在很多方面它與傳統的生物醫學方法相反，傳統的生物醫學方法通常我們等到人們生病了，然後我們嘗試治愈他們的疾病」。

The real obstacle here is a regulatory framework rooted in Medicine 2.0, which does not (yet) recognize “slowing aging” and “delaying disease” as fully legitimate end points. This would represent a Medicine 3.0 use for this drug, where we would be using a drug to help healthy people stay healthy, rather than to cure or relieve a specific ailment. Thus, it would face much more scrutiny and skepticism. But if we’re talking about preventing the diseases of aging, which kill 80 percent of us, then it’s certainly worth having a serious conversation about what level of risk is and isn’t acceptable in order to achieve that goal. Part of my aim in writing this book is to move that conversation forward.

這裡真正的障礙是植根於醫學 2.0 的監管框架，它尚未將「延緩老化」和「延緩疾病」視為完全合法的終點。這代表了該藥物的醫學 3.0 用途，我們將使用藥物來幫助健康人保持健康，而不是治癒或緩解特定疾病。因此，它將面臨更多的審查和懷疑。但如果我們談論的是預防導致 80% 人死亡的衰老疾病，那麼為了實現這一目標，認真討論什麼程度的風險是可以接受的，什麼是不可以接受的，這當然是值得的。我寫這本書的部分目的是推動這場對話的發展。

This may already be starting to happen. The FDA has given the green light for a clinical trial of another drug with potential longevity benefits, the diabetes medication metformin. This trial is called TAME (Targeting Aging with Metformin), and it came about in a very different way. Metformin has been taken by millions of people for years. Over time, researchers noticed (and studies appeared to confirm) that patients on metformin appeared to have a lower incidence of cancer than the general population. One large 2014 analysis seemed to show that diabetics on metformin actually lived longer than nondiabetics, which is striking. But none of these observations “prove” that metformin is geroprotective—hence the need for a clinical trial.

這可能已經開始發生。FDA 已經批准了另一種具有潛在長壽功效的藥物——糖尿病藥物二甲雙胍的臨床試驗。這項試驗被稱為 TAME（二甲雙胍靶向衰老），它以一種非常不同的方式進行。多年來，已有數百萬人服用二甲雙胍。隨著時間的推移，研究人員注意到（並且研究似乎證實）服用二甲雙胍的患者的癌症發生率似乎低於一般人群。2014 年的一項大型分析似乎表明，服用二甲雙胍的糖尿病患者實際上比非糖尿病患者壽命更長，這一點令人震驚。但這些觀察結果都沒有「證明」二甲雙胍具有老年保護作用，因此需要進行臨床試驗。

But aging itself is difficult—if not impossible—to measure with any accuracy. Instead, TAME lead investigator Nir Barzilai, whom we met in the previous chapter, decided to look at a different endpoint: whether giving metformin to healthy subjects delays the onset of aging-related diseases, as a proxy for its effect on aging. I’m hopeful that someday, maybe in the near future, we could attempt a similar human trial of rapamycin, which I believe has even greater potential as a longevity-promoting agent.^[*3]

但老化本身即使不是不可能，也很難準確地測量。相反，我們在上一章遇到的 TAME 首席研究員 Nir Barzilai 決定研究一個不同的終點：給健康受試者服用二甲雙胍是否會延遲與衰老相關的疾病的發作，作為其對衰老影響的代理。我希望有一天，也許在不久的將來，我們可以嘗試進行類似的雷帕黴素人體試驗，我相信雷帕黴素作為長壽劑具有更大的潛力。^[*3]

For the moment, though, let’s think about the fact that *all* of what we’ve

talked about in this chapter, from mTOR and rapamycin to caloric restriction, points in one direction: that what we eat and how we metabolize it appear to play an outsize role in longevity. In the next chapter, we will take a much more detailed look at how metabolic disorders help to instigate and promote chronic disease.

不過，目前讓我們考慮一下這樣一個事實：我們在本章中討論的所有內容，從mTOR 和雷帕黴素到熱量限制，都指向一個方向：我們吃的東西以及我們如何代謝它似乎發揮著一種影響。對長壽有著巨大的作用。在下一章中，我們將更詳細地了解代謝紊亂如何幫助引發和促進慢性疾病。

SKIP NOTES

跳過註釋

*1 A drug analog is a compound with similar but not identical molecular structure; e.g., oxycodone is an analog of codeine.

*1 藥物類似物是分子結構相似但不相同的化合物；例如，經考酮是可待因的類似物。

*2 This is where the nomenclature gets a bit confusing. Briefly, the drug rapamycin blocks or inhibits the activity of mTOR, mechanistic target of rapamycin, the protein complex found in cells. Adding to the confusion, mTOR was originally called *mammalian target of rapamycin*, to distinguish it from a version of *target of rapamycin*, TOR, that had first been discovered in yeast. TOR and mTOR are essentially the same, meaning this same basic mechanism is found up and down the tree of life, across a billion years of evolution.

*2 這是術語有點令人困惑的地方。簡而言之，藥物雷帕黴素阻斷或抑制 mTOR 的活性，mTOR 是雷帕黴素（細胞中發現的蛋白質複合物）的機制標靶。更令人困惑的是，mTOR 最初被稱為哺乳動物雷帕黴素靶點，以區別於雷帕黴素靶點 TOR，後者最初是在酵母中發現的。TOR 和 mTOR 本質上是相同的，這意味著在生命之樹上和下，經過十億年的進化，發現了相同的基本機制。

*3 Before leaving Rapa Nui, the four of us vowed to replace the missing plaque honoring the discovery of rapamycin with a new one saluting the island's unique contribution to molecular biology and the role of Suren Sehgal in preserving and elucidating the importance of this molecule.

*3 在離開拉帕努伊島之前，我們四人發誓要更換一塊新的紀念牌，紀念雷帕黴素的發現，以致敬該島對分子生物學的獨特貢獻，以及蘇倫·塞加爾(Suren Sehgal) 在保存和闡明該分子的重要性方面所發揮的作用。

CHAPTER 6

第 6 章

The Crisis of Abundance

豐富的危機

Can Our Ancient Genes Cope with Our Modern Diet?

我們古老的基因能適應我們現代的飲食嗎？

Avoidable human misery is more often caused not so much by stupidity as by ignorance, particularly our ignorance about ourselves.

本來可以避免的人類苦難更多不是由愚蠢造成的，而是由無知造成的，尤其是我們對自己的無知。

—CARL SAGAN

——卡爾·薩根

When it comes to managing junior surgical residents, there is a sort of unwritten rule that Hippocrates might have stated as follows: *First, let them do no harm.* That rule was in full effect during my early months at Johns Hopkins, in 2001, on the surgical oncology service. We were removing part of a patient's cancerous ascending colon, and one of my jobs was to "pre-op" him, which was basically like a briefing/semi-interrogation the day before surgery to be sure we knew everything that we needed to know about his medical history.

在管理初級外科住院醫生時，有一條希波克拉底可能說過的不成文的規則：首先，不要讓他們造成傷害。2001 年，我在約翰霍普金斯大學腫瘤外科服務部工作的最初幾個月裡，這條規則完全生效。我們正在切除患者的部分癌性升結腸，我的工作之一就是為他進行“術前準備”，這基本上就像手術前一天的簡報/半審訊，以確保我們知道我們需要知道的一切關於他的病史。

I met with this patient and outlined the procedure he was about to undergo, reminded him not to eat anything after 8 p.m., and asked him a series of routine questions, including whether or not he smoked and how much alcohol he drank. I had practiced asking this last one in a disarming, seemingly offhand way, but I knew it was among the most important items on my checklist. If we believed that a patient consumed significant amounts of alcohol (typically more than four or five drinks per day), we had to make sure that the anesthesiologists knew this, so they could administer specific drugs during recovery, typically benzodiazepines such as Valium, in order to ward off alcohol withdrawal. Otherwise, the patient could be at risk for delirium tremens, or the DTs, a potentially fatal condition.

我會見了這位患者，概述了他即將接受的手術，提醒他晚上 8 點之後不要吃任何東西，並問了他一系列常規問題，包括他是否吸煙、喝了多少酒。我已經練習過以一種令人放鬆的、看似隨意的方式詢問最後一個問題，但我知道這是我清單上最重要的項目之一。如果我們認為患者飲酒量很大（通常每天超過四杯或五杯），我們必須確保麻醉師知道這一點，以便他們可以在恢復期間服用特定藥物，通常是苯二氮

平類藥物，例如安定，以防止酒精戒斷。否則，患者可能面臨震顫性譫妄（DT）的風險，這是一種潛在的致命疾病。

I was relieved when he told me that he drank minimally. One less thing to worry about. The next day, I wheeled the patient into the OR and ran my checklist of mundane intern-level stuff. It would take a few minutes for the anesthesiologists to put him to sleep, after which I could place the Foley catheter into his bladder, swab his skin with Betadine, place the surgical drapes, and then step aside while the chief resident and attending surgeon made the first incision. If I was lucky, I would get to assist with the opening and closing of the abdomen. Otherwise, I was there to retract the liver, holding it out of the way so the senior surgeons could have an unobstructed view of the organ they needed to remove, which was sort of tucked in underneath the liver.

當他告訴我他喝得很少時，我鬆了一口氣。少了一件需要擔心的事。第二天，我把病人推進手術室，並檢查了我實習生的日常事務清單。麻醉師需要幾分鐘的時間才能讓他入睡，之後我可以將 Foley 導管插入他的膀胱，用 Betadine 擦拭他的皮膚，放置手術單，然後退到一邊，等待住院醫師和主治外科醫生進行手術。第一個切口。如果幸運的話，我可以協助打開和關閉腹部。否則，我會在那裡縮回肝臟，將其放在一邊，以便高級外科醫生可以無障礙地看到他們需要切除的器官，有點藏在肝臟下方。

As the surgery got under way, nothing seemed out of the ordinary. The surgeons had to make their way through a bit of abdominal fat before they could get to the peritoneal cavity, but nothing we didn't see most days. There is an incredible rush of anticipation one feels just before cutting through the last of several membranes separating the outside world from the inner abdominal cavity. One of the first things you see, as the incision grows, is the tip of the liver, which I've always considered to be a really underappreciated organ. The "cool kids" in medicine specialize in the brain or the heart, but the liver is the body's true workhorse—and also, it's simply breathtaking to behold. Normally, a healthy liver is a deep, dark purple color, with a gorgeous

silky-smooth texture. Hannibal Lecter was not too far off: it really does look as if it might be delicious with some fava beans and a nice Chianti.

隨著手術的進行，似乎沒有什麼異常。外科醫生必須穿過一些腹部脂肪才能到達腹膜腔，但大多數時候我們都沒有看到任何東西。在切開分隔外界與腹腔內部的最後幾層膜之前，人們會感到一種令人難以置信的期待感。隨著切口的增大，你首先看到的東西之一就是肝臟的尖端，我一直認為這是一個真正被低估的器官。醫學上的「酷孩子」專門研究大腦或心臟，但肝臟才是人體真正的主力——而且，它的外觀簡直令人驚嘆。通常，健康的肝臟呈現深紫色，具有華麗絲般光滑的質地。漢尼拔·萊克特 (Hannibal Lecter) 的想法並不遙遠：它看起來確實很美味，配上一些蠶豆和一杯美味的基安蒂酒。

This patient's liver appeared rather less appetizing as it emerged from beneath the omental fat. Instead of a healthy, rich purple, it was mottled and sort of orangish, with protruding nodules of yellow fat. It looked like foie gras gone bad. The attending looked up at me sharply. "You said this guy was not a drinker!" he barked.

這位患者的肝臟從網膜脂肪下方露出來，看起來不太有食慾。它不是健康、濃鬱的紫色，而是斑駁的、有點橙色的，有突出的黃色脂肪結節。看起來就像鵝肝壞了。主治醫生猛地抬頭看著我。“你說這傢伙不喝酒！”他咆哮道。

Clearly, this man was a very heavy drinker; his liver showed all the signs of it. And because I had failed to elicit that information, I had potentially placed his life in danger.

顯然，這個人是個酒鬼。他的肝臟出現了所有的症狀。由於我未能獲得這些信息，我有可能將他的生命置於危險之中。

But it turned out that I hadn't made a mistake. When the patient awoke after surgery, he confirmed that he rarely drank alcohol, if ever. In my experience, patients confronting cancer surgery rarely lied about drinking or anything else, especially when fessing up meant getting some Valium or even better, a couple of beers with their hospital dinner. But he definitely had the liver of an alcoholic, which struck everyone as odd.

但事實證明我沒有看錯。當病人在手術後醒來時，他證實自己很少喝酒，如果有的話。根據我的經驗，接受癌症手術的患者很少會在喝酒或其他事情上撒謊，尤其是當坦白意味著要喝一些安定，甚至更好的是，在醫院晚餐時喝幾杯啤酒時。但他確實有酒鬼的肝臟，這讓每個人都感到奇怪。

This would happen numerous times during my residency. Every time, we would scratch our heads. Little did we know that we were witnessing the beginning, or perhaps the flowering, of a silent epidemic.

在我住院期間，這種情況發生過很多次。每一次，我們都會摸不著頭緒。我們幾乎不知道，我們正在見證一場無聲的流行病的開始，或者也許是它的盛行。

—

Five decades earlier, a surgeon in Topeka, Kansas, named Samuel Zelman had encountered a similar situation: he was operating on a patient whom he knew personally, because the man was an aide in the hospital where he worked. He knew for a fact that the man did not drink any alcohol, so he was surprised to find out that his liver was packed with fat, just like that of my patient, decades later.

五年前，堪薩斯州托皮卡的一位外科醫生塞繆爾·澤爾曼也遇到過類似的情況：他正在為一位他認識的病人做手術，因為這個人是他工作的醫院的助手。他知道這個人沒有喝酒，所以他驚訝地發現他的肝臟充滿了脂肪，就像我的病人幾十年後的肝臟一樣。

This man did, in fact, drink a lot—of Coca-Cola. Zelman knew that he consumed a staggering quantity of soda, as many as twenty bottles (or more) in a single day. These were the older, smaller Coke bottles, not the supersizes we have now, but still, Zelman estimated that his patient was taking in an extra 1,600 calories per day on top of his already ample meals. Among his colleagues, Zelman noted, he was “distinguished for his appetite.”

事實上，這個人確實喝了很多——可口可樂。澤爾曼知道他每天消耗的蘇打水數量驚人，多達二十瓶（或更多）。這些是較舊、較小的可樂瓶，而不是我們現在擁有的超大瓶，但澤爾曼仍然估計，他的病人在已經足夠的膳食之外，每天還要攝入額外的 1,600 卡路里熱量。澤爾曼指出，在他的同事中，他「因其胃口而聞名」。

His curiosity piqued, Zelman recruited nineteen other obese but nonalcoholic subjects for a clinical study. He tested their blood and urine and conducted liver biopsies on them, a serious procedure performed with a serious needle. All of the subjects bore some sign or signs of impaired liver function, in a way eerily similar to the well-known stages of liver damage seen in alcoholics.

澤爾曼的好奇心激起了他，他招募了另外 19 名肥胖但不酗酒的受試者進行臨床研究。他測試了他們的血液和尿液，並對他們進行了肝臟活檢，這是用一支嚴肅的針進行的嚴肅程序。所有受試者都出現了一些肝功能受損的跡象，其方式與已知的酗酒者肝損傷階段非常相似。

This syndrome was often noticed but little understood. It was typically attributed to alcoholism or hepatitis. When it began to be seen in teenagers, in the 1970s and 1980s, worried doctors warned of a hidden epidemic of teenage binge drinking. But alcohol was not to blame. In 1980, a team at the Mayo Clinic dubbed this “hitherto unnamed disease” nonalcoholic steatohepatitis, or NASH. Since then, it has blossomed into a global plague. More than one in four people on this planet have some degree of NASH or its precursor, known as nonalcoholic fatty liver disease, or NAFLD, which is what we had observed in our patient that day in the operating room.

這種綜合症經常被注意到，但了解甚少。這通常歸因於酗酒或肝炎。1970 年代和 1980 年代，當青少年酗酒開始出現時，憂心忡忡的醫生警告說，青少年酗酒是一種隱藏的流行病。但酒精並不是罪魁禍首。1980 年，梅奧診所的一個團隊將這種「迄今為止未命名的疾病」稱為非酒精性脂肪性肝炎（NASH）。從那時起，它就發展成為一場全球性的瘟疫。這個地球上超過四分之一的人患有某種程度的 NASH 或其前

兆，稱為非酒精性脂肪肝病 (NAFLD)，這就是我們當天在手術室中在患者身上觀察到的情況。

NAFLD is highly correlated with both obesity and hyperlipidemia (excessive cholesterol), yet it often flies under the radar, especially in its early stages. Most patients are unaware that they have it—and so are their doctors, because NAFLD and NASH have no obvious symptoms. The first signs would generally show up only on a blood test for the liver enzyme alanine aminotransferase (ALT for short). Rising levels of ALT are often the first clue that something is wrong with the liver, although they could also be a symptom of something else, such as a recent viral infection or a reaction to a medication. But there are many people walking around whose physicians have no idea that they are in the early stages of this disease, because their ALT levels are still “normal.”

NAFLD 與肥胖和高脂血症（膽固醇過多）高度相關，但它經常被忽視，尤其是在早期階段。大多數患者並不知道自己患有這種疾病，他們的醫生也是如此，因為 NAFLD 和 NASH 沒有明顯的症狀。第一個跡象通常只在肝臟酵素丙胺酸轉氨酶（簡稱 ALT）的血液檢查中出現。ALT 值升高通常是肝臟出現問題的第一個線索，儘管它們也可能是其他疾病的症狀，例如最近的病毒感染或對藥物的反應。但有很多人的醫生並不知道他們正處於這種疾病的早期階段，因為他們的 ALT 水平仍然「正常」。

Next question: What is normal? According to Labcorp, a leading testing company, the acceptable range for ALT is below 33 IU/L for women and below 45 IU/L for men (although the ranges can vary from lab to lab). But “normal” is not the same as “healthy.” The reference ranges for these tests are based on current percentiles,^[*1] but as the population in general becomes less healthy, the average may diverge from optimal levels. It’s similar to what has happened with weight. In the late 1970s, the average American adult male weighed 173 pounds. Now the average American man tips the scale at nearly 200 pounds. In the 1970s, a 200-pound man would have been considered very overweight; today he is merely average. So you can see how in the twenty-first century, “average” is not necessarily optimal.

下一個問題：什麼是正常的？根據領先的檢測公司 Labcorp 的說法，女性 ALT 的可接受範圍是低於 33 IU/L，男性低於 45 IU/L（儘管各個實驗室的範圍可能有所不同）。但「正常」並不等於「健康」。這些測試的參考範圍是基於目前的百分位數，[*1]，但隨著整體人口健康狀況的惡化，平均值可能會偏離最佳水準。這與體重發生的情況類似。1970 年代末，美國成年男性的平均體重為 173 磅。現在美國男性的平均體重接近 200 磅。在 20 世紀 70 年代，一個體重 200 磅的男性會被認為非常超重；今天他只是個普通人。所以你可以看到，在二十一世紀，「平均」不一定是最佳的。

With regard to ALT liver values, the American College of Gastroenterology recently revised its guidelines to recommend clinical evaluation for liver disease in men with ALT above 33 and women with ALT above 25—significantly below the current “normal” ranges. Even that may not be low enough: a 2002 study that excluded people who *already* had fatty liver suggested upper limits of 30 for men, and 19 for women. So even if your liver function tests land within the reference range, that does not imply that your liver is actually healthy.

關於 ALT 肝臟值，美國胃腸病學會最近修訂了其指南，建議對 ALT 高於 33 的男性和 ALT 高於 25 的女性（明顯低於目前的「正常」範圍）進行肝臟疾病臨床評估。即使這個數字可能還不夠低：2002 年的一項研究排除了已經患有脂肪肝的人，建議男性的上限為 30，女性的上限為 19。因此，即使您的肝功能測試落在參考範圍內，也不代表您的肝臟實際上是健康的。

NAFLD and NASH are basically two stages of the same disease. NAFLD is the first stage, caused by (in short) more fat entering the liver or being produced there than exiting it. The next step down the metabolic gangplank is NASH, which is basically NAFLD plus inflammation, similar to hepatitis but without a viral infection. This inflammation causes scarring in the liver, but again, there are no obvious symptoms. This may sound scary, but all is not yet lost. Both NAFLD and NASH are still reversible. If you can somehow remove the fat from the liver (most commonly via weight loss), the inflammation will resolve, and liver function returns to normal. The liver is a highly resilient

organ, almost miraculously so. It may be the most regenerative organ in the human body. When a healthy person donates a portion of their liver, both donor and recipient end up with an almost full-sized, fully functional liver within about eight weeks of the surgery, and the majority of that growth takes place in just the first two weeks.

NAFLD 和 NASH 基本上是同一疾病的兩個階段。NAFLD 是第一階段，是由於（簡而言之）進入肝臟或在那裡產生的脂肪多於離開肝臟而引起的。代謝跳板的下一步是 NASH，它基本上是 NAFLD 加上炎症，類似於肝炎，但沒有病毒感染。這種發炎會導致肝臟形成疤痕，但同樣沒有明顯的症狀。這聽起來可能很可怕，但一切都還沒失去。NAFLD 和 NASH 仍然是可逆的。如果您能以某種方式去除肝臟中的脂肪（最常見的是透過減肥），發炎就會消退，肝功能也會恢復正常。肝臟是一個具有高度彈性的器官，這幾乎是個奇蹟。它可能是人體中最具再生能力的器官。當一個健康的人捐獻一部分肝臟時，捐贈者和接受者最終都會在手術後約八週內獲得幾乎全尺寸、功能齊全的肝臟，並且大部分生長發生在前兩週內。

In other words, your liver can recover from fairly extensive damage, up to and including partial removal. But if NASH is not kept in check or reversed, the damage and the scarring may progress into cirrhosis. This happens in about 11 percent of patients with NASH and is obviously far more serious. It now begins to affect the cellular architecture of the organ, making it much more difficult to reverse. A patient with cirrhosis is likely to die from various complications of their failing liver unless they receive a liver transplant. In 2001, when we did the operation on the man with the fatty liver, NASH officially accounted for just over 1 percent of liver transplants in the United States; by 2025, NASH with cirrhosis is expected to be the leading indication for liver transplantation.

換句話說，您的肝臟可以從相當廣泛的損傷中恢復，甚至包括部分切除。但如果 NASH 無法控制或逆轉，損傷和疤痕可能會發展為肝硬化。大約 11% 的 NASH 患者會出現這種情況，而且情況顯然要嚴重得多。現在它開始影響器官的細胞結構，使其更難逆轉。肝硬化患者可能會死於肝臟衰竭的各種併發症，除非接受肝臟移植。2001年，當我

們對一名脂肪肝患者進行手術時，NASH官方數據僅占美國肝臟移植手術的1%多一點；到2025年，伴隨肝硬化的NASH預計將成為肝臟移植的主要適應症。

As devastating as it is, cirrhosis is not the only end point I'm worried about here. I care about NAFLD and NASH—and you should too—because they represent the tip of the iceberg of a global epidemic of metabolic disorders, ranging from insulin resistance to type 2 diabetes. Type 2 diabetes is technically a distinct disease, defined very clearly by glucose metrics, but I view it as simply the last stop on a railway line passing through several other stations, including hyperinsulinemia, prediabetes, and NAFLD/NASH. If you find yourself anywhere on this train line, even in the early stages of NAFLD, you are likely also en route to one or more of the other three Horsemen diseases (cardiovascular disease, cancer, and Alzheimer's disease). As we will see in the next few chapters, metabolic dysfunction vastly increases your risk for all of these. So you can't fight the Horsemen without taking on metabolic dysfunction first.

儘管肝硬化具有毀滅性，但它並不是我擔心的唯一終點。我關心NAFLD和NASH，你也應該關心，因為它們代表了從胰島素抗性到第2型糖尿病等全球流行的代謝性疾病的冰山一角。從技術上講，2型糖尿病是一種獨特的疾病，透過血糖指標非常明確地定義，但我認為它只是鐵路線上的最後一站，途經其他幾個車站，包括高胰島素血症、糖尿病前期和NAFLD/NASH。如果您發現自己處於這條火車線路上的任何地方，即使處於NAFLD的早期階段，您也可能正在患上其他三種騎士疾病（心血管疾病、癌症和阿茲海默症）中的一種或多種。正如我們將在接下來的幾章中看到的，代謝功能障礙會大大增加您罹患所有這些疾病的風險。因此，如果不先解決代謝功能障礙，就無法與天啟騎士作戰。

Notice that I said “metabolic dysfunction” and not “obesity,” everybody's favorite public health bogeyman. It's an important distinction. According to the Centers for Disease Control (CDC), more than 40 percent of the US population is obese (defined as having a BMI[*2] greater than 30), while roughly another third is overweight (BMI of 25 to 30). Statistically, being

obese means someone is at greater risk of chronic disease, so a lot of attention is focused on the “obesity problem,” but I take a broader view: obesity is merely one symptom of an underlying metabolic derangement, such as hyperinsulinemia, that also happens to cause us to gain weight. But not everyone who is obese is metabolically unhealthy, and not everyone who is metabolically unhealthy is obese. There’s more to metabolic health than meets the eye.

請注意，我說的是“代謝功能障礙”，而不是“肥胖”，這是每個人最喜歡的公共衛生怪物。這是一個重要的區別。根據疾病管制中心 (CDC) 的數據，超過 40% 的美國人口肥胖（定義為 BMI [*2] 大於 30），而大約另外三分之一的人超重（BMI 為 25 至 30）。從統計數據來看，肥胖意味著某人患慢性病的風險更大，因此許多注意力都集中在「肥胖問題」上，但我有更廣泛的觀點：肥胖只是潛在代謝紊亂的一種症狀，例如高胰島素血症、這也會導致我們體重增加。但並不是所有肥胖的人都是代謝不健康的，也不是所有代謝不健康的人都是肥胖的。代謝健康的意義遠不止表面看起來那麼簡單。

As far back as the 1960s, before obesity had become a widespread problem, a Stanford endocrinologist named Gerald Reaven had observed that excess weight often traveled in company with certain other markers of poor health. He and his colleagues noticed that heart attack patients often had both high fasting glucose levels and high triglycerides, as well as elevated blood pressure and abdominal obesity. The more of these boxes a patient checked, the greater their risk of cardiovascular disease.

早在20世紀60年代，在肥胖成為一個普遍問題之前，史丹佛大學內分泌學家傑拉爾德·里文(Gerald Reaven) 就觀察到，體重過重往往與其他某些健康狀況不佳的標誌一起出現。他和他的同事注意到，心臟病患者往往空腹血糖和三酸甘油酯水平都很高，並且血壓升高和腹部肥胖。患者檢查的這些選項越多，心血管疾病的風險就越大。

In the 1980s, Reaven labeled this collection of related disorders “Syndrome X”—where the X factor, he eventually determined, was insulin resistance. Today we call this cluster of problems “metabolic syndrome” (or MetSyn), and it is defined in terms of the following five criteria:

20 世紀 80 年代，Reaven 將這些相關疾病稱為「X 症候群」——他最終確定，其中的 X 因素是胰島素阻抗。今天，我們將這一系列問題稱為「代謝症候群」（或 MetSyn），它是根據以下五個標準來定義的：

1. high blood pressure (>130/85)
高血壓 (>130/85)
2. high triglycerides (>150 mg/dL)
高三酸甘油酯 (>150 mg/dL)
3. low HDL cholesterol (<40 mg/dL in men or <50 mg/dL in women)
低 HDL 膽固醇（男性 <40 mg/dL 或女性 <50 mg/dL）
4. central adiposity (waist circumference >40 inches in men or >35 in women)
中心肥胖（男性腰圍 >40 吋或女性腰圍 >35 吋）
5. elevated fasting glucose (>110 mg/dL)
空腹血糖升高 (>110 mg/dL)

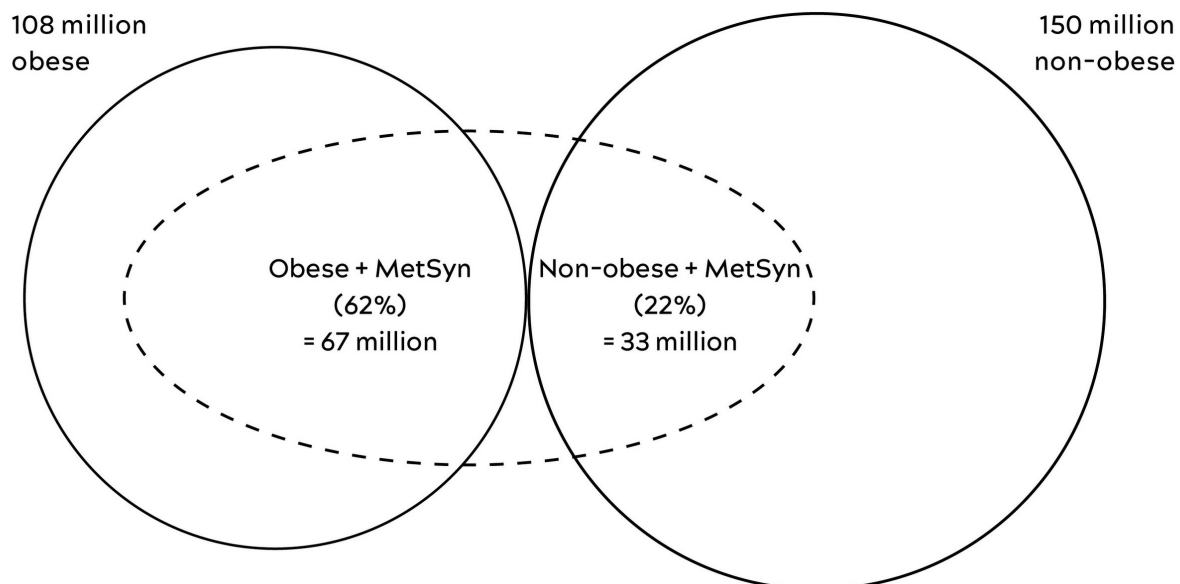
If you meet three or more of these criteria, then you have the metabolic syndrome—along with as many as 120 million other Americans, according to a 2020 article in *JAMA*. About 90 percent of the US population ticks at least one of these boxes. But notice that obesity is merely one of the criteria; it is *not* required for the metabolic syndrome to be diagnosed. Clearly the problem runs deeper than simply unwanted weight gain. This tends to support my view that obesity itself is not the issue but is merely a symptom of other problems.

根據 2020 年《美國醫學會雜誌》(JAMA) 上的一篇文章，如果您滿足其中三個或更多標準，那麼您就患有代謝綜合症，與多達 1.2 億其他美國人一樣。大約 90% 的美國人至少符合其中一項要求。但請注意，肥胖只是標準之一；診斷代謝症候群並不需要這樣做。顯然，這個問題不僅僅是不必要的體重增加。這傾向於支持我的觀點，即肥胖本身不是問題，而只是其他問題的症狀。

Studies have found that approximately one-third of those folks who are obese by BMI are actually metabolically *healthy*, by many of the same parameters used to define the metabolic syndrome (blood pressure, triglycerides, cholesterol, and fasting glucose, among others). At the same time, some studies have found that between 20 and 40 percent of nonobese adults may be metabolically unhealthy, by those same measures. A high percentage of obese people are also metabolically sick, of course—but as figure 3 illustrates, many normal-weight folks are in the same boat, which should be a wake-up call to all. This is *not* about how much you weigh. Even if you happen to be thin, you still need to read this chapter.

研究發現，根據許多用於定義代謝症候群的相同參數（血壓、三酸甘油酯、膽固醇和空腹血糖等），以 BMI 計算的肥胖者中大約有三分之一實際上是代謝健康的。同時，一些研究發現，以同樣的衡量標準，20% 至 40% 的非肥胖成年人可能代謝不健康。當然，很大比例的肥胖者也患有代謝疾病，但如圖 3 所示，許多體重正常的人也有同樣的情況，這應該會給所有人敲響警鐘。這與您的體重無關。即使你恰好很瘦，你仍然需要閱讀這一章。

Figure 3. Uncoupling Obesity from Metabolic Health



Source: Internal analysis based on data from National Institute of Diabetes and Digestive and Kidney Diseases (2021).

資料來源：根據國家糖尿病、消化和腎臟疾病研究所 (2021) 的數據進行的內部分析。

Relative prevalence of metabolic dysfunction (“MetSyn”) across the obese and nonobese segments of the population.

肥胖和非肥胖族群中代謝功能障礙（「MetSyn」）的相對盛行率。

This figure (based on NIH data and not the *JAMA* article just mentioned) shows quite dramatically how obesity and metabolic dysfunction are not the same thing—far from it, in fact. Some 42 percent of the US population is obese (BMI>30). Out of a conservatively estimated 100 million Americans who meet the criteria for the metabolic syndrome (i.e., metabolically unhealthy), almost exactly one-third are *not* obese. Many of these folks are overweight by BMI (25-29.9), but nearly 10 million Americans are normal weight (BMI 19-24.9) but metabolically unhealthy.

這個數字（基於 NIH 數據，而不是剛才提到的《JAMA》文章）非常戲劇性地表明，肥胖和代謝功能障礙並不是同一件事——事實上，兩者相差甚遠。約 42% 的美國人口肥胖（BMI>30）。保守估計，在符合代謝症候群（即代謝不健康）標準的 1 億美國人中，幾乎有三分之一的人不肥胖。其中許多人體重指數超重（BMI 25-29.9），但近 1,000 萬美國人體重正常（BMI 19-24.9），但代謝不健康。

Some research suggests that these people might be in the most serious danger. A large meta-analysis of studies with a mean follow-up time of 11.5 years showed that people in this category have more than triple the risk of all-cause mortality and/or cardiovascular events than metabolically healthy normal-weight individuals. Meanwhile, the metabolically healthy but obese subjects in these studies were *not* at significantly increased risk. The upshot is that it's not only obesity that drives bad health outcomes; it's metabolic dysfunction. That's what we're concerned with here.

一些研究表明，這些人可能面臨最嚴重的危險。對平均追蹤時間為 11.5 年的研究進行的大型薈萃分析表明，此類人群發生全因死亡和/或心血管事件的風險是代謝健康的正常體重人群的三倍多。同時，這些研究中代謝健康但肥胖的受試者的風險並未顯著增加。結果是，導致

不良健康結果的不僅是肥胖，還有肥胖。這是代謝功能障礙。這就是我們在這裡關心的。

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Metabolism is the process by which we take in nutrients and break them down for use in the body. In someone who is metabolically healthy, those nutrients are processed and sent to their proper destinations. But when someone is metabolically unhealthy, many of the calories they consume end up where they are not needed, at best—or outright harmful, at worst.

新陳代謝是我們吸收營養並將其分解以供體內使用的過程。對於代謝健康的人來說，這些營養素會被加工並發送到適當的目的地。但是，當一個人的新陳代謝不健康時，他們消耗的許多卡路里最終都會被用在不需要的地方，最好的情況是，或者最壞的情況是完全有害的。

If you eat a doughnut, for example, the body has to decide what to do with the calories in that doughnut. At the risk of oversimplifying a bit, the carbohydrate from our doughnut has two possible fates. First, it can be converted into glycogen, the storage form of glucose, suitable for use in the near term. About 75 percent of this glycogen ends up in skeletal muscle and the other 25 percent goes to the liver, although this ratio can vary. An adult male can typically store a total of about 1,600 calories worth of glycogen between these two sites, or about enough energy for two hours of vigorous endurance exercise. This is why if you are running a marathon or doing a long bike ride, and do not replenish your fuel stores in some way, you are likely to “bonk,” or run out of energy, which is not a pleasant experience.

例如，如果你吃一個甜甜圈，身體必須決定如何處理甜甜圈中的卡路里。冒著過度簡化的風險，甜甜圈中的碳水化合物有兩種可能的命運。首先，它可以轉化為肝糖，即葡萄糖的儲存形式，適合近期使用。大約 75% 的肝糖最終進入骨骼肌，另外 25% 進入肝臟，儘管這個比例可能有所不同。成年男性通常可以在這兩個部位之間儲存總計約 1,600 卡路里的肝糖原，或足夠進行兩個小時的劇烈耐力運動的能量。這就是為什麼如果您正在跑馬拉鬆或長途騎自行車，並且不以某

種方式補充燃料儲備，您可能會「崩潰」或耗盡能量，這不是一種愉快的經歷。

One of the liver's many important jobs is to convert this stored glycogen back to glucose and then to release it as needed to maintain blood glucose levels at a steady state, known as *glucose homeostasis*. This is an incredibly delicate task: an average adult male will have about five grams of glucose circulating in his bloodstream at any given time, or about a teaspoon. That teaspoon won't last more than a few minutes, as glucose is taken up by the muscles and especially the brain, so the liver has to continually feed in more, titrating it precisely to maintain a more or less constant level. Consider that five grams of glucose, spread out across one's entire circulatory system, is normal, while seven grams—a teaspoon and a half—means you have diabetes. As I said, the liver is an amazing organ.

肝臟的許多重要工作之一是將儲存的肝醣轉化回葡萄糖，然後根據需要釋放它以維持血糖水平處於穩定狀態，即葡萄糖穩態。這是一項極其微妙的任務：一個普通的成年男性在任何特定時間都會有大約五克或一茶匙的葡萄糖在他的血液中循環。那一茶匙的持續時間不會超過幾分鐘，因為葡萄糖會被肌肉，尤其是大腦吸收，因此肝臟必須不斷補充更多葡萄糖，並精確滴定以維持或多或少恆定的水平。考慮到分佈在整個循環系統中的五克葡萄糖是正常的，而七克（一茶匙半）則意味著您患有糖尿病。正如我所說，肝臟是一個神奇的器官。

We have a far greater capacity, almost unlimited, for storing energy as fat—the second possible destination for the calories in that doughnut. Even a relatively lean adult may carry ten kilograms of fat in their body, representing a whopping ninety thousand calories of stored energy.

我們有更大的能力，幾乎是無限的，可以將能量儲存為脂肪——甜甜圈中卡路里的第二個可能的目的地。即使是相對瘦弱的成年人，體內也可能攜帶十公斤脂肪，相當於儲存了九萬卡路里的能量。

That decision—where to put the energy from the doughnut—is made via hormones, chief among them insulin, which is secreted by the pancreas when the body senses the presence of glucose, the final breakdown product of most

carbohydrates (such as those in the doughnut). Insulin helps shuttle the glucose to where it's needed, while maintaining glucose homeostasis. If you happen to be riding a stage of the Tour de France while you eat the doughnut, or are engaged in other intense exercise, those calories will be consumed almost instantly in the muscles. But in a typical sedentary person, who is not depleting muscle glycogen rapidly, the excess energy from the doughnut will largely end up in fat cells (or more specifically, as triglycerides contained within fat cells).

這個決定——將甜甜圈中的能量放在哪裡——是透過荷爾蒙做出的，其中最主要的是胰島素，當身體感覺到葡萄糖的存在時，胰臟就會分泌胰島素，葡萄糖是大多數碳水化合物（例如碳水化合物中的碳水化合物）的最終分解產物。油炸圈餅）。胰島素有助於將葡萄糖運送到需要的地方，同時維持葡萄糖穩態。如果你在環法自行車賽的某個賽段邊吃甜甜圈，或者正在進行其他劇烈運動，那麼這些卡路里幾乎會立即在肌肉中消耗掉。但對於一個典型的久坐不動的人來說，他不會迅速消耗肌糖原，甜甜圈中多餘的能量將大部分最終進入脂肪細胞（或更具體地說，作為脂肪細胞內含有的甘油三酯）。

The twist here is that fat—that is, subcutaneous fat, the layer of fat just beneath our skin—is actually the *safest* place to store excess energy. Fat in and of itself is not bad. It's where we should put surplus calories. That's how we evolved. While fat might not be culturally or aesthetically desirable in our modern world, subcutaneous fat actually plays an important role in maintaining metabolic health. The Yale University endocrinologist Gerald Shulman, one of the leading researchers in diabetes, once published an elegant experiment demonstrating the necessity of fat: when he surgically implanted fat tissue into insulin-resistant mice, thereby making them *more* fat, he found that their metabolic dysfunction was cured almost instantly. Their new fat cells sucked up their excess blood glucose and stored it safely.

這裡的不同之處在於，脂肪——即皮下脂肪，我們皮膚下面的脂肪層——實際上是儲存多餘能量的最安全的地方。脂肪本身並不壞。這是我們應該放置多餘卡路里的地方。我們就是這樣進化的。雖然脂肪在現代世界中可能不符合文化或美學要求，但皮下脂肪實際上在維持代謝健康方面發揮著重要作用。耶魯大學內分泌學家傑拉爾德·舒爾曼

（Gerald Shulman）是糖尿病領域的頂尖研究人員之一，他曾發表過一項精妙的實驗，證明脂肪的必要性：當他透過手術將脂肪組織植入胰島素抗性小鼠體內，使它們變得更胖時，他發現它們的代謝功能障礙幾乎立刻就痊癒了。他們的新脂肪細胞吸收了多餘的血糖並安全地儲存起來。

Think of fat as acting like a kind of metabolic buffer zone, absorbing excess energy and storing it safely until it is needed. If we eat extra doughnuts, those calories are stored in our subcutaneous fat; when we go on, say, a long hike or swim, some of that fat is then released for use by the muscles. This fat flux goes on continually, and as long as you haven't exceeded your own fat storage capacity, things are pretty much fine.

脂肪就像一種代謝緩衝區，吸收多餘的能量並安全地儲存起來，直到需要為止。如果我們多吃甜甜圈，這些熱量就會儲存在我們的皮下脂肪中；當我們進行長途健行或游泳時，一些脂肪就會被釋放出來供肌肉使用。這種脂肪流動持續不斷，只要你沒有超過你自己的脂肪儲存能力，一切都很好。

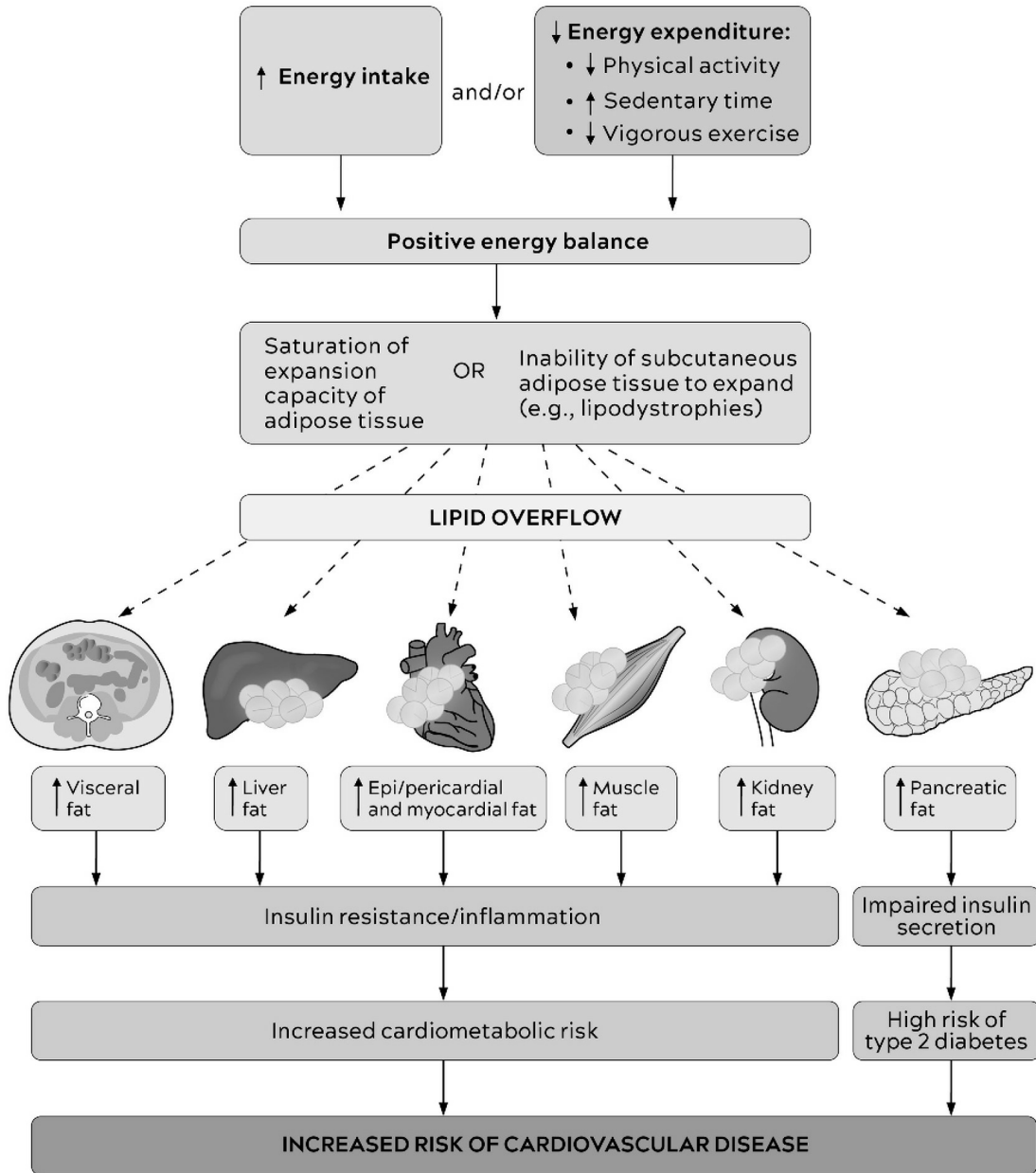
But if you continue to consume energy in excess of your needs, those subcutaneous fat cells will slowly fill up, particularly if little of that stored energy is being utilized. When someone reaches the limit of their capacity to store energy in their subcutaneous fat, yet they continue to take on excess calories, all that energy still has to go somewhere. The doughnuts or whatever they might be eating are probably still getting converted into fat, but now the body has to find other places to store it.

但如果你繼續消耗超過你的需要的能量，那些皮下脂肪細胞就會慢慢填滿，特別是如果儲存的能量很少被利用的話。當一個人的皮下脂肪儲存能量的能力達到極限時，但他們仍然攝取過量的卡路里，所有這些能量仍然必須去某個地方。甜甜圈或他們可能吃的任何東西可能仍在轉化為脂肪，但現在身體必須找到其他地方來儲存它。

It's almost as if you have a bathtub, and you're filling it up from the faucet. If you keep the faucet running even after the tub is full and the drain is closed (i.e., you're sedentary), water begins spilling over the rim of the tub, flowing

into places where it's not wanted or needed, like onto the bathroom floor, into the heating vents or down the stairs. It's the same with excess fat. As more calories flood into your subcutaneous fat tissue, it eventually reaches capacity and the surplus begins spilling over into other areas of your body: into your blood, as excess triglycerides; into your liver, contributing to NAFLD; into your muscle tissue, contributing directly to insulin resistance in the muscle (as we'll see); and even around your heart and your pancreas (figure 4). None of these, obviously, are ideal places for fat to collect; NAFLD is just one of many undesirable consequences of this fat spillover.

這幾乎就像你有一個浴缸，你可以從水龍頭給它注水。如果即使在浴缸已滿且排水管已關閉（即您久坐）後仍保持水龍頭運轉，水就會開始溢出浴缸邊緣，流到不需要或不需要的地方，例如浴室地板、暖氣通風口或下樓梯。多餘的脂肪也是如此。隨著更多的卡路里湧入您的皮下脂肪組織，它最終會達到容量，多餘的熱量開始溢出到您身體的其他區域：作為多餘的甘油三酯進入您的血液；進入肝臟，導致 NAFLD；進入你的肌肉組織，直接導致肌肉中的胰島素抗性（正如我們將看到的）；甚至心臟和胰臟周圍（圖 4）。顯然，這些都不是脂肪聚集的理想地點。NAFLD 只是這種脂肪溢出帶來的眾多不良後果之一。

Figure 4. How Excess Fat Increases Cardiometabolic Risk

Source: Tchernof and Després (2013).

資料來源：Tchernof 和 Després (2013)。

Fat also begins to infiltrate your abdomen, accumulating in between your organs. Where subcutaneous fat is thought to be relatively harmless, this

“visceral fat” is anything but. These fat cells secrete inflammatory cytokines such as TNF-alpha and IL-6, key markers and drivers of inflammation, in close proximity to your most important bodily organs. This may be why visceral fat is linked to increased risk of both cancer and cardiovascular disease.

脂肪也開始滲入腹部，並積聚在器官之間。皮下脂肪被認為相對無害，但這種「內臟脂肪」卻絕非如此。這些脂肪細胞緊鄰您最重要的身體器官，分泌發炎細胞因子，例如 TNF- α 和 IL-6，它們是發炎的關鍵標記物和驅動因素。這可能是為什麼內臟脂肪與癌症和心血管疾病風險增加有關。

Fat storage capacity varies widely among individuals. Going back to our tub analogy, some people have subcutaneous fat-storage capacity equivalent to a regular bathtub, while others may be closer to a full-sized Jacuzzi or hot tub. Still others may have only the equivalent of a five-gallon bucket. It also matters, obviously, how much “water” is flowing *into* the tub via the faucet (as calories in food) and how much is flowing *out* via the drain (or being consumed via exercise or other means).

脂肪儲存能力因人而異。回到我們的浴缸類比，有些人的皮下脂肪儲存能力相當於普通浴缸，而有些人可能更接近全尺寸的按摩浴缸或熱水浴缸。還有一些人可能只有相當於五加侖的水桶。顯然，有多少“水”通過水龍頭流入浴缸（作為食物中的卡路里）以及有多少“水”通過排水管流出（或通過運動或其他方式消耗）也很重要。

Individual fat-storage capacity seems to be influenced by genetic factors. This is a generalization, but people of Asian descent (for example), tend to have much lower capacity to store fat, on average, than Caucasians. There are other factors at play here as well, but this explains in part why some people can be obese but metabolically healthy, while others can appear “skinny” while still walking around with three or more markers of metabolic syndrome. It’s these people who are most at risk, according to research by Mitch Lazar at the University of Pennsylvania, because a “thin” person may simply have a much lower capacity to safely store fat. All other things being equal, someone

who carries a bit of body fat may also have greater fat-storage capacity, and thus more metabolic leeway than someone who appears to be more lean.

個體脂肪儲存能力似乎受到遺傳因素的影響。這是一個概括，但平均而言，亞裔人（例如）儲存脂肪的能力往往比白人低得多。這裡還有其他因素在起作用，但這在一定程度上解釋了為什麼有些人可能肥胖但代謝健康，而另一些人可能看起來“瘦”，但仍然帶著三種或更多代謝綜合徵的標誌。根據賓州大學米奇·拉扎爾的研究，這些人面臨的風險最大，因為「瘦」人安全儲存脂肪的能力可能要低得多。在其他條件相同的情況下，體內脂肪較多的人也可能具有更大的脂肪儲存能力，因此比看起來更瘦的人有更多的代謝空間。

It doesn't take much visceral fat to cause problems. Let's say you are a forty-year-old man who weighs two hundred pounds. If you have 20 percent body fat, making you more or less average (50th percentile) for your age and sex, that means you are carrying 40 pounds of fat throughout your body. Even if just 4.5 pounds of that is visceral fat, you would be considered at exceptionally high risk for cardiovascular disease and type 2 diabetes, in the top 5 percent of risk for your age and sex. This is why I insist my patients undergo a DEXA scan annually—and I am far more interested in their visceral fat than their total body fat.

不需要太多的內臟脂肪就會造成問題。假設您是一位四十歲的男子，體重兩百磅。如果您的身體脂肪含量為 20%，相當於您的年齡和性別的平均值（第 50 個百分位數），則表示您的全身脂肪含量為 40 磅。即使其中只有 4.5 磅是內臟脂肪，您也會被視為心血管疾病和 2 型糖尿病的風險極高，在您的年齡和性別中屬於前 5% 的風險。這就是為什麼我堅持讓我的患者每年接受一次 DEXA 掃描，而且我對他們的內臟脂肪比他們的全身脂肪更感興趣。

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It may have taken you a long time to get there, but now you are in trouble—even if you, and your doctor, may not yet realize it. You have fat accumulating in many places where it should not be, such as in your liver, between your

abdominal organs, even around your heart—regardless of your actual weight. But one of the first places where this overflowing fat will cause problems is in your muscle, as it worms its way in between your muscle fibers, like marbling on a steak. As this continues, microscopic fat droplets even appear *inside* your muscle cells.

您可能花了很長時間才到達那裡，但現在您遇到了麻煩 - 即使您和您的醫生可能還沒有意識到這一點。脂肪會積聚在許多不該積聚的地方，例如肝臟、腹部器官之間，甚至心臟周圍——無論您的實際體重如何。但這種溢出的脂肪首先會引起問題的地方之一是你的肌肉，因為它會在你的肌肉纖維之間蠕動，就像牛排上的大理石花紋一樣。隨著這種情況的持續，微小的脂肪滴甚至會出現在你的肌肉細胞內。

This is where insulin resistance likely begins, Gerald Shulman concludes from three decades' worth of investigation. These fat droplets may be among the first destinations of excess energy/fat spillover, and as they accumulate they begin to disrupt the complex network of insulin-dependent transport mechanisms that normally bring glucose in to fuel the muscle cell. When these mechanisms lose their function, the cell becomes “deaf” to insulin's signals. Eventually, this insulin resistance will progress to other tissues, such as the liver, but Shulman believes that it originates in muscle. It's worth noting that one key ingredient in this process seems to be inactivity. If a person is not physically active, and they are not consuming energy via their muscles, then this fat-spillover-driven insulin resistance develops much more quickly. (This is why Shulman requires his study subjects, mostly young college students, to refrain from physical activity, in order to push them towards insulin resistance.)

傑拉爾德·舒爾曼（Gerald Shulman）根據三十年的調查得出結論，這可能是胰島素阻抗的開始。這些脂肪滴可能是多餘能量/脂肪溢出的第一個目的地，當它們累積時，它們開始破壞胰島素依賴性運輸機制的複雜網絡，這些機制通常將葡萄糖帶入肌肉細胞。當這些機制失去功能時，細胞就會對胰島素訊號「充耳不聞」。最終，這種胰島素阻抗會發展到其他組織，例如肝臟，但舒爾曼認為它起源於肌肉。值得注意的是，這過程中的一個關鍵因素似乎是不活躍。如果一個人不進行

體力活動，並且不透過肌肉消耗能量，那麼這種脂肪溢出驅動的胰島素抗性就會發展得更快。（這就是為什麼舒爾曼要求他的研究對象（主要是年輕大學生）避免體力活動，以促使他們產生胰島素抗性。）

Insulin resistance is a term that we hear a lot, but what does it really mean? Technically, it means that cells, initially muscle cells, have stopped listening to insulin's signals, but another way to visualize it is to imagine the cell as a balloon being blown up with air. Eventually, the balloon expands to the point where it gets more difficult to force more air inside. You have to blow harder and harder. This is where insulin comes in, to help facilitate the process of blowing air into the balloon. The pancreas begins to secrete even more insulin, to try to remove excess glucose from the bloodstream and cram it into cells. For the time being it works, and blood glucose levels remain normal, but eventually you reach a limit where the "balloon" (cells) cannot accept any more "air" (glucose).

胰島素阻抗是我們經常聽到的術語，但它的真正意義是什麼？從技術上講，這意味著細胞（最初是肌肉細胞）已經停止聆聽胰島素的信號，但另一種可視化的方法是將細胞想像成一個被空氣吹脹的氣球。最終，氣球會膨脹到難以將更多空氣壓入其中的程度。你必須越來越用力地吹。這就是胰島素發揮作用的地方，以幫助促進將空氣吹入氣球的過程。胰臟開始分泌更多的胰島素，試圖從血液中去掉多餘的葡萄糖並將其塞入細胞中。暫時它有效，血糖水平保持正常，但最終會達到“氣球”（細胞）無法接受更多“空氣”（葡萄糖）的極限。

This is when the trouble shows up on a standard blood test, as fasting blood glucose begins to rise. This means you have high insulin levels *and* high blood glucose, and your cells are shutting the gates to glucose entry. If things continue in this way, then the pancreas becomes fatigued and less able to mount an insulin response. This is made worse by, you guessed it, the fat now residing in the pancreas itself. You can see the vicious spiral forming here: fat spillover helps initiate insulin resistance, which results in the accumulation of still more fat, eventually impairing our ability to store calories as anything *other* than fat. There are many other hormones involved in the production and

distribution of fat, including testosterone, estrogen, hormone-sensitive lipase[*3] and cortisol. Cortisol is especially potent, with a double-edged effect of depleting subcutaneous fat (which is generally beneficial) and replacing it with more harmful visceral fat. This is one reason why stress levels and sleep, both of which affect cortisol release, are pertinent to metabolism. But insulin seems to be the most potent as far as promoting fat accumulation because it acts as kind of a one-way gate, allowing fat to enter the cell while impairing the release of energy from fat cells (via a process called lipolysis). Insulin is all about fat storage, not fat utilization.

當空腹血糖開始上升時，標準血液檢查就會出現問題。這意味著您的胰島素水平和血糖水平都很高，並且您的細胞正在關閉葡萄糖進入的大門。如果事情繼續這樣下去，那麼胰臟就會變得疲勞，並且無法產生胰島素反應。你猜對了，現在駐留在胰臟本身的脂肪使情況變得更糟。您可以看到這裡正在形成惡性循環：脂肪溢出有助於引發胰島素阻抗，從而導致更多脂肪的積累，最終損害我們以脂肪以外的方式儲存卡路里的能力。還有許多其他荷爾蒙參與脂肪的產生和分配，包括睪固酮、雌激素、荷爾蒙敏感脂肪酶 [*3] 和皮質醇。皮質醇尤其有效，具有消耗皮下脂肪（這通常是有益的）並用更有害的內臟脂肪取而代之的雙重作用。這就是為什麼壓力水平和睡眠（兩者都會影響皮質醇的釋放）與新陳代謝有關的原因之一。但就促進脂肪累積而言，胰島素似乎是最有效的，因為它充當單向門，允許脂肪進入細胞，同時削弱脂肪細胞釋放能量（透過稱為脂解的過程）。胰島素主要是關於脂肪儲存，而不是脂肪利用。

When insulin is chronically elevated, more problems arise. Fat gain and ultimately obesity are merely one symptom of this condition, known as hyperinsulinemia. I would argue that they are hardly even the most serious symptoms: as we'll see in the coming chapters, insulin is also a potent growth-signaling hormone that helps foster both atherosclerosis and cancer. And when insulin resistance begins to develop, the train is already well down the track toward type 2 diabetes, which brings a multitude of unpleasant consequences.

當胰島素長期升高時，會出現更多問題。脂肪增加和最終肥胖只是這種稱為高胰島素血症的症狀之一。我認為它們甚至不是最嚴重的症

狀：正如我們將在接下來的章節中看到的，胰島素也是一種有效的生長信號激素，有助於促進動脈粥狀硬化和癌症。當胰島素阻抗開始出現時，這列火車就已經駛向第 2 型糖尿病，這會帶來許多令人不快的後果。

Our slowly dawning awareness of NAFLD and NASH mirrors the emergence of the global epidemic of type 2 diabetes a century ago. Like cancer, Alzheimer's, and heart disease, type 2 diabetes is known as a "disease of civilization," meaning it has only come to prominence in the modern era. Among primitive tribes and in prior times, it was largely unknown. Its symptoms had been recognized for thousands of years, going back to ancient Egypt (as well as ancient India), but it was the Greek physician Aretaeus of Cappadocia who named it *diabetes*, describing it as "a melting down of the flesh and limbs into urine."

我們對 NAFLD 和 NASH 的認識逐漸覺醒，這反映了一個世紀前全球 2 型糖尿病流行的出現。就像癌症、阿茲海默症和心臟病一樣，2 型糖尿病被稱為“文明疾病”，這意味著它只是在現代才變得突出。在原始部落和以前的時代，它基本上是未知的。幾千年來人們就已經認識到它的症狀，可以追溯到古埃及（以及古印度），但卡帕多西亞的希臘醫生阿雷泰烏斯將其命名為糖尿病，並將其描述為「肉體和四肢融化成糖尿病」。尿。”

Back then, it was vanishingly rare, observed only occasionally. As type 2 diabetes emerged, beginning in the early 1700s, it was at first largely a disease of the superelite, popes and artists and wealthy merchants and nobles who could afford this newly fashionable luxury food known as sugar. The composer Johann Sebastian Bach is thought to have been afflicted, among other notable personages. It also overlapped with gout, a more commonly recognized complaint of the decadent upper classes. This, as we'll soon see, was not a coincidence.

那時，這種情況非常罕見，只是偶爾觀察到。隨著 2 型糖尿病從 1700 年代初期開始出現，它最初主要是超級精英、教皇、藝術家、富有的商人和貴族的疾病，他們買得起這種新時尚的奢侈食品——糖。作曲家約翰·塞巴斯蒂安·巴赫和其他著名人物都被認為受到了折磨。它也與痛風重疊，痛風是頹廢上層階級更常見的疾病。我們很快就會看到，這並非巧合。

By the early twentieth century, diabetes was becoming a disease of the masses. In 1940 the famed diabetologist Elliott Joslin estimated that about one person in every three to four hundred was diabetic, representing an enormous increase from just a few decades earlier, but it was still relatively uncommon. By 1970, around the time I was born, its prevalence was up to one in every fifty people. Today over 11 percent of the US adult population, one in nine, has clinical type 2 diabetes, according to a 2022 CDC report, including more than 29 percent of adults over age sixty-five. Another 38 percent of US adults—more than one in three—meet at least one of the criteria for prediabetes. That means that nearly half of the population is either on the road to type 2 diabetes or already there.

到了二十世紀初，糖尿病已成為一種大眾疾病。1940 年，著名糖尿病學家艾利奧特·喬斯林(Elliott Joslin) 估計，大約每三到四百人中就有一個患有糖尿病，這與幾十年前相比大幅增加，但仍然相對不常見。到 1970 年，也就是我出生的時候，這種疾病的盛行率已達到每 50 人中就有 1 人。根據 2022 年 CDC 報告，目前超過 11% 的美國成年人（即九分之一）患有臨床 2 型糖尿病，其中超過 29% 的 65 歲以上成年人患有臨床 2 型糖尿病。另外 38% 的美國成年人（超過三分之一）至少符合糖尿病前期的標準之一。這意味著近一半的人口要么正在患有第 2 型糖尿病，要么已經患有第 2 型糖尿病。

One quick note: diabetes ranks as only the seventh or eighth leading cause of death in the United States, behind things like kidney disease, accidents, and Alzheimer's disease. In 2020, a little more than one hundred thousand deaths were attributed to type 2 diabetes, a fraction of the number due to either cardiovascular disease or cancer. By the numbers, it barely qualifies as a Horseman. But I believe that the actual death toll due to type 2 diabetes is

much greater and that we undercount its true impact. Patients with diabetes have a much greater risk of cardiovascular disease, as well as cancer and Alzheimer's disease and other dementias; one could argue that diabetes with related metabolic dysfunction is one thing that all these conditions have in common. This is why I place such emphasis on metabolic health, and why I have long been concerned about the epidemic of metabolic disease not only in the United States but around the world.

簡單說明一下：糖尿病僅在美國排名第七或第八位，僅次於腎臟病、意外和阿茲海默症。2020年，2型糖尿病導致的死亡人數略高於十萬人，僅佔心血管疾病或癌症死亡人數的一小部分。從數字上看，它勉強符合騎士的資格。但我相信第2型糖尿病造成的實際死亡人數要高得多，而且我們低估了它的真正影響。糖尿病患者罹患心血管疾病、癌症、阿茲海默症和其他失智症的風險要大得多；有人可能會說，糖尿病伴隨相關代謝功能障礙是所有這些疾病的共同點之一。這就是為什麼我如此重視代謝健康，也是為什麼我長期以來不僅關注美國而且在世界各地的代謝疾病的流行。

Why is this epidemic happening now?

為什麼現在才會發生這種流行病？

The simplest explanation is likely that our metabolism, as it has evolved over millennia, is not equipped to cope with our ultramodern diet, which has appeared only within the last century or so. Evolution is no longer our friend, because our environment has changed much faster than our genome ever could. Evolution wants us to get fat when nutrients are abundant: the more energy we could store, in our ancestral past, the greater our chances of survival and successful reproduction. We needed to be able to endure periods of time without much food, and natural selection obliged, endowing us with genes that helped us conserve and store energy in the form of fat. That enabled our distant ancestors to survive periods of famine, cold climates, and physiologic stressors such as illness and pregnancy. But these genes have proved less advantageous in our present environment, where many people in the developed world have access to almost unlimited calories.

最簡單的解釋可能是，我們的新陳代謝已經進化了數千年，無法適應我們上個世紀左右才出現的超現代飲食。演化不再是我們的朋友，因為我們的環境變化速度比我們的基因組變化速度快得多。演化希望我們在營養豐富時變胖：在我們祖先的過去，我們儲存的能量越多，我們生存和成功繁殖的機會就越大。我們需要能夠忍受一段時間沒有太多食物的情況，自然選擇賦予我們基因，幫助我們以脂肪的形式保存和儲存能量。這使得我們的遠祖能夠度過飢荒、寒冷氣候以及疾病和懷孕等生理壓力的時期。但事實證明，這些基因在我們目前的環境中不太有利，因為已開發國家的許多人可以獲得幾乎無限的卡路里。

Another problem is that not all of these calories are created equal, and not all of them are metabolized in the same way. One abundant source of calories in our present diet, fructose, also turns out to be a very powerful driver of metabolic dysfunction if consumed to excess. Fructose is not a novel nutrient, obviously. It's the form of sugar found in nearly all fruits, and as such it is essential in the diets of many species, from bats and hummingbirds up to bears and monkeys and humans. But as it turns out, we humans have a unique capacity for turning calories from fructose into fat.

另一個問題是，並非所有這些卡路里都是平等產生的，也並非所有卡路里都以相同的方式代謝。果糖是我們目前飲食中豐富的熱量來源之一，如果攝取過量，果糖也會成為代謝功能障礙的強大驅動因素。顯然，果糖並不是一種新的營養素。它幾乎是所有水果中都含有的糖形式，因此它在許多物種的飲食中至關重要，從蝙蝠、蜂鳥到熊、猴子和人類。但事實證明，我們人類具有將卡路里從果糖轉化為脂肪的獨特能力。

Lots of people like to demonize fructose, especially in the form of high-fructose corn syrup, without really understanding why it's supposed to be so harmful. The story is complicated but fascinating. The key factor here is that fructose is metabolized in a manner different from other sugars. When we metabolize fructose, along with certain other types of foods, it produces large amounts of uric acid, which is best known as a cause of gout but which has also been associated with elevated blood pressure.

許多人喜歡妖魔化果糖，尤其是高果糖玉米糖漿的形式，但沒有真正理解為什麼它如此有害。這個故事很複雜，但很精彩。這裡的關鍵因素是果糖的代謝方式與其他糖不同。當我們代謝果糖以及某些其他類型的食物時，它會產生大量的尿酸，這是眾所周知的痛風原因，但也與血壓升高有關。

More than two decades ago, a University of Colorado nephrologist named Rick Johnson noticed that fructose consumption appeared to be an especially powerful driver not only of high blood pressure but also of fat gain. “We realized fructose was having effects that could not be explained by its calorie content,” Johnson says. The culprit seemed to be uric acid. Other mammals, and even some other primates, possess an enzyme called uricase, which helps them clear uric acid. But we humans lack this important and apparently beneficial enzyme, so uric acid builds up, with all its negative consequences.

二十多年前，科羅拉多大學的腎臟病學家里克·約翰遜注意到，果糖的攝取似乎不僅是高血壓的一個特別強大的驅動因素，而且也是導致脂肪增加的一個特別強大的驅動因素。「我們意識到果糖所產生的影響無法用其卡路里含量來解釋，」約翰遜說。罪魁禍首似乎是尿酸。其他哺乳動物，甚至其他一些靈長類動物，都擁有一種稱為尿酸酶的酶，可以幫助它們清除尿酸。但我們人類缺乏這種重要且明顯有益的酶，因此尿酸會積聚，並產生所有負面後果。

Johnson and his team began investigating our evolutionary history, in collaboration with a British anthropologist named Peter Andrews, a retired researcher at the Natural History Museum in London and an expert on primate evolution. Others had observed that our species had lost this uricase enzyme because of some sort of random genetic mutation, far back in our evolutionary past, but the reason why had remained mysterious. Johnson and Andrews scoured the evolutionary and fossil record and came up with an intriguing theory: that this mutation may have been essential to the very emergence of the human species.

約翰遜和他的團隊開始與英國人類學家彼得·安德魯斯合作，研究我們的進化史。彼得·安德魯斯是倫敦自然歷史博物館的退休研究員，也是

靈長類進化的專家。其他人觀察到，我們的物種由於某種隨機基因突變而失去了這種尿酸酶，這種突變早在我們的演化歷史中就已存在，但原因仍然是個謎。約翰遜和安德魯斯研究了演化和化石記錄，並提出了一個有趣的理論：這種突變可能對人類物種的出現至關重要。

The story they uncovered was that, millions of years ago, our primate ancestors migrated north from Africa into what is now Europe. Back then, Europe was lush and semitropical, but as the climate slowly cooled, the forest changed. Deciduous trees and open meadows replaced the tropical forest, and the fruit trees on which the apes depended for food began to disappear, especially the fig trees, a staple of their diets. Even worse, the apes now had to endure a new and uncomfortably cold season, which we know as “winter.” In order to survive, these apes now needed to be able to store some of the calories they did eat as fat. But storing fat did not come naturally to them because they had evolved in Africa, where food was always available. Thus, their metabolism did not prioritize fat storage.

他們發現的故事是，數百萬年前，我們的靈長類祖先從非洲向北遷移到現在的歐洲。當時的歐洲植被茂盛，屬於亞熱帶地區，但隨著氣候慢慢變冷，森林發生了變化。落葉樹木和開闊的草地取代了熱帶森林，猿類賴以為生的果樹開始消失，尤其是無花果樹，它們是它們的主食。更糟的是，類人猿現在必須忍受一個新的、令人不舒服的寒冷季節，我們稱之為「冬天」。為了生存，這些猿類現在需要能夠將攝取的部分卡路里儲存為脂肪。但儲存脂肪對它們來說並不是天生的，因為它們是在非洲進化的，那裡總是有食物。因此，他們的新陳代謝並不優先考慮脂肪儲存。

At some point, our primate ancestors underwent a random genetic mutation that effectively switched on their ability to turn fructose into fat: the gene for the uricase enzyme was “silenced,” or lost. Now, when these apes consumed fructose, they generated lots of uric acid, which caused them to store many more of those fructose calories as fat. This newfound ability to store fat enabled them to survive in the colder climate. They could spend the summer gorging themselves on fruit, fattening up for the winter.

在某個時刻，我們的靈長類祖先經歷了隨機基因突變，有效地開啟了

它們將果糖轉化為脂肪的能力：尿酸酶的基因被「沉默」或丟失。現在，當這些猿類消耗果糖時，它們會產生大量尿酸，這導致它們將更多的果糖卡路里儲存為脂肪。這種新發現的儲存脂肪的能力使它們能夠在寒冷的氣候中生存。他們可以在夏天大吃水果，在冬天增肥。

These same ape species, or their evolutionary successors, migrated back down into Africa, where over time they evolved into hominids and then *Homo sapiens*—while also passing their uricase-silencing mutation down to us humans. This, in turn, helped enable humans to spread far and wide across the globe, because we could store energy to help us survive cold weather and seasons without abundant food.

這些相同的猿類，或它們的進化繼承者，遷回非洲，隨著時間的推移，它們進化成原始人類，然後進化成智人，同時也將尿酸酶沉默突變遺傳給我們人類。這反過來又幫助人類在全球範圍內廣泛傳播，因為我們可以儲存能量來幫助我們在沒有充足食物的情況下度過寒冷的天氣和季節。

But in our modern world, this fat-storage mechanism has outlived its usefulness. We no longer need to worry about foraging for fruit or putting on fat to survive a cold winter. Thanks to the miracles of modern food technology, we are almost literally swimming in a sea of fructose, especially in the form of soft drinks, but also hidden in more innocent-seeming foods like bottled salad dressing and yogurt cups.^[*4]

但在我們的現代世界，這種脂肪儲存機制已經不再有用。我們不再需要擔心尋找水果或增加脂肪來度過寒冷的冬天。由於現代食品科技的奇蹟，我們幾乎真正沐浴在果糖的海洋中，尤其是軟性飲料形式的果糖，但也隱藏在瓶裝沙拉醬和優格杯等看似無辜的食物中。[*4]

Whatever form it takes, fructose does not pose a problem when consumed the way that our ancestors did, before sugar became a ubiquitous commodity: mostly in the form of actual fruit. It is very difficult to get fat from eating too many apples, for example, because the fructose in the apple enters our system relatively slowly, mixed with fiber and water, and our gut and our metabolism

can handle it normally. But if we are drinking quarts of apple juice, it's a different story, as I'll explain in a moment.

無論採取何種形式，在糖成為無所不在的商品之前，果糖以我們祖先的方式消費時都不會造成問題：主要以實際水果的形式存在。例如，吃太多蘋果很難發胖，因為蘋果中的果糖進入我們的系統相對較慢，與纖維和水混合，而我們的腸道和新陳代謝可以正常處理它。但如果我們喝誇脫的蘋果汁，情況就不同了，我稍後會解釋。

Fructose isn't the only thing that creates uric acid; foods high in chemicals called purines, such as certain meats, cheeses, anchovies, and beer, also generate uric acid. This is why gout, a condition of excess uric acid, was so common among gluttonous aristocrats in the olden days (and still today). I test my patients' levels of uric acid, not only because high levels may promote fat storage but also because it is linked to high blood pressure. High uric acid is an early warning sign that we need to address a patient's metabolic health, their diet, or both.

果糖並不是唯一會產生尿酸的物質。富含嘌呤化學物質的食物，如某些肉類、起司、鰵魚和啤酒，也會產生尿酸。這就是為什麼痛風（一種尿酸過多的病症）在過去（至今仍然是）貪吃的貴族中如此常見。我測試了患者的尿酸水平，不僅因為高尿酸水平可能會促進脂肪儲存，還因為它與高血壓有關。高尿酸是早期預警信號，表明我們需要解決患者的代謝健康、飲食或兩者兼而有之的問題。

Another issue is that glucose and fructose are metabolized very differently at the cellular level. When a brain cell, muscle cell, gut cell, or any other type of cell breaks down glucose, it will almost instantly have more ATP (adenosine triphosphate), the cellular energy “currency,” at its disposal. But this energy is not free: the cell must expend a small amount of ATP in order to make more ATP, in the same way that you sometimes have to spend money to make money. In glucose metabolism, this energy expenditure is regulated by a specific enzyme that prevents the cell from “spending” too much of its ATP on metabolism.

另一個問題是葡萄糖和果糖在細胞層面的代謝非常不同。當腦細胞、肌肉細胞、腸道細胞或任何其他類型的細胞分解葡萄糖時，它幾乎會立即擁有更多的 ATP（三磷酸腺苷），即細胞能量「貨幣」可供使用。但這種能量並不是免費的：細胞必須消耗少量的 ATP 才能產生更多的 ATP，就像你有時必須花錢才能賺錢一樣。在葡萄糖代謝中，這種能量消耗由特定的酶調節，該酶可防止細胞在代謝中「消耗」過多的 ATP。

But when we metabolize fructose in large quantities, a different enzyme takes over, and this enzyme does *not* put the brakes on ATP “spending.” Instead, energy (ATP) levels inside the cell drop rapidly and dramatically. This rapid drop in energy levels makes the cell think that we are still hungry. The mechanisms are a bit complicated, but the bottom line is that even though it is rich in energy, fructose basically tricks our metabolism into thinking that we are depleting energy—and need to take in still more food and store more energy as fat.^[*5]

但當我們大量代謝果糖時，另一種酵素就會接管，而這種酵素不會阻止 ATP「消耗」。相反，細胞內的能量 (ATP) 水平迅速急劇下降。能量水平的迅速下降使細胞認為我們仍然飢餓。其機制有點複雜，但底線是，儘管果糖富含能量，但它基本上會欺騙我們的新陳代謝，讓我們認為我們正在耗盡能量，並且需要攝取更多的食物並將更多的能量儲存為脂肪。^[*5]

On a more macro level, consuming large quantities of liquid fructose simply overwhelms the ability of the gut to handle it; the excess is shunted to the liver, where many of those calories are likely to end up as fat. I've seen patients work themselves into NAFLD by drinking too many “healthy” fruit smoothies, for the same reason: they are taking in too much fructose, too quickly. Thus, the almost infinite availability of liquid fructose in our already high-calorie modern diet sets us up for metabolic failure if we're not careful (and especially if we are not physically active).

從更宏觀的層面來看，攝取大量液體果糖只會壓倒腸道處理它的能力。多餘的熱量會被分流到肝臟，其中許多卡路里最終可能會轉化為

脂肪。我曾看過患者因飲用過多「健康」水果冰沙而患上 NAFLD，原因相同：他們攝取過多、過快的果糖。因此，如果我們不小心（特別是如果我們不進行身體活動），我們本已高熱量的現代飲食中幾乎無限量的液體果糖將使我們代謝失敗。

I sometimes think back to that patient who first introduced me to fatty liver disease. He and Samuel Zelman's Patient Zero, the man who drank a dozen Cokes a day, had the same problem: they consumed many more calories than they needed. In the end, I still think excess calories matter the most.

有時我會回想起那位先向我介紹脂肪肝疾病的患者。他和塞繆爾·澤爾曼飾演的零號病人，每天喝一打可樂，也有同樣的問題：他們消耗的卡路里比他們需要的多很多。最後，我仍然認為過量的卡路里是最重要的。

Of course, my patient was in the hospital not because of his NAFLD, but because of his colon cancer. His operation turned out beautifully: we removed the cancerous part of his colon and sent him off to a speedy recovery. His colon cancer was well established, but it had not metastasized or spread. I remember the attending surgeon feeling pretty good about the operation, as we had caught the cancer in time. This man was maybe forty or forty-five, with a long life still ahead of him.

當然，我的病人住院不是因為 NAFLD，而是因為結腸癌。他的手術結果很順利：我們切除了他結腸的癌症部分，讓他很快康復。他的結腸癌已經確診，但尚未轉移或擴散。我記得主治醫生對這次手術感覺很好，因為我們及時發現了癌症。這個人大概有四十歲或四十五歲了，他的人生還很長。

But what became of him? He was obviously also in the early stages of metabolic disease. I keep wondering whether the two might have been connected in some way, his fatty liver and his cancer. What did he look like, metabolically, ten years before he came in for surgery that day? As we'll see in chapter 8, obesity and metabolic dysfunction are both powerful risk factors

for cancer. Could this man's underlying metabolic issues have been fueling his cancer somehow? What would have happened if his underlying issues, which his fatty liver made plain as day, had been recognized a decade or more earlier? Would we have ever even met?

但他後來怎麼樣了呢？他顯然也處於代謝疾病的早期階段。我一直想知道他的脂肪肝和癌症這兩者是否可能以某種方式聯繫在一起。那天他來接受手術前十年，他的新陳代謝又是什麼樣子？正如我們將在第 8 章中看到的，肥胖和代謝功能障礙都是癌症的強大危險因子。這個人潛在的代謝問題是否會以某種方式助長他的癌症？如果他的潛在問題（他的脂肪肝顯而易見）早十年或更早被發現，會發生什麼事？我們還會見面嗎？

It seems unlikely that Medicine 2.0 would have addressed his situation at all. The standard playbook, as we touched on in chapter 1, is to wait until someone's HbA1c rises above the magic threshold of 6.5 percent before diagnosing them with type 2 diabetes. But by then, as we've seen in this chapter, the person may already be in a state of elevated risk. To address this rampant epidemic of metabolic disorders, of which NAFLD is merely a harbinger, we need to get a handle on the situation much earlier.

醫學 2.0 似乎根本不可能解決他的情況。正如我們在第 1 章中提到的，標準策略是等到某人的 HbA1c 升至 6.5% 的神奇閾值以上，然後再診斷其患有 2 型糖尿病。但到那時，正如我們在本章中所看到的，這個人可能已經處於高風險狀態。為了解決這種猖獗的代謝紊亂流行病（NAFLD 只是其中的一個預兆），我們需要更早控制這種情況。

One reason I find value in the concept of metabolic syndrome is that it helps us see these disorders as part of a continuum and not a single, binary condition. Its five relatively simple criteria are useful for predicting risk at the population level. But I still feel that reliance on it means waiting too long to declare that there is a problem. Why wait until someone has three of the five markers? Any one of them is generally a bad sign. A Medicine 3.0 approach would be to look for the warning signs years earlier. We want to intervene *before* a patient actually develops metabolic syndrome.

我發現代謝症候群概念有價值的一個原因是，它幫助我們將這些疾病視為連續體的一部分，而不是單一的二元病症。它的五個相對簡單的標準對於預測人群層面的風險很有用。但我仍然覺得依賴它意味著等待太久才宣布有問題。為什麼要等到有人擁有五個標記中的三個呢？其中任何一個通常都是一個壞兆頭。醫學 3.0 方法是提前幾年尋找警告信號。我們希望在患者真正出現代謝症候群之前進行幹預。

This means keeping watch for the earliest signs of trouble. In my patients, I monitor several biomarkers related to metabolism, keeping a watchful eye for things like elevated uric acid, elevated homocysteine, chronic inflammation, and even mildly elevated ALT liver enzymes. Lipoproteins, which we will discuss in detail in the next chapter, are also important, especially triglycerides; I watch the ratio of triglycerides to HDL cholesterol (it should be less than 2:1 or better yet, less than 1:1), as well as levels of VLDL, a lipoprotein that carries triglycerides—all of which may show up many years before a patient would meet the textbook definition of metabolic syndrome. These biomarkers help give us a clearer picture of a patient's overall metabolic health than HbA1c, which is not very specific by itself.

這意味著要密切注意最早的麻煩跡象。在我的患者中，我監測了幾種與新陳代謝相關的生物標記物，密切關注尿酸升高、同型半胱氨酸升高、慢性炎症，甚至輕度升高的 ALT 肝酶等情況。脂蛋白也很重要，尤其是三酸甘油酯，我們將在下一章詳細討論。我觀察三酸甘油酯與高密度脂蛋白膽固醇的比例（它應該小於2:1 或更好，小於1:1），以及極低密度脂蛋白（一種攜帶三酸甘油酯的脂蛋白）的水平，所有這些可能會在很多年出現在患者滿足代謝症候群教科書定義之前。與 HbA1c 相比，這些生物標記有助於我們更清楚地了解患者的整體代謝健康狀況，而 HbA1c 本身並不十分具體。

But the first thing I look for, the canary in the coal mine of metabolic disorder, is elevated insulin. As we've seen, the body's first response to incipient insulin resistance is to produce *more* insulin. Think back to our analogy with the balloon: as it gets harder to get air (glucose) into the balloon (the cell), we have to blow harder and harder (i.e., produce more insulin). At first, this appears to be successful: the body is still able to maintain glucose

homeostasis, a steady blood glucose level. But insulin, especially postprandial insulin, is already on the rise.

但我首先要尋找的是代謝紊亂煤礦中的金絲雀——胰島素升高。如我們所見，身體對初期胰島素抗性的第一個反應是產生更多的胰島素。回想我們與氣球的類比：隨著空氣（葡萄糖）進入氣球（細胞）變得越來越困難，我們必須越來越用力地吹氣（即產生更多的胰島素）。起初，這似乎是成功的：身體仍然能夠維持葡萄糖穩態，即穩定的血糖水平。但胰島素，尤其是餐後胰島素，已經在上升。

One test that I like to give patients is the oral glucose tolerance test, or OGTT, where the patient swallows ten ounces of a sickly-sweet, almost undrinkable beverage called Glucola that contains seventy-five grams of pure glucose, or about twice as much sugar as in a regular Coca-Cola.^[*6] We then measure the patient's glucose *and* their insulin, every thirty minutes over the next two hours. Typically, their blood glucose levels will rise, followed by a peak in insulin, but then the glucose will steadily decrease as insulin does its job and removes it from circulation.

我喜歡為患者做的一項測試是口服葡萄糖耐量測試(OGTT)，患者吞下 10 盎司一種甜得令人作嘔、幾乎無法飲用的飲料，稱為Glucola，其中含有75 克純葡萄糖，大約是其兩倍。與普通可口可樂中的糖一樣。^[*6] 然後，我們在接下來的兩個小時內每三十分鐘測量一次患者的血糖和胰島素。通常，他們的血糖水平會上升，隨後胰島素達到峰值，但隨著胰島素發揮作用並將其從循環中去除，血糖會穩定下降。

On the surface, this is fine: insulin has done its job and brought glucose under control. But the insulin in someone at the early stages of insulin resistance will rise very dramatically in the first thirty minutes and then remain elevated, or even rise further, over the next hour. This postprandial insulin spike is one of the biggest early warning signs that all is not well.

從表面上看，這很好：胰島素已經完成了它的工作並控制了血糖。但處於胰島素抗性早期階段的人的胰島素會在前三十分鐘內急劇上升，然後在接下來的一個小時內保持升高狀態，甚至進一步上升。餐後胰島素飆升是一切不順利的最大早期預警之一。

Gerald Reaven, who died in 2018 at the age of eighty-nine, would have agreed. He had to fight for decades for insulin resistance to be recognized as a primary cause of type 2 diabetes, an idea that is now well accepted. Yet diabetes is only one danger: Studies have found that insulin resistance itself is associated with huge increases in one's risk of cancer (up to twelvefold), Alzheimer's disease (fivefold), and death from cardiovascular disease (almost sixfold)—all of which underscores why addressing, and ideally preventing, metabolic dysfunction is a cornerstone of my approach to longevity.

於 2018 年去世、享年 89 歲的傑拉爾德·里文 (Gerald Reaven) 可能會同意。他花了幾十年的時間才將胰島素阻抗視為第 2 型糖尿病的主要原因，這一觀點現在已被廣泛接受。然而，糖尿病只是一種危險：研究發現，胰島素抗性本身與癌症（高達十二倍）、阿茲海默症（五倍）和心血管疾病死亡（幾乎六倍）的風險大幅增加有關，所有這些都強調了這一點。為什麼解決並最好預防代謝功能障礙是我長壽之道的基石。

It seems at least plausible that my patient with the fatty liver had developed elevated insulin at some point, well before his surgery. But it is also extremely unlikely that Medicine 2.0 would have even considered treating him, which boggles my mind. If any other hormone got out of balance like this, such as thyroid hormone or even cortisol, doctors would act swiftly to rectify the situation. The latter might be a symptom of Cushing's disease, while the former could be a possible sign of Graves' disease or some other form of hyperthyroidism. Both of these endocrine (read: *hormone*) conditions require and receive treatment as soon as they are diagnosed. To do nothing would constitute malpractice. But with hyperinsulinemia, for some reason, we wait and do nothing. Only when type 2 diabetes has been diagnosed do we take any serious action. This is like waiting until Graves' disease has caused *exophthalmos*, the signature bulging eyeballs in people with untreated hyperthyroidism, before stepping in with treatment.

我的脂肪肝患者在手術前的某個時間點就出現了胰島素升高，這似乎至少是合理的。但醫學 2.0 也極不可能考慮治療他，這讓我感到難以置信。如果任何其他激素像這樣失去平衡，例如甲狀腺激素甚至皮質

醇，醫生會迅速採取行動糾正這種情況。後者可能是庫欣氏症的症狀，而前者可能是格雷夫茲病或其他形式的甲狀腺功能亢進的症狀。這兩種內分泌（讀作：荷爾蒙）病症一經診斷就需要並接受治療。不採取任何行動將構成瀆職。但對於高胰島素血症，出於某種原因，我們只能等待而不採取任何行動。只有當診斷出第 2 型糖尿病時，我們才會採取任何認真的行動。這就像等到格雷夫茲病引起眼球突出（未經治療的甲狀腺亢進患者的標誌性眼球凸出）才開始治療。

It is beyond backwards that we do not treat hyperinsulinemia like a bona fide endocrine disorder of its own. I would argue that doing so might have a greater impact on human health and longevity than any other target of therapy. In the next three chapters, we will explore the three other major diseases of aging—cardiovascular disease, cancer, and neurodegenerative diseases—all of which are fueled in some way by metabolic dysfunction. It will hopefully become clear to you, as it is to me, that the logical first step in our quest to delay death is to get our metabolic house in order.

我們不把高胰島素血症當作一種真正的內分泌疾病來治療，這實在是太落後了。我認為這樣做可能比任何其他治療目標對人類健康和壽命產生更大的影響。在接下來的三章中，我們將探討老化的另外三種主要疾病——心血管疾病、癌症和神經退化性疾病——所有這些疾病在某種程度上都是由代謝功能障礙引起的。希望你和我都清楚，我們尋求延遲死亡的邏輯第一步就是讓我們的新陳代謝房子保持秩序。

The good news is that we have tremendous agency over this. Changing how we exercise, what we eat, and how we sleep (see Part III) can completely turn the tables in our favor. The bad news is that these things require effort to escape the default modern environment that has conspired against our ancient (and formerly helpful) fat-storing genes, by overfeeding, undermoving, and undersleeping us all.

好消息是我們對此擁有巨大的代理權。改變我們的運動方式、飲食和睡眠方式（請參閱第三部分）可以完全扭轉局面，對我們有利。壞消息是，這些事情需要努力擺脫預設的現代環境，這種環境透過過度餵食、運動不足和睡眠不足來損害我們古老的（以前有用的）脂肪儲存基因。

[*1](#) Typically, “normal” means between the 2.5th and 97.5th percentiles, a very wide range.

*1 通常，「正常」是指第 2.5 個百分位數到第 97.5 個百分位數之間，這是一個非常寬的範圍。

[*2](#) BMI is far from perfect, as it does not capture the proportion of fat to muscle, but is good enough for our purposes here.

*2 BMI 遠非完美，因為它沒有反映脂肪與肌肉的比例，但對於我們的目的來說已經足夠了。

[*3](#) An enzyme expressed in fat cells that helps convert stored triglycerides into free fatty acids.

*3 一種在脂肪細胞中表現的酶，有助於將儲存的三酸甘油酯轉化為遊離脂肪酸。

[*4](#) While it may be in vogue to vilify high-fructose corn syrup, which is 55 percent fructose and 45 percent glucose, it's worth pointing out that good old table sugar (sucrose) is about the same, consisting of 50 percent fructose and 50 percent glucose. So there's really not much of a difference between the two.

*4 雖然詆毀高果糖玉米糖漿（其中含有 55% 果糖和 45% 葡萄糖）可能很流行，但值得指出的是，傳統的食糖（蔗糖）大致相同，由 50% 果糖和 50% 葡萄糖組成。葡萄糖百分比。所以兩者之間確實沒有太大差別。

[*5](#) This drop in cellular ATP triggers an enzyme called *AMP deaminase*, or AMPD, which is sort of like the evil twin to AMPK, the reverse-fuel gauge enzyme that we discussed in the previous chapter. When AMPK is activated, it triggers all sorts of cellular survival programs, including the burning of stored fat, that help enable the organism to survive without food. When fructose triggers AMPD, on the other hand, it sends us down the path of fat storage. (This cascade also triggers hunger by blocking the satiety hormone leptin.)

*5 細胞 ATP 的下降會觸發一種稱為 AMP 脫氨酶 (AMPD) 的酶，它有點像 AMPK（我們在上一章中討論的反向電量計酶）的邪惡雙胞胎。當 AMPK 被激活時，它會觸發各種細胞生存程序，包括燃燒儲存的脂肪，這有助於有機體在沒有食物的情況下生存。另一方面，當果糖觸發 AMPD 時，它會讓我們沿著脂肪儲存的道路前進。（這種級聯反應也會透過阻斷飽足感激素瘦素來引發飢餓感。）

[*6](#) For comparison, a regular twelve-ounce Coca-Cola contains thirty-nine grams of high-fructose corn syrup, about half of which is glucose and half is fructose.

*6 作為比較，普通的 12 盎司可口可樂含有 39 克高果糖玉米糖漿，其中大約一半是葡萄糖，一半是果糖。

CHAPTER 7

第7章

The Ticker

股票行情指示器

Confronting—and Preventing—Heart Disease, the
Deadliest Killer on the Planet

面對並預防心臟病這一地球上最致命的殺手

There is some risk involved in action, there always is.

But there is far more risk in failure to act.

行動中總是存在一些風險。但不採取行動的風險
要大得多。

—HARRY S. TRUMAN

——哈里·S·杜魯門

One downside of my profession is that too much knowledge can become its own kind of curse. As I delved back into the practice of medicine, after my hiatus in the business world, it dawned on me that I already know how I am likely to die: I seem destined to die from heart disease.

我這個職業的一個缺點是，太多的知識本身就會變成一種詛咒。當我在商業世界中斷一段時間後，當我重新鑽研醫學實踐時，我突然意識到我已經知道我可能會如何死亡：我似乎注定會死於心臟病。

I wonder what took me so long to get the hint. When I was five, my father's older brother Francis—his favorite of eight siblings—died of a sudden heart attack at forty-six. When my own brother Paul was born two days later, my grief-stricken father chose Francis as his middle name. Just as certain names run in families, a propensity for early cardiovascular disease seems to run in mine. Another uncle suffered a fatal heart attack at forty-two, while a third made it to age sixty-nine before his heart killed him, which is perhaps more typical but still way too young.

我想知道為什麼我花了這麼長時間才得到提示。當我五歲的時候，我父親的哥哥弗朗西斯——他在八個兄弟姐妹中最喜歡的一個——在四十六歲時因心臟病突發去世。兩天後，當我自己的兄弟保羅出生時，我悲痛欲絕的父親選擇了方濟各作為他的中間名。正如某些家族的名字一樣，我的名字似乎也有早期心血管疾病的傾向。另一位叔叔在四十二歲時因心臟病發作而死亡，而第三位叔叔則在六十九歲時心臟病發作，這也許更典型，但仍然太年輕了。

My dad is lucky, because he has lived to the ripe old age of eighty-five (so far). But even he has a stent in one of his coronary arteries, a souvenir of his own minor event in his midsixties. He felt chest pain one day at the limestone quarry where he worked, and ended up in the ER, where it was determined that he had had a recent infarction. The stent, a little sleeve of metal wire, was put in a year or so later. I'm not actually convinced that the stent did anything—he was not experiencing symptoms at the time it was placed—but perhaps it scared him enough to be more diligent with his medications and his diet.

我爸爸很幸運，因為他已經活到了八十五歲的高齡（至今）。但即使是他的一條冠狀動脈也裝有支架，這是他自己六十多歲時發生的一件小事的紀念品。有一天，他在他工作的石灰石採石場感到胸痛，最後被送進了急診室，在那裡被確定他最近患有梗塞。支架是一個金屬絲的小套管，大約一年後植入。我實際上並不相信支架有什麼作用——放置支架時他沒有出現任何症狀——但也許這足以讓他害怕，從而更加勤奮地服用藥物和飲食。

So even though my cholesterol profile is excellent, and I eat sensibly, never smoke, have normal blood pressure, and rarely drink alcohol, I'm still at risk. I feel like I'm trapped in that Charlie Munger anecdote, about the guy who just wants to know *where* he's going to die, so he'll make sure never to go there. Unfortunately, too often heart disease finds you.

因此，儘管我的膽固醇水平非常好，而且我飲食合理、從不吸煙、血壓正常、很少飲酒，但我仍然處於危險之中。我覺得我陷入了查理·蒙格的軼事中，講的是一個只想知道自己會死在哪裡的人，所以他會確保永遠不會去那裡。不幸的是，心臟病常常找上你。

When I was in medical school, my first-year pathology professor liked to ask a trick question: What is the most common “presentation” (or symptom) of heart disease? It wasn't chest pain, left arm pain, or shortness of breath, the most common answers; it was sudden death. You know the patient has heart disease because he or she has just died from it. This is why, he claimed, the only doctors who truly understand cardiovascular disease are pathologists. His point: by the time a pathologist sees your arterial tissue, you are dead.

當我在醫學院時，我一年級的病理學教授喜歡問一個棘手的問題：心臟病最常見的「表現」（或症狀）是什麼？最常見的答案不是胸痛、左臂疼痛或氣短；而是胸痛、左臂疼痛或氣短。這是猝死。您知道患者患有心臟病，因為他或她剛剛死於心臟病。他聲稱，這就是為什麼唯一真正了解心血管疾病的醫生是病理學家。他的觀點是：當病理學家看到你的動脈組織時，你就已經死了。

While mortality rates from those first, surprise heart attacks have dropped significantly, thanks to improvements in basic cardiac life support and time-

sensitive interventions such as cardiac catheterization and clot-obliterating drugs that can halt a heart attack almost in its tracks, they are still fatal roughly one-third of the time, according to Ron Krauss, senior scientist and director of atherosclerosis research at Children's Hospital Oakland Research Institute.

儘管由於基本心臟生命支持的改善和時間敏感的干預措施（例如心導管插入術和幾乎可以阻止心臟病發作的血栓消除藥物）的改善，意外心臟病發作的死亡率已顯著下降，但死亡率仍處於上升趨勢。奧克蘭兒童醫院研究所的高級科學家兼動脈粥狀硬化研究主任 Ron Krauss 表示，大約三分之一的情況是致命的。

Globally, heart disease and stroke (or cerebrovascular disease), which I lump together under the single heading of atherosclerotic cardiovascular disease, or ASCVD, represent the leading cause of death, killing an estimated 2,300 people every day in the United States, according to the CDC—more than any other cause, including cancer. It's not just men who are at risk: American women are up to ten times more likely to die from atherosclerotic disease than from breast cancer (not a typo: one in three versus one in thirty). But pink ribbons for breast cancer far outnumber the American Heart Association's red ribbons for awareness of heart disease among women.

在全球範圍內，心臟病和中風（或腦血管疾病）（我將其歸類為動脈粥狀硬化性心血管疾病（ASCVD））是導致死亡的主要原因。CDC 比其他任何原因都重要，包括癌症。面臨風險的不僅是男性：美國女性死於動脈粥狀硬化疾病的可能性比死於乳癌的可能性高出十倍（不是拼字錯誤：三分之一對三十之一）。但針對乳癌的粉紅絲帶遠遠多於美國心臟協會針對女性心臟病意識的紅絲帶。

My uncles' deaths remain a mystery to me. They lived in Egypt, and I have no idea what their blood work looked like or, more importantly, what kind of shape their coronary arteries were in. I'm pretty sure they smoked, but perhaps if they had had access to better medical care they too might have survived their heart attacks, as my father did. Or perhaps their fates were inescapable, tied to their genes. All I know is that forty-two seems really young to keel over from a heart attack.

我叔叔的死對我來說仍然是個謎。他們住在埃及，我不知道他們的血液檢查是什麼樣子，更重要的是，他們的冠狀動脈是什麼樣的。我很確定他們吸煙，但也許如果他們能夠獲得更好的醫療護理的話他們也可能像我父親一樣從心臟病發作中倖存下來。或者也許他們的命運是不可避免的，與他們的基因息息相關。我所知道的是，四十二歲似乎很年輕，就因心臟病發作而倒下。

I'd known about my uncles all my life, but the implication of their stories only really hit me in my midthirties, when I became a father for the first time. All of a sudden, the awareness of my own mortality crashed over my head like a rogue wave, coming out of nowhere on one of my long swims. This book probably wouldn't have been written if not for that family history.

我一生都了解我的叔叔們，但他們的故事的含義直到我三十幾歲第一次成為父親時才真正觸動了我。突然間，我對自己必死無疑的認識像一股洶湧的海浪從我的一次長途游泳中不知從何而來，衝過我的頭頂。如果沒有這段家族史，這本書可能不會寫成。

Like most thirty-six-year-olds, Not-Thin Peter scarcely gave a thought to heart disease. Why should I have? My heart was strong enough to have propelled me across the twenty-one-mile-wide Catalina Channel, working steadily for more than fourteen hours, like a Mercedes diesel engine purring along smoothly inside my chest. I was in great shape, I thought. But I was nevertheless worried, on account of my family history. So I insisted that my doctor order a CT scan of my heart, and it wound up changing my whole outlook on life.

像大多數三十六歲的人一樣，不瘦的彼得幾乎沒有想到心臟病。為什麼我應該有？我的心臟足夠強大，可以推動我穿過二十一英里寬的卡特利娜海峽，穩定地工作了十四多小時，就像一輛梅賽德斯柴油發動機在我的胸腔裡平穩地運轉。我想，我的狀態很好。但考慮到我的家族史，我仍然很擔心。所以我堅持讓醫生對我的心臟進行 CT 掃描，結果改變了我的整個人生觀。

The scan was calibrated to detect calcification in my coronary arteries, a sign of advanced atherosclerosis. The results showed that I had a calcium

“score” of 6. That sounds low, and in absolute terms it was; someone with severe disease could return a score well over 1,000. But for someone age thirty-six, it should have been zero. My score of 6 meant that I had more calcium in my coronary arteries than 75 to 90 percent of people my age. As I dug deeper into the pathology of this disease, I was dismayed to learn that it was already fairly late in the game. A calcium score is treated as a predictor of future risk, which it is, but it is also a measure of historical and existing damage. And I was already off the charts. I was only in my midthirties, but I had the arteries of a fifty-five-year-old.

掃描經過校準以檢測我的冠狀動脈鈣化，這是晚期動脈粥狀硬化的跡象。結果顯示，我的鈣「分數」為 6。這聽起來很低，但從絕對值來看確實如此；患有嚴重疾病的人可能會返回遠遠超過 1,000 分的分數。但對三十六歲的人來說，它應該是零。我的得分為 6 分，這意味著我的冠狀動脈中的鈣含量比同齡人中的 75% 到 90% 還要多。當我更深入地研究這種疾病的病理學時，我沮喪地發現，事情已經發展到相當晚了。鈣分數被視為未來風險的預測指標（事實確實如此），但它也是歷史和現有損害的衡量標準。我已經超出了記錄。我才三十幾歲，但我的動脈卻像五十五歲的人一樣。

I was upset by this revelation, although knowing what I know now, it's not at all surprising. At the time, I was overweight and borderline insulin resistant, two huge risk factors that by themselves help create an environment that fosters and accelerates the development of atherosclerotic lesions. Yet because my calcium score was “only” 6, and my all-important LDL (“bad”) cholesterol was “normal,” the medical advice I received was—wait for it—to do nothing. Sound familiar?

我對這個消息感到不安，儘管知道我現在所知道的，但這一點也不奇怪。當時，我體重超重，並且處於臨界胰島素抗性狀態，這兩個巨大的危險因子本身就有助於創造一個促進和加速動脈粥狀硬化病變發展的環境。然而，因為我的鈣分數“只有”6，而我最重要的 LDL（“壞”）膽固醇卻“正常”，所以我收到的醫療建議是——等等——什麼也不做。聽起來有點熟？

Doing nothing is not my style, as you may have gathered by now. I sensed

that I was not on a good trajectory, and I needed to figure out how to change it. My curiosity launched me on a years-long quest to truly understand atherosclerosis. The story I uncovered, with the generous help of my mentors Tom Dayspring, Allan Sniderman, and Ron Krauss (among others), all of whom are world-renowned experts in cardiac pathology and/or the study of lipids, was flabbergasting.

什麼都不做不是我的風格，你現在可能已經明白了。我感覺自己的發展軌跡不太好，我需要想辦法改變它。我的好奇心促使我進行了長達數年的探索，以真正了解動脈粥狀硬化。在我的導師湯姆·戴斯普林（Tom Dayspring）、艾倫·斯尼德曼（Allan Sniderman）和羅恩·克勞斯（Ron Krauss）（以及其他人士）的慷慨幫助下，我發現的故事令人震驚，他們都是心臟病病理學和/或脂質研究領域的世界知名專家。

While heart disease is the most prevalent age-related condition, it is also more easily prevented than either cancer or Alzheimer's disease. We know a lot about how and why it begins and the manner in which it progresses. While it can't exactly be cured or reversed the way type 2 diabetes (sometimes) can, it is relatively easy to delay if you're smart and you get on the case early. It's also the rare example of a chronic disease where Medicine 2.0 already does focus on prevention, to some extent. We have a cabinet full of blood pressure—and cholesterol—lowering medications that really do reduce the risk of death for many patients, and we have blood tests and imaging tests (like my calcium scan) that can at least give us a snapshot, however blurry, of someone's cardiovascular health. It's a start.

雖然心臟病是最常見的與年齡相關的疾病，但它也比癌症或阿茲海默症更容易預防。我們非常了解它如何開始、為何開始以及進展的方式。雖然它不能像第 2 型糖尿病（有時）那樣完全治癒或逆轉，但如果您足夠聰明並且儘早開始治療，那麼延遲治療相對容易。這也是醫學 2.0 在某種程度上已經將重點放在預防的慢性病的罕見例子。我們有一櫃子的降血壓和降膽固醇藥物，確實可以降低許多患者的死亡風險，而且我們還進行了血液檢查和影像學檢查（比如我的鈣掃描），至少可以給我們一個快照。某人的心血管健康狀況模糊。這是一個開始。

In spite of how well we understand atherosclerotic disease and its progression, and how many tools we have to prevent it, it *still* kills more people than cancer in the United States each year, many of them completely out of the blue. We're losing the war. I don't claim to have all the answers, but I think this is at least partly due to the fact that we still have some major blind spots in our understanding of what truly drives our risk for the disease, how it develops, and most of all when we need to act to counter its momentum.

儘管我們非常了解動脈粥狀硬化疾病及其進展，並且我們有許多工具來預防它，但在美國，每年死於該疾病的人數仍然比癌症還要多，其中許多人完全是出乎意料的。我們正在輸掉戰爭。我並不聲稱擁有所有答案，但我認為這至少部分是由於我們在理解真正導致我們患這種疾病的風險、它是如何發展的以及大多數疾病的風險方面仍然存在一些重大盲點。尤其是當我們需要採取行動遏制其勢頭時。

The fundamental problem, I believe, is classic Medicine 2.0: guidelines for managing cardiovascular risk are based on an overly short time horizon, compared to the time line of the disease. We need to begin treating it, and preventing it, much earlier. If we could get it right, the potential payoff would be huge: the high prevalence of male centenarians on the island of Sardinia, for example, has largely been attributed to their ability to avoid or delay circulatory disease. Fewer Sardinian men die from heart disease between the ages of eighty and one hundred than anywhere else in Italy.

我認為，根本問題是經典醫學 2.0：與疾病的時間線相比，管理心血管風險的指南基於的時間範圍過短。我們需要更早開始治療和預防它。如果我們能做對，潛在的回報將是巨大的：例如，撒丁島男性百歲老人的高盛行率很大程度上歸因於他們避免或延緩循環系統疾病的能力。撒丁島在八十歲至一百歲之間死於心臟病的男性比義大利其他地方都要少。

But we're nowhere near that. Heart disease remains our deadliest killer, the worst of the Horsemen. In the next few pages, I hope to convince you that it need not be—that with the right strategy, and attention to the correct risk factors *at the correct time*, it should be possible to eliminate much of the

morbidity and mortality that is still associated with atherosclerotic cardiovascular and cerebrovascular disease.

但我們還遠遠未達到這個目標。心臟病仍然是我們最致命的殺手，也是最糟糕的騎士。在接下來的幾頁中，我希望讓您相信，不必如此——通過正確的策略，並在正確的時間關注正確的風險因素，應該有可能消除仍然存在的大部分發病率和死亡率。與動脈粥狀硬化性心臟和腦血管疾病有關。

Bluntly put: this should be the tenth leading cause of death, not the first.

直白地說：這應該是第十大死因，而不是第一名。

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Scientists have been exploring the medical mysteries of the human heart for almost as long as poets have been probing its metaphorical depths. It is a wondrous organ, a tireless muscle that pumps blood around the body every moment of our lives. It pounds hard when we are exercising, slows down when we sleep, and even microadjusts its rate between beats, a hugely important phenomenon called heart rate variability. And when it stops, we stop.

科學家探索人類心臟的醫學奧秘的時間幾乎和詩人探索其隱喻深度的時間一樣長。它是一個奇妙的器官，是一塊不知疲倦的肌肉，在我們生命中的每時每刻都將血液輸送到身體各處。當我們運動時，它會劇烈運動，當我們睡覺時，它會減慢速度，甚至會微調心跳之間的速率，這是一種非常重要的現象，稱為心率變異性。當它停止時，我們就停止。

Our vascular network is equally miraculous, a web of veins, arteries, and capillaries that, if stretched out and laid end to end, would wrap around the earth more than twice (about sixty thousand miles, if you're keeping score). Each individual blood vessel is a marvel of material science and engineering, capable of expanding and contracting dozens of times per minute, allowing vital substances to pass through its membranes, and accommodating huge swings in fluid pressure, with minimal fatigue. No material created by man

can even come close to matching this. If one vessel is injured, others regrow to take its place, ensuring continuous blood flow throughout the body.

我們的血管網絡同樣神奇，是一個由靜脈、動脈和毛細血管組成的網絡，如果伸展並首尾相接，將環繞地球兩圈以上（如果你記分的話，大約六萬英里）。每一根血管都是材料科學和工程的奇蹟，每分鐘能夠擴張和收縮數十次，允許重要物質通過其膜，並適應流體壓力的巨大波動，同時將疲勞降至最低。人類創造的任何材料都無法與此相媲美。如果一條血管受傷，其他血管就會重新生長取代它，確保全身的血液持續流動。

Incredible as it is, however, our circulatory system is far from perfect—in fact, it is almost perfectly designed to generate atherosclerotic disease, just in the course of daily living. This is in large part because of another important function of our vasculature. In addition to transporting oxygen and nutrients to our tissues and carrying away waste, our blood traffics cholesterol molecules between cells.

然而，令人難以置信的是，我們的循環系統遠非完美——事實上，它幾乎是完美設計的，只是在日常生活過程中就會產生動脈粥狀硬化疾病。這在很大程度上是因為我們脈管系統的另一個重要功能。除了將氧氣和營養物質輸送到我們的組織並帶走廢物之外，我們的血液還在細胞之間運輸膽固醇分子。

It's practically a dirty word, *cholesterol*. Your doctor will probably utter it with a frown, because as everyone knows, cholesterol is evil stuff. Well, some of it is—you know, the LDL or “bad” cholesterol, which is inevitably counterpoised against the HDL, or “good” cholesterol. I practically need to be restrained when I hear these terms, because they're so meaningless. And your “total cholesterol,” the first number that people offer up when we're talking about heart disease, is only slightly more relevant to your cardiovascular risk than the color of your eyes. So let's hit rewind and look at what cholesterol really is, what it does, and how it contributes to heart disease.

膽固醇，其實是一個骯髒的字眼。你的醫生可能會皺著眉頭說出來，因為眾所周知，膽固醇是邪惡的東西。嗯，其中一些是——你知道

的，低密度脂蛋白或「壞」膽固醇，它不可避免地與高密度脂蛋白或「好」膽固醇相抵消。當我聽到這些術語時，我實際上需要保持克制，因為它們毫無意義。當我們談論心臟病時，人們提出的第一個數字「總膽固醇」與心血管風險的相關性僅比眼睛的顏色稍高一些。那麼，讓我們倒帶一下，看看膽固醇到底是什麼、它有什麼作用，以及它如何導致心臟病。

Cholesterol is essential to life. It is required to produce some of the most important structures in the body, including cell membranes; hormones such as testosterone, progesterone, estrogen, and cortisol; and bile acids, which are necessary for digesting food. All cells can synthesize their own cholesterol, but some 20 percent of our body's (large) supply is found in the liver, which acts as a sort of cholesterol repository, shipping it out to cells that need it and receiving it back via the circulation.

膽固醇對生命至關重要。它是產生體內一些最重要的結構所必需的，包括細胞膜；激素，例如睪固酮、黃體酮、雌激素和皮質醇；和膽汁酸，這是消化食物所必需的。所有細胞都可以合成自己的膽固醇，但我們身體（大量）供應的大約20% 是在肝臟中發現的，肝臟充當一種膽固醇儲存庫，將其運送到需要它的細胞並通過循環將其接收回來。

Because cholesterol belongs to the lipid family (that is, fats), it is not water soluble and thus cannot dissolve in our plasma like glucose or sodium and travel freely through our circulation. So it must be carted around in tiny spherical particles called *lipoproteins*—the final “L” in LDL and HDL—which act like little cargo submarines. As their name suggests, these lipoproteins are part lipid (inside) and part protein (outside); the protein is essentially the vessel that allows them to travel in our plasma while carrying their water-insoluble cargo of lipids, including cholesterol, triglycerides, and phospholipids, plus vitamins and other proteins that need to be distributed to our distant tissues.

因為膽固醇屬於脂質家族（即脂肪），所以它不溶於水，因此不能像葡萄糖或鈉一樣溶解在我們的血漿中並在我們的循環中自由流動。因此，它必須以稱為脂蛋白（LDL 和 HDL 的最後一個“L”）的微小球形顆粒形式運輸，其作用就像小型貨運潛艇一樣。顧名思義，這些脂蛋

白部分是脂質（內部），部分是蛋白質（外部）；蛋白質本質上是一種容器，允許它們在我們的血漿中移動，同時攜帶不溶於水的脂質貨物，包括膽固醇、三酸甘油酯和磷脂，以及需要分佈到我們遠處組織的維生素和其他蛋白質。

The reason they're called high- and low-density lipoproteins (HDL and LDL, respectively) has to do with the amount of fat relative to protein that each one carries. LDLs carry more lipids, while HDLs carry more protein in relation to fat, and are therefore more dense. Also, these particles (and other lipoproteins) frequently exchange cargo with one another, which is part of what drives me crazy about labeling them “good” and “bad.” When an HDL transfers its “good cholesterol” to an LDL particle, does that cholesterol suddenly become “bad”?

它們被稱為高密度脂蛋白和低密度脂蛋白（分別為 HDL 和 LDL）的原因與每種脂蛋白攜帶的脂肪相對於蛋白質的量有關。低密度脂蛋白攜帶更多的脂質，而高密度脂蛋白攜帶更多與脂肪相關的蛋白質，因此密度更大。此外，這些顆粒（和其他脂蛋白）經常會相互交換貨物，這也是讓我瘋狂地給它們貼上「好」和「壞」標籤的部分原因。當高密度脂蛋白將其「好膽固醇」轉移到低密度脂蛋白顆粒時，該膽固醇會突然變得「壞」嗎？

The answer is no—because it's not the cholesterol per se that causes problems but the nature of the particle in which it's transported. Each lipoprotein particle is enwrapped by one or more large molecules, called apolipoproteins, that provide structure, stability, and, most importantly solubility to the particle. HDL particles are wrapped in a type of molecule called apolipoprotein A (or apoA), while LDL is encased in apolipoprotein B (or apoB). This distinction may seem trivial, but it goes to the very root cause of atherosclerotic disease: every single lipoprotein that contributes to atherosclerosis—not only LDL but several others^[*1]—carries this apoB protein signature.

答案是否定的，因為造成問題的不是膽固醇本身，而是運輸膽固醇的顆粒的性質。每個脂蛋白顆粒都被一個或多個稱為載脂蛋白的大分子包裹，為顆粒提供結構、穩定性，以及最重要的是溶解度。HDL 顆粒

包裹在一種稱為載脂蛋白 A（或 apoA）的分子中，而 LDL 則包裹在載脂蛋白 B（或 apoB）中。這種差異看似微不足道，但它涉及動脈粥狀硬化疾病的根本原因：每一種導致動脈粥狀硬化的脂蛋白（不僅是 LDL，還有其他幾種脂蛋白[*1]）都帶有這種apoB 蛋白特徵。

Another major misconception about heart disease is that it is somehow caused by the cholesterol that we eat in our diet. According to this dated and simplistic view, eating cholesterol-rich foods causes the so-called bad cholesterol to accumulate in our blood and then build up on our artery walls, as if you poured bacon grease down the kitchen drain every time you made breakfast. Sooner or later, your sink will back up.

關於心臟病的另一個主要誤解是，它是由我們飲食中攝取的膽固醇引起的。根據這種過時且簡單化的觀點，吃富含膽固醇的食物會導致所謂的壞膽固醇在我們的血液中積聚，然後在我們的動脈壁上積聚，就像您每次做早餐時將培根油脂倒入廚房下水道一樣。遲早，你的水槽會恢復正常。

The humble egg, in particular, was singled out in a 1968 proclamation by the American Heart Association, accused of causing heart disease because of its high cholesterol content. It has remained in nutritional purgatory for decades, even after reams of research papers showing that dietary cholesterol (and particularly egg consumption) may not have much to do with heart disease at all. Eating lots of saturated fat *can* increase levels of atherosclerosis-causing lipoproteins in blood, but most of the actual cholesterol that we consume in our food ends up being excreted out our backsides. The vast majority of the cholesterol in our circulation is actually produced by our own cells. Nevertheless, US dietary guidelines warned Americans away from consuming foods high in cholesterol for decades, and nutrition labels still inform American consumers about how much cholesterol is contained in each serving of packaged foods.

特別是這種不起眼的雞蛋，在 1968 年美國心臟協會的聲明中被特別提及，指責其高膽固醇含量導致心臟病。幾十年來，它一直處於營養煉獄之中，即使大量研究論文表明膳食膽固醇（尤其是雞蛋攝入量）可能與心臟病根本沒有太大關係。吃大量的飽和脂肪會增加血液中導致動脈粥狀硬化的脂蛋白水平，但我們在食物中攝取的大部分實際膽固醇最終都會被排出體外。我們循環中的絕大多數膽固醇實際上是由我們自己的細胞產生的。儘管如此，美國飲食指南警告美國人幾十年內不要食用高膽固醇食品，營養標示仍告知美國消費者每份包裝食品中含有多少膽固醇。

Even Ancel Keys, the famed nutrition scientist who was one of the founding fathers of the notion that saturated fat causes heart disease, knew this was nonsense. The problem he recognized was that much of the basic research into cholesterol and atherosclerosis had been conducted in rabbits, which have a unique ability to absorb cholesterol into their blood from their food and form atherosclerotic plaques from it; the mistake was to assume that humans also absorb dietary cholesterol as readily. “There’s no connection whatsoever between cholesterol in food and cholesterol in blood,” Keys said in a 1997 interview. “None. And we’ve known that all along. Cholesterol in the diet doesn’t matter at all unless you happen to be a chicken or a rabbit.”

就連著名營養學家安塞爾凱斯 (Ancel Keys) 也知道這是無稽之談，他是飽和脂肪導致心臟病這一觀點的創始人之一。他認識到的問題是，許多關於膽固醇和動脈粥樣硬化的基礎研究都是在兔子身上進行的，兔子具有獨特的能力，可以從食物中吸收膽固醇到血液中，並從中形成動脈粥樣硬化斑塊；錯誤在於假設人類也同樣容易吸收膳食膽固醇。「食物中的膽固醇和血液中的膽固醇之間沒有任何联系，」凱斯在 1997 年的一次採訪中說道。「沒有任何。我們一直都知道這一點。飲食中的膽固醇根本不重要，除非你碰巧是一隻雞或一隻兔子。」

It took nearly two more decades before the advisory committee responsible for the US government dietary guidelines finally conceded (in 2015) that “cholesterol is not a nutrient of concern for overconsumption.” Glad we settled that.

又過了近二十年，負責美國政府飲食指南的諮詢委員會最終（2015年）承認「膽固醇不是一種需要過度消費的營養素」。很高興我們解決了這個問題。

The final myth that we need to confront is the notion that cardiovascular disease primarily strikes “old” people and that therefore we don’t need to worry much about prevention in patients who are in their twenties and thirties and forties. Not true. I’ll never forget the one-question pop quiz that Allan Sniderman dropped on me over dinner at Dulles Airport, back in 2014: “What proportion of heart attacks occur in people younger than age sixty-five?” I guessed high, one in four, but I was way low. Fully *half* of all major adverse cardiovascular events in men (and a third of those in women), such as heart attack, stroke, or any procedure involving a stent or a graft, occur before the age of sixty-five. In men, one-quarter of all events occur before age fifty-four.

我們需要面對的最後一個誤解是，心血管疾病主要侵襲“老年人”，因此我們不需要太擔心二、三、四十歲患者的預防問題。不對。我永遠不會忘記 2014 年在杜勒斯機場吃晚飯時艾倫·斯尼德曼 (Allan Sniderman) 向我提出的一個簡單問題：“65 歲以下的人中心臟病發作的比例是多少？”我猜得很高，四分之一，但我的預測太低了。男性所有主要不良心血管事件的一半（以及女性的三分之一），例如心臟病發作、中風或任何涉及支架或移植物的手術，發生在六十五歲之前。對男性來說，四分之一的的事件發生在五十四歲之前。

But while the events themselves may have seemed sudden, the problem was likely lurking for years. Atherosclerosis is a slow-moving, sneaky disease, which is why I take such a hard line on it. Our risk of these “events” rises steeply in the second half of our lifespan, but some scientists believe the underlying processes are set into motion in late adolescence, even as early as our teens. The risk builds throughout our lives, and the critical factor is time. Therefore it is critical that we understand how it develops, and progresses, so we can develop a strategy to try to slow or stop it.

然而，儘管這些事件本身似乎很突然，但問題可能已經潛伏多年。動脈粥狀硬化是一種進展緩慢、不易察覺的疾病，這就是為什麼我對它

採取如此強硬的態度。在我們生命的後半段，我們發生這些「事件」的風險急劇上升，但一些科學家認為，潛在的過程在青春期末期，甚至早在我們十幾歲的時候就開始了。風險貫穿我們的一生，而關鍵因素是時間。因此，了解它的發展和進展至關重要，這樣我們就可以制定策略來嘗試減緩或阻止它。

Back when I had an office, pre-COVID, I kept a clutter-free desk, but one book in particular was always there: *Atlas of Atherosclerosis Progression and Regression*, by Herbert C. Stary. It will never be a bestseller, but in the field of cardiovascular pathology it is legendary. It also happens to be a highly effective tool for communicating the seriousness of this disease to my patients, thanks to its lavish and gruesome photographs of arterial lesions as they form, develop, and rupture—all taken of the arteries of dead people, many of them in their twenties and thirties. The story it lays out, in graphic detail, is equal parts fascinating and terrifying. By the time I finished, my patients would often have this kind of harrowed expression on their faces, as if they'd just leafed through a coffee-table book documenting their own death.

在新冠疫情爆發之前，當我有一間辦公室時，我的桌子很整潔，但總是放著一本書：《動脈粥樣硬化進展與回歸圖譜》，作者是赫伯特·C·斯塔里(Herbert C. Stary)。它永遠不會成為暢銷書，但在心血管病理學領域是傳奇。它也恰好是向我的患者傳達這種疾病的嚴重性的一個非常有效的工具，這要歸功於它對動脈病變形成、發展和破裂的大量而可怕的照片——所有這些都是從死者的動脈中拍攝的，其中許多是死者的動脈。他們二、三十歲。它以生動的細節講述的故事既令人著迷又令人恐懼。當我結束時，我的病人臉上常常帶著這種痛苦的表情，就好像他們剛剛翻閱了一本記錄自己死亡的咖啡桌書一樣。

This isn't a perfect analogy, but I think of atherosclerosis as kind of like the scene of a crime—breaking and entering, more or less. Let's say we have a street, which represents the blood vessel, and the street is lined with houses, representing the arterial wall. The fence in front of each house is analogous to

something called the endothelium, a delicate but critical layer of tissue that lines all our arteries and veins, as well as certain other tissues, such as the kidneys. Composed of just a single layer of cells, the endothelium acts as a semipermeable barrier between the vessel lumen (i.e., the street, where the blood flows) and the arterial wall proper, controlling the passage of materials and nutrients and white blood cells into and out of the bloodstream. It also helps maintain our electrolyte and fluid balance; endothelial problems can lead to edema and swelling. Another very important job it does is to dilate and contract to allow increased or decreased blood flow, a process modulated by nitric oxide. Last, the endothelium regulates blood-clotting mechanisms, which can be important if you accidentally cut yourself. It's a pretty important little structure.

這不是一個完美的類比，但我認為動脈粥狀硬化有點像犯罪現場——破門而入，或多或少。假設我們有一條街道，代表血管，街道兩旁都是房屋，代表動脈壁。每棟房子前面的柵欄類似於一種叫做內皮的東西，這是一層脆弱但關鍵的組織，排列在我們所有的動脈和靜脈以及某些其他組織（例如腎臟）上。內皮細胞僅由單層細胞組成，充當血管腔（即血液流動的街道）和動脈壁之間的半透性屏障，控制物質和營養物質以及白血球進入和進入血管。從血液中出來。它也有助於維持我們的電解質和液體平衡；內皮問題可導致水腫和腫脹。它所做的另一項非常重要的工作是擴張和收縮以增加或減少血流量，這是由一氧化氮調節的過程。最後，內皮細胞調節凝血機制，如果您不小心割傷了自己，這一點可能很重要。這是一個非常重要的小結構。

The street is very busy, with a constant flow of blood cells and lipoproteins and plasma and everything else that our circulation carries, all brushing past the endothelium. Inevitably, some of these cholesterol-bearing lipoprotein particles will penetrate the barrier, into an area called the subendothelial space—or in our analogy, the front porch. Normally, this is fine, like guests stopping by for a visit. They enter, and then they leave. This is what HDL particles generally do: particles tagged with apoA (HDL) can cross the endothelial barrier easily in both directions, in and out. LDL particles and

other particles with the apoB protein are far more prone to getting stuck inside.

街道非常繁忙，血細胞、脂蛋白、血漿以及我們循環中攜帶的其他所有東西不斷流動，所有這些都擦過內皮細胞。不可避免地，這些帶有膽固醇的脂蛋白顆粒中的一些將穿透屏障，進入稱為內皮下空間的區域，或在我們的類比中，前廊。通常情況下，這很好，就像有客人來拜訪一樣。他們進來，然後離開。這就是 HDL 顆粒通常的作用：帶有 apoA (HDL) 標記的顆粒可以輕鬆地在兩個方向（進出）穿過內皮屏障。LDL 顆粒和其他含有 apoB 蛋白的顆粒更容易被卡在裡面。

This is what actually makes HDL particles potentially “good” and LDL particles potentially “bad”—not the cholesterol, but the particles that carry it. The trouble starts when LDL particles stick in the arterial wall and subsequently become oxidized, meaning the cholesterol (and phospholipid) molecules they contain come into contact with a highly reactive molecule known as a reactive oxygen species, or ROS, the cause of oxidative stress. It's the oxidation of the lipids on the LDL that kicks off the entire atherosclerotic cascade.

這實際上是使高密度脂蛋白顆粒潛在「好」而低密度脂蛋白顆粒潛在的「壞」原因——不是膽固醇，而是攜帶膽固醇的顆粒。當低密度脂蛋白顆粒黏附在動脈壁上並隨後被氧化時，問題就開始了，這意味著它們所含的膽固醇（和磷脂）分子與一種被稱為活性氧（ROS）的高活性分子接觸，這是氧化壓力的原因。低密度脂蛋白上的脂質氧化引發了整個動脈粥狀硬化級聯反應。

Now that it is lodged in the subendothelial space and oxidized, rendering it somewhat toxic, the LDL/apoB particle stops behaving like a polite guest, refusing to leave—and inviting its friends, other LDLs, to join the party. Many of these also are retained and oxidized. It is not an accident that the two biggest risk factors for heart disease, smoking and high blood pressure, cause damage to the endothelium. Smoking damages it chemically, while high blood pressure does so mechanically, but the end result is endothelial harm that, in turn, leads to greater retention of LDL. As oxidized LDL accumulates, it causes still more damage to the endothelium.

現在，它被困在內皮下空間並被氧化，使其具有一定的毒性，LDL/apoB 顆粒不再表現得像一個有禮貌的客人，拒絕離開，並邀請它的朋友，其他 LDL，加入聚會。其中許多也被保留和氧化。心臟病的兩個最大危險因子——吸菸和高血壓——對內皮細胞造成損害並非偶然。吸菸會造成化學損傷，而高血壓會造成機械性損傷，但最終結果是內皮損傷，進而導致低密度脂蛋白滯留更多。隨著氧化低密度脂蛋白的積累，它會對內皮細胞造成更大的傷害。

I've been saying LDL, but the key factor here is actually *exposure* to apoB-tagged particles, over time. The more of these particles that you have in your circulation, not only LDL but VLDL and some others, the greater the risk that some of them will penetrate the endothelium and get stuck. Going back to our street analogy, imagine that we have, say, one ton of cholesterol moving down the street, divided among four pickup trucks. The chance of an accident is fairly small. But if that same total amount of cholesterol is being carried on five hundred of those little rental scooters that swarm around cities like Austin, where I live, we are going to have absolute mayhem^[*2] on our hands. So to gauge the true extent of your risk, we *have* to know how many of these apoB particles are circulating in your bloodstream. That number is much more relevant than the total quantity of cholesterol that these particles are carrying.

我一直在說 LDL，但這裡的關鍵因素實際上是隨著時間的推移，暴露於 apoB 標記的顆粒。循環中的這些顆粒越多，不僅是低密度脂蛋白，還有極低密度脂蛋白和其他一些顆粒，它們中的一些顆粒穿透內皮而卡住的風險就越大。回到我們的街道類比，想像一下，我們有一噸膽固醇沿著街道運輸，分裝到四輛皮卡車中。發生事故的可能性相當小。但是，如果五百輛小型出租摩托車攜帶著同樣總量的膽固醇，這些小型出租摩托車聚集在我居住的奧斯汀等城市周圍，那麼我們將面臨絕對的混亂^[*2]。因此，為了衡量您的風險的真實程度，我們必須知道您的血液中循環的 apoB 顆粒數量。這個數字比這些顆粒攜帶的膽固醇總量更重要。

If you take a healthy coronary artery and expose it to high enough concentrations of apoB particles, over a long enough time, a certain amount of LDL (and VLDL) will get stuck in that subendothelial space and become

oxidized, which then leads to it sticking together in clumps or aggregates. In response to this incursion, the endothelium dials up the biochemical equivalent of 911, summoning specialized immune cells called monocytes to the scene to confront the intruders. Monocytes are large white blood cells that enter the subendothelial space and transform into macrophages, larger and hungrier immune cells that are sometimes compared to Pac-Man. The macrophage, whose name means “big eater,” swallows up the aggregated or oxidized LDL, trying to remove it from the artery wall. But if it consumes too much cholesterol, then it blows up into a foam cell, a term that you may have heard—so named because under a microscope it looks foamy or soapy. When enough foam cells gather together, they form a “fatty streak”—literally a streak of fat that you can see with your naked eye during an autopsy of a splayed-open coronary artery.

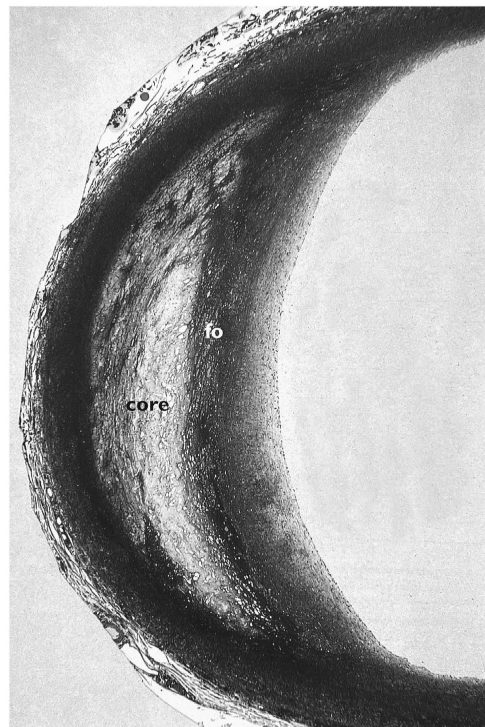
如果您將健康的冠狀動脈暴露於足夠高濃度的 apoB 顆粒中，經過足夠長的時間，一定量的 LDL（和 VLDL）將卡在該內皮下空間並被氧化，從而導致其粘附聚集成團塊或聚集體。為了應對這種入侵，內皮細胞會調出相當於 911 的生化訊號，召喚稱為單核細胞的特殊免疫細胞來對抗入侵者。單核細胞是進入內皮下空間並轉化為巨噬細胞的大型白血球，巨噬細胞是更大、更飢餓的免疫細胞，有時與吃豆人比較。巨噬細胞的名字意思是“大食者”，它吞噬聚集或氧化的低密度脂蛋白，試圖將其從動脈壁上清除。但如果它消耗了太多的膽固醇，那麼它就會膨脹成泡沫細胞，你可能聽說過這個術語——如此命名是因為在顯微鏡下它看起來呈泡沫狀或肥皂狀。當足夠多的泡沫細胞聚集在一起時，它們會形成「脂肪條紋」——字面意思是在對張開的冠狀動脈進行屍檢時用肉眼可以看到的脂肪條紋。

The fatty streak is a precursor of an atherosclerotic plaque, and if you are reading this and are older than fifteen or so, there is a good chance you already have some of these lurking in your arteries. Yes, I said “fifteen” and not “fifty”—this is a lifelong process and it starts very early. Autopsy data from young people who died from accidents, homicides, or other noncardiovascular causes have revealed that as many as a third of sixteen-

twenty-year-olds *already* had actual atherosclerotic lesions or plaques in their coronary arteries when they died. As teenagers.

脂肪條紋是動脈粥狀硬化斑塊的前兆，如果您正在閱讀本文並且年齡超過 15 歲左右，那麼您的動脈中很可能已經潛伏著其中一些脂肪條紋。是的，我說的是「十五」而不是「五十」——這是一個終生的過程，而且很早就開始了。死於事故、兇殺或其他非心血管原因的年輕人的屍檢數據顯示，多達三分之一的16 至20 歲年輕人在死亡時，其冠狀動脈中已經存在實際的動脈粥樣硬化病變或斑塊。作為青少年。

Figure 5. Atherosclerotic Disease in a 23-Year-Old



Source: Sary, (2003).

來源：Sary，（2003）。

This is a cross-sectional view of the proximal left anterior descending artery, one of the key vessels supplying blood to the heart, from a twenty-three-year-old male homicide victim. Note that he already has extensive atherosclerotic damage in the wall of this artery: a significant core (“core”) of accumulated lipids, and macrophages and foam cells (“fo”) in the subendothelial space, beginning to encroach on the lumen, the passage where blood flows. He would likely not suffer a heart attack anytime soon, but this is very advanced disease nonetheless.

這是一名 23 歲男性兇殺案受害者的左前降支近端的橫斷面圖，左前降支是向心臟供血的關鍵血管之一。請注意，他的動脈壁已經出現廣泛的動脈粥樣硬化損傷：內皮下空間中積累的脂質、巨噬細胞和泡沫細胞（“fo”）的顯著核心（“核心”）開始侵入管腔，血液流動的通道。他可能不會很快心臟病發作，但這仍然是一種非常晚期的疾病。

It's not as if they were about to have heart attacks. The atherosclerotic process moves very slowly. This may be partly because of the action of HDLs. If an HDL particle arrives at our crime scene, with the foam cells and fatty streaks, it can suck the cholesterol back *out* of the macrophages in a process called delipidation. It then slips back across the endothelial layer and into the bloodstream, to deliver the excess cholesterol back to the liver and other tissues (including fat cells and hormone-producing glands) for reuse.

他們並不像是心臟病發作。動脈粥狀硬化過程進展非常緩慢。這可能部分是由於 HDL 的作用。如果高密度脂蛋白顆粒帶著泡沫細胞和脂肪條紋到達我們的犯罪現場，它可以透過稱為脫脂的過程將膽固醇從巨噬細胞中吸回。然後它滑回內皮層並進入血液，將多餘的膽固醇輸送回肝臟和其他組織（包括脂肪細胞和產生激素的腺體）以供再利用。

Its role in this process of “cholesterol efflux” is one reason why HDL is considered “good,” but it does more than that. Newer research suggests that HDL has multiple other atheroprotective functions that include helping maintain the integrity of the endothelium, lowering inflammation, and neutralizing or stopping the oxidation of LDL, like a kind of arterial antioxidant.

它在「膽固醇流出」過程中的作用是高密度脂蛋白被認為「好」的原因之一，但它的作用不止於此。最新的研究表明，HDL 具有多種其他

動脈粥狀硬化功能，包括幫助維持內皮的完整性、降低發炎以及中和或阻止 LDL 的氧化，就像一種動脈抗氧化劑。

The role of HDL is far less well understood than that of LDL. The cholesterol content in your LDL particles, your “bad” cholesterol number (technically expressed as LDL-C),^[*3] is actually a decent if imperfect proxy for its biologic impact; lots of studies have shown a strong correlation between LDL-C and event risk. But the all-important “good cholesterol” number on your blood test, your HDL-C, doesn’t actually tell me very much if anything about your overall risk profile. Risk does seem to decline as HDL-C rises to around the 80th percentile. But simply raising HDL cholesterol concentrations by brute force, with specialized drugs, has not been shown to reduce cardiovascular risk at all. The key seems to be to increase the *functionality* of the particles—but as yet we have no way to do that (or measure it).

高密度脂蛋白的作用遠不如低密度脂蛋白那麼了解。低密度脂蛋白顆粒中的膽固醇含量，即「壞」膽固醇數量（技術上表示為低密度脂蛋白膽固醇），^[*3]實際上是其生物影響的一個不錯的指標，儘管並不完美；大量研究顯示 LDL-C 與事件風險之間有強烈的相關性。但血液檢測中最重要的「好膽固醇」數字，即高密度脂蛋白膽固醇（HDL-C），實際上並不能告訴我有關您整體風險狀況的任何資訊。隨著 HDL-C 上升到第 80 個百分位數左右，風險似乎確實下降了。但僅僅使用專門藥物強力提高高密度脂蛋白膽固醇濃度，並沒有被證明可以降低心血管風險。關鍵似乎是增加粒子的功能，但到目前為止我們還沒有辦法做到這一點（或測量它）。

HDL may or may not explain why centenarians develop heart disease two decades later than average, if at all; remember, three of the most prominent “longevity genes” discovered to date are involved with cholesterol transport and processing (APOE and two others, CETP and APOC3). And it’s not just centenarians: I have patients walking around whose lipoprotein panels read like a death sentence, with sky-high LDL-C and apoB, but by every single measure that we have—calcium score, CT angiogram, you name it—they show no sign of disease. Yet as of now, we cannot give a satisfactory explanation for why. I feel strongly that if we are to make any further progress

attacking cardiovascular disease with drugs, we must start by better understanding HDL and hopefully figuring out how to enhance its function.

高密度脂蛋白可能或可能無法解釋為什麼百歲老人患心臟病的時間比平均晚二十年（如果有的話）；請記住，迄今為止發現的三個最著名的「長壽基因」與膽固醇運輸和加工有關（APOE 和另外兩個基因，CETP 和 APOC3）。不只是百歲老人：我身邊有一些患者，他們的脂蛋白檢測結果就像判了死刑一樣，LDL-C 和 apoB 都極高，但根據我們所掌握的每一項指標（鈣分數、CT血管攝影，凡是你能想到的），他們沒有任何疾病跡象。但到目前為止，我們還無法給出令人滿意的解釋。我強烈認為，如果我們要在藥物治療心血管疾病方面取得進一步進展，我們必須從更好地了解 HDL 開始，並希望弄清楚如何增強其功能。

But I digress. Back at the crime scene, the ever-growing number of foam cells begin to sort of ooze together into a mass of lipids, like the liquefying contents of a pile of trash bags that have been dumped on the front lawn. This is what becomes the core of our atherosclerotic plaque. And this is the point where breaking and entering tilts over into full-scale looting. In an attempt to control the damage, the “smooth muscle” cells in the artery wall then migrate to this toxic waste site and secrete a kind of matrix in an attempt to build a kind of barrier around it, like a scar. This matrix ends up as the fibrous cap on your brand-new arterial plaque.

但我離題了。回到犯罪現場，越來越多的泡沫細胞開始滲出，形成大量脂質，就像傾倒在前草坪上的一堆垃圾袋中液化的內容物一樣。這就是動脈粥狀硬化斑塊的核心。這就是破門而入轉變為全面搶劫的關鍵點。為了控制損傷，動脈壁中的「平滑肌」細胞會遷移到這個有毒廢物部位，並分泌一種基質，試圖在其周圍建立一種屏障，就像疤痕一樣。此基質最終成為全新動脈斑塊上的纖維帽。

More bad news: None of what's gone on so far is easily detectable in the various tests we typically use to assess cardiovascular risk in patients. We might expect to see evidence of inflammation, such as elevated levels of C-reactive protein, a popular (but poor) proxy of arterial inflammation. But it's still mostly flying below our medical radar. If you look at the coronary arteries

with a CT scan at this very early stage, you will likely miss this if you're looking only for calcium buildup. (You have a better chance of spotting this level of damage if using a more advanced type of CT scan, called a CT angiogram, which I much prefer to a garden-variety calcium scan^[*4] because it can also identify the noncalcified or “soft” plaque that precedes calcification.)

更多壞消息：到目前為止，我們通常用來評估患者心血管風險的各種測試都無法輕易檢測到所發生的情況。我們可能期望看到發炎的證據，例如 C 反應蛋白水平升高，這是動脈發炎的一種流行（但效果不佳）的指標。但它仍然大部分在我們的醫療雷達範圍內飛行。如果您在早期階段透過 CT 掃描觀察冠狀動脈，如果您只關注鈣沉積，您可能會錯過這一點。（如果使用更先進的CT 掃描（稱為CT 血管造影），您更有可能發現這種程度的損傷，我更喜歡這種掃描，而不是普通的鈣掃描^[*4]，因為它還可以識別非鈣化或鈣化的病變。鈣化之前的“軟”斑塊。）

As this maladaptive repair or remodeling process continues, the plaque will continue to grow. At first, this expansion is directed toward the outer arterial wall, but as it continues it may encroach on the lumen, the passage through which blood flows—in our analogy, blocking traffic in the street itself. This luminal narrowing, known as *stenosis*, can also be seen in an angiogram.

隨著這種不適應的修復或重塑過程的繼續，斑塊將繼續生長。起初，這種擴張是針對外動脈壁的，但隨著它的繼續，它可能會侵入管腔，即血液流動的通道——用我們的比喻來說，阻塞街道本身的交通。這種管腔變窄，稱為狹窄，也可以在血管攝影中看到。

At a certain point in this process, the plaque may start to become calcified. This is what (finally) shows up on a regular calcium scan. Calcification is merely another way in which the body is trying to repair the damage, by stabilizing the plaque to protect the all-important arteries. But it's like pouring concrete on the Chernobyl reactor: you're glad it's there, but you know there's been an awful lot of damage in the area to warrant such an intervention. A

positive calcium score is really telling us that there are almost certainly other plaques around that may or may not be stabilized (calcified).

在這個過程的某個時刻，斑塊可能會開始鈣化。這就是（最終）在常規鈣掃描中顯示的結果。鈣化只是身體試圖修復損傷的另一種方式，透過穩定斑塊來保護最重要的動脈。但這就像在切爾諾貝利反應器上澆築混凝土：你很高興它在那裡，但你知道該地區已經遭受了嚴重的破壞，需要進行這樣的干預。正面的鈣分數實際上告訴我們，幾乎可以肯定周圍有其他斑塊可能會或可能不會穩定（鈣化）。

If the plaque does become unstable, eroding or even rupturing, you've really got problems. The damaged plaque may ultimately cause the formation of a clot, which can narrow and ultimately block the lumen of the blood vessel—or worse, break free and cause a heart attack or stroke. This is why we worry more about the noncalcified plaques than the calcified ones.

如果牙菌斑確實變得不穩定、腐蝕甚至破裂，那麼你就真的遇到了問題。受損的斑塊最終可能會形成凝塊，凝塊會變窄並最終阻塞血管腔，或者更糟的是，凝塊會脫落並導致心臟病發作或中風。這就是為什麼我們更擔心非鈣化斑塊而不是鈣化斑塊。

Normally, however, most atherosclerotic plaques are fairly undramatic. They grow silently and invisibly, gradually occluding the blood vessel until one day the obstruction, due to the plaque itself or a plaque-induced clot, becomes a problem. For example, a sedentary person may not notice that she has a partially blocked coronary artery until she goes outside to shovel snow. The sudden demands on her circulatory system can trigger ischemia (decreased blood delivery of oxygen) or infarction (tissue death from no blood flow)—or, in layman's terms, a heart attack or a stroke.

然而，通常情況下，大多數動脈粥狀硬化斑塊都相當平淡。它們默默地、無形地生長，逐漸堵塞血管，直到有一天，由於斑塊本身或斑塊引起的凝塊而導致的阻塞成為一個問題。例如，久坐的人可能不會注意到她的冠狀動脈部分阻塞，直到她出去鏟雪。循環系統的突然需求可能會引發缺血（血液輸送氧氣減少）或梗塞（因沒有血液流動而導致組織死亡），或者用外行的話來說，引發心臟病或中風。

It may seem sudden, but the danger was lurking all along.
看似突然，但危險其實一直潛伏著。

When I finally recognized my own cardiovascular risk, back in my thirties, I had no idea about how any of this complex disease process worked. Looking back, it's clear that I had quite a few of the major and lesser risk factors already checked off. I didn't smoke, which is perhaps the most potent environmental risk driver, and my blood pressure was normal, but I had other problems. And as my calcium score revealed, I already had a small, calcified plaque in the upper part of my left anterior descending (LAD) artery, one of the main arteries supplying my heart. There may have been other bad things happening there as well, but because I did not have a CT angiogram at this time, I had no sense of what kind of damage existed elsewhere in my coronary arteries. Anything shy of calcification is *not* identified by the calcium score.

當我三十多歲時終於認識到自己的心血管風險時，我不知道這種複雜的疾病過程是如何發生的。回顧過去，很明顯我已經檢查了相當多的主要和次要風險因素。我不吸煙，這可能是最有力的環境風險驅動因素，而且我的血壓正常，但我還有其他問題。正如我的鈣評分顯示，我的左前降支 (LAD) 動脈（供應心臟的主要動脈之一）上部已經有一個小的鈣化斑塊。那裡可能還發生了其他不好的事情，但因為我當時沒有做CT血管造影，所以我不知道我的冠狀動脈其他地方有什麼樣的損傷。鈣評分無法辨識任何未鈣化的情況。

Clearly, Not-Thin Peter was already on the road to heart disease. My waist size was on track to hit 40 by the time I turned forty, a clear sign of my metabolic dysfunction. Underneath my belt, I was likely accumulating visceral fat. I was also insulin resistant, an enormous risk driver for cardiovascular disease. Though my blood pressure was fine, I suspect it would have deteriorated fairly rapidly as I aged, as hypertension seems rampant in my family. I probably also had high levels of uric acid, which as we saw in the previous chapter is often found in the company of high blood pressure and

other signs of metabolic dysfunction. All of these contribute to another necessary (but not sufficient) condition that is required for atherosclerosis to develop, and that is inflammation. The endothelial barrier, in particular, is uniquely vulnerable to damage from inflammation.

顯然，不瘦的彼得已經走上了心臟病的道路。到四十歲時，我的腰圍有望達到 40，這是我代謝功能障礙的明顯跡象。在我的腰帶下面，我可能正在累積內臟脂肪。我還患有胰島素阻抗，這是心血管疾病的巨大風險驅動因素。雖然我的血壓很好，但我懷疑隨著年齡的增長，血壓會很快惡化，因為高血壓在我的家族中似乎很猖獗。我的尿酸水平可能也很高，正如我們在前一章中看到的那樣，尿酸水平通常伴隨著高血壓和其他代謝功能障礙的跡象。所有這些都會導致動脈粥狀硬化發展所需的另一個必要（但不是充分）條件，那就是發炎。尤其是內皮屏障，特別容易受到發炎的損害。

But no physician would likely have treated me for any of this. My blood panel did not signal any significant risk. My LDL-C tested at 110 to 120 mg/dL, just slightly higher than normal but not a cause for concern, particularly in a younger person. My triglycerides were on the higher side, slightly north of 150 mg/dL, but that did not set off any alarm bells either. I now know that these numbers almost certainly indicated a high concentration of atherogenic apoB particles—but no one bothered to test my apoB number, either.

但沒有醫生可能會為此治療我。我的血液檢查沒有顯示任何重大風險。我的 LDL-C 測試值為 110 至 120 mg/dL，僅略高於正常值，但不必擔心，尤其是對於年輕人。我的三酸甘油酯偏高，略高於 150 毫克/分升，但這也沒有引起任何警鐘。我現在知道，這些數字幾乎肯定表明致動脈粥樣硬化的 apoB 顆粒濃度很高，但也沒有人費心測試我的 apoB 數值。

Back then, nearly fifteen years ago, the apoB test (simply, measuring the concentration of apoB-tagged particles) was not commonly done. Since then, evidence has piled up pointing to apoB as far more predictive of cardiovascular disease than simply LDL-C, the standard “bad cholesterol” measure. According to an analysis published in *JAMA Cardiology* in 2021,

each standard-deviation increase in apoB raises the risk of myocardial infarction by 38 percent in patients without a history of cardiac events or a diagnosis of cardiovascular disease (i.e., primary prevention). That's a powerful correlation. Yet even now, the American Heart Association guidelines still favor LDL-C testing instead of apoB. I have all my patients tested for apoB regularly, and you should ask for the same test the next time you see your doctor. (Don't be waved off by nonsensical arguments about "cost": It's about twenty to thirty dollars.)

當時，大約十五年前，apoB 測試（簡單來說，測量 apoB 標記顆粒的濃度）並不常見。從那時起，越來越多的證據表明，apoB 比標準的「壞膽固醇」指標 LDL-C 更能預測心血管疾病。根據2021 年《美國醫學會雜誌心臟病學》(JAMA Cardiology) 發表的一項分析，對於沒有心臟事件史或沒有心血管疾病診斷（即一級預防）的患者，apoB 每增加一個標準差，心肌梗塞的風險就會增加38%。這是一種很強的相關性。然而即使是現在，美國心臟協會的指導方針仍然傾向於 LDL-C 檢測而不是 apoB。我定期對所有患者進行 apoB 檢測，您下次看醫生時應該要求進行相同的檢測。（不要被關於「成本」的無意義爭論所打動：大約是二十到三十美元。）

I was still in my thirties, yet I likely already had all three of the major prerequisites for heart disease: significant lipoprotein burden or apoB, LDL oxidation or modification (leading to the plaques that my calcium scan revealed), and a high level of background inflammation. None of these is enough to *guarantee* that someone will develop heart disease, but all three are *necessary* to develop it. We are fortunate that many of these conditions can be modulated or nearly eliminated—including apoB, by the way—via lifestyle changes and medications. As we'll discuss in the final section, I take a very hard line on lowering apoB, the particle that causes all this trouble. (In short: get it as low as possible, as early as possible.)

我當時才三十多歲，但我可能已經具備了心臟病的所有三個主要先決條件：顯著的脂蛋白負荷或apoB、LDL 氧化或修飾（導致我的鈣掃描顯示出斑塊）以及高水平的背景炎。這些都不足以保證某人會罹患心臟病，但這三者都是罹患心臟病所必需的。幸運的是，許多這些病症

都可以透過改變生活方式和藥物來調節或幾乎消除——順便說一句，包括 apoB。正如我們將在最後一節中討論的那樣，我對降低 apoB（導致所有這些問題的粒子）採取非常強硬的態度。（簡而言之：盡可能低、儘早獲得。）

But before we go there, I want to talk about another deadly but relatively little-known lipoprotein that is likely responsible for graveyards full of sudden cardiac arrest victims, people whose conventional cholesterol panels and risk factor profiles otherwise looked fine. I don't have this particular issue, thankfully, but a very good friend of mine does, and finding out about it in a timely manner likely saved his life.

但在我們討論之前，我想談談另一種致命但相對鮮為人知的脂蛋白，它可能是導致墓地裡充滿心臟驟停受害者的原因，這些人的傳統膽固醇面板和危險因素概況在其他方面看起來都很好。謝天謝地，我沒有這個特殊的問題，但我的一個很好的朋友有，及時發現這個問題可能救了他的命。

—

I met Anahad O'Connor in 2012 on a junket to France, courtesy of the French-American Foundation and an award we had both won, and we immediately bonded. I think it was because we were the only two guys on the trip who skipped the *pain au chocolat* and spent our spare time in the gym. Also, he wrote about health and science for *The New York Times*, so we had plenty to talk about.

2012 年，我在去法國的一次中介中認識了阿納哈德·奧康納（Anahad O'Connor），受到法美基金會的惠顧，我們都贏得了一個獎項，我們很快就結下了不解之緣。我想這是因為我們是這次旅行中唯一兩個跳過巧克力痛苦並在健身房度過空閒時間的人。此外，他也為《紐約時報》撰寫有關健康和科學的文章，因此我們有很多主題可以討論。

Because I am a cholesterol nerd, I badgered Anahad into doing a comprehensive lipoprotein panel when we got back to the United States. He looked at me funny—Why should he do that? He was only in his early thirties,

an extremely fit vegetarian with maybe 6 or 7 percent body fat. He should have been fine in the lipid department. But you never know; his father had died of an aneurysm, which may have been a sign of circulatory problems.

因為我是一個膽固醇迷，所以當我們回到美國時，我纏著阿納哈德做一個全面的脂蛋白檢查。他奇怪地看著我——他為什麼要這麼做？他只有三十歲出頭，是個非常健康的素食者，體脂大約有百分之六七。他在血脂科應該沒問題。但你永遠不知道；他的父親死於動脈瘤，可能是循環系統問題的徵兆。

As expected, his standard lipid numbers looked great. There was only one thing that seemed off, so I suggested that he should probably also get a calcium scan, as I had done, so we could get a better sense of the state of his arteries. That's where things got interesting. Recall, my calcium score had come back at 6, placing me at higher risk than 75 to 90 percent of people my age. Anahad's calcium score was 125—off the charts for someone so young and otherwise healthy. “Can this be real?” he said.

正如預期的那樣，他的標準血脂數值看起來不錯。只有一件事似乎不對勁，所以我建議他也應該像我一樣進行鈣掃描，這樣我們就可以更了解他的動脈狀況。這就是事情變得有趣的地方。回想一下，我的鈣分數恢復為 6，這使我比 75% 至 90% 的同齡人面臨更高的風險。阿納哈德的鈣分數為 125，對於如此年輕且健康的人來說，這是超乎尋常的。“這可能是真的嗎？”他說。

It was. It turned out that the culprit was a little-known but very deadly type of particle called Lp(a) (pronounced “el-pee-little-A”). This hot mess of a lipoprotein is formed when a garden-variety LDL particle is fused with another, rarer type of protein called apolipoprotein(a), or apo(a) for short (not to be confused with apolipoprotein A or apoA, the protein that marks HDL particles). The apo(a) wraps loosely around the LDL particle, with multiple looping amino acid segments called “kringles,” so named because their structure resembles the ring-shaped Danish pastry by that name. The kringles are what make Lp(a) so dangerous: as the LDL particle passes through the bloodstream, they scoop up bits of oxidized lipid molecules and carry them along.

它是。事實證明，罪魁禍首是一種鮮為人知但非常致命的粒子，稱為 Lp(a)（發音為“el-pee-little-A”）。當普通的 LDL 顆粒與另一種較罕見的蛋白質（稱為載脂蛋白(a)，簡稱 apo(a)）融合時，就會形成這種熱亂的脂蛋白（不要與載脂蛋白 A 或 apoA 混淆，該蛋白質是載脂蛋白 A 或 apoA）。標記 HDL 顆粒）。 apo(a) 鬆散地包裹著 LDL 顆粒，具有多個稱為「kringles」的環狀氨基酸片段，之所以如此命名，是因為它們的結構類似於同名的環形丹麥糕點。這些三環使 Lp(a) 如此危險：當低密度脂蛋白顆粒通過血液時，它們會舀起一些氧化的脂質分子並將其帶走。

As my lipid guru Tom Dayspring points out, this isn't entirely bad. There is some evidence that Lp(a) may act as a sort of cleansing agent, like a street-sweeping truck that gathers up unpleasant and potentially harmful lipid junk and delivers it to the liver. But because Lp(a) is a member of the apoB particle family, it also has the potential to penetrate the endothelium and get lodged in an artery wall; because of its structure, Lp(a) may be even more likely than a normal LDL particle to get stuck, with its extra cargo of lipids gone bad. Even worse, once in there, it acts partly as a thrombotic or proclotting factor, which helps to speed the formation of arterial plaques.

正如我的脂質專家湯姆·戴斯普林（Tom Dayspring）指出的那樣，這並不完全是壞事。有一些證據表明，Lp(a) 可能充當一種清潔劑，就像一輛掃街車，收集令人不愉快且可能有害的脂質垃圾並將其輸送到肝臟。但由於 Lp(a) 是 apoB 顆粒家族的一員，因此它也有可能穿透內皮並滯留在動脈壁中；由於其結構，Lp(a) 可能比正常的低密度脂蛋白顆粒更容易被卡住，因為其中多餘的脂質會變質。更糟的是，一旦進入其中，它就會部分地充當血栓形成或凝血因子，這有助於加速動脈斑塊的形成。

Often, the way Lp(a) announces itself is via a sudden, seemingly premature heart attack. This is what happened to *Biggest Loser* host Bob Harper, who suffered cardiac arrest at a gym in New York in 2017, at age fifty-two. Harper's life was saved by a bystander who performed CPR until the paramedics arrived. He woke up in the hospital two days later, wondering

what had hit him. Turns out, his very high level of Lp(a) was what had hit him. He had no idea that he was at risk.

通常，Lp(a) 的表現是透過突然的、看似過早的心臟病發作。這就是《減肥達人》主持人鮑勃哈珀 (Bob Harper) 的遭遇，他於 2017 年在紐約一家健身房遭遇心臟驟停，當時他年僅 52 歲。一名旁觀者對哈珀進行了心肺復甦，直到醫護人員趕到，才救了哈珀的命。兩天後，他在醫院醒來，想知道發生了什麼事。事實證明，他的 Lp(a) 水平非常高，這就是對他造成打擊的原因。他不知道自己正處於危險之中。

This is not an atypical scenario: when a patient comes to me and says their father or grandfather or aunt, or all three, died of “premature” heart disease, elevated Lp(a) is the first thing I look for. It is the most prevalent hereditary risk factor for heart disease, and its danger is amplified by the fact that it is still largely flying under the radar of Medicine 2.0, although that is beginning to change.

這並不是一種不典型的情況：當一位患者來找我並說他們的父親、祖父或阿姨，或者三人都死於「過早」心臟病時，我首先要尋找的就是升高的Lp(a)。它是心臟病最常見的遺傳性危險因素，儘管這種情況正在開始改變，但它仍然很大程度上處於醫學 2.0 的雷達之下，這一事實放大了它的危險。

Most people have relatively small concentrations of this particle, but some individuals can have as much as one hundred times more than others. The variation is largely genetic, and an estimated 20 to 30 percent of the US population has levels high enough that they are at increased risk; also, people of African descent tend to have higher levels of Lp(a), on average, than Caucasians. This is why, if you have a history of premature heart attacks in your family, you should definitely ask for an Lp(a) test. We test every single patient for Lp(a) during their first blood draw. Because elevated Lp(a) is largely genetic, the test need only be done once (and cardiovascular disease guidelines are beginning to advise a once-a-lifetime test for it anyway).

大多數人的這種顆粒濃度相對較低，但有些人的濃度可能比其他人高出一百倍。這種變異主要是遺傳性的，估計 20% 至 30% 的美國人的

病毒水平足夠高，導致他們面臨更高的風險；此外，平均而言，非洲人後裔的 Lp(a) 水平往往高於白人。這就是為什麼，如果您的家族中有過早心臟病發作的病史，您絕對應該要求進行 Lp(a) 測試。我們在每位患者第一次抽血時檢測 Lp(a)。由於 Lp(a) 升高主要是遺傳性的，因此該測試只需進行一次（心血管疾病指南開始建議一生進行一次測試）。

Anahad was fortunate that he found out about his situation when he did. His calcium score meant that he had already suffered significant atherosclerotic damage due to his Lp(a). Beyond the harm it causes to coronary arteries, Lp(a) is particularly destructive to the aortic valve, one of the more important structures in the heart, by promoting the formation of tiny, bony particles in the valve leaflets, which leads to stenosis or narrowing of the aortic outlet.

阿納哈德很幸運，他當時發現了自己的處境。他的鈣分數意味著他已經因 Lp(a) 遭受了嚴重的動脈粥狀硬化損傷。除了對冠狀動脈造成傷害之外，Lp(a) 對主動脈瓣（心臟中更重要的結構之一）的破壞性尤其大，它會促進瓣膜小葉中微小骨顆粒的形成，從而導致狹窄或主動脈出口變窄。

There was no quick fix for Anahad, or anyone else with elevated Lp(a). It does not seem to respond to behavioral interventions such as exercise and dietary changes the way that, say, LDL-C does. A class of drug called PCSK9 inhibitors, aimed at lowering apoB concentrations, does seem to be able to reduce Lp(a) levels by approximately 30 percent, but as yet there are no data suggesting that they reduce the excess events (heart attacks) attributable to that particle. Thus, the only real treatment for elevated Lp(a) right now is aggressive management of apoB overall. Though we can't reduce Lp(a) directly, beyond what a PCSK9 inhibitor can do, we can lower the remaining apoB concentration sufficiently that we can reduce a patient's overall risk.^[*5] Because Anahad is relatively young, he also has more time to address his other risk factors.

對於阿納哈德或其他 Lp(a) 升高的人來說，沒有快速的解決方案。它似乎不像低密度脂蛋白膽固醇那樣對運動和飲食改變等行為幹預做出

反應。一類名為PCSK9 抑制劑的藥物旨在降低apoB 濃度，似乎確實能夠將Lp(a) 水平降低約30%，但迄今為止還沒有數據表明它們可以減少可歸因於的過度事件（心臟病發作）。到那個粒子。因此，目前 Lp(a) 升高的唯一真正治療方法是對 apoB 進行整體積極管理。儘管我們無法直接降低 Lp(a)，但超出 PCSK9 抑制劑的作用，我們可以充分降低剩餘的 apoB 濃度，從而降低患者的整體風險。 [*5] 由於阿納哈德相對年輕，他也有更多的時間來解決其他風險因素。

Luckily, we found the trouble before the trouble found him.

幸運的是，我們在麻煩找到他之前就發現了麻煩。

How to Reduce Cardiovascular Risk

如何降低心血管風險

In a way, Not-Thin Peter and Anahad O'Connor were like two sides of the same coin. While our stories don't seem to have much in common, both underscore the insidious, almost sneaky nature of heart disease: my risk should have been obvious, based on my family history, while Anahad's disease remained all but invisible until he happened to have a calcium scan, which is not normally done on healthy-seeming people in their thirties. We only learned of our risk thanks to dumb luck, because few doctors would have considered screening either of us for heart disease at our ages.

在某種程度上，不瘦彼得和阿納哈德·奧康納就像同一枚硬幣的兩面。雖然我們的故事似乎沒有太多共同點，但都強調了心臟病的陰險、幾乎是鬼祟的本質：根據我的家族史，我的風險應該是顯而易見的，而阿納哈德的疾病幾乎是看不見的，直到他碰巧患上了心臟病。鈣掃描，通常不會對看起來健康的三十多歲的人進行這項檢查。由於運氣不好，我們才了解到自己的風險，因為很少有醫生會考慮在我們這個年紀對我們進行心臟病篩檢。

Together, our stories illustrate three blind spots of Medicine 2.0 when it comes to dealing with atherosclerotic disease: first, an overly simplistic view

of lipids that fails to understand the importance of total lipoprotein burden (apoB) and how much one needs to reduce it in order to truly reduce risk; second, a general lack of knowledge about other bad actors such as Lp(a); and third, a failure to fully grasp the lengthy time course of atherosclerotic disease, and the implications this carries if we seek true prevention.

總之，我們的故事說明了醫學2.0 在治療動脈粥狀硬化疾病方面的三個盲點：第一，對脂質的看法過於簡單化，無法理解總脂蛋白負荷 (apoB) 的重要性以及人們需要將其減少多少。才能真正降低風險；其次，普遍缺乏對 Lp(a) 等其他不良行為者的了解；第三，未能充分掌握動脈粥狀硬化疾病的漫長病程，以及如果我們尋求真正的預防，其所帶來的影響。

When I look at a patient's blood panel for the first time, my eyes immediately dart to two numbers: apoB and Lp(a). I look at the other numbers, too, but these two tell me the most when it comes to predicting their risk of ASCVD. ApoB not only tells me the concentration of LDL particles (which, you'll recall, is more predictive of disease than the concentration of cholesterol found *within* LDL particles, LDL-C), but it also captures the concentration of VLDL particles, which as members of the apoB family can also contribute to atherosclerosis. Furthermore, even someone whose apoB is low can still have a dangerously elevated Lp(a).[*6]

當我第一次查看患者的血液檢測結果時，我的眼睛立即看到兩個數字：apoB 和 Lp(a)。我也會查看其他數字，但這兩個數字在預測 ASCVD 風險方面最能告訴我。ApoB 不僅告訴我 LDL 顆粒的濃度（您可能還記得，它比 LDL 顆粒中膽固醇的濃度 LDL-C 更能預測疾病），而且還能捕捉 VLDL 顆粒的濃度，apoB 家族的成員也會導致動脈粥樣硬化。此外，即使 apoB 較低的人的 Lp(a) 仍然可能危險地升高。[*6]

Once you establish the central importance of apoB, the next question becomes, By how much does one need to lower it (or its proxy LDL-C) to achieve meaningful risk reduction? The various treatment guidelines specify target ranges for LDL-C, typically 100 mg/dL for patients at normal risk, or 70 mg/dL for high-risk individuals. In my view, this is still far too high.

Simply put, I think you can't lower apoB and LDL-C too much, provided there are no side effects from treatment. You want it as low as possible.

一旦確定了 apoB 的核心重要性，下一個問題就變成了，需要將其（或其替代 LDL-C）降低多少才能實現有意義的風險降低？各種治療指引指定了 LDL-C 的目標範圍，通常對於正常風險患者為 100 mg/dL，對於高風險個體為 70 mg/dL。在我看來，這仍然太高了。簡而言之，我認為只要治療沒有副作用，就不能將 apoB 和 LDL-C 降低太多。你希望它盡可能低。

As Peter Libby, one of the leading authorities on cardiovascular disease, and colleagues wrote in *Nature Reviews* in 2019, “Atherosclerosis *probably would not occur* [emphasis mine] in the absence of LDL-C concentrations in excess of physiological needs (on the order of 10 to 20 mg/dL).” Furthermore, the authors wrote: “If the entire population maintained LDL concentrations akin to those of a neonate (or to those of adults of most other animal species), atherosclerosis might well be an orphan disease.”

正如心血管疾病領域的權威人士之一 Peter Libby 及其同事在 2019 年《自然評論》中所寫的那樣，「如果 LDL-C 濃度不超過生理需求（約為 10 至 20 毫克/分升）。」此外，作者寫道：“如果整個種群的低密度脂蛋白濃度維持在與新生兒（或大多數其他動物物種的成年人）相似的水平，那麼動脈粥樣硬化很可能是一種罕見疾病。”

Translation: if we all maintained the apoB levels we had when we were babies, there wouldn't be enough heart disease on the planet for people to know what it was. Kind of like 3-hydroxyisobutyric aciduria. What, you haven't heard of it? Well, that's because there have been only thirteen reported cases. Ever. That is an orphan disease. I'm being a bit facetious, but my point is that atherosclerotic disease shouldn't even be in the top ten causes of death, if we treated it more aggressively. Instead, we have over eighteen million cases of fatal atherosclerotic disease per year globally.

換句話說：如果我們都保持嬰兒時期的 apoB 水平，那麼地球上就不會有足夠的心臟病讓人們知道它是什麼。有點像 3-羥基異丁酸尿症。什麼，你沒聽過嗎？嗯，那是因為只有 13 例報告病例。曾經。那是一種

孤兒病。我有點開玩笑，但我的觀點是，如果我們更積極地治療動脈粥狀硬化疾病，它甚至不應該成為十大死因之一。相反，全球每年有超過一千八百萬致命動脈粥狀硬化病例。

Many doctors, and in fact many of you reading this, might be shocked to see such a low LDL-C target: 10 to 20 mg/dL? Most guidelines consider lowering LDL-C to 70 mg/dL to be “aggressive,” even for secondary prevention in high-risk patients, such as those who have already had a heart attack. It’s also natural to ask whether such extremely low levels of LDL-C and apoB are safe, given the ubiquity and importance of cholesterol in the human body. But consider the following: infants, who presumably require the *most* cholesterol, in order to meet the enormous demands of their rapidly growing central nervous system, have similarly low levels of circulating cholesterol, without any developmental impairment. Why? Because the total amount of cholesterol contained in all our lipoproteins—not just LDL, but also HDL and VLDL—represents only about 10 to 15 percent of our body’s total pool of cholesterol. So the concern is unwarranted, as demonstrated by scores of studies showing no ill effects from extremely low LDL concentrations.

許多醫生，事實上你們中的許多人讀到這篇文章，可能會驚訝地發現如此低的 LDL-C 目標：10 至 20 mg/dL？大多數指南認為將 LDL-C 降低至 70 mg/dL 是“積極的”，即使對於高風險患者（例如已經心臟病發作的患者）進行二級預防也是如此。鑑於膽固醇在人體內的普遍性和重要性，人們自然會問如此低水平的 LDL-C 和 apoB 是否安全。但請考慮以下情況：嬰兒可能需要最多的膽固醇，以滿足其快速生長的中樞神經系統的巨大需求，但其循環膽固醇水平同樣較低，且沒有任何發育障礙。為什麼？因為我們所有脂蛋白（不僅包括 LDL，還包括 HDL 和 VLDL）中所含的膽固醇總量僅占我們體內膽固醇總量的 10% 至 15% 左右。因此，這種擔憂是沒有根據的，大量研究顯示極低的低密度脂蛋白濃度不會產生不良影響。

This is my starting point with any patient, whether they are like Anahad (with one prominent risk factor) or like me (lots of smaller risk factors). Our first order of business is to reduce the burden of apoB particles, primarily

LDLs but also VLDLs, which can be dangerous in their own right. And do so dramatically, not marginally or incrementally. We want it as low as possible, sooner rather than later. We must also pay attention to other markers of risk, notably those associated with metabolic health, such as insulin, visceral fat, and homocysteine, an amino acid that in high concentrations^[*7] is strongly associated with increased risk of heart attack, stroke, and dementia.

這是我對任何患者的出發點，無論他們是像阿納哈德（有一個突出的風險因素）還是像我（有許多較小的風險因素）。我們的首要任務是減少 apoB 顆粒的負擔，主要是 LDL，但也包括 VLDL，它們本身可能是危險的。並且要戲劇性地這樣做，而不是邊際或漸進。我們希望它盡可能低，宜早不宜遲。我們還必須注意其他風險標記物，特別是那些與代謝健康相關的標誌物，例如胰島素、內臟脂肪和同型半胱氨酸，高半胱氨酸是一種高濃度的氨基酸[*7]，與心臟病、中風的風險增加密切相關和癡呆症。

You'll note that I don't pay much attention to HDL-C, because while having very low HDL-C is *associated* with higher risk, it does not appear to be *causal*. This is why drugs aimed at raising HDL-C have generally failed to reduce risk and events in clinical trials. The reasons why are suggested by two elegant Mendelian randomization studies that examined both sides of the HDL-C question: Does low HDL-C *causally* increase the risk of myocardial infarction? No. Does raising HDL-C *causally* lower the risk of myocardial infarction? No.

您會注意到，我不太關注 HDL-C，因為雖然 HDL-C 非常低與較高的風險有關，但它似乎不存在因果關係。這就是為什麼旨在提高 HDL-C 的藥物在臨床試驗中通常無法降低風險和事件。兩項優雅的孟德爾隨機化研究提出了原因，該研究檢視了 HDL-C 問題的雙方：低 HDL-C 是否會增加心肌梗塞的風險？不會。提高 HDL-C 是否會降低心肌梗塞的風險？不。

Why? Probably because whatever benefit HDLs provide in the battle for arterial supremacy, it (again) seems to be driven by their *function*—which doesn't seem to be related to their cholesterol content. But we cannot test for

HDL functionality, and until we have a better grasp on how HDL actually works, it will likely remain elusive as a target of therapy.

為什麼？可能是因為無論高密度脂蛋白在動脈霸權之戰中提供什麼好處，它（再次）似乎都是由它們的功能驅動的——這似乎與它們的膽固醇含量無關。但我們無法測試 HDL 的功能，在我們更好地掌握 HDL 的實際工作原理之前，它作為治療目標可能仍然難以捉摸。

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Lipoproteins aren't the only significant risk factors for cardiovascular disease; as noted earlier, smoking and high blood pressure both damage the endothelium directly. Smoking cessation and blood pressure control are thus non-negotiable first steps in reducing cardiovascular risk.

脂蛋白並不是心血管疾病的唯一重要危險因子；如前所述，吸煙和高血壓都會直接損害內皮細胞。因此，戒菸和控制血壓是降低心血管風險無法妥協的第一步。

We'll talk about nutrition in much more detail, but my first step in controlling my own cardiovascular risk was to begin to change my own diet, so as to lower my triglycerides (a contributor to apoB when they are high, as mine were), but more importantly to manage my insulin levels. I needed to get my metabolic house in order. I should note that my own solution at the time, a ketogenic diet, might not work for everyone, nor is it a diet to which I continue to adhere. In my clinical experience, about a third to half of people who consume high amounts of saturated fats (which sometimes goes hand in hand with a ketogenic diet) will experience a dramatic *increase* in apoB particles, which we obviously don't want.^[*8] Monounsaturated fats, found in high quantities in extra virgin olive oil, macadamia nuts, and avocados (among other foods), do not have this effect, so I tend to push my patients to consume more of these, up to about 60 percent of total fat intake. The point is not necessarily to limit fat overall but to shift to fats that promote a better lipid profile.

我們將更詳細地討論營養，但我控制自己心血管風險的第一步是開始改變自己的飲食，以降低我的三酸甘油酯（apoB 在高時會產生三酸甘油酯，就像我的一樣），但更重要的是管理我的胰島素水平。我需要讓我的新陳代謝室井然有序。我應該指出，我當時自己的解決方案，生酮飲食，可能不適合所有人，也不是我繼續堅持的飲食方式。根據我的臨床經驗，大約三分之一到一半食用大量飽和脂肪（有時與生酮飲食同時進行）的人會經歷 apoB 顆粒的急劇增加，這顯然是我們不希望看到的。[*8] 特級初榨橄欖油、澳洲堅果和酪梨（以及其他食物）含有大量的單元不飽和脂肪，但沒有這種效果，所以我傾向於促使我的患者攝取更多這些脂肪，最多約佔總脂肪攝取量的60%。重點不一定是限制整體脂肪，而是轉向促進改善血脂狀況的脂肪。

But for many patients, if not for most, lowering apoB to the levels we aim for—the physiologic levels found in children—cannot be accomplished with diet alone, so we need to use nutritional interventions in tandem with drugs. Here we are fortunate because we have more preventive options in our armamentarium than we do for cancer or neurodegenerative disease. Statins are far and away the most prescribed class of drugs for lipid management, but there are several other options that might be right for a given individual, and often we need to combine classes of drugs, so it's not uncommon for a patient to take two lipid-lowering drugs that operate via distinct mechanisms. These are typically thought of as “cholesterol-lowering” medications, but I think we are better served to think about them in terms of increasing apoB *clearance*, enhancing the body's ability to get apoBs out of circulation. That's really our goal. Mostly this is done by amplifying the activity of LDL receptors (LDLR) in the liver, which absorb cholesterol from the bloodstream.

但對於許多患者（如果不是大多數）來說，將 apoB 降低到我們的目標水平（兒童的生理水平）無法僅透過飲食來實現，因此我們需要將營養幹預與藥物結合使用。在這裡，我們很幸運，因為我們的軍備庫中有比癌症或神經退化性疾病更多的預防選擇。他汀類藥物無疑是最常用的血脂管理藥物，但還有其他幾種可能適合特定個體的選擇，而且我們通常需要結合使用多種藥物，因此患者服用兩種藥物的情況並不少見。透過不同機制發揮作用的降血脂藥物。這些通常被認為是「降

低膽固醇」的藥物，但我認為我們最好從增加 apoB 清除率、增強身體將 apoB 排出循環的能力來考慮它們。這確實是我們的目標。這主要是透過增強肝臟中低密度脂蛋白受體（LDLR）的活性來實現的，該受體可從血液中吸收膽固醇。

Different drugs arrive at this effect via different paths. Typically our first line of defense (or attack), statins inhibit cholesterol synthesis, prompting the liver to increase the expression of LDLR, taking more LDL out of circulation. They may have other benefits too, including an apparent anti-inflammatory effect, so while I don't think statins should be dissolved into the drinking water, as some have suggested, I do think they are very helpful drugs for reducing apoB or LDL concentration in many patients. Not everyone can take statins comfortably; about 5 percent of patients experience deal-breaking side effects, most notably statin-related muscle pain. Also, a smaller but nonzero subset of patients taking statins experience a disruption in glucose homeostasis, which may explain why statins are associated with a small increase in the risk for type 2 diabetes. Another fraction of patients experience an asymptomatic rise in liver enzymes, which is even more common in patients also taking the drug ezetimibe. All these side effects are completely and rapidly reversible when the drug is discontinued. But for those who can tolerate them (i.e., most people), I deploy them early and often. (For more on specific statin and other apoB-lowering medications, see the sidebar on [this page](#).)

不同的藥物透過不同的途徑達到這種效果。他汀類藥物通常是我們的第一道防線（或攻擊線），它會抑制膽固醇合成，促使肝臟增加 LDLR 的表達，從而將更多的 LDL 排出循環。它們也可能有其他好處，包括明顯的抗發炎作用，所以雖然我不認為他汀類藥物應該像一些人建議的那樣溶解到飲用水中，但我確實認為它們是降低 apoB 或 LDL 濃度非常有用的藥物在許多患者中。並不是每個人都能輕鬆服用他汀類藥物；約 5% 的患者會出現嚴重的副作用，最明顯的是與他汀類藥物相關的肌肉疼痛。此外，一小部分服用他汀類藥物的患者會出現葡萄糖穩態紊亂，這可能解釋了為什麼他汀類藥物與第 2 型糖尿病風險小幅增加有關。另一部分患者出現肝酵素無症狀升高，這在同時

服用依折麥布藥物的患者中更為常見。停藥後，所有這些副作用都可以完全且快速地逆轉。但對於那些能夠容忍它們的人（即大多數人），我會儘早且頻繁地部署它們。（有關特定他汀類藥物和其他降apoB 藥物的更多信息，請參閱本頁側邊欄。）

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This brings us to the final, and perhaps greatest, major blind spot of Medicine 2.0: time.

這讓我們看到了醫學 2.0 的最後一個，也許是最大的主要盲點：時間。

The process I've outlined in this chapter unfolds very slowly—not over two or three or even five years, but over many decades. The fact that younger people have been found to have lesions and plaques, without suffering many events, tells us that there is a considerable period of time when the disease is not harmful. Dying from cardiovascular disease is certainly not inevitable: the centenarians delay it for decades, and many avoid it altogether, their arteries remaining as clean as those of people a generation younger. Somehow, they manage to slow the process down.

我在本章中概述的過程展開得非常緩慢——不是兩年、三年甚至五年，而是幾十年。年輕人被發現有病變和斑塊，而沒有遭受許多事件的事實告訴我們，這種疾病在相當長的時間內是無害的。死於心血管疾病當然不是不可避免的：百歲老人將死亡推遲了數十年，許多人完全避免了死亡，他們的動脈與年輕一代的人一樣乾淨。不知何故，他們設法減慢了這個過程。

Nearly all adults are coping with some degree of vascular damage, no matter how young and vital they may seem, or how pristine their arteries appear on scans. There is always damage, especially in regions of shear stress and elevated local blood pressure, such as curves and splits in the vasculature. Atherosclerosis is with us, in some form, throughout our life course. Yet most doctors consider it “overtreatment” to intervene if a patient's computed ten-year risk of a major adverse cardiac event (e.g., heart attack or stroke) is

below 5 percent, arguing that the benefits are not greater than the risks, or that treatment costs too much. In my opinion, this betrays a broader ignorance about the inexorable, long-term unfolding of heart disease. Ten years is far too short a time horizon. If we want to reduce deaths from cardiovascular disease, we need to begin thinking about prevention in people in their forties and even thirties.

幾乎所有成年人都在應對某種程度的血管損傷，無論他們看起來多麼年輕和充滿活力，或者他們的動脈在掃描中顯得多麼原始。損傷總是存在的，特別是在剪切應力和局部血壓升高的區域，例如脈管系統的彎曲和分裂。動脈粥狀硬化以某種形式伴隨著我們的一生。然而，大多數醫生認為，如果患者計算出的10年發生重大不良心臟事件（例如心臟病發作或中風）的風險低於5%，則進行幹預是“過度治療”，認為獲益並不大於風險，或認為介入是「過度治療」。治療費用太大。在我看來，這暴露了人們對心臟病不可阻擋的長期發展的更廣泛的無知。十年的時間跨度太短了。如果我們想減少心血管疾病的死亡，我們需要開始考慮對四十幾歲甚至三十多歲的人進行預防。

Another way to think of all this is that someone might be considered “low risk” at a given point—but on what time horizon? The standard is ten years. But what if our time horizon is “the rest of your life”?

思考這一切的另一種方式是，某人在某個特定點可能被視為「低風險」——但在什麼時間範圍內呢？標準是十年。但如果我們的時間範圍是「你的餘生」呢？

Then nobody is at low risk.

那麼沒有人處於低風險。

When I had my first calcium scan in 2009, at the age of thirty-six, my ten-year risk was incalculably low—literally. The dominant mathematical models for risk assessment have a lower limit for age of forty or forty-five. My parameters could not even be entered into the models. So it's no wonder nobody was alarmed by my findings. Despite my calcium score of 6, my ten-year risk of a heart attack was far less than 5 percent.

2009 年，當我 36 歲時第一次進行鈣掃描時，我的 10 年患病風險簡直低得難以估量。風險評估的主流數學模型的下限為四十或四十五歲。我的參數甚至無法輸入模型。因此，難怪沒有人對我的發現感到震驚。儘管我的鈣分數為 6，但我十年內心臟病發作的風險遠低於 5%。

In 2016, seven years after my initial calcium scan, I had a CT angiogram (the better, higher-res scan), which showed the same small speck of calcium but no evidence of additional soft plaque elsewhere. In 2022, I went back again for a repeat CT angiogram, and the result was the same. There was no indication whatsoever of soft plaque this time either, and only that tiny speck of calcium remained from 2009.^[*9] Thus, at least at the resolution of the sharpest CT scanner commercially available, there is no reason to believe that my atherosclerosis has progressed over thirteen years.

2016 年，也就是我初次鈣掃描七年後，我進行了CT 血管造影（效果更好、分辨率更高的掃描），結果顯示出同樣的小鈣斑點，但沒有證據表明其他地方有額外的軟斑塊。2022年，我又回去做了CT血管攝影，結果還是一樣。這次也沒有任何軟斑的跡象，只留下了 2009 年的那個微小的鈣斑點。^[*9] 因此，至少在市售最清晰的 CT 掃描儀的分辨率下，沒有理由相信我的動脈粥狀硬化已經發展了十三年。

I have no idea if this means I'm free from risk—I frankly doubt it—but I no longer fear dying from cardiovascular disease the way I once did. My long, comprehensive program of prevention seems to have paid off. I feel a lot better now, at age fifty, than I did at age thirty-six, and my risk is a lot lower by any metric other than age. One major reason for this is that I started early, well before Medicine 2.0 would have suggested *any* intervention.

我不知道這是否意味著我沒有風險——坦白說我對此表示懷疑——但我不再像以前那樣擔心死於心血管疾病。我長期、全面的預防計劃似乎取得了成效。現在我五十歲了，比三十六歲時感覺好多了，而且按照年齡以外的任何指標來衡量，我的風險要低得多。造成這種情況的一個主要原因是我很早就開始了，遠早於醫學 2.0 提出任何干預措施。

Yet most physicians and cardiology experts would still insist that one's thirties are too young to begin to focus on primary prevention of cardiac disease. This viewpoint is directly challenged by a 2018 *JAMA Cardiology* paper coauthored by Allan Sniderman, comparing ten-year versus thirty-year risk horizons in terms of prevention. Sniderman and colleagues' analysis found that looking at a thirty-year time frame rather than the standard ten years and taking aggressive precautionary measures *early*—like beginning statin treatment earlier in certain patients—could prevent hundreds of thousands more cardiac events, and by implication could save many lives.

然而，大多數醫生和心臟病學專家仍然堅持認為，三十多歲開始關注心臟病的一級預防還太年輕。這一觀點受到 Allan Sniderman 與人合著的 2018 年《美國醫學會雜誌》心臟病學論文直接挑戰，該論文比較了預防方面十年與三十年的風險範圍。斯尼德曼及其同事的分析發現，著眼於三十年而不是標準的十年，並儘早採取積極的預防措施（例如對某些患者儘早開始他汀類藥物治療）可以預防數十萬例心臟事件，這意味著可以拯救許多人的生命。

For context, most studies of statins used in primary prevention (that is, prevention of a first cardiac event) last about five years and typically find a “number needed to treat” (or NNT, the number of patients who need to take a drug in order for it to save one life) of between about 33 and 130, depending on the baseline risk profile of the patients. (Amazingly, the *longest* statin trials to date have lasted just seven years.) But looking at their risk reduction potential over a thirty-year time frame, as the Sniderman study did, reduces the NNT down to less than 7: For every seven people who are put on a statin at this early stage, we could potentially save one life. The reason for this is simple math: risk is proportional to apoB exposure over time. The sooner we lower apoB exposure, thus lowering risk, the more the benefits compound over time—and the greater our overall risk reduction.

就背景而言，大多數用於一級預防（即預防首次心臟事件）的他汀類藥物研究持續約五年，通常會發現「需要治療的人數」（或 NNT，需要服用藥物的患者人數）為了挽救一個生命）大約 33 到 130 人之間，取決於患者的基線風險狀況。（令人驚訝的是，迄今為止最長的他汀

類藥物試驗只持續了七年。)但是，正如斯尼德曼的研究那樣，從三十年的時間範圍內觀察其風險降低潛力，將NNT降低至不到7：每七個人在早期階段使用他汀類藥物的患者，我們有可能挽救一個生命。原因很簡單：隨著時間的推移，風險與 apoB 暴露量成正比。我們越早降低 apoB 暴露，從而降低風險，隨著時間的推移，收益複合得越多，我們的整體風險降低得就越多。

This encapsulates the fundamental difference between Medicine 2.0 and Medicine 3.0 when it comes to cardiovascular disease. The former views prevention largely as a matter of managing relatively short-term risk. Medicine 3.0 takes a much longer view—and more importantly seeks to identify and eliminate the *primary causative agent* in the disease process: apoB. This changes our approach to treatment completely. For example, a forty-five-year-old with elevated apoB has a lower ten-year risk than a seventy-five-year-old with low apoB. Medicine 2.0 would say to treat the seventy-five-year-old (because of their age), but not the forty-five-year-old. Medicine 3.0 says to disregard the ten-year risk and instead treat the causal agent in *both* cases—lowering the forty-five-year-old's apoB as much as possible.

這概括了醫學2.0和醫學3.0在心血管疾病方面的根本差異。前者將預防主要視為管理相對短期風險的問題。醫學 3.0 的視野更為長遠，更重要的是尋求識別和消除疾病過程中的主要致病因子：apoB。這完全改變了我們的治療方法。例如，apoB 升高的 45 歲老人的十年風險低於 apoB 較低的 75 歲老人。醫學2.0會說要治療七十五歲的人（因為他們的年齡），但不是四十五歲的人。醫學 3.0 表示，忽略十年風險，而是對這兩種情況的致病因素進行治療——盡可能降低 45 歲患者的 apoB。

Once you understand that apoB particles—LDL, VLDL, Lp(a)—are *causally* linked to ASCVD, the game completely changes. The only way to stop the disease is to remove the cause, and the best time to do that is now.

一旦您了解 apoB 顆粒（LDL、VLDL、Lp(a)）與 ASCVD 有因果關係，情況就會完全改變。阻止疾病的唯一方法是消除原因，而現在就是最好的時機。

Still struggling with this idea? Consider the following example. We know that smoking is causally linked to lung cancer. Should we tell someone to stop smoking only after their ten-year risk of lung cancer reaches a certain threshold? That is, do we think it's okay for people to keep smoking until they are sixty-five and then quit? Or should we do everything we can to help young people, who have maybe just picked up the habit, quit altogether?

還在為這個想法掙扎嗎？考慮以下範例。我們知道吸菸與肺癌有因果關係。我們是否應該在某人十年內患肺癌的風險達到一定閾值後才告訴他們停止吸煙？也就是說，我們認為人們可以繼續吸菸直到六十五歲然後戒菸嗎？或者我們應該盡一切努力幫助可能剛剛養成這種習慣的年輕人完全戒掉？

When viewed this way, the answer is unambiguous. The sooner you cut the head off the snake, the lower the risk that it will bite you.

從這個角度來看，答案是明確的。越早砍掉蛇的頭，它咬你的風險就越低。

Brief Overview of Lipid-Lowering Medications

降血脂藥物概述

While there are seven statins on the market, I tend to start with **rosuvastatin (Crestor)** and only pivot from that if there is some negative effect from the drug (e.g., a symptom or biomarker). My goal is aggressive: as rationalized by Peter Libby, I want to knock someone's apoB concentration down to 20 or 30 mg/dL, about where it would be for a child.

雖然市面上有七種他汀類藥物，但我傾向於從瑞舒伐他汀（Crestor）開始，只有在藥物出現一些負面影響（例如症狀或生物標記）時才會轉向該藥物。我的目標非常積極：正如 Peter Libby 所闡述的那樣，我希望將某人的 apoB 濃度降至 20 或 30 mg/dL，大約是兒童的水平。

For people who can't tolerate statins, I like to use a newer drug, called **bempedoic acid (Nexletol)**, which manipulates a different pathway to accomplish much the same end: inhibiting cholesterol synthesis as a way to force the liver to increase LDLR and therefore LDL clearance. But where statins inhibit

cholesterol synthesis throughout the body, and most notably in the muscles, bempedoic acid does so only in the liver. Therefore, it does not cause the side effects associated with statins, especially muscle soreness. The main issue with this drug is cost.

對於無法耐受他汀類藥物的人，我喜歡使用一種名為 **Bempedoic Acid (Nexletol)** 的新藥，它通過操縱不同的途徑來達到大致相同的目的：抑制膽固醇合成，從而迫使肝臟增加 **LDLR**，因此低密度脂蛋白清除率。但他汀類藥物會抑制全身膽固醇的合成，尤其是肌肉的膽固醇合成，而貝培多酸則僅在肝臟中發揮作用。因此，它不會引起他汀類藥物的副作用，特別是肌肉酸痛。這種藥物的主要問題是成本。

Another drug called **ezetimibe (Zetia)** blocks absorption of cholesterol in the GI tract.^[*10] That in turn depletes the amount of cholesterol in the liver, leading once again to increased **LDLR** expression and greater clearance of apoB particles, which is what we want. Ezetimibe pairs very well with statins because statins, which block cholesterol synthesis, tend to cause the body to reflexively increase cholesterol reabsorption in the gut—exactly the thing that ezetimibe so effectively prevents.

另一種名為依折麥布 (**Zetia**) 的藥物可阻止胃腸道中膽固醇的吸收。^[*10] 這反過來會消耗肝臟中的膽固醇量，再次導致 **LDLR** 表達增加和 apoB 顆粒的更大清除，這正是我們想要的。依折麥布與他汀類藥物搭配得很好，因為他汀類藥物可以阻止膽固醇合成，往往會導致身體反射性地增加腸道中的膽固醇重吸收，而這正是依折麥布可以有效防止的情況。

LDL receptors can be upregulated by a class of drugs that we mentioned earlier, called **PCSK9 inhibitors**, which attack a protein called **PCSK9** that degrades **LDL** receptors. This increases the receptors' half-life, thus improving the liver's ability to clear apoB. As a monotherapy they have about the same apoB- or **LDL-C**-lowering potency as high-dose statins, but their most common use is in addition to statins; the combination of statins plus **PCSK9** inhibitors is the most powerful pharmacological tool that we have against apoB. Alas, statins do not reduce **Lp(a)**, but **PCSK9** inhibitors do in most patients, typically to the tune of about 30 percent.

我們先前提到的一類稱為 **PCSK9** 抑制劑的藥物可以上調 **LDL** 受體，這種藥物會攻擊一種名為 **PCSK9** 的蛋白質，從而降解 **LDL** 受體。這會增加受體的半衰期，從而提高肝臟清除 apoB 的能力。作為單一療法，它們具有與高劑量他汀類藥物大致相同的 apoB 或 **LDL-C** 降低效力，但它們最常見的用途是除了他汀類藥物之外；他汀類藥物合併 **PCSK9** 抑制劑的組合是我們對抗 apoB 的最強大的藥理學工具。遺憾的是，他汀類藥物不會降低 **Lp(a)**，但 **PCSK9** 抑制劑可以降低大多數患者的 **Lp(a)**，通常降低 30% 左右。

Triglycerides also contribute to the apoB particle burden, because they are largely transported in **VLDLs**. Our dietary interventions are aimed at reducing

triglycerides, but in cases where nutritional changes are insufficient, and in cases where genetics render dietary interventions useless, **fibrates** are the drug of choice.

三酸甘油酯也會增加 apoB 顆粒的負擔，因為它們主要在極低密度脂蛋白 (VLDL) 中運輸。我們的飲食幹預旨在降低三酸甘油酯，但在營養改變不足的情況下，以及在遺傳學使飲食幹預無效的情況下，貝特類藥物是首選藥物。

Ethyl eicosapentaenoic acid (Vascepa), a drug derived from fish oil and consisting of four grams of pharmaceutical-grade eicosapentaenoic acid (EPA), also has FDA approval to reduce LDL in patients with elevated triglycerides.

乙基二十碳五烯酸(Vascepa) 是一種從魚油中提取的藥物，由4 克醫藥級二十碳五烯酸(EPA) 組成，也已獲得FDA 批准用於降低甘油三酯升高患者的LDL。

[SKIP NOTES](#)

[跳過註釋](#)

*1 There are also very-low-density lipoproteins, or VLDLs, which we mentioned in the previous chapter, as well as intermediate-density lipoproteins, or IDLs. These carry even more fat than the LDLs, much of it in the form of triglycerides, and they are also marked with apoB. Also: While HDL particles have multiple apoAs, each LDL (or VLDL, or IDL) has only one apoB particle, making it relatively easy to measure their concentration.

*1 還有我們在上一章提到的極低密度脂蛋白（VLDL），以及中密度脂蛋白（IDL）。它們比低密度脂蛋白攜帶更多的脂肪，其中大部分以三酸甘油酯的形式存在，而且它們還帶有 apoB 標記。另外：雖然 HDL 顆粒具有多個 apoA，但每個 LDL（或 VLDL 或 IDL）只有一個 apoB 顆粒，因此測量其濃度相對容易。

*2 The scientific term for this is *stochastic*, meaning it's a largely random process.

*2 科學術語是隨機的，這意味著它是一個很大程度上隨機的過程。

*3 A brief word about nomenclature: When we say LDL or HDL, we are typically referring to a type of *particle*; when we say LDL-C or HDL-C, we are talking about a laboratory measurement of the *concentration* of cholesterol within those particles.

*3 關於術語的簡要說明：當我們說 LDL 或 HDL 時，我們通常指的是一種顆粒；當我們說低密度脂蛋白膽固醇或高密度脂蛋白膽固醇時，我們談論的是這些顆粒內膽固醇濃度的實驗室測量結果。

*4 While the CT angiogram costs a bit more, requires IV dye, and exposes the patient to slightly more radiation, I struggle to find credible arguments against its use. Approximately 15 percent of people who have a normal calcium score (0) are still found to have soft plaque or even small calcifications on CT angiograms, and as many as 2 to 3 percent of people with a zero calcium score are found on CT angiogram to have high-risk plaques. For this reason, I almost always prefer my patients to have a CT angiogram over a calcium scan if we opt to look for evidence of disease via imaging studies.

*4 雖然 CT 血管造影的費用稍高，需要靜脈注射染料，並且使患者接受稍多的輻射，但我很難找到反對其使用的可信論點。大約15% 的鈣評分正常(0) 的人在CT 血管造影中仍發現有軟斑塊甚至小鈣化，多達2% 至3% 的鈣評分為零的人在CT 血管造影中發現有軟斑塊甚至小鈣化，有高危斑塊。因此，如果我們選擇透過影像學研究尋找疾病證據，我幾乎總是更喜歡患者進行 CT 血管造影而不是鈣掃描。

*5 There is a new class of drug called antisense oligonucleotides, or ASOs, which are currently in clinical trials to virtually eliminate Lp(a) in circulation. So far, these trials look promising in that they dramatically reduce Lp(a) concentration, but it's too soon to know if they are effective at doing what matters most: reducing cardiovascular events.

*5 有一種新的藥物稱為反義寡核苷酸（ASO），目前正在進行臨床試驗，以幾乎消除循環中的 Lp(a)。到目前為止，這些試驗看起來很有希望，因為它們顯著降低了 Lp(a) 濃度，但現在判斷它們是否能有效地完成最重要的事情：減少心血管事件還為時過早。

*6 This is because the total number of LDL particles is far higher than the number of Lp(a) particles, but Lp(a) still has an outsize ability to cause damage, even in relatively small numbers.

*6 這是因為 LDL 顆粒的總數遠高於 Lp(a) 顆粒的數量，但 Lp(a) 仍然具有巨大的造成損害的能力，即使數量相對較少。

*7 Homocysteine is broken down by B vitamins, which is why deficiency in B vitamins or genetic mutations in enzymes involved in their metabolism (*e.g.*, *MTHFR*) can raise homocysteine.

*7 同型半胱氨酸被 B 群維生素分解，這就是為什麼 B 群維生素缺乏或參與其代謝的酶（例如 MTHFR）基因突變會導致同型半胱氨酸升高。

*8 There are at least two reasons for this. First, it seems saturated fat contributes directly to the synthesis of excess cholesterol. Second, and more importantly, excess saturated fat causes the liver to reduce expression of LDL receptors, thereby reducing the amount of LDL removed from circulation.

*8 至少有兩個原因。首先，飽和脂肪似乎直接導致過量膽固醇的合成。其次，更重要的是，過量的飽和脂肪會導致肝臟減少 LDL 受體的表達，從而減少從循環中清除的 LDL 量。

*9 The only difference was that the 2016 test gave me a calcium score of 0; in 2022 my calcium score was 2, and the original CT scan scored this same tiny plaque as a 6. This reinforces my belief that while calcium scores are useful, they are by no means sufficient on their own.

*9 唯一的差別是，2016年的測驗給我的鈣分數為0；2022年，我的鈣評分為2，而最初的CT掃描對這個小斑塊的評分為6。這強化了我的信念，即雖然鈣評分很有用，但僅憑這些評分還遠遠不夠。

*10 Not the cholesterol you eat, which is not being absorbed anyway, but the cholesterol you make and recycle via your liver and biliary system.

*10 不是您吃進去的膽固醇，它無論如何也不會被吸收，而是您透過肝臟和膽道系統產生和回收的膽固醇。

CHAPTER 8

第 8 章

The Runaway Cell

失控的細胞

New Ways to Address the Killer That Is Cancer

解決癌症殺手的新方法

You may have to fight a battle more than once to win it.

您可能需要多次戰鬥才能贏得勝利。

—MARGARET THATCHER

-柴契爾夫人

Steve Rosenberg was still a young resident when he encountered the patient who would determine the course of his career—and, possibly, of cancer treatment in general. He was on a rotation at a VA hospital in

Massachusetts in 1968 when a man in his sixties came in needing a relatively simple gallbladder operation. The man, whose name was James DeAngelo, already had a large scar across his abdomen, which he said was from a long-ago operation to remove a stomach tumor. He had also had metastatic tumors that had spread to his liver, he added, but the surgeons had not touched those.

當史蒂夫·羅森伯格（Steve Rosenberg）遇到這位患者時，他還是一名年輕的住院醫生，這位患者將決定他的職業生涯，甚至可能決定整個癌症治療的進展。1968年，他在馬薩諸塞州的一家退伍軍人管理局醫院輪值，當時一名60多歲的男子需要進行相對簡單的膽囊手術。這名男子的名字叫詹姆斯·迪安傑洛，他的腹部已經有一道大疤痕，他說這是很久以前的一次胃腫瘤切除手術留下的。他補充說，他的轉移性腫瘤已經擴散到肝臟，但外科醫生沒有觸及這些腫瘤。

Rosenberg was sure that his patient was confused. It would have been a miracle if he had survived even six months with metastatic stomach cancer. But according to DeAngelo's hospital records, that was exactly what had happened. Twelve years earlier, he had walked into the same hospital complaining of malaise and low energy. At the time, his chart noted, he was drinking his way through three or four bottles of whiskey per week and smoking a pack or two of cigarettes every day. Surgeons had discovered a fist-sized tumor in his stomach and smaller metastatic tumors in his liver. They removed the stomach tumor, along with half of his stomach, but they left the liver tumors alone, deciding that it was too risky to try to remove them at the same time. And then they had sewn him up and sent him home to die, which he had obviously failed to do.

羅森伯格確信他的病人很困惑。如果他罹患轉移性胃癌還能活六個月，那就是一個奇蹟了。但根據迪安吉洛的醫院記錄，事實確實如此。十二年前，他曾因身體不適和精力不足而走進同一家醫院。他的圖表顯示，當時他每週喝三到四瓶威士忌，每天吸一兩包菸。外科醫生在他的胃裡發現了一個拳頭大小的腫瘤，在他的肝臟裡發現了更小的轉移性腫瘤。他們切除了胃腫瘤和他的半個胃，但他們留下了肝臟腫瘤，認為同時切除它們風險太大。然後他們把他縫起來送回家等死，但他顯然沒有這麼做。

Rosenberg went ahead with the gallbladder operation, and while he was in there he decided to take a look around in DeAngelo's abdomen. He felt behind the liver, gingerly working his way under its soft purple lobes, expecting to feel lumps of remnant tumors—an unmistakable feeling, hard and round, almost alien-like—but he found absolutely no trace of any growths. "This man had had a virulent and untreatable cancer that should have killed him quickly," Rosenberg wrote in his 1992 book *The Transformed Cell*. "He had received no treatment whatsoever for his disease from us or from anyone else. And he had been cured."

羅森博格繼續進行膽囊手術，當他在那裡時，他決定看看迪安吉洛的腹部。他摸索著肝臟後面，小心翼翼地，在柔軟的紫色葉下摸索，期望能摸到殘餘腫瘤的腫塊——一種明顯的感覺，又硬又圓，幾乎像外星人一樣——但他完全沒有發現任何生長的痕跡。「這個人患有一種致命且無法治癒的癌症，他本應該很快就會死去，」羅森伯格在 1992 年出版的《轉化的細胞》一書中寫道。「他沒有從我們或其他任何人那裡得到任何治療。而且他已經被治癒了。」

How could this be? In all the medical literature, Rosenberg could find only four instances of complete and spontaneous remission of metastatic stomach cancer. He was mystified. But he eventually came up with a hypothesis: he believed that DeAngelo's own immune system had fought off the cancer and killed the remaining tumors in his liver, the way you or I might shake off a cold. His own body had cured his cancer. Somehow.

怎麼會這樣？在所有醫學文獻中，羅森博格只能找到四個轉移性胃癌完全自發性緩解的例子。他很困惑。但他最終提出了一個假設：他相信迪安吉洛自己的免疫系統已經抵抗了癌症，並殺死了肝臟中剩餘的腫瘤，就像你我擺脫感冒一樣。他自己的身體治癒了他的癌症。不知何故。

At the time, this notion was well out of the mainstream of cancer research. But Rosenberg suspected that he was onto something important. *The Transformed Cell* told the story of Rosenberg's quest to harness the immune system to fight cancer. Despite small successes peppered here and there, however, whatever phenomenon had erased James DeAngelo's tumors proved

to be elusive; for the first ten years, not a single one of Rosenberg's patients had survived. Not one. But still he kept at it.

當時，這個概念遠遠超出了癌症研究的主流。但羅森伯格懷疑他正在做一些重要的事情。《轉化的細胞》講述了羅森伯格尋求利用免疫系統對抗癌症的故事。儘管到處都取得了一些小成功，但事實證明，無論什麼現象能夠消除詹姆斯·迪安吉洛的腫瘤，都是難以捉摸的。在最初的十年裡，羅森伯格的病人無一倖存。不是一個。但他仍然堅持了下來。

He was doing better as a cancer surgeon than a cancer researcher: he operated on President Ronald Reagan in 1985, removing cancerous polyps from his colon, and that had gone fine. But Rosenberg's goal was to eliminate the need for cancer surgeries, period. Finally, in the mid-1980s, he had a glimmer of success—just enough to keep him going.

作為一名癌症外科醫生，他比癌症研究員做得更好：1985 年，他為羅納德·雷根總統進行了手術，切除了結腸中的癌性息肉，一切進展順利。但羅森伯格的目標是消除癌症手術的需要。最終，在 20 世紀 80 年代中期，他獲得了一絲成功——這足以讓他繼續前進。

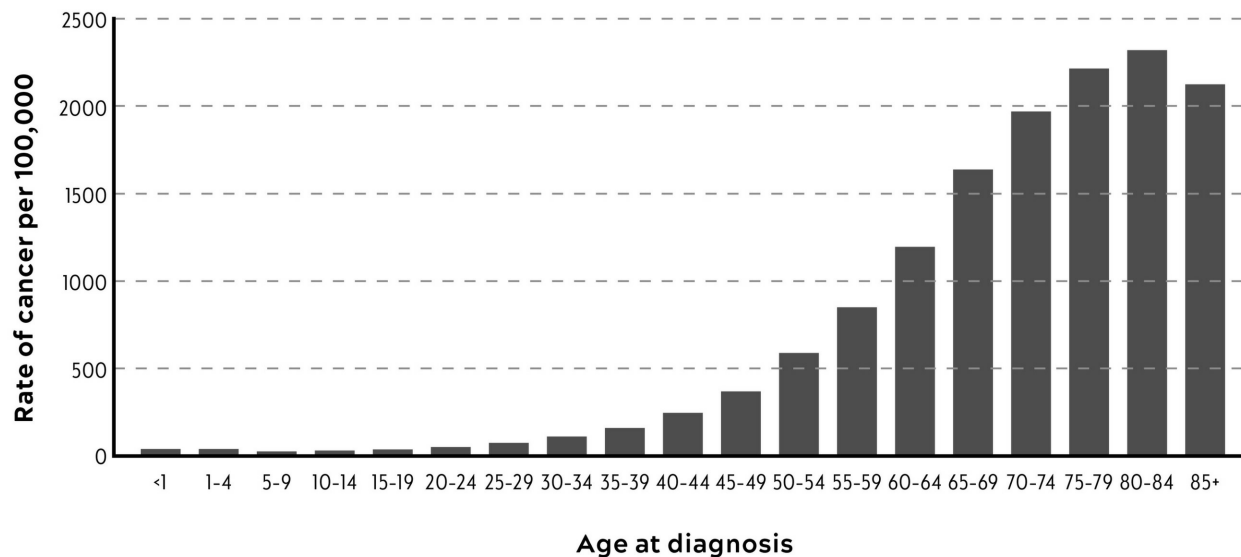
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As soon as I read *The Transformed Cell*, as a medical student, I knew that I wanted to be a surgical oncologist and that I had to work with Steve Rosenberg. Cancer had been on my mind since before I had even applied to medical school. During my postbac year, while taking med school prerequisite courses, I volunteered on the pediatric cancer ward of Kingston General Hospital in Ontario, spending time with kids who were undergoing cancer treatment. Thankfully, childhood leukemia is one area where Medicine 2.0 has made real progress. But not all the kids survived, and the bravery of these children, the pain that they and their parents endured, and the compassion of their medical teams moved me more deeply than any engineering or mathematical problem. It confirmed my decision to switch from engineering to medicine.

作為一名醫學生，當我讀到《轉化的細胞》時，我就知道我想成為一名腫瘤外科醫師，並且我必須與史蒂夫·羅森伯格一起工作。在我申請醫學院之前，癌症就一直在我的腦海裡。在我讀完大學後的一年裡，在修讀醫學院的先修課程的同時，我在安大略省金斯頓綜合醫院的兒科癌症病房做志願者，與正在接受癌症治療的孩子們共度時光。值得慶幸的是，兒童白血病是醫學 2.0 真正進展的領域之一。但並不是所有的孩子都活了下來，這些孩子的勇敢、他們和他們的父母所承受的痛苦以及他們的醫療團隊的同情心比任何工程或數學問題都更讓我感動。它堅定了我從工程轉向醫學的決定。

In my third year of medical school, I got the opportunity to spend four months in Rosenberg's lab, at the epicenter of American cancer research. By the time I arrived, it had been nearly three decades since Richard Nixon had declared a national War on Cancer in 1971. Initially, the hope was that cancer would be "cured" within five years, in time for the Bicentennial. Yet it remained stubbornly undefeated in 1976, and still by the time I finished medical school in 2001. And today, for all intents and purposes.

在醫學院的第三年，我有機會在美國癌症研究中心羅森伯格的實驗室待了四個月。當我到達時，距離理查德·尼克松(Richard Nixon) 1971 年向全國癌症宣戰已經過去了近三十年。最初，人們希望癌症能在五年內“治愈”，正好趕上二百週年紀念日。然而，它在 1976 年仍然頑強地保持不敗，直到 2001 年我從醫學院畢業時仍然如此。直到今天，無論出於何種意圖和目的。

Figure 6. Cancer Incidence by Age in the United States

Source: National Cancer Institute (2021).

資料來源：國家癌症研究所（2021 年）。

Despite well over \$100 billion spent on research via the National Cancer Institute, plus many billions more from private industry and public charities—despite all the pink ribbons and yellow bracelets, and literally millions of published papers on the PubMed database—cancer is the second leading cause of death in the United States, right behind heart disease. Together, these two conditions account for almost one in every two American deaths. The difference is that we understand the genesis and progression of heart disease fairly well, and we have some effective tools with which to prevent and treat it. As a result, mortality rates from cardiovascular disease and cerebrovascular disease have dropped by two-thirds since the middle of the twentieth century. But cancer still kills Americans at almost exactly the same rate as it did fifty years ago.

儘管美國國家癌症研究所在研究上花費了超過1000 億美元，再加上私營企業和公共慈善機構投入了數十億美元——儘管有粉紅絲帶和黃手鐲，並且PubMed 數據庫上確實發表了數百萬篇論文——癌症仍是第二大癌症在美國，死亡原因僅次於心臟病。這兩種情況加起來幾乎占美國死亡人數的二分之一。不同之處在於，我們相當了解心臟病的起源

和進展，我們擁有一些有效的工具來預防和治療心臟病。結果，自二十世紀中葉以來，心血管疾病和腦血管疾病的死亡率下降了三分之二。但癌症殺死美國人的速度仍然與五十年前幾乎完全相同。

We have made some progress against a few specific cancers, notably leukemia (especially childhood leukemia, as I noted earlier). For adults with leukemia, ten-year survival rates nearly doubled between 1975 and 2000, leaping from 23 percent to 44 percent. Survival rates for Hodgkin's and non-Hodgkin's lymphomas have increased as well, especially the former. Yet these represent relatively small victories in a "war" that has not gone particularly well.

我們在對抗一些特定癌症方面取得了一些進展，特別是白血病（特別是兒童白血病，正如我之前提到的）。1975 年至 2000 年間，成人白血病患者十年存活率幾乎翻了一番，從 23% 躍升至 44%。霍奇金淋巴瘤和非何杰金氏淋巴瘤的存活率也有所增加，尤其是前者。然而，這些只是一場進展不太順利的「戰爭」中相對較小的勝利。

Like heart disease, cancer is a disease of aging. That is, it becomes exponentially more prevalent with each decade of life, as figure 6 shows. But it can be deadly at almost any age, especially middle age. The median age of a cancer diagnosis is sixty-six, but in 2017 there were more cancer deaths among people between forty-five and sixty-four than from heart disease, liver disease, and stroke combined. This year, if recent trends continue, that same age group will also account for nearly 40 percent of the estimated 1.7 million new cases of cancer that are likely to be diagnosed in the United States, according to the National Cancer Institute. By the time cancer is detected, however, it has probably already been progressing for years and possibly decades. As I write these words, I reflect sadly on three of my friends from high school who died of cancer in the past ten years, all younger than forty-five. I was able to say goodbye to only one of them before she died. Everyone reading this book probably has a few similar stories.

與心臟病一樣，癌症是一種老化疾病。也就是說，隨著生命的每十年，它的流行程度呈指數級增長，如圖 6 所示。但幾乎任何年齡，尤其是中年，它都可能是致命的。癌症診斷的中位數年齡為 66 歲，但

2017 年，45 歲至 64 歲之間的癌症死亡人數比心臟病、肝病和中風死亡人數的總和還要多。根據美國國家癌症研究所的數據，今年，如果最近的趨勢持續下去，同一年齡層也將占美國可能診斷的 170 萬個新癌症病例中的近 40%。然而，當癌症被發現時，它可能已經發展了數年甚至數十年。當我寫下這些文字時，我悲傷地想起過去十年因癌症去世的三位高中朋友，他們的年齡都在四十五歲以下。在她去世之前，我只能與其中一位告別。每個讀過這本書的人可能都有一些類似的故事。

The problem we face is that once cancer is established, we lack highly effective treatments for it. Our toolbox is limited. Many (though not all) solid tumors can be removed surgically, a tactic that dates back to ancient Egypt. Combining surgery and radiation therapy is pretty effective against most local, solid-tumor cancers. But while we've gotten fairly good at this approach, we have essentially maxed out our ability to treat cancers this way. We are not getting any more juice from the squeeze. And surgery is of limited value when cancer has metastasized, or spread. Metastatic cancers can be slowed by chemotherapy, but they virtually always come back, often more resistant to treatment than ever. Our benchmark for success in a patient, or remission, is typically five-year survival, nothing more. We don't dare utter the word *cure*.

我們面臨的問題是，一旦癌症確診，我們就缺乏高效率的治療方法。我們的工具箱是有限的。許多（儘管不是全部）實體腫瘤可以透過手術切除，這種策略可以追溯到古埃及。手術和放射治療相結合對於大多數局部實體瘤癌症非常有效。雖然我們已經相當擅長這種方法，但我們基本上已經最大限度地發揮了這種方法治療癌症的能力。我們不會再從榨汁中得到更多的果汁了。當癌症已經轉移或擴散時，手術的價值有限。化療可以減緩轉移性癌症的進展，但它們實際上總是會復發，而且往往比以往任何時候都對治療產生更強的抵抗力。我們對患者成功或緩解的基準通常是五年存活期，僅此而已。我們不敢說出治愈這個字。

The second problem is that our ability to detect cancer at an early stage remains very weak. Far too often, we discover tumors only when they cause other symptoms, by which point they are often too locally advanced to be

removed—or worse, the cancer has already spread to other parts of the body. I saw this happen many times during my training: we would remove a patient's tumor (or tumors), only to have them die a year later because that same cancer had taken hold elsewhere, like their liver or their lungs.

第二個問題是我們早期發現癌症的能力仍然非常薄弱。很多時候，我們只有在腫瘤引起其他症狀時才發現腫瘤，此時腫瘤往往已經局部晚期而無法切除，或者更糟的是，癌症已經擴散到身體的其他部位。我在訓練期間多次看到這種情況發生：我們會切除患者的一個或多個腫瘤，但一年後他們就會死亡，因為同樣的癌症已經在其他地方發生，例如他們的肝臟或肺部。

This experience informs our three-part strategy for dealing with cancer. Our first and most obvious wish is to avoid getting cancer at all, like the centenarians—in other words, prevention. But cancer prevention is tricky, because we do not yet fully understand what drives the initiation and progression of the disease with the same resolution that we have for atherosclerosis. Further, plain bad luck seems to play a major role in this largely stochastic process. But we do have some clues, which is what we'll talk about in the next two sections.

這一經驗為我們治療癌症的三部分策略提供了資訊。我們第一個也是最明顯的願望是像百歲老人一樣完全避免罹患癌症，換句話說，就是預防。但癌症的預防是很棘手的，因為我們還沒有完全了解是什麼驅動了疾病的發生和進展，其解決方案與我們對動脈粥狀硬化的解決方案相同。此外，運氣不好似乎在這個很大程度上是隨機的過程中發揮了重要作用。但我們確實有一些線索，這就是我們將在接下來的兩節中討論的內容。

Next is the use of newer and smarter treatments targeting cancer's manifold weaknesses, including the insatiable metabolic hunger of fast-growing cancer cells and their vulnerability to new immune-based therapies, the outcome of decades of work by scientists like Steve Rosenberg. I feel that immunotherapy, in particular, has enormous promise.

接下來是使用更新、更聰明的治療方法來針對癌症的多種弱點，包括快速生長的癌細胞無法滿足的代謝飢餓以及它們對新免疫療法的脆弱性，這是史蒂夫·羅森伯格等科學家數十年工作的成果。我認為免疫療法尤其具有巨大的前景。

Third, and perhaps most importantly, we need to try to detect cancer as early as possible so that our treatments can be deployed more effectively. I advocate early, aggressive, and broad screening for my patients—such as colonoscopy (or other colorectal cancer screening) at age forty, as opposed to the standard recommendation of forty-five or fifty—because the evidence is overwhelming that it's much easier to deal with most cancers in their early stages. I am also cautiously optimistic about pairing these tried-and-true staples of cancer screening with emerging methods, such as “liquid biopsies,” which can detect trace amounts of cancer-cell DNA via a simple blood test.

第三，也許也是最重要的一點，我們需要儘早發現癌症，以便更有效地部署我們的治療方法。我主張對我的患者進行早期、積極和廣泛的篩檢，例如在四十歲時進行大腸鏡檢查（或其他結直腸癌篩檢），而不是標準建議的四十五歲或五十歲，因為有壓倒性的證據表明，在四十歲時進行大腸鏡檢查（或其他結直腸癌篩檢）要容易得多。治療大多數癌症的早期階段。我還對將這些經過驗證的癌症篩檢主要方法與新興方法（例如「液體活檢」）結合起來持謹慎樂觀的態度，「液體活檢」可以透過簡單的血液測試檢測出微量的癌細胞 DNA。

Five decades into the war on cancer, it seems clear that no single “cure” is likely to be forthcoming. Rather, our best hope likely lies in figuring out better ways to attack cancer on all three of these fronts: prevention, more targeted and effective treatments, and comprehensive and accurate early detection.

對抗癌症的戰爭已經進行了五十年，很明顯，不可能出現任何單一的「治癒方法」。相反，我們最大的希望可能在於在這三個方面找出更好的方法來攻擊癌症：預防、更有針對性和有效的治療以及全面和準確的早期檢測。

What Is Cancer?

什麼是癌症？

One major reason why cancer is so deadly—and so scary—is that we still know relatively little about how it begins and why it spreads.

癌症如此致命且如此可怕的一個主要原因是，我們對它是如何開始以及為何傳播仍然知之甚少。

Cancer cells are different from normal cells in two important ways. Contrary to popular belief, cancer cells don't grow faster than their noncancerous counterparts; they just don't *stop* growing when they are supposed to. For some reason, they stop listening to the body's signals that tell them when to grow and when to stop growing. This process is thought to begin when normal cells acquire certain genetic mutations. For example, a gene called *PTEN*, which normally stops cells from growing or dividing (and eventually becoming tumors), is often mutated or “lost” in people with cancer, including about 31 percent of men with prostate cancer and 70 percent of men with advanced prostate cancer. Such “tumor suppressor” genes are critically important to our understanding of the disease.

癌細胞在兩個重要方面不同於正常細胞。與一般看法相反，癌細胞的生長速度並不比非癌細胞快。他們只是在應該停止生長的時候並沒有停止生長。由於某種原因，他們不再傾聽身體的信號，告訴他們何時生長以及何時停止生長。這個過程被認為是在正常細胞獲得某些基因突變時開始的。例如，一種名為PTEN 的基因通常會阻止細胞生長或分裂（並最終成為腫瘤），但它經常在癌症患者體內發生突變或“丟失”，其中包括約31% 的前列腺癌男性和70% 的前列腺癌男性。晚期前列腺癌。這種「腫瘤抑制」基因對於我們了解這種疾病至關重要。

The second property that defines cancer cells is their ability to travel from one part of the body to a distant site where they should not be. This is called *metastasis*, and it is what enables a cancerous cell in the breast to spread to the lung. This spreading is what turns a cancer from a local, manageable problem to a fatal, systemic disease.

定義癌細胞的第二個特性是它們能夠從身體的一個部位移動到它們不應該到達的遠處部位。這稱為轉移，它使乳房中的癌細胞擴散到肺部。這種擴散使得癌症從一個可控制的局部問題變成了一種致命的全身性疾病。

Beyond these two common properties, however, the similarities among different cancers largely end. One of the biggest obstacles to a “cure” is the fact that cancer is not one single, simple, straightforward disease, but a condition with mind-boggling complexity.

然而，除了這兩個共同特性之外，不同癌症之間的相似性基本上消失了。「治癒」的最大障礙之一是癌症不是一種單一、簡單、直接的疾病，而是一種具有令人難以置信的複雜性的疾病。

About two decades ago, the National Cancer Institute launched a huge and ambitious study called The Cancer Genome Atlas, whose goal was to sequence cancer tumor cells in hopes of finding the precise genetic changes that cause various types of cancer, such as breast, kidney, and liver cancer. Armed with this knowledge, scientists would be able to develop therapies targeted at these exact mutations. As one of the scientists who proposed the project said, “These are the starting blocks that we need to develop a cure.”

大約二十年前，美國國家癌症研究所發起了一項名為「癌症基因組圖譜」的龐大而雄心勃勃的研究，其目標是對癌症腫瘤細胞進行測序，希望找到導致各種類型癌症（如乳腺癌、腎癌、癌症）的精確基因變化。和肝癌。有了這些知識，科學家將能夠開發針對這些確切突變的療法。正如提出該計畫的一位科學家所說，“這些是我們開發治療方法所需的起點。”

But the early results of The Cancer Genome Atlas, published in a series of papers beginning in 2008, revealed more confusion than clarity. Rather than uncovering a definite pattern of genetic changes driving each type of cancer, the study found enormous complexity. Each tumor had more than one hundred different mutations, on average, and those mutations almost appeared to be random. A handful of genes emerged as drivers, including *TP53* (also known as p53, found in half of all cancers), *KRAS* (common in pancreatic

cancer), *PIC3A* (common in breast cancer), and *BRAF* (common in melanoma), but very few if any of these well-known mutations were shared across all tumors. In fact, there didn't seem to be any individual genes that "caused" cancer at all; instead, it seemed to be random somatic mutations that *combined* to cause cancers. So not only is breast cancer genetically distinct from colon cancer (as the researchers expected), but no two breast cancer tumors are very much alike. If two women have breast cancer, at the same stage, their tumor genomes are likely to be very different from each other. Therefore, it would be difficult if not impossible to devise one treatment for both women based on the genetic profile of their tumors. Rather than revealing the shape of the forest, then, The Cancer Genome Atlas merely dragged us deeper into the maze of the trees.

但從 2008 年開始在一系列論文中發表的《癌症基因組圖譜》的早期結果顯示，混亂多於清晰。該研究並沒有揭示驅動每種癌症的基因變化的明確模式，而是發現了巨大的複雜性。每個腫瘤平均有一百多個不同的突變，而且這些突變幾乎是隨機的。少數基因成為驅動因素，包括 TP53（也稱為 p53，在一半的癌症中都有發現）、KRAS（常見於胰腺癌）、PIC3A（常見於乳腺癌）和 BRAF（常見於黑色素瘤），但這些眾所周知的突變幾乎沒有在所有腫瘤中共有。事實上，似乎根本沒有任何單一基因「引發」癌症；相反，它似乎是隨機的體細胞突變結合起來導致癌症。因此，乳癌不僅在基因上與結腸癌不同（正如研究人員預期的那樣），而且沒有兩種乳癌腫瘤非常相似。如果兩名女性患有乳癌，處於同一階段，她們的腫瘤基因組可能彼此非常不同。因此，根據腫瘤的遺傳特徵為這兩位女性設計一種治療方法即使不是不可能，也是很困難的。那麼，癌症基因組圖譜並沒有揭示森林的形狀，只是將我們拖入了樹木迷宮的更深處。

Or so it seemed at the time. Ultimately, genome sequencing has proved to be a very powerful tool against cancer—just not in the way that was envisioned two decades ago.

或者說當時看起來是這樣。最終，基因組定序已被證明是一種非常強大的抗癌工具，只是與二十年前設想的方式不同。

Even when we treat a local cancer successfully, we can never be sure that it's entirely gone. We have no way of knowing whether cancer cells may have already spread and are lurking in other organs, waiting to establish a foothold there. It is this metastatic cancer that is responsible for most cancer deaths. If we want to reduce cancer mortality by a significant amount, we must do a better job of preventing, detecting, and treating metastatic cancers.

即使我們成功治療了局部癌症，我們也無法確定它是否已完全消失。我們無法知道癌細胞是否可能已經擴散並潛伏在其他器官中，等待在那裡立足。正是這種轉移性癌症導致了大多數癌症死亡。如果我們想大幅降低癌症死亡率，我們必須更好地預防、檢測和治療轉移性癌症。

With a few exceptions, such as glioblastoma or other aggressive brain tumors, as well as certain lung and liver cancers, solid organ tumors typically kill you only when they spread to other organs. Breast cancer kills only when it becomes metastatic. Prostate cancer kills only when it becomes metastatic. You could live without either of those organs. So when you hear the sad story of someone dying from breast or prostate cancer, or even pancreatic or colon cancer, they died because the cancer spread to other, more critical organs such as the brain, the lungs, the liver, and bones. When cancer reaches those places, survival rates drop precipitously.

除了少數例外，例如膠質母細胞瘤或其他侵襲性腦瘤，以及某些肺癌和肝癌，實體器官腫瘤通常只有在擴散到其他器官時才會致命。乳癌只有在轉移時才會致命。前列腺癌只有在發生轉移時才會致命。沒有這些器官你也可以生存。因此，當你聽到某人死於乳腺癌或前列腺癌，甚至胰腺癌或結腸癌的悲傷故事時，他們的死亡是因為癌症擴散到其他更重要的器官，如大腦、肺、肝臟和骨骼。當癌症到達這些地方時，存活率急劇下降。

But what causes cancer to spread? We don't really know, and we are unlikely to find out anytime soon because only about 5 to 8 percent of US cancer research funding goes to the study of metastasis. Our ability to detect

cancer metastasis is also very poor, although I do believe we are on the verge of some key breakthroughs in cancer screening, as we'll discuss later. Most of our energy has been focused on treating metastatic cancer, which is an extremely difficult problem. Once cancer has spread, the entire game changes: we need to treat it *systemically* rather than locally.

但是是什麼原因導致癌症擴散呢？我們真的不知道，而且不太可能很快找到答案，因為美國癌症研究經費中只有約 5% 到 8% 用於轉移研究。我們檢測癌症轉移的能力也很差，儘管我確實相信我們即將在癌症篩檢方面取得一些關鍵突破，正如我們稍後將討論的那樣。我們大部分的精力都集中在治療轉移性癌症上，這是一個極其困難的問題。一旦癌症擴散，整個遊戲就會發生變化：我們需要系統地而不是局部地治療它。

Right now, this usually means chemotherapy. Contrary to popular belief, killing cancer cells is actually pretty easy. I've got a dozen potential chemotherapy agents in my garage and under my kitchen sink. Their labels identify them as glass cleaner or drain openers, but they would easily kill cancer cells too. The problem, of course, is that these poisons will also slaughter every normal cell in between, likely killing the patient in the process. The game is won by killing cancers while sparing the normal cells. *Selective* killing is the key.

目前，這通常意味著化療。與普遍的看法相反，殺死癌細胞實際上非常容易。我的車庫和廚房水槽下有十幾種潛在的化療藥物。它們的標籤將它們標記為玻璃清潔劑或排水溝開啟器，但它們也很容易殺死癌細胞。當然，問題是這些毒藥也會殺死其間的每一個正常細胞，很可能會在過程中殺死病人。這場遊戲的勝利在於殺死癌症，同時不傷害正常細胞。選擇性殺傷是關鍵。

Traditional chemotherapy occupies a fuzzy region between poison and medicine; the mustard gas used as a weapon during World War I was a direct precursor to some of the earliest chemotherapy agents, some of which are still in use. These drugs attack the replicative cycle of cells, and because cancer cells are rapidly dividing, the chemo agents harm them more severely than normal cells. But many important noncancerous cells are also dividing

frequently, such as those in the lining of the mouth and gut, the hair follicles, and the nails, which is why typical chemotherapy agents cause side effects like hair loss and gastrointestinal misery. Meanwhile, as cancer researcher Robert Gatenby points out, those cancer cells that do manage to survive chemotherapy often end up acquiring mutations that make them stronger, like cockroaches that develop resistance to insecticides.

傳統化療處於毒藥與藥物之間的模糊地帶。第一次世界大戰期間用作武器的芥子氣是一些最早的化療藥物的直接前身，其中一些仍在使用中。這些藥物會攻擊細胞的複製週期，由於癌細胞快速分裂，化療藥物對它們的傷害比正常細胞更嚴重。但許多重要的非癌細胞也經常分裂，例如口腔和腸道內壁、毛囊和指甲中的細胞，這就是為什麼典型的化療藥物會導致脫髮和胃腸道不適等副作用。同時，正如癌症研究人員羅伯特·蓋滕比（Robert Gatenby）指出的那樣，那些確實能夠在化療中存活下來的癌細胞最終往往會獲得使它們變得更強的突變，就像蟑螂對殺蟲劑產生抗藥性一樣。

The side effects of chemo might seem at the outset to be a fair trade for a “chance for a few more useful years,” as the late author Christopher Hitchens noted in his cancer memoir *Mortality*. But as his treatment for metastatic esophageal cancer dragged on, he changed his mind. “I lay for days on end, trying in vain to postpone the moment when I would have to swallow. Every time I did swallow, a hellish tide of pain would flow up my throat, culminating in what felt like a mule kick in the small of my back....And then I had an unprompted rogue thought: If I had been told about all this in advance, would I have opted for the treatment?”

正如已故作家克里斯托弗·希欽斯(Christopher Hitchens) 在他的癌症回憶錄《死亡率》中所指出的那樣，化療的副作用一開始似乎是一種公平的交易，可以換取「多活幾年的機會」。但隨著轉移性食道癌治療的拖延，他改變了主意。「我連續躺了好幾天，徒勞地試圖推遲我必須吞嚥的時刻。每次我吞嚥下去，一股地獄般的疼痛就會湧上我的喉嚨，最終感覺就像是騾子踢我的後腰.....然後我就有了一個無意識的想法：如果有人告訴我這一切如果提前的話，我會選擇接受治療嗎？」

Hitchens was experiencing the primary flaw of modern chemotherapy: It

is systemic, but still not specific enough to target only cancerous cells and not normal healthy cells. Hence the horrible side effects he suffered. Ultimately, successful treatments will need to be both systemic *and* specific to a particular cancer type. They will be able to exploit some weakness that is unique to cancer cells, while largely sparing normal cells (and, obviously, the patient). But what might those weaknesses be?

希欽斯正在經歷現代化療的主要缺陷：它是系統性的，但仍然不夠具體，無法只針對癌細胞而不是正常的健康細胞。因此他遭受了可怕的副作用。最終，成功的治療需求既是系統性的又是針對特定癌症類型的。他們將能夠利用癌細胞特有的一些弱點，同時很大程度上保護正常細胞（顯然，還有患者）。但這些弱點可能是什麼？

Just because cancer is powerful does not mean it is invincible. In 2011, two leading cancer researchers named Douglas Hanahan and Robert Weinberg identified two key hallmarks of cancer that may lead—and in fact have led—to new treatments, as well as potential methods of reducing cancer risk. The first such hallmark is the fact that many cancer cells have an altered metabolism, consuming huge amounts of glucose. Second, cancer cells seem to have an uncanny ability to evade the immune system, which normally hunts down damaged and dangerous cells—such as cancerous cells—and targets them for destruction. This second problem is the one that Steve Rosenberg and others have been trying to solve for decades.

癌症很強大並不意味著它是無敵的。2011年，兩位著名的癌症研究人員道格拉斯·哈納漢(Douglas Hanahan)和羅伯特·溫伯格(Robert Weinberg)發現了癌症的兩個關鍵特徵，這些特徵可能導致（而且實際上已經導致）新的治療方法以及降低癌症風險的潛在方法。第一個特徵是許多癌細胞的新陳代謝發生了改變，消耗了大量的葡萄糖。其次，癌細胞似乎具有逃避免疫系統的不可思議的能力，免疫系統通常會追捕受損和危險的細胞（例如癌細胞）並將其作為目標進行破壞。第二個問題是史蒂夫羅森伯格和其他人幾十年來一直試圖解決的問題。

Metabolism and immune surveillance excite me because they are both systemic, a necessary condition for any new treatment to combat metastatic

cancers. They both exploit features of cancer that are potentially more specific to tumors than simply runaway cell replication. But neither the metabolic nor the immune-based approaches to cancer are exactly new: dogged researchers have been laying the groundwork for progress in both of these areas for decades.

新陳代謝和免疫監視讓我感到興奮，因為它們都是系統性的，是任何對抗轉移性癌症的新療法的必要條件。它們都利用了癌症的特徵，這些特徵可能比單純的細胞複製失控更具腫瘤特異性。但代謝和基於免疫的癌症治療方法都不是全新的：數十年來，頑強的研究人員一直在為這兩個領域的進展奠定基礎。

Cancer Metabolism

癌症代謝

As you might have gathered by now, we tend to think of cancer as primarily a genetic disease, driven by mutations of unknown cause. Clearly, cancer cells are genetically distinct from normal human cells. But for the last century or so, a handful of researchers have been investigating another unique property of cancer cells, and that is their metabolism.

正如您現在可能已經了解的那樣，我們傾向於認為癌症主要是一種遺傳性疾病，由未知原因的突變驅動。顯然，癌細胞在遺傳上與正常人類細胞不同。但在上個世紀左右，一些研究人員一直在研究癌細胞的另一個獨特特性，那就是它們的新陳代謝。

In the 1920s, a German physiologist named Otto Warburg discovered that cancer cells had a strangely gluttonous appetite for glucose, devouring it at up to forty times the rate of healthy tissues. But these cancer cells weren't "respiring" the way normal cells do, consuming oxygen and producing lots of ATP, the energy currency of the cell, via the mitochondria. Rather, they appeared to be using a different pathway that cells normally use to produce energy under anaerobic conditions, meaning without sufficient oxygen, such

as when we are sprinting. The strange thing was that these cancer cells were resorting to this inefficient metabolic pathway despite having plenty of oxygen available to them.

1920 年代，一位名叫奧托·瓦爾堡 (Otto Warburg) 的德國生理學家發現，癌細胞對葡萄糖有著奇怪的貪婪胃口，其吞噬葡萄糖的速度高達健康組織的四十倍。但這些癌細胞並不像正常細胞那樣“呼吸”，透過粒線體消耗氧氣並產生大量 ATP（細胞的能量貨幣）。相反，它們似乎使用了細胞通常在無氧條件下產生能量的不同途徑，即沒有足夠的氧氣，例如當我們短跑時。奇怪的是，儘管這些癌細胞有充足的氧氣，但它們仍然採取這種低效的代謝途徑。

This struck Warburg as a very strange choice. In normal aerobic respiration, a cell can turn one molecule of glucose into as many as thirty-six units of ATP. But under anaerobic conditions, that same amount of glucose yields only two net units of ATP. This phenomenon was dubbed the Warburg effect, and even today, one way to locate potential tumors is by injecting the patient with radioactively labeled glucose and then doing a PET scan to see where most of the glucose is migrating. Areas with abnormally high glucose concentrations indicate the possible presence of a tumor.

瓦爾堡覺得這是一個很奇怪的選擇。在正常的有氧呼吸中，細胞可以將一分子葡萄糖轉化為多達三十六個單位的 ATP。但在無氧條件下，相同量的葡萄糖只會產生兩個淨單位的 ATP。這種現象被稱為瓦伯格效應，即使在今天，定位潛在腫瘤的一種方法是向患者注射放射性標記的葡萄糖，然後進行 PET 掃描以查看大部分葡萄糖遷移的位置。葡萄糖濃度異常高的區域表示可能有腫瘤。

Warburg was awarded the Nobel Prize in Physiology or Medicine in 1931 for his discovery of a crucial enzyme in the electron transport chain (a key mechanism for producing energy in the cell). By the time he died in 1970, the weird quirk of cancer metabolism that he had discovered had been all but forgotten. The discovery of the structure of DNA by James Watson, Francis Crick, Maurice Wilkins, and Rosalind Franklin in 1953 had caused a seismic paradigm shift, not just in cancer research but in biology in general.

瓦爾堡因發現電子傳遞鏈（細胞產生能量的關鍵機制）中的關鍵酶而獲得 1931 年諾貝爾生理學或醫學獎。1970 年他去世時，他發現的癌症代謝的怪異現象幾乎被遺忘了。1953 年，詹姆斯·沃森(James Watson)、弗朗西斯·克里克(Francis Crick)、莫里斯·威爾金斯(Maurice Wilkins) 和羅莎琳德·富蘭克林(Rosalind Franklin) 對DNA 結構的發現引起了巨大的典範轉移，不僅在癌症研究領域，而且在整個生物學領域。

As Watson recounted in a 2009 *New York Times* op-ed: “In the late 1940s, when I was working toward my doctorate, the top dogs of biology were its biochemists who were trying to discover how the intermediary molecules of metabolism were made and broken down. After my colleagues and I discovered the double helix of DNA, biology’s top dogs then became its molecular biologists, whose primary role was finding out how the information encoded by DNA sequences was used to make the nucleic acid and protein components of cells.”

正如華森在2009 年《紐約時報》專欄中所敘述的：「20 世紀40 年代末，當我攻讀博士學位時，生物學界的頂尖人物是生物化學家，他們試圖發現新陳代謝的中間分子是如何形成和分解的。向下。在我和我的同事發現 DNA 雙螺旋之後，生物學界的頂尖人物就成為了分子生物學家，他們的主要職責是找出 DNA 序列編碼的訊息如何被用來製造細胞的核酸和蛋白質成分。」

Nearly forty years into the War on Cancer, however, Watson himself had become convinced that genetics did not hold the key to successful cancer treatment after all. “We may have to turn our main research focus away from decoding the genetic instructions behind cancer and toward understanding the chemical reactions within cancer cells,” he wrote. It was time, he argued, to start looking at therapies that targeted cancer’s metabolism as well as its genetics.

然而，在與癌症的戰爭進行了近四十年後，沃森本人開始相信，遺傳學畢竟不是成功治療癌症的關鍵。他寫道：“我們可能不得不將主要研

究重點從解碼癌症背後的遺傳指令轉向了解癌細胞內的化學反應。”他認為，是時候開始尋找針對癌症代謝及其遺傳學的療法了。

A handful of scientists had been pursuing the metabolic aspects of cancer all along. Lew Cantley, now at Harvard's Dana-Farber Cancer Center, has been investigating cancer metabolism since the 1980s, when the idea was unfashionable. One of the more puzzling questions he has tackled was *why* cancer cells needed to produce energy in this highly inefficient way. Because the inefficiency of the Warburg effect may be the point, as Cantley, Matthew Vander Heiden, and Craig Thompson argued in a 2009 paper. While it may not yield much in the way of energy, they found, the Warburg effect generates lots of by-products, such as lactate, a substance that is also produced during intense exercise. In fact, turning glucose into lactate creates so many extra molecules that the authors argued that the relatively small amount of energy it produces may actually be the “by-product.”

一些科學家一直在研究癌症的代謝方面。盧·坎特利 (Lew Cantley) 現任職於哈佛大學丹納法伯癌症中心，自 1980 年代以來一直在研究癌症代謝，當時這個想法並不流行。他解決的更令人費解的問題之一是為什麼癌細胞需要以這種效率極低的方式產生能量。因為正如坎特利、馬修·范德·海登和克雷格·湯普森在 2009 年的一篇論文中所指出的那樣，瓦爾堡效應的低效率可能是問題所在。他們發現，雖然瓦伯格效應可能不會產生太多能量，但它會產生大量副產品，例如乳酸，這種物質在劇烈運動時也會產生。事實上，將葡萄糖轉化為乳酸會產生如此多的額外分子，以至於作者認為，它產生的相對少量的能量實際上可能是「副產品」。

There's a logic to this seeming madness: when a cell divides, it doesn't simply split into two smaller cells. The process requires not only the division of the nucleus, and all that stuff we learned in high school biology, but the actual physical materials required to construct a whole new cell. Those don't just appear out of nowhere. Normal aerobic cellular respiration produces only energy, in the form of ATP, plus water and carbon dioxide, which aren't much use as building materials (also, we exhale the latter two). The Warburg effect, also known as anaerobic glycolysis, turns the same amount of glucose into a

little bit of energy and a whole lot of chemical building blocks—which are then used to build new cells rapidly. Thus, the Warburg effect is how cancer cells fuel their own proliferation. But it also represents a potential vulnerability in cancer's armor.^[*1]

這種看似瘋狂的現象是有邏輯的：當細胞分裂時，它並不是簡單地分裂成兩個較小的細胞。這個過程不僅需要細胞核的分裂以及我們在高中生物學中學到的所有東西，還需要建造全新細胞所需的實際物理材料。這些並不是憑空出現的。正常的有氧細胞呼吸僅產生 ATP 形式的能量，以及水和二氧化碳，這些能量並不能作為建築材料使用（而且，我們呼出後兩者）。瓦伯格效應，也稱為無氧糖解，可將等量的葡萄糖轉化為少量能量和大量化學構件，然後用於快速建立新細胞。因此，瓦爾堡效應是癌細胞促進自身增生的方式。但它也代表了癌症盔甲的潛在脆弱性。^[*1]

This remains a controversial view in mainstream cancer circles, but it has gotten harder and harder to ignore the link between cancer and metabolic dysfunction. In the 1990s and early 2000s, as rates of smoking and smoking-related cancers declined, a new threat emerged to take the place of tobacco smoke. Obesity and type 2 diabetes were snowballing into national and then global epidemics, and they seemed to be driving increased risk for many types of cancers, including esophageal, liver, and pancreatic cancer. The American Cancer Society reports that excess weight is a leading risk factor for both cancer cases and deaths, second only to smoking.

這在主流癌症界仍然是一個有爭議的觀點，但人們越來越難以忽視癌症與代謝功能障礙之間的關聯。在 1990 年代和 2000 年代初，隨著吸煙和與吸煙相關的癌症發病率下降，出現了一種新的威脅來取代菸草煙霧。肥胖和第 2 型糖尿病像滾雪球一樣在全國乃至全球範圍內流行，它們似乎導致多種癌症的風險增加，包括食道癌、肝癌和胰臟癌。美國癌症協會報告稱，體重過重是癌症病例和死亡的主要危險因素，僅次於吸菸。

Globally, about 12 to 13 percent of all cancer cases are thought to be attributable to obesity. Obesity itself is strongly associated with thirteen different types of cancers, including pancreatic, esophageal, renal, ovarian,

and breast cancers, as well as multiple myeloma (see [figure 7](#)). Type 2 diabetes also increases the risk of certain cancers, by as much as double in some cases (such as pancreatic and endometrial cancers). And extreme obesity ($\text{BMI} \geq 40$) is associated with a 52 percent greater risk of death from all cancers in men, and 62 percent in women.

在全球範圍內，大約 12% 至 13% 的癌症病例被認為是由肥胖引起的。肥胖本身與 13 種不同類型的癌症密切相關，包括胰臟癌、食道癌、腎癌、卵巢癌和乳癌，以及多發性骨髓瘤（見圖 7）。2 型糖尿病也會增加某些癌症的風險，在某些情況下會增加兩倍（例如胰臟癌和子宮內膜癌）。極度肥胖（ $\text{BMI} \geq 40$ ）與男性死於所有癌症的風險增加 52% 相關，而女性則增加 62%。

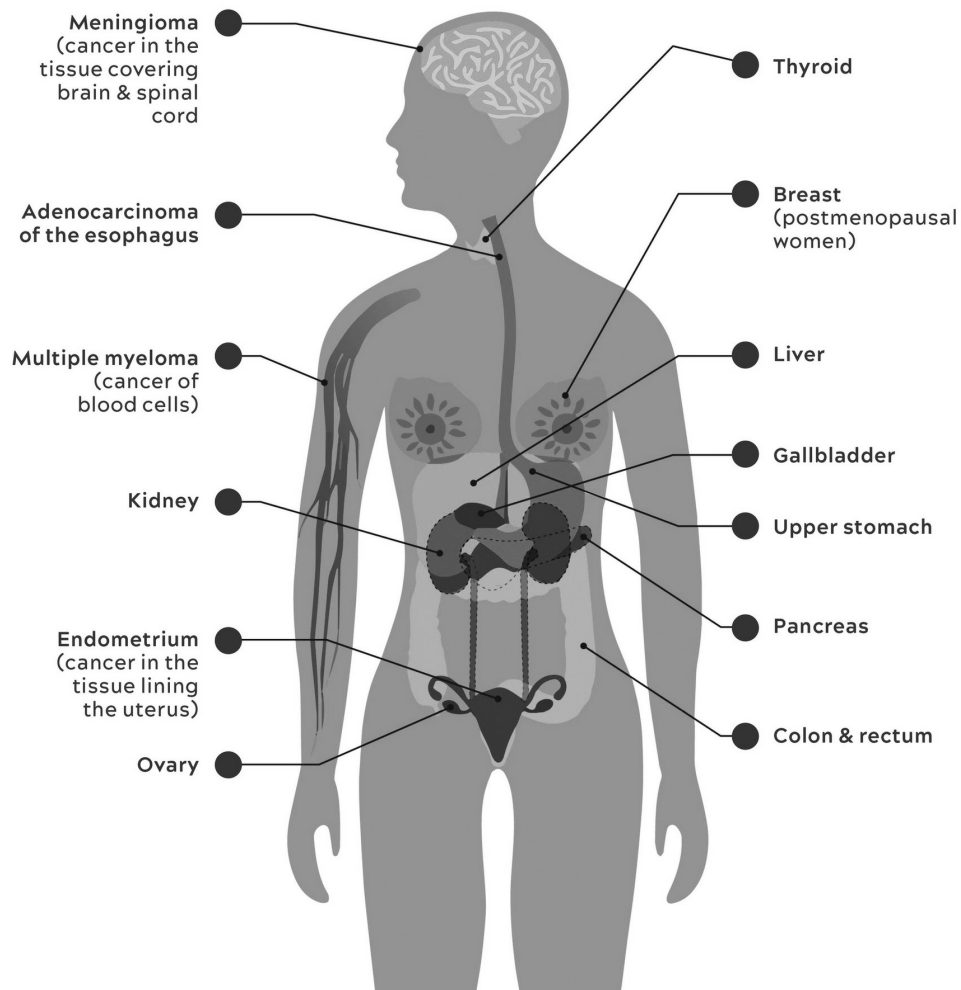
I suspect that the association between obesity, diabetes, and cancer is primarily driven by inflammation and growth factors such as insulin. Obesity, especially when accompanied by accumulation of visceral fat (and other fat outside of subcutaneous storage depots), helps promote inflammation, as dying fat cells secrete an array of inflammatory cytokines into the circulation (see [figure 4](#) in chapter 6). This chronic inflammation helps create an environment that could induce cells to become cancerous. It also contributes to the development of insulin resistance, causing insulin levels to creep upwards—and, as we'll see shortly, insulin itself is a bad actor in cancer metabolism.

我懷疑肥胖、糖尿病和癌症之間的關聯主要是由發炎和胰島素等生長因子所驅動的。肥胖，特別是當伴隨著內臟脂肪（以及皮下儲存庫之外的其他脂肪）積累時，有助於促進炎症，因為垂死的脂肪細胞會向循環中分泌一系列炎症細胞因子（參見第6章中的圖4）。這種慢性發炎有助於創造一個可能誘導細胞癌變的環境。它還會導致胰島素抵抗的發展，導致胰島素水平上升——而且，正如我們很快就會看到的，胰島素本身在癌症代謝中是一個壞因素。

This insight comes courtesy of further work by Lew Cantley. He and his colleagues discovered a family of enzymes called PI3-kinases, or PI3K, that play a major role in fueling the Warburg effect by speeding up glucose uptake into the cell. In effect, PI3K helps to open a gate in the cell wall, allowing

glucose to flood in to fuel its growth. Cancer cells possess specific mutations that turn up PI3K activity while shutting down the tumor-suppressing protein PTEN, which we talked about earlier in this chapter. When PI3K is activated by insulin and IGF-1, the insulin-like growth factor, the cell is able to devour glucose at a great rate to fuel its growth. Thus, insulin acts as a kind of cancer enabler, accelerating its growth.

這項見解得益於盧·坎特利 (Lew Cantley) 的進一步工作。他和他的同事發現了一個稱為 PI3 激酶 (PI3K) 的酶家族，它們透過加速細胞對葡萄糖的攝取，在推動瓦伯格效應方面發揮重要作用。實際上，PI3K 有助於打開細胞壁的大門，讓葡萄糖大量湧入，促進其生長。癌細胞具有特定的突變，可以提高 PI3K 活性，同時關閉腫瘤抑制蛋白 PTEN，我們在本章前面討論過。當 PI3K 被胰島素和 IGF-1（胰島素樣生長因子）活化時，細胞能夠以極快的速度吞噬葡萄糖以促進其生長。因此，胰島素充當一種癌症促進劑，加速其生長。

Figure 7. Cancers Associated with Excess Weight and Obesity

Source: NCI (2022a).

資料來源：NCI (2022a)。

This in turn suggests that metabolic therapies, including dietary manipulations that lower insulin levels, could potentially help slow the growth of some cancers and reduce cancer risk. There is already some evidence that tinkering with metabolism can affect cancer rates. As we have seen, laboratory animals on calorically restricted (CR) diets tend to die from cancer at far lower rates than control animals on an *ad libitum* (all-they-can-eat) diet. Eating less appears to give them some degree of protection. The same may hold true in people: one study of caloric restriction in humans found that limiting caloric intake directly turns down the PI3K-associated pathway, albeit

in muscle (which is not susceptible to cancer). This may be a function of lowered insulin rather than lower glucose levels.

這反過來表明代謝療法，包括降低胰島素水平的飲食控制，可能有助於減緩某些癌症的生長並降低癌症風險。已經有一些證據表明，調整新陳代謝會影響癌症發生率。正如我們所看到的，採用熱量限制（CR）飲食的實驗動物死於癌症的比率往往遠低於採用隨意飲食（所有食物都可以吃）的對照動物。少吃似乎可以為他們帶來一定程度的保護。同樣的情況也適用於人類：一項針對人類熱量限制的研究發現，限制熱量攝取會直接降低 PI3K 相關通路，儘管是在肌肉中（不易患癌症）。這可能是胰島素水平降低而不是血糖水平降低的結果。

While it's tricky to impossible to avoid or prevent the genetic mutations that help give rise to cancer, it is relatively easy to address the metabolic factors that feed it. I'm not suggesting that it's possible to "starve" cancer or that any particular diet will magically make cancer go away; cancer cells always seem to be able to obtain the energy supply they need. What I am saying is that we don't want to be anywhere on that spectrum of insulin resistance to type 2 diabetes, where our cancer risk is clearly elevated. To me, this is the low-hanging fruit of cancer prevention, right up there with quitting smoking. Getting our metabolic health in order is essential to our anticancer strategy. In the next section, we'll look at how metabolic interventions have also been used to potentiate other kinds of cancer therapy.

雖然避免或預防導致癌症的基因突變很棘手甚至不可能，但解決導致癌症的代謝因素卻相對容易。我並不是說可以「餓死」癌症，也不是說任何特定的飲食都能神奇地讓癌症消失。癌細胞似乎總是能夠獲得它們所需的能量供應。我想說的是，我們不想陷入胰島素抗性到第 2 型糖尿病的任何階段，因為我們的癌症風險明顯升高。對我來說，這是預防癌症的唾手可得的成果，與戒菸一樣。保持代謝健康有序對於我們的抗癌策略至關重要。在下一節中，我們將了解代謝幹預措施如何用於加強其他類型的癌症治療。

New Treatments

新療法

Lew Cantley's discovery of the PI3K pathway led to the development of a whole class of drugs that target cancer metabolism. Three of these drugs, known as PI3K inhibitors, have been FDA approved for certain relapsed leukemias and lymphomas, and a fourth was approved in late 2019 for breast cancer. But they haven't seemed to work as well as predicted, based on PI3K's prominent role in the growth pathways of cancer cells. Also, they had the annoying side effect of raising blood glucose, which in turn provoked a jump in insulin levels and IGF-1 as the cell tried to work around PI3K inhibition—the very thing we would want to avoid, under this theory.

Lew Cantley 對 PI3K 路徑的發現導致了一整類針對癌症代謝的藥物的開發。其中三種藥物稱為 PI3K 抑制劑，已獲得 FDA 批准用於治療某些復發性白血病和淋巴瘤，第四種藥物於 2019 年底被批准用於治療乳癌。但由於 PI3K 在癌細胞生長途徑中的突出作用，它們的作用似乎沒有預期的那麼好。此外，它們還有令人討厭的副作用，即升高血糖，當細胞試圖繞過 PI3K 抑制時，這反過來會引起胰島素水平和 IGF-1 的跳躍——根據這個理論，這正是我們想要避免的事。

This situation came up at a dinner in 2014, when I joined Cantley, who was then director of the Meyer Cancer Center at Weill Cornell Medical College in Manhattan, and Siddhartha Mukherjee, who is a practicing oncologist, research scientist, and Pulitzer Prize-winning author of *The Emperor of All Maladies*, a “biography” of cancer. I was a huge fan of Sid's work, so I was excited to sit down with these two giants in oncology.

這種情況是在 2014 年的一次晚宴上出現的，當時我加入了 Cantley（當時擔任曼哈頓威爾康奈爾醫學院邁耶癌症中心主任）和 Siddhartha Mukherjee（一位執業腫瘤學家、研究科學家、普立茲獎得主）。《萬病之王》的作者，一本癌症「傳記」。我是 Sid 工作的超級粉絲，所以我很高興能與腫瘤學領域的兩位巨頭坐在一起。

Over dinner, I shared a story about a case where a PI3K-inhibiting drug treatment had been enhanced by a kind of metabolic therapy. I couldn't stop

thinking about it, because the patient was the wife of a very close friend of mine. Sandra (not her real name) had been diagnosed with breast cancer six years earlier. It had already spread to her lymph nodes and her bones. Because of her poor prognosis, she qualified for a clinical trial of an experimental PI3K-inhibitor drug, in combination with standard therapies.

晚餐時，我分享了一個關於 PI3K 抑制藥物治療透過某種代謝療法增強的案例的故事。我無法停止思考這個問題，因為病人是我一個非常親密的朋友的妻子。桑德拉（化名）六年前被診斷出罹患乳癌。它已經擴散到她的淋巴結和骨骼。由於預後不良，她有資格參加實驗性 PI3K 抑制劑藥物與標準療法相結合的臨床試驗。

Sandra was a very motivated patient. From the day of her diagnosis, she had become obsessed with doing anything possible to stack the odds in her favor. She devoured everything she could read on the impact of nutrition on cancer, and she had concluded that a diet that reduced insulin and IGF-1 would aid in her treatment. So she worked out a regimen that consisted primarily of leafy vegetables, olive oil, avocados, nuts, and modest amounts of protein, mostly from fish, eggs, and poultry. The diet was just as notable for what it did not contain: added sugar and refined carbohydrates. All along, she underwent frequent blood tests to make sure her insulin and IGF-1 levels stayed low, which they did.

桑德拉是一位非常積極主動的患者。從確診那天起，她就沉迷於盡一切可能增加對自己有利的機會。她閱讀了所有有關營養對癌症影響的書籍，並得出結論：減少胰島素和 IGF-1 的飲食將有助於她的治療。因此，她制定了一種主要由葉菜類、橄欖油、酪梨、堅果和適量蛋白質（主要來自魚、雞蛋和家禽）組成的飲食方案。這種飲食同樣因其不含添加糖和精緻碳水化合物而引人注目。一直以來，她都經常接受血液檢查，以確保她的胰島素和 IGF-1 水平保持在較低水平，而他們也做到了。

Over the next few years, every other woman who was enrolled at her trial site had died. Every single one. The patients had been on state-of-the-art chemotherapy plus the PI3K inhibitor, yet their metastatic breast cancer had still overtaken them. The trial had to be stopped because it was clear that the

drugs were not working. Except for Sandra. Why was she still alive, while hundreds of other women with the same disease, at the same stage, were not? Was she merely lucky? Or could her very strict diet, which likely inhibited her insulin and IGF-1, have played a role in her fate?

在接下來的幾年裡，在她的試驗地點登記的所有其他女性都死亡了。每一個。這些患者接受了最先進的化療加上 PI3K 抑制劑，但轉移性乳癌仍然困擾著他們。試驗必須停止，因為很明顯這些藥物不起作用。除了桑德拉。為什麼她還活著，而其他數百名患有同樣疾病、處於同一階段的女性卻死了？她只是幸運嗎？或者說，她非常嚴格的飲食可能會抑制她的胰島素和 IGF-1，從而影響了她的命運？

I had a hunch that it may have. I believe that we have to pay attention to these outliers, these “miraculous” survivors. Even if they are only anecdotal, their stories may contain some useful insight into this lethal, mysterious disease. As Steve Rosenberg used to say, “These patients help us ask the right questions.”

我有預感，可能有。我相信我們必須關注這些異常值，這些「奇蹟」的倖存者。即使它們只是軼事，他們的故事也可能包含對這種致命的神秘疾病的一些有用的見解。正如史蒂夫·羅森伯格曾經說過的那樣：“這些患者幫助我們提出正確的問題。”

Yet in his 592-page magnum opus on cancer, published in 2010, Mukherjee had barely written a word about metabolism and metabolic therapies. It seemed premature to write about it, he later told me. Now, as I told this story over dinner, he seemed interested but skeptical. Cantley grabbed a napkin and started scribbling a graphic: the problem with PI3K inhibitors, he explained, is that by turning down the insulin-related PI3K pathway, they actually end up *raising* insulin and glucose levels. Because glucose is blocked from entering the cell, more of it stays in the bloodstream. The body then thinks it needs to produce more insulin to get rid of all that glucose, possibly negating some of the effects of the drug by activating PI3K. So what if we combined PI3K inhibitors with an insulin-minimizing or ketogenic diet?

然而，在 2010 年出版的長達 592 頁的癌症鉅作中，慕克吉幾乎隻字未提新陳代謝和代謝療法。他後來告訴我，現在寫這件事似乎還太早。現在，當我在晚餐時講述這個故事時，他似乎很感興趣，但又持懷疑態度。Cantley 抓起一張餐巾紙，開始畫圖：他解釋說，PI3K 抑制劑的問題在於，透過關閉胰島素相關的 PI3K 通路，它們實際上最終會升高胰島素和血糖水平。由於葡萄糖無法進入細胞，因此更多的葡萄糖會留在血液中。然後，身體認為需要產生更多的胰島素來消除所有葡萄糖，可能會透過活化 PI3K 來抵消藥物的一些作用。那麼，如果我們將 PI3K 抑制劑與胰島素最小化或生酮飲食結合會怎麼樣？

From that crude drawing on a napkin, a study was born. Published in *Nature* in 2018, with Mukherjee and Cantley as senior authors, the study found that a combination of a ketogenic diet *and* PI3K inhibitors improved the responses to treatment of mice that had been implanted with human cancer tumors. The results are important because they show not only that a cancer cell's metabolism is a valid target for therapy but that a patient's metabolic state can affect the efficacy of a drug. In this case, the animals' ketogenic diet seemed to synergize with what was otherwise a somewhat disappointing treatment, and together they proved to be far more powerful than either one alone. It's like in boxing, where a combination often proves to be much more effective than any single punch. If your first punch misses, the second is already in motion, aimed directly at the spot where you anticipate your opponent will move. (Mukherjee and Cantley have since partnered on a start-up company to further explore this idea of combining drug treatment with nutritional interventions.)

從餐巾紙上的粗略繪圖中，一項研究誕生了。該研究於 2018 年發表在《自然》雜誌上，由 Mukherjee 和 Cantley 擔任高級作者，研究發現生酮飲食和 PI3K 抑制劑的組合可以改善植入人類癌症腫瘤的小鼠對治療的反應。這些結果很重要，因為它們不僅表明癌細胞的代謝是治療的有效目標，而且患者的代謝狀態也會影響藥物的療效。在這種情況下，動物的生酮飲食似乎與原本有些令人失望的治療方法產生了協同作用，事實證明，它們組合起來比單獨使用任何一種方法都更有效。就像在拳擊中一樣，組合拳通常比任何單拳更有效。如果你的第一拳

沒有打中，第二拳就已經開始了，直接瞄準你預期對手會移動的地方。（慕克吉和坎特利此後合作成立了一家新創公司，以進一步探索將藥物治療與營養幹預相結合的想法。）

Other types of dietary interventions have been found to help improve the effectiveness of chemotherapy, while limiting its collateral damage to healthy tissues. Work by Valter Longo of the University of Southern California and others has found that fasting, or a fasting-like diet, increases the ability of normal cells to resist chemotherapy, while rendering cancer cells more vulnerable to the treatment. It may seem counterintuitive to recommend fasting to cancer patients, but researchers have found that it caused no major adverse events in chemotherapy patients, and in some cases it may have improved the patients' quality of life. A randomized trial in 131 cancer patients undergoing chemotherapy found that those who were placed on a "fasting-mimicking diet" (basically, a very low-calorie diet designed to provide essential nutrients while reducing feelings of hunger) were more likely to respond to chemotherapy and to feel better physically and emotionally.

人們發現其他類型的飲食幹預有助於提高化療的有效性，同時限制其對健康組織的附帶損害。南加州大學的 Valter Longo 等人的研究發現，禁食或類似禁食的飲食可以提高正常細胞抵抗化療的能力，同時使癌細胞更容易受到治療的影響。建議癌症患者禁食似乎有違常理，但研究人員發現，它不會對化療患者造成重大不良事件，而且在某些情況下可能改善了患者的生活品質。一項針對131 名接受化療的癌症患者進行的隨機試驗發現，那些採用「模擬禁食飲食」（基本上是一種低熱量飲食，旨在提供必需營養同時減少飢餓感）的患者更有可能對化療產生反應並在身體和情感上感覺更好。

This flies in the face of traditional practice, which is to try to get patients on chemotherapy to eat as much as they can tolerate, typically in the form of high-calorie and even high-sugar diets. The American Cancer Society suggests using ice cream "as a topping on cake." But the results of these studies suggest that maybe it's not such a good idea to increase the level of insulin in someone who has cancer. More studies need to be done, but the working hypothesis is that because cancer cells are so metabolically greedy, they are therefore more

vulnerable than normal cells to a reduction in nutrients—or more likely, a reduction in insulin, which activates the PI3K pathway essential to the Warburg effect.

這與傳統做法背道而馳，傳統做法是嘗試讓化療患者吃盡可能多的食物，通常是高熱量甚至高糖飲食。美國癌症協會建議使用冰淇淋「作為蛋糕的配料」。但這些研究的結果表明，提高癌症患者的胰島素水平也許不是一個好主意。還需要進行更多的研究，但有效的假設是，由於癌細胞的代謝非常貪婪，因此它們比正常細胞更容易受到營養物質減少的影響，或者更可能是胰島素減少，而胰島素會激活PI3K 通路必需的物質瓦爾堡效應。

This study and the Mukherjee-Cantley study we discussed earlier also point toward another important takeaway from this chapter, which is that there is rarely only *one* way to treat a cancer successfully. As Keith Flaherty, a medical oncologist and the director of developmental therapeutics at Massachusetts General Hospital, explained to me, the best strategy to target cancer is likely by targeting multiple vulnerabilities of the disease at one time, or in sequence. By stacking different therapies, such as combining a PI3K inhibitor with a ketogenic diet, we can attack cancer on multiple fronts, while also minimizing the likelihood of the cancer developing resistance (via mutations) to any single treatment. This is becoming a more common practice in conventional chemotherapy—but for it to be truly effective, we need more efficacious treatments to work with in the first place, ones that do a better job of singling out cancer cells for destruction while leaving healthy cells, and the patient, unharmed.

這項研究和我們之前討論的 Mukherjee-Cantley 研究也指出了本章的另一個重要結論，即成功治療癌症的方法很少只有一種。正如馬薩諸塞州總醫院的腫瘤內科醫生兼發育治療主任 Keith Flaherty 向我解釋的那樣，針對癌症的最佳策略可能是一次性或依次針對該疾病的多個脆弱性。透過疊加不同的療法，例如將 PI3K 抑制劑與生酮飲食相結合，我們可以從多個方面攻擊癌症，同時也最大限度地減少癌症對任何單一療法產生抗藥性（透過突變）的可能性。這在傳統化療中已成為一種更常見的做法，但為了使其真正有效，我們首先需要更有效的治療

方法，能夠更好地挑選出癌細胞並進行破壞，同時保留健康細胞，和病人，安然無恙。

In the next section, we'll look at how the once-outlandish notion of immunotherapy has yielded multiple potentially game-changing cancer therapies that could fit this bill.

在下一節中，我們將了解曾經古怪的免疫療法概念如何產生多種可能改變遊戲規則的癌症療法，這些療法可以滿足這項要求。

The Promise of Immunotherapy

免疫療法的前景

Like metabolism, immunotherapy did not figure in *The Emperor of All Maladies*. It was barely on the radar when the book was published in 2010. But when Ken Burns made his documentary based on the book just five years later, both immunotherapy and Steve Rosenberg were featured very prominently, which speaks to the degree to which our thinking about cancer and especially immunotherapy has begun to change, just in the last decade.

與新陳代謝一樣，免疫療法在《萬病之王》中也沒有出現。當這本書2010年出版時，它幾乎沒有引起人們的注意。但僅僅五年後，當肯·伯恩斯(Ken Burns)根據這本書製作他的紀錄片時，免疫療法和史蒂夫·羅森伯格(Steve Rosenberg)都得到了非常突出的關注，這說明了我們對癌症，尤其是免疫療法，僅在過去十年就開始發生變化。

The immune system is programmed to distinguish “nonself” from “self”—that is, to recognize invading pathogens and foreign bodies among our own healthy native cells, and then to kill or neutralize the harmful agents. An immunotherapy is any therapy that tries to boost or harness the patient's immune system to fight an infection or other condition (example: vaccines). The problem with trying to treat cancer this way is that while cancer cells are abnormal and dangerous, they are technically still our cells (“self”). They have cleverly evolved to hide from the immune system and specifically our T cells,

the immune system's assassins that would ordinarily kill foreign cells. So for a cancer immunotherapy to succeed, we essentially need to teach the immune system to recognize and kill our own cells that have turned cancerous. It needs to be able to distinguish "bad self" (cancer) from "good self" (everything else).

免疫系統被編程為區分「非己」和「自我」——也就是說，識別我們自己健康的原生細胞中入侵的病原體和外來物，然後殺死或中和有害物質。免疫療法是什麼試圖增強或利用患者免疫系統來對抗感染或其他疾病的療法（例如：疫苗）。嘗試以這種方式治療癌症的問題在於，雖然癌細胞是異常且危險的，但從技術上講它們仍然是我們的細胞（「自身」）。它們巧妙地進化來躲避免疫系統，特別是我們的 T 細胞，而 T 細胞是免疫系統的殺手，通常會殺死外來細胞。因此，為了使癌症免疫療法成功，我們本質上需要教導免疫系統識別並殺死我們自己已經癌變的細胞。它需要能夠區分「壞自我」（癌症）和「好自我」（其他一切）。

Rosenberg wasn't the first person to try to harness the immune system against cancer. Back in the late nineteenth century, a Harvard-trained surgeon named William Coley had noticed that a patient with a serious tumor had been miraculously cured, apparently as a result of a major postsurgical infection. Coley began experimenting with bacterial inoculations that he hoped would trigger a similar immune response in other patients. But his medical colleagues were appalled by the notion of injecting patients with germs, and when others failed to reproduce Coley's results, his ideas were sidelined and condemned as quackery. Yet cases of spontaneous cancer remission—like the one Rosenberg had observed as a young resident—kept occurring, and nobody could really explain them. They offered a tantalizing glimpse of the healing power of the human body.

羅森伯格並不是第一個嘗試利用免疫系統對抗癌症的人。早在十九世紀末，一位名叫威廉·科利（William Coley）的哈佛培訓外科醫生注意到，一名患有嚴重腫瘤的患者奇蹟般地痊癒了，這顯然是由於嚴重的術後感染所致。科利開始試驗細菌接種，他希望這能在其他患者身上引發類似的免疫反應。但他的醫學同事對病人注射細菌的想法感到震驚，當其他人未能重現科利的結果時，他的想法被邊緣化並被譴責為

庸醫。然而，癌症自發性緩解的病例——就像羅森伯格年輕時觀察到的那樣——不斷發生，但沒有人能真正解釋它們。它們讓我們對人體的治癒能力有了誘人的了解。

It wasn't an easy problem to solve. Rosenberg tried one approach after another, without success. A cancer "vaccine" went nowhere. He spent many years experimenting with interleukin-2 (IL-2), a cytokine that plays a major role in the immune response (it basically amplifies the activity of lymphocytes, white blood cells that fight infection). It had worked in animal models of metastatic cancer, but results in human subjects were more mixed: patients had to spend days, if not weeks, in the ICU, and they could very easily die from its massive side effects. Finally, in 1984, a late-stage melanoma patient named Linda Taylor was put into remission by high-dose IL-2 alone.

這不是一個容易解決的問題。羅森伯格嘗試了一種又一種方法，但沒有成功。癌症「疫苗」毫無進展。他花了很多年時間對白血球介素 2 (IL-2) 進行實驗，這是一種在免疫反應中發揮重要作用的細胞激素（它基本上增強了淋巴細胞、白血球對抗感染的活性）。它在轉移性癌症的動物模型中發揮了作用，但在人類受試者中的結果則更加複雜：患者必須在ICU 中度過數天甚至數週的時間，而且他們很容易因其巨大的副作用而死亡。最終，1984 年，一位名叫琳達·泰勒 (Linda Taylor) 的晚期黑色素瘤患者僅透過高劑量 IL-2 病情緩解。

This was a huge turning point, because it showed that the immune system *could* fight off cancer. But the failures still outnumbered the successes, as high-dose IL-2 seemed to be effective only against melanoma and renal cell cancers, and only in 10 to 20 percent of patients with these two cancers.^[*2] It was a shotgun approach to a problem that required more precision. So Rosenberg turned his attention to the T cells directly. How could they be trained to spot and attack cancer cells?

這是一個巨大的轉折點，因為它表明免疫系統可以抵抗癌症。但失敗的次數仍然多於成功的次數，因為高劑量 IL-2 似乎只對黑色素瘤和腎細胞癌有效，而且僅對 10% 至 20% 的這兩種癌症患者有效。[*2] 這是解決需要更高精準度問題的霰彈槍方法。於是羅森伯格將注意力直接轉向了T細胞。如何訓練它們發現和攻擊癌細胞？

It took many more years and several iterations, but Rosenberg and his team adapted a technique that had been developed in Israel that involved taking T cells from a patient's blood, then using genetic engineering to add antigen receptors that were specifically targeted to the patient's tumors. Now the T cells were programmed to attack the patient's cancer. Known as chimeric antigen receptor T cells (or CAR-T), these modified T cells could be multiplied in the lab and then infused back into the patient.

又花了很多年的時間和幾次迭代，但羅森伯格和他的團隊採用了以色列開發的一項技術，從患者的血液中提取T 細胞，然後使用基因工程添加專門針對患者腫瘤的抗原受體。現在，T 細胞被編程為攻擊患者的癌症。這些經過修飾的 T 細胞稱為嵌合抗原受體 T 細胞（或 CAR-T），可以在實驗室中進行增殖，然後回輸到患者體內。

In 2010, Rosenberg and his team reported their first success with a CAR-T treatment, in a patient with advanced follicular lymphoma who had undergone multiple rounds of conventional treatments, including chemotherapy, as well as a different kind of immunotherapy, all without success. Other groups pursued the technique as well, and finally, in 2017, the first two CAR-T-based treatments were approved by the FDA (making them the first cell and gene therapies ever approved by the FDA), one for adult lymphoma and another for acute lymphoblastic leukemia, the most common cancer in children. It had taken nearly fifty years, but Steve Rosenberg's once-outlandish theory had finally yielded a breakthrough.

2010 年，Rosenberg 和他的團隊報告了他們首次成功使用CAR-T 療法治療一名晚期濾泡性淋巴瘤患者，該患者接受了多輪常規治療，包括化療以及不同類型的免疫療法，但均未成功。其他團體也在追求這項技術，最終，在2017 年，前兩種基於CAR-T 的治療方法獲得了FDA 批准（使它們成為FDA 批准的第一種細胞和基因療法），一種用於成人淋巴瘤，另一種用於治療成人淋巴瘤。用於急性淋巴細胞白血病，這是兒童最常見的癌症。花了近五十年的時間，史蒂夫羅森伯格曾經荒誕的理論終於取得了突破。

As elegant as they are, however, CAR-T treatments have proven successful only against one specific type of cancer called B-cell lymphoma. All B-cells, normal and cancerous alike, express a protein called CD19, which is the target used by the CAR-T cell to zero in and kill them. Since we can live without B-cells, CAR-T works by obliterating *all* CD19-bearing cells. Unfortunately, we have not yet identified a similar marker for other cancers.

然而，儘管 CAR-T 療法很優雅，但事實證明，它只對一種稱為 B 細胞淋巴瘤的特定類型的癌症有效。所有 B 細胞，無論正常或癌變，都表達一種名為 CD19 的蛋白質，這是 CAR-T 細胞用於歸零並殺死它們的標靶。由於我們可以在沒有 B 細胞的情況下生存，因此 CAR-T 的作用是消除所有攜帶 CD19 的細胞。不幸的是，我們尚未發現其他癌症的類似標記。

If we are going to bring down overall cancer death rates, we need a more broadly successful class of treatments. Luckily, the immunotherapy approach continued to evolve. Now, a bit more than a decade later, a handful of immunotherapy-based cancer drugs have been approved. In addition to CAR-T, there is a class of drugs called “checkpoint inhibitors,” which take an opposite approach to the T cell-based therapies. Instead of activating T cells to go kill the cancer, the checkpoint inhibitors help make the cancer visible to the immune system.

如果我們要降低整體癌症死亡率，我們需要更廣泛的成功治療方法。幸運的是，免疫治療方法不斷發展。現在，十多年後，一些基於免疫療法的癌症藥物已獲得批准。除了CAR-T之外，還有一類稱為「檢查點抑制劑」的藥物，其採用與基於T細胞的療法相反的方法。檢查點抑制劑不是活化 T 細胞來殺死癌症，而是幫助免疫系統發現癌症。

To simplify a very long and fascinating story,^[*3] a researcher from Texas named James Allison, who has been working on immunotherapy for almost as long as Steve Rosenberg, figured out how cancer cells hide from the immune system by exploiting so-called checkpoints that are normally supposed to regulate our T cells and keep them from going overboard and attacking our

normal cells, which would lead to autoimmune disease. Essentially, the checkpoints ask the T cells, one last time, “Are you *sure* you want to kill this cell?”

為了簡化一個非常漫長而引人入勝的故事，[*3] 一位來自德克薩斯州的研究人員詹姆斯·艾利森（James Allison）研究免疫療法的時間幾乎與史蒂夫·羅森伯格一樣長，他弄清楚了癌細胞如何透過利用所謂的「免疫療法」來躲避免疫系統。檢查點通常負責調節我們的 T 細胞，防止它們過度攻擊我們的正常細胞，從而導致自身免疫性疾病。本質上，檢查點最後一次詢問 T 細胞：“你確定要殺死這個細胞嗎？”

Allison found that if you blocked specific checkpoints, particularly one called CTLA-4, you effectively outed or unmasked the cancer cells, and the T cells would then destroy them. He tried the technique on cancer-prone mice, and in one early experiment he arrived at his lab one morning to find that all the mice who had received checkpoint-inhibiting therapy were still alive, while the ones without it were all dead. It's nice when your results are so clear that you don't even really need statistical analysis.

艾利森發現，如果你阻斷特定的檢查點，特別是一種名為 CTLA-4 的檢查點，你就可以有效地排除或揭露癌細胞，然後 T 細胞就會消滅它們。他在易患癌症的老鼠身上嘗試了這項技術，在一項早期實驗中，一天早上他到達實驗室，發現所有接受檢查點抑制治療的老鼠都還活著，而沒有接受檢查點抑制治療的老鼠都死了。當您的結果如此清晰以至於您甚至不需要統計分析時，這真是太好了。

In 2018, Allison shared the Nobel Prize with a Japanese scientist named Tasuku Honjo, who had been working on a slightly different checkpoint called PD-1. The work of these two scientists has led to two approved checkpoint-inhibiting drugs, ipilimumab (Yervoy) and pembrolizumab (Keytruda), targeting CTLA-4 and PD-1, respectively.

2018 年，艾利森與一位名叫 Tasuku Honjo 的日本科學家分享了諾貝爾獎，他一直在研究一種略有不同的檢查點，稱為 PD-1。這兩位科學家的工作導致了兩種已獲批准的檢查點抑制藥物：ipilimumab (Yervoy) 和 pembrolizumab (Keytruda)，分別針對 CTLA-4 和 PD-1。

All Nobel Prizes are impressive, but I'm pretty biased toward this one. Checkpoint inhibitors not only saved the life of a third Nobel laureate, former US president Jimmy Carter, who was treated with Keytruda for his metastatic melanoma in 2015, but they also came to the rescue of a very good friend of mine, a former colleague whom I'll call Michael. When he was only in his early forties, Michael was diagnosed with a very large colon tumor that required immediate surgery. I still remember the cover of the magazine that I flipped through anxiously while I was sitting in the waiting room during his procedure. Michael is the kindest soul I think I've ever known, and his brilliance and wit could make the worst day seem enjoyable during the years we worked together. I could not imagine losing him.

所有諾貝爾獎都令人印象深刻，但我對這個有很大偏見。檢查點抑制劑不僅拯救了第三位諾貝爾獎得主、美國前總統吉米·卡特（Jimmy Carter）的生命，他於2015 年因轉移性黑色素瘤接受了Keytruda 治療，而且還拯救了我的一位非常好的朋友，一位前同事，我會打電話給麥可。當麥可四十歲出頭時，他被診斷出患有非常大的結腸腫瘤，需要立即進行手術。我還記得在他的手術過程中，我坐在候診室裡焦急地翻閱著那本雜誌的封面。麥可是我所認識的最善良的人，他的才華和智慧可以讓我們一起工作的這些年裡最糟糕的一天變得愉快。我無法想像失去他。

His family and friends were elated when his surgery proved successful and the pathology report found no sign of cancer in his nearby lymph nodes, despite the advanced size of the primary tumor. A few months later, our joy was turned back to despair as we learned that Michael's cancer had been the result of a genetic condition called Lynch syndrome. People with Lynch syndrome usually know they have it, because it is inherited in a dominant fashion. But Michael had been adopted, so he had no idea he was at risk. The mutations that define Lynch syndrome all but guarantee that its carriers develop early-onset colon cancer, as Michael had, but they are also at very high risk for other cancers. Sure enough, five years after he dodged that first bullet with colon cancer, Michael called to say that he now had pancreatic

adenocarcinoma. This was even more distressing, because as we both well knew, this cancer is almost uniformly fatal.

當他的手術被證明是成功的，並且病理報告在他附近的淋巴結中沒有發現癌症的跡象時，他的家人和朋友都很高興，儘管原發腫瘤已經很大了。幾個月後，當我們得知麥可的癌症是由一種稱為林奇症候群的遺傳性疾病引起時，我們的喜悅又變成了絕望。患有林奇症候群的人通常知道自己患有這種疾病，因為它是以顯性方式遺傳的。但麥可是被收養的，所以他不知道自己是有危險。定義林奇症候群的突變幾乎保證了其攜帶者會像邁克爾一樣患上早發性結腸癌，但他們患其他癌症的風險也非常高。果然，在他躲過第一顆結腸癌子彈五年後，麥可打電話說他現在患有胰腺癌。這更痛苦，因為我們都知道，這種癌症幾乎都是致命的。

Michael went to see the top pancreatic surgeon in his area, who confirmed the worst: surgery was not possible. The cancer was too advanced. Michael would have, at most, nine to twelve months to live. Making this all the more heart-wrenching was the fact that Michael and his wife had just welcomed their first children, twin girls, into the world that year. But *The New England Journal of Medicine* had recently reported that some patients with mismatch-repair deficiency (common in Lynch syndrome) had been successfully treated with Keytruda, the anti-PD-1 drug. It was a long shot, but it seemed at least plausible that Michael might benefit from this drug. Michael's doctors agreed to test him, and the tests confirmed that Michael was indeed a candidate for Keytruda. He was immediately enrolled in a clinical trial. While it is not guaranteed to work on all such patients, it worked on Michael, turning his immune system against his tumor and eventually eradicating all signs of pancreatic cancer in his body.

麥可去看了他所在地區的頂級胰臟外科醫生，他證實了最糟糕的情況：手術是不可能的。癌症已經太晚期了。麥可最多還能活九到十二個月。更令人心碎的是，麥可和他的妻子那一年剛剛迎來了他們的第一個孩子，雙胞胎女兒。但《新英格蘭醫學雜誌》最近報道稱，一些錯配修復缺陷（常見於林奇症候群）的患者已成功接受抗 PD-1 藥物 Keytruda 的治療。雖然可能性不大，但至少邁克爾可能會從這種藥物

中受益似乎是合理的。麥可的醫生同意對他進行測試，測試證實麥可確實是 Keytruda 的候選人。他立即參加了一項臨床試驗。雖然不能保證它對所有此類患者都有效，但它對邁克爾有效，使他的免疫系統對抗腫瘤，並最終消除了他體內所有胰腺癌的跡象。

So now he is cancer-free for a second time, and beyond grateful to have survived a disease that should have killed him when his twin girls were still in diapers. Now he gets to see them grow up. The price he paid is that while his immune system was attacking his cancer, it went a bit overboard and also destroyed his pancreas in the process. As a result, he now has type 1 diabetes, since he can't produce insulin anymore. He lost his pancreas, but his life was saved. Seems like a fair trade, on balance.

現在，他第二次擺脫了癌症，他非常慶幸自己能從一種本應在他的雙胞胎女兒還穿著尿布時殺死他的疾病中倖存下來。現在他可以看到他們長大了。他付出的代價是，雖然他的免疫系統正在攻擊他的癌症，但它有點太過分了，並且在此過程中破壞了他的胰腺。結果，他現在患有第 1 型糖尿病，因為他無法再產生胰島素。他失去了胰腺，但生命得到了挽救。總的來說，這似乎是公平交易。

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Michael was one of the lucky ones. As of yet, the various immunotherapy treatments that have been approved still benefit only a fairly small percentage of patients. About a third of cancers can be treated with immunotherapy, and of those patients, just one-quarter will actually benefit (i.e., survive). That means that only 8 percent of potential cancer deaths could be prevented by immunotherapy, according to an analysis by oncologists Nathan Gay and Vinay Prasad. They work when they work, but only in a small number of patients and at great cost. Nevertheless, just two decades ago—when I was feeling frustration as a cancer surgeon in training—patients like former president Carter or my friend Michael, and countless others, would have all died.

麥可是幸運者之一。到目前為止，已批准的各種免疫治療方法仍然只使一小部分患者受益。大約三分之一的癌症可以透過免疫療法治療，而在這些患者中，只有四分之一會真正受益（即存活）。根據腫瘤學家 Nathan Gay 和 Vinay Prasad 的分析，這意味著只有 8% 的潛在癌症死亡可以透過免疫療法預防。它們在發揮作用時發揮作用，但僅限於少數患者，且成本高昂。然而，就在二十年前，當我作為一名正在接受培訓的癌症外科醫生感到沮喪時，像前總統卡特或我的朋友邁克爾以及無數其他人一樣的患者都會死去。

But I (and others who know much more than I do) believe that we have had only a small taste of what can be accomplished via immunotherapy.

但我（以及其他比我了解更多的人）相信，我們對透過免疫療法可以實現的目標只了解了一小部分。

One idea that is currently being explored is the notion of combining immunotherapies with other treatments. One recent paper describes a clinical trial where a platinum-based chemotherapy was used in combination with a checkpoint inhibitor, resulting in improved overall survival in patients with lung cancer. These patients were not sensitive to the checkpoint inhibitor alone, but something about the chemo made the cancer more sensitive, or more “visible” if you will, to the immunotherapy. It’s an extension of the idea of “stacking” therapies that we mentioned earlier.

目前正在探索的一個想法是將免疫療法與其他治療方法結合。最近的一篇論文描述了一項臨床試驗，其中鉑類化療與檢查點抑制劑聯合使用，從而提高了肺癌患者的整體存活率。這些患者對檢查點抑制劑本身並不敏感，但化療中的某些因素使癌症對免疫療法更加敏感，或更「明顯」（如果你願意的話）。這是我們之前提到的「堆疊」療法理念的延伸。

To make immunotherapy more widely effective, we need to devise ways to help our immune cells detect and kill a broader array of cancers, not just a few specific types. Genetic analysis reveals that some 80 percent of epithelial cancers (that is, solid organ tumors) possess mutations that the immune system

can recognize—thus making them potentially vulnerable to immune-based treatments.

為了使免疫療法更廣泛有效，我們需要設計方法來幫助我們的免疫細胞檢測和殺死更廣泛的癌症，而不僅僅是少數特定類型。基因分析顯示，約 80% 的上皮癌（即實體器官腫瘤）具有免疫系統可以識別的突變，使它們可能容易受到基於免疫的治療的影響。

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One very promising technique is called adoptive cell therapy (or adoptive cell transfer, ACT). ACT is a class of immunotherapy whereby supplemental T cells are transferred into a patient, like adding reinforcements to an army, to bolster their ability to fight their own tumor. These T cells have been genetically programmed with antigens specifically targeted at the patient's individual tumor type. It is similar to CAR-T cell therapy, which we discussed earlier, but much broader in scope. As cancer grows, it quickly outruns the immune system's ability to detect and kill it; there simply aren't enough T cells to do the job, particularly when the cancer reaches the point of clinical detection. This is why spontaneous remission, as happened with James DeAngelo, is so rare. The idea behind ACT is basically to overwhelm the cancer with a huge number of targeted T cells, like supplementing an army with a brigade of trained assassins.

一種非常有前景的技術稱為過繼性細胞療法（或過繼性細胞轉移，ACT）。ACT 是一類免疫療法，將補充 T 細胞轉移到患者體內，就像為軍隊增援一樣，以增強他們對抗自身腫瘤的能力。這些 T 細胞經過基因編程，含有專門針對患者個別腫瘤類型的抗原。它類似於我們之前討論過的 CAR-T 細胞療法，但範圍更廣泛。隨著癌症的生長，它很快就會超越免疫系統檢測和殺死它的能力。根本沒有足夠的 T 細胞來完成這項工作，特別是當癌症達到臨床檢測階段時。這就是為什麼像詹姆斯·迪安吉洛那樣的自發性緩解如此罕見。ACT 背後的想法基本上是用大量的靶向 T 細胞來壓倒癌症，就像用一隊訓練有素的刺客來補充一支軍隊一樣。

There are two ways to do ACT. First, we can take a sample of a patient's tumor and isolate those T cells that do recognize the tumor as a threat. These are called tumor-infiltrating lymphocytes (TILs), but there may only be a few million of them, not enough to mount a complete response against the tumor. By removing the TILs from the body and multiplying them by a factor of 1,000 or so, and then reinfusing them into the patient, we can expect to see a much better response. Alternatively, T cells can be harvested from the patient's blood and genetically modified to recognize his or her specific tumor. Each of these approaches has advantages and disadvantages,^[*4] but the interesting part is that ACT effectively means designing a new, customized anticancer drug for each individual patient.

有兩種方法可以進行 ACT。首先，我們可以採集患者的腫瘤樣本，並分離那些確實將腫瘤視為威脅的 T 細胞。這些細胞被稱為腫瘤浸潤淋巴細胞（TIL），但它們的數量可能只有數百萬個，不足以對腫瘤產生完全的反應。透過從體內取出 TIL 並將其乘以 1,000 倍左右，然後將其重新注入患者體內，我們預計會看到更好的反應。或者，可以從患者的血液中收集 T 細胞，並進行基因改造以識別他或她的特定腫瘤。這些方法各有優點和缺點，[*4] 但有趣的是，ACT 實際上意味著為每位患者設計一種新的、客製化的抗癌藥物。

This is obviously a costly proposition, and a very labor-intensive process, but it has a lot of promise. The proof of principle is here, but much more work is needed, not only to improve the efficacy of this approach but also to enable us to deliver this treatment more widely and more easily. And while the cost may seem prohibitive at first, I would point out that conventional chemotherapy is also very expensive—and its remissions are almost never permanent.

這顯然是一個成本高昂的提議，也是一個非常耗費勞動力的過程，但它有很大的希望。原理證明已經完成，但還需要做更多的工作，不僅要提高這種方法的功效，還要使我們能夠更廣泛、更輕鬆地提供這種治療方法。雖然費用乍看之下似乎令人望而卻步，但我要指出的是，傳統化療也非常昂貴，而且其緩解幾乎不會是永久性的。

One striking feature of immune-based cancer treatment is that when it

works, it really works. It is not uncommon for a patient with metastatic cancer to enter remission after chemotherapy. The problem is that it virtually never lasts. The cancer almost always comes back in some form. But when patients do respond to immunotherapy, and go into complete remission, they often *stay* in remission. Between 80 and 90 percent of so-called complete responders to immunotherapy remain disease-free fifteen years out. This is extraordinary—far better than the short-term, five-year time horizon at which we typically declare victory in conventional cancer treatment. One hesitates to use the word *cured*, but in patients who do respond to immunotherapy, it's safe to assume that the cancer is pretty much gone.

基於免疫的癌症治療的一個顯著特徵是，當它有效時，它確實有效。轉移性癌症患者在化療後進入緩解期並不罕見。問題是它幾乎永遠不會持續。癌症幾乎總是會以某種形式復發。但當患者對免疫療法確實有反應並進入完全緩解狀態時，他們通常會保持緩解狀態。80% 到 90% 的所謂免疫療法完全反應者在 15 年後仍然沒有疾病。這是非同尋常的——遠遠好於我們通常宣布傳統癌症治療取得勝利的短期五年時間範圍。人們對使用「治癒」這個詞猶豫不決，但對於對免疫療法有反應的患者來說，可以安全地假設癌症基本上已經消失。

The important message here is that there is hope. For the first time in my lifetime, we are making progress in the War on Cancer, if we can even still call it that. There are now treatments that can, and do, save the lives of thousands of people who would have inevitably died just a decade ago. Twenty years ago, someone with metastatic melanoma could expect to live about six more months, on average. Now that number is twenty-four months, with about 20 percent of such patients being completely cured. This represents measurable progress—almost entirely thanks to immunotherapy. Improved early detection of cancer, which we will discuss in the final section of this chapter, will likely make our immunotherapy treatments still more effective.

這裡重要的訊息是，還有希望。這是我一生中第一次，我們在對抗癌症的戰爭中取得了進展，如果我們仍然可以這樣稱呼它的話。現在的治療方法可以而且確實可以挽救成千上萬在十年前不可避免地死亡的人的生命。二十年前，患有轉移性黑色素瘤的人平均可以多活六個月

左右。現在這個數字是 24 個月，其中大約 20% 的患者完全治癒。這代表著可衡量的進展——幾乎完全歸功於免疫療法。我們將在本章最後一節討論改進癌症的早期檢測，這可能會使我們的免疫療法更加有效。

Immunotherapy traveled a rocky road, and it could have been abandoned completely at many points along the way. In the end, it survived because its chimerical successes turned out to be not so chimerical, but mostly thanks to the determination and persistence of visionary scientists such as James Allison, Tasuku Honjo, Steve Rosenberg, and others, who kept going even when their work seemed pointless and possibly crazy.

免疫療法的道路崎嶇不平，一路上許多地方都可能被完全放棄。最終，它得以倖存，因為它的幻想成功並不那麼幻想，而主要歸功於詹姆斯·艾利森、本廬佑、史蒂夫·羅森伯格等有遠見的科學家的決心和堅持，他們即使在工作完成後仍堅持不懈。看起來毫無意義，而且可能很瘋狂。

Early Detection

早期發現

The final and perhaps most important tool in our anticancer arsenal is early, aggressive screening. This remains a controversial topic, but the evidence is overwhelming that catching cancer early is almost always net beneficial.

我們的抗癌武器庫中最後的、也許是最重要的工具是早期、積極的篩檢。這仍然是一個有爭議的話題，但大量證據表明，及早發現癌症幾乎總是有益的。

Unfortunately, the same problem that I encountered in residency applies today: too many cancers are detected too late, after they've grown and spread via metastasis. Very few treatments work against these advanced cancers; in most cases, outside of the few cancers that respond to immunotherapies, the best we can hope for is to delay death slightly. The ten-year survival rate for

patients with metastatic cancer is virtually the same now as it was fifty years ago: zero. We need to do more than hope for novel therapies.

不幸的是，我在住院醫師實習中遇到的同樣的問題今天也適用：太多的癌症在生長和通過轉移擴散後被發現得太晚了。很少有治療方法可以對抗這些晚期癌症。在大多數情況下，除了少數對免疫療法有反應的癌症之外，我們所能期望的最佳結果就是稍微延遲死亡。轉移性癌症患者的十年存活率現在與五十年前幾乎相同：零。我們需要做的不僅僅是希望新的療法。

When cancers are detected early, in stage I, survival rates skyrocket. This is partly because of simple math: these earlier-stage cancers comprise fewer total cancerous cells, with fewer mutations, and thus are more vulnerable to treatment with the drugs that we do have, including some immunotherapies. I would go so far as to argue that early detection is our *best* hope for radically reducing cancer mortality.

當癌症在第一階段早期被發現時，存活率會飆升。這部分是因為簡單的數學計算：這些早期癌症包含的癌細胞總數較少，突變也較少，因此更容易接受我們所用藥物的治療有，包括一些免疫療法。我甚至認為早期檢測是我們從根本上降低癌症死亡率的最佳希望。

This claim makes intuitive sense, but it is supported by even a cursory look at data comparing success rates at treating specific cancers in the metastatic versus adjuvant (i.e., postsurgical) setting. Let's look at colon cancer first. A patient with metastatic colon cancer, which means the cancer has spread past their colon and adjacent lymph nodes to another part of the body, such as the liver, will typically be treated with a combination of three drugs known as the FOLFOX regimen. This treatment yields a median survival time of about 31.5 months,^[*5] meaning about half of patients live longer than this, and half do not. Regardless, virtually none of these patients will be alive in ten years. If a patient undergoes successful surgery for stage III colon cancer, which means all the cancer was removed and there was no visible spread to distant organs, then the follow-up care is treatment with the exact same FOLFOX treatment regimen. But in this scenario, fully 78.5 percent of these patients will survive for another *six* years—more than twice as long as median survival for the

metastatic patients—and 67 percent of them will still be alive ten years after surgery. That’s an impressive difference.

這種說法具有直觀意義，但即使是粗略地查看比較轉移性與輔助（即術後）環境中治療特定癌症的成功率的數據也可以支持這一說法。我們先來看看結腸癌。患有轉移性結腸癌的患者（這意味著癌症已透過結腸和鄰近淋巴結擴散到身體的其他部位，例如肝臟）通常會接受三種藥物的組合治療，稱為 FOLFOX 方案。這種治療的中位存活時間約為 31.5 個月，[*5] 意味著大約一半患者的壽命比此長，另一半則不然。無論如何，十年後這些患者中幾乎沒有一個能活著。如果患者成功接受了 III 期結腸癌手術，這意味著所有癌症都被切除，並且沒有明顯的遠端器官擴散，那麼後續護理就是採用完全相同的 FOLFOX 治療方案進行治療。但在這種情況下，78.5% 的患者將再存活六年，是轉移性患者中位數存活期的兩倍多，其中 67% 的患者在手術後十年仍能存活。這是一個令人印象深刻的差異。

So what explains it? The difference has to do with the overall burden of cancer cells in each patient. In advanced, metastatic cancer there are tens if not hundreds of billions of cancer cells in need of treatment. In less advanced cancers, while there are undoubtedly still millions, if not billions, of cancer cells that have escaped the surgeon’s scalpel, the far lower population means they will also have fewer mutations and thus less resistance to the treatment.

那麼如何解釋呢？這種差異與每個患者體內癌細胞的整體負擔有關。在晚期轉移性癌症中，有數百億甚至數千億的癌細胞需要治療。在不太晚期的癌症中，儘管毫無疑問仍然有數百萬甚至數十億的癌細胞逃脫了外科醫生的手術刀，但數量少得多意味著它們的突變也更少，因此對治療的抵抗力也更小。

It’s a similar story for patients with breast cancer. Patients with HER2-positive metastatic breast cancer[*6] can expect a median survival time of just under five years, with standard treatment consisting of three chemotherapy drugs. But if our patient has a smaller (< 3 cm), localized, HER2+ tumor that is removed surgically, plus adjuvant treatment with just two of these chemo drugs, she will have a 93 percent chance of living for at least another seven years without disease. The lower a patient’s overall tumor burden, the more

effective our drugs tend to be—and the greater the patient's odds of survival. Again, just as with immunotherapy treatment, it's a numbers game: the fewer cancerous cells we have, the greater our likelihood of success.

對於乳癌患者來說，情況也類似。HER2 陽性轉移性乳癌 [*6] 患者的中位存活時間預計略低於五年，標準治療包括三種化療藥物。但是，如果我們的患者有一個較小（< 3 公分）的局部HER2+ 腫瘤，透過手術切除，再加上僅使用其中兩種化療藥物的輔助治療，她將有93% 的機會至少再存活7 年而不患病。患者的整體腫瘤負荷越低，我們的藥物就越有效，患者的生存幾率就越大。再次強調，就像免疫療法一樣，這是一場數字遊戲：癌細胞越少，成功的可能性就越大。

The problem is that we're still not very good at detecting cancer in these early stages—yet. Out of dozens of different types of cancers, we have agreed-upon, reliable screening methods for only *five*: lung (for smokers), breast, prostate, colorectal, and cervical. Even so, mainstream guidelines have been waving people away from some types of early screening, such as mammography in women and blood testing for PSA, prostate-specific antigen, in men. In part this has to do with cost, and in part this has to do with the risk of false positives that may lead to unnecessary or even dangerous treatment (entailing further costs). Both are valid issues, but let's set aside the cost issue and focus on the false-positive problem.

問題是我們仍然不太擅長在早期階段檢測癌症。在數十種不同類型的癌症中，我們僅針對五種癌症制定了商定的可靠篩檢方法：肺癌（針對吸菸者）、乳癌、攝護腺癌、大腸癌和子宮頸癌。即便如此，主流指引仍然勸阻人們放棄某些類型的早期篩檢，例如女性乳房X光檢查和男性PSA（前列腺特異性抗原）血液檢測。這部分與成本有關，部分與誤報風險有關，誤報可能導致不必要甚至危險的治療（帶來進一步的費用）。兩者都是有效的問題，但讓我們拋開成本問題，並專注於誤報問題。

Medicine 2.0 says that because there are significant false positives with certain tests, we shouldn't do these tests on most people, period. But if we put on our Medicine 3.0 glasses, we see it differently: these tests are potentially

useful, and they're just about all we have. So how can we make them more useful and accurate?

Medicine 2.0 表示，由於某些測試有明顯的誤報，因此我們不應該對大多數人進行這些測試。但如果我們戴上醫學 3.0 眼鏡，我們會看到不同的結果：這些測試可能有用，而且它們就是我們所擁有的一切。那麼我們如何才能使它們更加有用和準確呢？

With all diagnostic tests, there is a trade-off between *sensitivity*, or the ability of the test to detect an existing condition (i.e., its true positive rate, expressed as a percentage), and *specificity*, which is the ability to determine that someone does *not* have that condition (i.e., true negative rate). Together, these represent the test's overall accuracy. In addition, however, we have to consider the prevalence of the disease in our target population. How likely is it that the person we are testing actually has this condition? Mammography has a sensitivity in the mideighties and a specificity in the low nineties. But if we are examining a relatively low-risk population, perhaps 1 percent of whom actually have breast cancer, then even a test with decent sensitivity is going to generate a fairly large number of false positives. In fact, in this low-risk group, the “positive predictive value” of mammography is only about 10 percent—meaning that if you do test positive, there is only about a one-in-ten chance that you actually have breast cancer. In other populations, with greater overall prevalence (and risk), the test performs much better.

對於所有診斷測試，靈敏度或測試檢測現有病症的能力（即其真實陽性率，以百分比表示）和特異性之間存在權衡，特異性是確定某人的能力不具備該條件（即真負率）。這些共同代表了測試的整體準確性。然而，此外，我們還必須考慮該疾病在目標族群中的盛行率。我們正在測試的人實際上患有這種疾病的可能性有多大？乳房X光照相術在八十年代中期具有敏感性，在九十年代下旬具有特異性。但如果我們檢查的是相對低風險的人群，其中可能有 1% 的人實際上患有乳癌，那麼即使是靈敏度不錯的測試也會產生相當多的假陽性。事實上，在這個低風險群體中，乳房X 光檢查的「陽性預測值」僅為10%左右，這意味著如果您的檢測結果呈陽性，那麼您實際上患有乳癌的

可能性只有大約十分之一。在其他人群中，由於整體盛行率（和風險）較高，該測試的效果要好得多。

The situation with mammography illustrates why we need to be very strategic about *who* we are testing and what their risk profile might be, and to understand what our test can and can't tell us. No single diagnostic test, for anything, is 100 percent accurate. So it is foolish to rely on just one test, not only for breast cancer but in many other areas as well. We need to think in terms of stacking test modalities—incorporating ultrasound and MRI in addition to mammography, for example, when looking for breast cancer. With multiple tests, our resolution improves and fewer unnecessary procedures will be performed.

乳房X光檢查的情況說明了為什麼我們需要對我們正在測試的對象以及他們的風險狀況可能是什麼採取非常戰略性的態度，並了解我們的測試可以告訴我們什麼，不能告訴我們什麼。對於任何事情，沒有任何一項診斷測試是 100% 準確的。因此，僅依賴一項測試是愚蠢的，不僅針對乳癌，而且在許多其他領域也是如此。我們需要考慮疊加測試方式，例如在尋找乳癌時，除了乳房 X 光攝影之外，還需要結合超音波和 MRI。透過多次測試，我們的分辨率得到提高，並且將執行更少的不必要的程序。

In short, the problem is not the tests themselves but how we use them. Prostate cancer screening provides an even better example. It's no longer as simple as "Your PSA number is X or higher, and therefore we must biopsy your prostate, a painful procedure with many unpleasant possible side effects." Now we know to look at other parameters, such as PSA velocity (the speed at which PSA has been changing over time), PSA density (PSA value normalized to the volume of the prostate gland), and free PSA (comparing the amount of PSA that is bound versus unbound to carrier proteins in the blood). When those factors are taken into account, PSA becomes a much better indicator of prostate cancer risk.

簡而言之，問題不在於測試本身，而是我們如何使用它們。前列腺癌篩檢提供了一個更好的例子。它不再是「您的 PSA 值為 X 或更高，因此我們必須對您的前列腺進行活檢，這是一個痛苦的過程，可能會產

生許多令人不快的副作用」那麼簡單。現在我們知道要查看其他參數，例如 PSA 速度（PSA 隨時間變化的速度）、PSA 密度（根據前列腺體積標準化的 PSA 值）和遊離 PSA（比較 PSA 的量）與血液中的載體蛋白結合或未結合）。當考慮到這些因素時，PSA 就成為前列腺癌風險的更好指標。

Then there are other tests, such as the 4K blood test, which looks for specific proteins that might give us a better idea of how aggressive and potentially dangerous the patient's prostate cancer might be. The key question we want to answer is, Will our patient die *with* prostate cancer, as many men do, or will he die *from* it? We'd rather not disrupt his life, and potentially do him harm, in the course of finding out. Combining these blood tests I've just described with the techniques of multiparametric MRI imaging means that the likelihood of performing an unnecessary biopsy or surgery is now very low.

然後還有其他測試，例如 4K 血液測試，它尋找特定的蛋白質，這些蛋白質可能會讓我們更了解患者前列腺癌的侵襲性和潛在危險性。我們要回答的關鍵問題是，我們的病人會像許多男性一樣死於攝護腺癌，還是會死於攝護腺癌？我們不想在尋找答案的過程中擾亂他的生活，並可能對他造成傷害。將我剛剛描述的這些血液測試與多參數 MRI 成像技術相結合意味著現在進行不必要的活檢或手術的可能性非常低。

There is a similar but quieter controversy around screening for colorectal cancer (CRC), which has long been a rite of passage for those in middle age. [7] The purpose of the colonoscopy is to look not only for full-fledged tumors but also for polyps, which are growths that form in the lining of the colon. Most polyps remain small and harmless and never become cancerous, but some have the potential to become malignant and invade the wall of the colon. Not all polyps become cancer, but all colon cancers came from polyps. This is what makes a colonoscopy such a powerful tool. The endoscopist is able not only to spot potentially cancerous growths before they become dangerous but also to intervene on the spot, using instruments on the colonoscope to remove polyps for later examination. It combines screening and surgery into one procedure. It's an amazing tool.

關於大腸直腸癌（CRC）篩檢也存在類似但更安靜的爭議，長期以來，大腸癌篩檢一直是中年人的必經之路。[*7] 大腸鏡檢查的目的不僅是尋找成熟的腫瘤，還包括息肉，息肉是在結腸內壁形成的生長物。大多數息肉很小且無害，永遠不會癌變，但有些息肉有可能惡性化並侵入結腸壁。並非所有息肉都會變成癌症，但所有結腸癌都來自息肉。這就是為什麼大腸鏡檢查如此強大的工具的原因。內視鏡醫師不僅能夠在潛在的癌性生長變得危險之前發現它們，而且能夠在現場進行幹預，使用結腸鏡上的儀器去除息肉以供以後檢查。它將篩檢和手術合而為一。這是一個了不起的工具。

Traditional guidelines have recommended colorectal cancer screenings for average-risk people ages fifty to seventy-five. These preventive screenings are fully covered under the Affordable Care Act, and if no polyps are found and the patient is of average risk, the procedure needs to be repeated only every ten years, according to consensus guidelines. But there is ample evidence out there that age fifty may be too old for a first screening, even in patients with average risk factors (that is, no family history of colon cancer and no personal history of inflammatory bowel disease). About 70 percent of people who are diagnosed with CRC before the age of fifty have no family history or hereditary conditions linked to the disease. In 2020, some 3,640 Americans died from colorectal cancer before they turned fifty—and given the slow-moving nature of the disease, it's likely that many of those who died later than that already had the disease on their fiftieth birthday. This is why the American Cancer Society updated its guidelines in 2018, lowering the age to forty-five for people at average risk.

傳統指引建議對 50 至 75 歲的平均風險族群進行大腸癌篩檢。這些預防性篩檢完全涵蓋在《平價醫療法案》的範圍內，如果沒有發現息肉並且患者處於中等風險，則根據共識指南，只需每十年重複該程序。但有充足的證據表明，50 歲對於首次篩檢來說可能太高了，即使對於具有一般風險因素（即沒有結腸癌家族史和發炎性腸道疾病個人史）的患者也是如此。大約 70% 在 50 歲之前被診斷出患有 CRC 的人沒有與該疾病相關的家族史或遺傳性疾病。2020 年，約 3,640 名美國人在 50 歲之前死於結直腸癌，考慮到這種疾病傳播緩慢的性質，許多晚於

該日期死亡的人很可能在50 歲生日時就已經患有這種疾病。這就是為什麼美國癌症協會在 2018 年更新了指南，將平均風險族群的年齡降低至 45 歲。

In my practice, we go further, typically encouraging average-risk individuals to get a colonoscopy by age forty—and even sooner if anything in their history suggests they may be at higher risk. We then repeat the procedure as often as every two to three years, depending on the findings from the previous colonoscopy. If a sessile (flat) polyp is found, for example, we're inclined to do it sooner than if the endoscopist finds nothing at all. Two or three years might seem like a very short window of time to repeat such an involved procedure, but colon cancer has been documented to appear within the span of as little as six months to two years after a normal colonoscopy. Better safe than sorry.^[*8]

在我的實踐中，我們走得更遠，通常鼓勵中等風險的人在四十歲之前接受大腸鏡檢查，如果他們的病史表明他們可能面臨更高的風險，甚至更早。然後，我們每兩到三年重複一次該程序，具體取決於先前大腸鏡檢查的結果。例如，如果發現無蒂（扁平）息肉，我們傾向於比內視鏡醫生什麼也沒發現的情況更早採取行動。重複這樣一個複雜的手術似乎需要兩到三年的時間，但據記錄，結腸癌在正常結腸鏡檢查後短短六個月到兩年的時間內就會出現。安全總比後悔好。[*8]

Why do I generally recommend a colonoscopy before the guidelines do? Mostly because, of all the major cancers, colorectal cancer is one of the easiest to detect, with the greatest payoff in terms of risk reduction. It remains one of the top five deadliest cancers in the United States, behind lung (#1) and breast/prostate (#2 for women/men), and just ahead of pancreas (#4) and liver (#5) cancers. Of these five, though, CRC is the one we have the best shot at catching early. As it grows in a relatively accessible location, the colon, we can see it without any need for imaging techniques or a surgical biopsy. Because it is so easily observed, we understand its progression from normal tissue to polyp to tumor. Finding it early makes a huge difference, since we can effectively eliminate polyps or growths on the spot. If only we could do that with arterial plaques.

為什麼我通常建議在指南之前進行大腸鏡檢查？主要是因為，在所有主要癌症中，大腸癌是最容易發現的癌症之一，在降低風險方面回報最大。它仍然是美國最致命的五種癌症之一，僅次於肺癌（排名第一）和乳腺癌/前列腺癌（女性/男性排名第二），略高於胰腺癌（排名第四）和肝癌（排名第五）。不過，在這五個中，**CRC** 是我們最有可能儘早發現的一個。由於它生長在相對容易接近的位置，即結腸，我們無需任何成像技術或手術活檢就可以看到它。因為它很容易觀察，我們了解它從正常組織到息肉再到腫瘤的進展。及早發現它會產生巨大的影響，因為我們可以有效地當場消除息肉或增生。如果我們能用動脈斑塊做到這一點就好了。

My bottom line is that it is far better to screen early than risk doing it too late. Think asymmetric risk: It's possible that *not* screening early and frequently enough is the most dangerous option.^[*9]

我的底線是，儘早篩檢比冒著太晚篩檢的風險要好得多。考慮不對稱風險：不及早且頻繁地進行篩檢可能是最危險的選擇。[*9]

Other cancers that are relatively easy to spot on visual examination include skin cancer and melanomas. The pap smear for cervical cancer is another well-established, minimally invasive test that I recommend my patients do yearly. When we're talking about cancers that develop *inside* the body, in our internal organs, things get trickier. We can't see them directly, so we must rely on imaging technologies such as low-dose CT scans for lung cancer. These scans are currently recommended in smokers and former smokers, but (as always) I think they should be used more widely, because about 15 percent of lung cancers are diagnosed in people who have *never* smoked. Lung cancer is the #1 cause of cancer deaths overall, but lung cancer in never-smokers ranks seventh, all by itself.

其他透過目視檢查相對容易發現的癌症包括皮膚癌和黑色素瘤。子宮頸癌子宮頸抹片檢查是另一種成熟的微創檢查，我建議我的患者每年進行一次。當我們談論體內、內臟器官中發生的癌症時，事情變得更加棘手。我們無法直接看到它們，所以我們必須依靠影像技術，例如肺癌的低劑量CT掃描。目前建議吸菸者和前吸菸者進行這些掃描，但（一如既往）我認為它們應該更廣泛地使用，因為大約 15% 的肺癌是

在從未吸菸的人中診斷出來的。肺癌是整體癌症死亡的第一大原因，但從不吸菸者的肺癌單獨排名第七。

MRI has a distinct advantage over CT in that it does not produce any ionizing radiation but still provides good resolution. One newer technique that can enhance the ability of a screening MRI to differentiate between a cancer and noncancer is something called diffusion-weighted imaging with background subtraction, or DWI for short. The idea behind DWI is to look at water movement in and around tissue, at different points in time very close to each other (between ten and fifty microseconds, typically). If the water is held or trapped, then it could indicate the presence of a tightly packed cluster of cells, a possible tumor. So the higher the density of cells, the brighter the signal on the DWI phase of MRI, making DWI functionally a radiographic “lump detector.” Right now, DWI works best in the brain because it suffers least from movement artifacts.

MRI 與 CT 相比具有明顯的優勢，因為它不會產生任何電離輻射，但仍提供良好的解析度。一種可以增強篩檢 MRI 區分癌症和非癌症能力的新技術稱為背景扣除擴散加權成像（DWI），簡稱 DWI。DWI 背後的想法是在彼此非常接近的不同時間點（通常在十到五十微秒之間）觀察組織內部和周圍的水運動。如果水被保留或滯留，則可能表示存在緊密堆積的細胞簇，可能是腫瘤。因此，細胞密度越高，MRI 的 DWI 階段的訊號越亮，使得 DWI 在功能上成為放射線照相「腫塊偵測器」。目前，DWI 在大腦中效果最好，因為它受到運動偽影的影響最小。

I remain optimistic that this technique can be improved over time, with optimization of software and standardization of technique. Despite all this, even something as advanced as the best DWI MRI is not without problems, if used in isolation. While the sensitivity of this test is very high (meaning it's very good at finding cancer if cancer is there, hence very few false negatives), the specificity is relatively low (which means it's not as good at telling you when you don't have cancer, hence a lot of false positives). This is the inevitable trade-off, the yin and yang if you will, between sensitivity and specificity. The more you increase one, the more you decrease the other.^[*10]

我仍然樂觀地認為，隨著時間的推移，透過軟體的最佳化和技術的標準化，這項技術可以得到改進。儘管如此，即使是像最好的 DWI MRI 這樣先進的技術，如果單獨使用也並非沒有問題。雖然該測試的敏感性非常高（這意味著如果存在癌症，它非常擅長發現癌症，因此假陰性很少），但特異性相對較低（這意味著當您沒有癌症時，它不能很好地告訴您）癌症，因此有很多假陽性）。這是敏感性和特異性之間不可避免的權衡，如果你願意的話，可以說是陰陽。增加其中一項越多，減少另一項就越多。[*10]

I tell patients, if you're going to have a whole-body screening MRI, there is a good chance we'll be chasing down an insignificant thyroid (or other) nodule in exchange for getting such a good look at your other organs. As a result of this, about a quarter of my patients, understandably, elect not to undergo such screening. Which brings me to the next tool in the cancer screening tool kit, a tool that can complement the high sensitivity / low specificity problem of imaging tests.

我告訴患者，如果您要進行全身篩檢 MRI，我們很有可能會追蹤一個微不足道的甲狀腺（或其他）結節，以換取對您其他器官的良好觀察。因此，我的大約四分之一的患者選擇不接受此類篩檢，這是可以理解的。這讓我想到了癌症篩檢工具包中的下一個工具，可以補充影像測試的高靈敏度/低特異性問題。

I am cautiously optimistic about the emergence of so-called “liquid biopsies” that seek to detect the presence of cancers via a blood test.[*11] These are used in two settings: to detect recurrences of cancer in patients following treatment and to screen for cancers in otherwise healthy patients, a fast-moving and exciting field called multicancer early detection.

我對所謂的「液體活檢」的出現持謹慎樂觀的態度，這種活檢旨在透過血液檢測來檢測癌症的存在。[*11] 這些用於兩種情況：檢測治療後患者的癌症復發，以及篩檢其他健康患者的癌症，這是一個快速發展且令人興奮的領域，稱為多癌早期檢測。

Max Diehn, one of my med school classmates and now an oncology professor at Stanford, has been on the forefront of this research since 2012.

Max and his colleagues set out to ask a seemingly simple question initially. After a patient with lung cancer has had a resection of their tumor, is there any way a blood test can be used to screen the patient for signs of tumor recurrence?

馬克斯·迪恩(Max Diehn) 是我的醫學院同學，現在是史丹佛大學的腫瘤學教授，自2012 年以來一直處於這項研究的最前沿。馬克斯和他的同事最初提出了一個看似簡單的問題。肺癌患者切除腫瘤後，有什麼方法可以透過血液檢查來篩檢患者是否有腫瘤復發的跡象？

Historically, this has been done via imaging tests, such as CT scans, that enable us to “see” a tumor. Radiation exposure notwithstanding, the main issue is that these tests don’t have very high resolution. It’s very difficult for these imaging technologies to discern a cancer smaller than about one centimeter in diameter. Even if you assume that this one-centimeter nodule is the only collection of cancer cells in the patient’s body (not a great assumption; the mouse in the trap is rarely the only one in the house), you’re still talking about more than a billion cancer cells by the time you reach the threshold of traditional detection. If we could catch these recurrent cancers sooner, we might have a better shot at keeping patients in remission—for the same reasons that it’s easier to treat adjuvant versus metastatic cancer, as we discussed a few pages ago.

從歷史上看，這是透過成像測試（例如 CT 掃描）來完成的，這使我們能夠「看到」腫瘤。儘管存在輻射暴露，但主要問題是這些測試沒有很高的分辨率。這些成像技術很難識別直徑小於一公分的癌症。即使您假設這個一厘米的結節是患者體內唯一的癌細胞集合（這不是一個很好的假設；陷阱中的老鼠很少是房子裡唯一的一隻），您仍然在談論超過當達到傳統檢測的閾值時，癌細胞已達十億個。如果我們能夠更快地發現這些復發性癌症，我們可能有更好的機會讓患者保持緩解狀態——正如我們在幾頁前討論的那樣，輔助治療比轉移性癌症更容易治療是同樣的原因。

Max and his colleagues came up with a wholly different method. Because cancer cells are growing constantly, they tend to shed cellular matter, including bits of tumor DNA, into the circulation. What if there were a blood

test that could detect this so-called cell-free DNA? We would already know the genetic signature of the tumor from the surgery—that is, how the lung cancer cells differ from normal lung cells. Thus, it should be possible to screen for this cell-free DNA in a patient's plasma and thereby determine the presence of cancer.

馬克斯和他的同事想出了一個完全不同的方法。由於癌細胞不斷生長，它們往往會將細胞物質（包括腫瘤 DNA 片段）釋放到循環系統中。如果有一種血液檢查可以檢測這種所謂的遊離 DNA 會怎麼樣？我們已經透過手術了解了腫瘤的遺傳特徵，即肺癌細胞與正常肺細胞的差異。因此，應該可以在患者血漿中篩選這種無細胞 DNA，從而確定癌症的存在。

Make no mistake about it, this is still akin to looking for a needle in a haystack. In an early-stage cancer, which are the cancers we would most want to find via liquid biopsies, we might be talking about 0.01 to 0.001 percent of cell-free DNA coming from the cancer (or about one part in ten thousand to one hundred thousand). Only with the help of next-generation, high-throughput DNA screening technology is this possible. These tests are becoming more widely used in the postsurgical setting, but the technology is still relatively young. The key is that you must know what you're looking for—the patterns of mutations that distinguish cancer from normal cells.

毫無疑問，這仍然類似大海撈針。在早期癌症中，也就是我們最想透過液體活檢發現的癌症，我們可能會談論 0.01% 到 0.001% 的遊離 DNA 來自癌症（或大約萬分之一到百分之一）。千）。只有借助下一代高通量 DNA 篩選技術，這才有可能實現。這些測試在術後環境中的應用越來越廣泛，但該技術仍然相對較年輕。關鍵是你必須知道你在尋找什麼——區分癌症和正常細胞的突變模式。

Some researchers are beginning to develop ways to use blood tests to screen for cancer generally, in otherwise healthy people. This is an order of magnitude more difficult, like looking for a needle in ten haystacks; worse, in this case we don't even know what the needle should look like. We don't know anything about the patient's tumor mutation patterns, because we're not yet certain that they *have* cancer. Thus we must look for other potential markers.

One company leading the charge with this type of assay is called Grail, a subsidiary of the genetic-sequencing company Illumina. The Grail test, known as Galleri, looks at methylation patterns of the cell-free DNA, which are basically chemical changes to the DNA molecules that suggest the presence of cancer. Using very-high-throughput screening and a massive AI engine, the Galleri test can glean two crucial pieces of information from this sample of blood: Is cancer present? And if so, where is it? From what part of the body did it most likely originate?

一些研究人員開始開發使用血液檢查來普遍篩檢健康人群癌症的方法。這就像大海撈針一樣困難一個數量級；更糟的是，在這種情況下，我們甚至不知道針應該是什麼樣子。我們對患者的腫瘤突變模式一無所知，因為我們還不確定他們是否有癌症。因此我們必須尋找其他潛在的標記。在此類檢測領域處於領先地位的公司稱為 Grail，它是基因定序公司 Illumina 的子公司。Grail 測試，稱為 Galleri，著眼於無細胞 DNA 的甲基化模式，這些甲基化模式基本上是 DNA 分子的化學變化，表明癌症的存在。Galleri 測試使用非常高通量的篩選和大型人工智慧引擎，可以從該血液樣本中收集兩個關鍵資訊：是否存在癌症？如果是的話，它在哪裡？它最有可能源自於身體的哪個部位？

With any diagnostic test, a decision has to be made with respect to how to calibrate, or tune, it. Is it going to be geared toward higher sensitivity or higher specificity? Galleri has been validated against a database called the Circulating Cell-free Genome Atlas (CCGA), which is based on blood samples from more than fifteen thousand patients both with and without cancer. In this study, the Galleri test proved to have a very high specificity, about 99.5 percent, meaning only 0.5 percent of tests yielded a false positive. If the test says you have cancer, somewhere in your body, then it is likely that you do. The trade-off is that the resulting sensitivity can be low, depending on the stage. (That is, even if the test says you don't have cancer, you are not necessarily in the clear.)

對於任何診斷測試，都必須決定如何校準或調整它。它會面向更高的靈敏度還是更高的特異性？Galleri 已根據名為循環無細胞基因組圖譜 (CCGA) 的資料庫進行了驗證，該資料庫基於超過一萬五千名癌症患

者和非癌症患者的血液樣本。在這項研究中，Galleri 測試被證明具有非常高的特異性，約為 99.5%，這意味著只有 0.5% 的測試產生假陽性。如果測試顯示您體內某個部位患有癌症，那麼您很可能患有癌症。權衡是最終的靈敏度可能較低，具體取決於階段。（也就是說，即使測試表明您沒有患有癌症，您也不一定是安全的。）

The thing to keep in mind here, however, is that this test still has much higher resolution than radiographic tests such as MRI or mammogram. Those imaging-based tests require “seeing” the tumor, which can happen only when the tumor reaches a certain size. With Galleri, the test is looking at cell-free DNA, which can come from any size tumor—even ones that remain invisible to imaging tests.

然而，這裡要記住的是，該測試的分辨率仍然比 MRI 或乳房 X 光檢查等放射線測試高得多。這些基於影像的測試需要「看到」腫瘤，而這只有當腫瘤達到一定大小時才會發生。Galleri 的測試著眼於無細胞 DNA，它可以來自任何大小的腫瘤，甚至是成像測試中看不見的腫瘤。

One early observation of the CCGA study was that detectability was associated not only with the stage of tumor, which would be expected (the more advanced the tumor, the greater the likelihood of finding cell-free DNA in the blood), but also with the subtype of tumor. For example, the detection rate for stage I/II hormone receptor-*positive* breast cancer is about 25 percent, while the detection rate for stage I/II hormone receptor-*negative* breast cancer is about 75 percent. What does this difference tell us? We know that breast cancer is not a uniform disease and that the hormone receptor-negative tumors are more lethal than hormone receptor-positive tumors. Thus, the test proves more accurate in detecting the more lethal subtype of breast cancer.

CCGA 研究的一項早期觀察結果是，可檢測性不僅與預期的腫瘤分期相關（腫瘤越晚期，在血液中發現無細胞 DNA 的可能性就越大），而且與腫瘤的亞型。例如，I/II期荷爾蒙受體陽性乳癌的檢出率約為 25%，而I/II期荷爾蒙受體陰性乳癌的檢出率約為75%。這種差異告訴我們什麼？我們知道乳癌不是統一的疾病，荷爾蒙受體陰性腫瘤比荷

爾蒙受體陽性腫瘤更致命。因此，該測試在檢測更致命的乳癌亞型方面被證明更加準確。

Liquid biopsies could be viewed as having two functions: first, to determine cancer's presence or absence, a binary question; and second and perhaps more important, to gain insight into the specific cancer's biology. How dangerous is this particular cancer likely to be? The cancers that shed more cell-free DNA, it seems, also tend to be more aggressive and deadly—and are thus the cancers that we want to detect, and treat, as soon as possible. This technology is still in its infancy, but I'm hopeful that pairing different diagnostic tests ranging from radiographic (e.g., MRI) to direct visualization (e.g., colonoscopy) to biological/genetic (e.g., liquid biopsy) will allow us to correctly identify the cancers that need treatment the soonest, with the fewest possible false positives.

液體活檢可以被視為具有兩個功能：第一，確定癌症是否存在，這是一個二元問題；第二，確定癌症是否存在。其次，也許更重要的是，深入了解特定癌症的生物學。這種特殊的癌症有多危險？脫落更多遊離 DNA 的癌症似乎也更具侵襲性和致命性，因此是我們希望盡快檢測和治療的癌症。這項技術仍處於起步階段，但我希望將不同的診斷測試（從放射線照相（例如MRI）到直接可視化（例如大腸鏡檢查）再到生物/遺傳（例如液體活檢））配對，將使我們能夠正確識別需要最快治療的癌症，假陽性率最少。

The implications of this, I think, are seismic: if liquid biopsies deliver on their promise, we could completely flip the time line of cancer so that we are routinely intervening early, when we have a chance of controlling or even eliminating the cancer—rather than the way we typically do it now, coming in at a late stage, when the odds are already stacked against the patient, and hoping for a miracle.

我認為，這一點的影響是巨大的：如果液體活檢兌現了它們的承諾，我們就可以完全扭轉癌症的時間線，這樣我們就可以在有機會控制甚至消除癌症時定期進行早期幹預——而不是與我們現在通常採取的方式不同，我們在晚期才介入，當時患者的可能性已經對患者不利，並希望奇蹟出現。



Of all the Horsemen, cancer is probably the hardest to prevent. It is probably also the one where bad luck in various forms plays the greatest role, such as in the form of accumulated somatic mutations. The only modifiable risks that really stand out in the data are smoking, insulin resistance, and obesity (all to be avoided)—and maybe pollution (air, water, etc.), but the data here are less clear.

在所有騎士中，癌症可能是最難預防的。這也可能是各種形式的壞運氣發揮最大作用的原因，例如以累積的體細胞突變的形式。數據中真正突出的唯一可改變的風險是吸煙、胰島素阻抗和肥胖（所有這些都需要避免）——也許還有污染（空氣、水等），但這裡的數據不太清楚。

We do have some treatment options for cancer, unlike with Alzheimer's disease (as we'll see in the next chapter), and immunotherapy in particular has great promise. Yet our treatment and prevention strategies remain far less effective than the tools that we have to address cardiovascular disease and the spectrum of metabolic dysfunction from insulin resistance to type 2 diabetes.

與阿茲海默症不同（我們將在下一章中看到），我們確實有一些癌症治療選擇，尤其是免疫療法有很大的前景。然而，我們的治療和預防策略仍然遠不如我們應對心血管疾病以及從胰島素阻抗到第 2 型糖尿病等一系列代謝功能障礙的工具有效。

Until we learn how to prevent or “cure” cancer entirely, something I do not see happening in our lifetime, short of some miraculous breakthroughs, we need to focus far more energy on early detection of cancer, to enable better targeting of specific treatments at specific cancers while they are at their most vulnerable stages. If the first rule of cancer is “Don't get cancer,” the second rule is “Catch it as soon as possible.”

在我們學會如何完全預防或「治癒」癌症之前（我在有生之年看不到這種事情發生，除了一些奇蹟般的突破），我們需要將更多的精力集

中在癌症的早期檢測上，以便能夠更好地針對特定治療當特定癌症處於最脆弱階段。如果癌症的第一條規則是“不要得癌症”，那麼第二條規則就是“盡快感染”。

This is why I'm such an advocate for early screening. It's a simple truth that treating smaller tumors with fewer mutations is far easier than if we wait for the cancer to advance and potentially acquire mutations that help it evade our treatments. The only way to catch it early is with aggressive screening.

這就是為什麼我如此倡導早期篩檢。這是一個簡單的事實，用較少的突變來治療較小的腫瘤比我們等待癌症進展並可能獲得有助於其逃避治療的突變要容易得多。儘早發現它的唯一方法是積極篩檢。

This does come at significant cost, which is why Medicine 2.0 tends to be more conservative about screening. There is a financial cost, of course, but there is also an emotional cost, particularly of tests that may generate false positives. And there are other, incidental risks, such as the slight risk from a colonoscopy or the more significant risk from an unnecessary biopsy. These three costs must be weighed against the cost of missing a cancer, or not spotting it early, when it is still susceptible to treatment.

這確實需要付出巨大的代價，這就是為什麼醫學 2.0 在篩檢方面往往更加保守。當然，這有經濟成本，但也有情感成本，尤其是可能產生誤報的測試。還有其他偶然的風險，例如大腸鏡檢查帶來的輕微風險或不必要的活檢帶來更大的風險。必須權衡這三項成本與錯過癌症或在癌症仍易於治療時未及早發現癌症的成本。

Nobody said this was going to be easy. We still have a very long way to go. But there is finally hope, on multiple fronts—far more than when I was training to become a cancer surgeon. More than fifty years into the War on Cancer, we can finally see a path to a world where a cancer diagnosis typically means an early detection of a treatable problem rather than a late discovery of a grim one. Thanks to better screening and more effective treatments such as immunotherapy, cancer could someday become a manageable disease, perhaps no longer even qualifying as a Horseman.

沒有人說這會很容易。我們還有很長的路要走。但在多個方面終於有了希望——遠遠超過我接受癌症外科醫生培訓時的希望。對抗癌症的戰爭已經過去了五十多年，我們終於可以看到一條通往這樣一個世界的道路：癌症診斷通常意味著早期發現可治療的問題，而不是晚期發現嚴峻的問題。由於更好的篩檢和更有效的治療（例如免疫療法），癌症有一天可能成為一種可以控制的疾病，甚至可能不再有資格成為騎士。

[SKIP NOTES](#)

[跳過註釋](#)

[*1](#) This is not the only explanation for how the Warburg effect benefits a cancer cell. Another theory is that it helps protect the tumor from immune cells by making the tumor microenvironment less hospitable because of lower pH (i.e., more acidic) caused by the generation of lactic acid and reactive oxygen species. For an excellent review of these topics, see Liberti and Locasale (2016).

*1 這並不是瓦爾堡效應如何有益於癌細胞的唯一解釋。另一種理論認為，它有助於保護腫瘤免受免疫細胞的侵害，因為乳酸和活性氧的產生導致 pH 值降低（即酸性更強），從而使腫瘤微環境變得不太適宜。有關這些主題的精彩回顧，請參閱 Liberti 和 Locasale (2016)。

[*2](#) At the time it was not clear why this was the case, but today it's clear that this approach worked because these two cancers tend to have a large number of genetic mutations, meaning the immune system is more likely to recognize the cancerous cells as harmful and target them.

*2 當時還不清楚為什麼會出現這種情況，但現在很明顯這種方法有效，因為這兩種癌症往往有大量基因突變，這意味著免疫系統更有可能將癌細胞識別為有害並針對他們。

[*3](#) To learn more about the story of immunotherapy, read Charles Graeber's 2018 book, *Breakthrough*, which goes into greater detail about Jim Allison's work with checkpoint inhibitors.

*3 要了解有關免疫療法故事的更多信息，請閱讀 Charles Graeber 2018 年出版的書《Breakthrough》，其中更詳細地介紹了 Jim Allison 在檢查點抑制劑方面的工作。

[*4](#) For example, TILs by definition have already demonstrated an affinity for the tumor; however, they may “age” more as they are multiplied (cells “age” every time they divide), losing some of their potency. Conversely, genetically modified T cells tend to be younger and easier to grow, but they don't necessarily have the same ability to kill tumors as TILs.

*4 例如，根據定義，TIL 已表現出對腫瘤的親和力；然而，隨著它們的繁殖，它們可能會「老化」得更多（細胞每次分裂時都會「老化」），從而失去一些效力。相反，基因改造 T 細胞往往更年輕、更容易生長，但它們不一定具有與 TIL 相同的殺死腫瘤的能力。

[*5](#) For 95 percent of metastatic colon cancer patients.

*5 對於 95% 的轉移性結腸癌患者。

[*6](#) This means the expression of human epidermal growth factor receptor 2, which is a protein receptor on the surface of breast cancer cells that promotes growth. This is overexpressed in roughly 30 percent of breast cancers.

*6 這意味著人類表皮生長因子受體2的表達，它是乳癌細胞表面的一種促進生長的蛋白質受體。它在大約 30% 的乳腺癌中過度表達。

[*7](#) There are several different colon cancer screening methods that break down into two categories: stool-based tests and direct visualization tests. Stool-based tests are essentially a screening test for a screening test. A positive stool-based test prompts a direct visualization test of the colon: either a flexible sigmoidoscopy, which allows the endoscopist to view the lower part of the colon (including the sigmoid and descending colon), or a traditional colonoscopy, which examines the entire colon. In my opinion, none of the other tests compares to a colonoscopy.

*7 有幾種不同的大腸癌篩檢方法，可分為兩類：基於糞便的測試和直接可視化測試。基於糞便的測試本質上是篩選測試的篩選測試。基於糞便的測試呈陽性，提示對結腸進行直接可視化測試：要么是靈活的乙狀結腸鏡檢查，允許內視鏡醫生觀察結腸的下部（包括乙狀結腸和降結腸），要么是傳統的結腸鏡檢查，檢查整個結腸盲腸。在我看來，其他檢查都無法與大腸鏡檢查相比。

[*8](#) A study published in 2022 found that the risk of CRC was only reduced by 18 percent (relative) and 0.22 percent (absolute) in people advised to get one colonoscopy in a ten-year period versus those not advised to. However, only 42 percent of those advised to get a colonoscopy actually did so, and they only underwent one during the period of the study. I would argue this was not a test of the efficacy of frequent colonoscopy for prevention of CRC and was, instead, a test of the effectiveness of telling people to get (infrequent) colonoscopy.

*8 2022 年發表的一項研究發現，與不建議在 10 年內進行一次大腸鏡檢查的人相比，建議在 10 年內進行一次大腸鏡檢查的人患 CRC 的風險僅降低了 18%（相對）和 0.22%（絕對）。然而，在建議接受大腸鏡檢查的人中，只有 42% 的人真正這樣做了，而且他們在研究期間只接受了一次大腸鏡檢查。我認為這不是對頻繁大腸鏡檢查預防大腸直腸癌的有效性的測試，而是對告訴人們（不頻繁）進行大腸鏡檢查的有效性的測試。

[*9](#) For those seeking more detailed guidance, this is what I wrote (Attia 2020a) in a blog post on CRC screening a few years ago: “Before you get your first colonoscopy, there are [a] few things you can do that may improve your risk-to-benefit ratio. You should ask what your endoscopist’s adenoma detection rate (ADR) is. The ADR is the proportion of individuals undergoing a colonoscopy who have one or more adenomas (or colon polyps) detected. The benchmarks for ADR are greater than 30% in men and greater than 20% in women. You should also ask your endoscopist how many perforations he or she has caused, specifically, as well as any other serious complications, like major intestinal bleeding episodes (in a routine screening setting). Another question you should ask is what is your endoscopist’s withdrawal time, defined as the amount of time spent viewing as the colonoscope is withdrawn during a colonoscopy. A longer withdrawal time suggests a more thorough inspection. A 6-minute withdrawal time is currently the standard of care.”

*9 對於那些尋求更詳細指導的人，這是我幾年前在一篇有關 CRC 篩檢的部落格文章中所寫的內容(Attia 2020a)：「在您進行第一次大腸鏡檢查之前，您可以做一些事情來提高您的風

險收益比。您應該詢問內視鏡醫師的腺瘤檢出率 (ADR) 是多少。ADR 是指在接受大腸鏡檢查時發現一個或多個腺瘤（或結腸息肉）的個體的比例。男性 ADR 基準高於 30%，女性高於 20%。您還應該詢問您的內視鏡醫生他或她造成了多少次穿孔，特別是以及任何其他嚴重併發症，例如大腸出血事件（在常規篩檢環境中）。您應該問的另一個問題是內視鏡醫生的撤回時間是多少，定義為在大腸鏡檢查期間撤回大腸鏡所花費的時間。較長的撤藥時間顯示檢查更加徹底。6 分鐘撤藥時間是目前的護理標準。”

*10 The specificity of MRI is particularly reduced by glandular tissue. MRI is so good at detecting glandular cancer that it significantly overdoes it. The thyroid gland might be the worst offender.

*10 MRI 的特異性尤其會因腺體組織而降低。MRI 非常擅長偵測腺癌，但它的效果明顯有些過頭了。甲狀腺可能是最嚴重的罪魁禍首。

*11 These are called liquid biopsies to distinguish them from traditional solid-tissue biopsies.

*11 這些被稱為液體活檢，以區別於傳統的固體組織活檢。

CHAPTER 9

第9章

Chasing Memory

追逐記憶

Understanding Alzheimer's Disease and Other
Neurodegenerative Diseases

了解阿茲海默症和其他神經退化性疾病

The greatest obstacle to discovery is not ignorance—it is
the illusion of knowledge.

發現的最大障礙不是無知，而是知識的幻覺。

—DANIEL J. BOORSTIN

——丹尼爾·J·布爾斯汀

Most people tend to go to the doctor when they are sick or think they might be. Nearly all my patients first come to see me when they are relatively healthy, or think they are. That was the case with Stephanie, a forty-year-old woman who walked into my office for her initial visit in early 2018 with no real complaint. She was simply “interested” in longevity.

大多數人在生病或認為自己可能生病時傾向於去看醫生。幾乎所有的病人第一次來找我時，他們都相對健康，或認為自己相對健康。史蒂芬妮 (Stephanie) 就是這樣的情況，她是一位 40 歲的女性，她於 2018 年初首次來到我的辦公室，沒有任何真正的抱怨。她只是對長壽「感興趣」。

Her family history was not remarkable. Three of her four grandparents had died from complications of atherosclerosis in their late seventies or early eighties, and the fourth had died from cancer. Pretty much par for the course for the Greatest Generation. The only red flag was the fact that her mother, otherwise healthy at seventy, was beginning to suffer some memory loss, which Stephanie attributed to “old age.”

她的家族史並不顯著。她的四位祖父母中的三位在七十年代末或八十年代初死於動脈粥樣硬化併發症，第四位則死於癌症。與最偉大的一代的課程幾乎相同。唯一的危險信號是，她的母親雖然七十歲了，身體健康，但開始出現一些記憶喪失，史蒂芬妮將其歸因於「年老」。

We set up another appointment for a week later to review her initial blood work. I rely as much as one can on biomarkers, so we run a comprehensive array of tests, but there are a few things that I immediately scan for when I get a new patient's results back. Among them is their level of Lp(a), the high-risk lipoprotein that we talked about in chapter 7, along with their apoB concentration. A third thing that I always check is their *APOE* genotype, the gene related to Alzheimer's disease risk that we mentioned in chapter 4.

我們在一周後安排了另一次預約，以檢查她的初步血液檢查。我盡可能依賴生物標誌物，因此我們進行了一系列全面的測試，但當我收到新患者的結果時，我會立即掃描一些內容。其中包括 Lp(a)（我們在第 7 章中討論過的高風險脂蛋白）水平以及 apoB 濃度。我經常檢查的第

三件事是他們的 APOE 基因型，該基因與我們在第 4 章中提到的阿茲海默症風險相關。

Stephanie's labs revealed that she had the *APOE e4* allele, which is associated with a greater risk of Alzheimer's disease—and not just one copy, but two (*e4/e4*), which meant her risk of developing Alzheimer's disease was up to twelve times greater than that of someone with two copies of the common *e3* allele. The *e2* version of *APOE* appears to protect carriers against Alzheimer's disease: 10 percent reduced risk for someone with *e2/e3*, and about 20 percent for *e2/e2*. Stephanie was unlucky.

史蒂芬妮的實驗室發現，她攜帶 APOE e4 等位基因，該等位基因與阿茲海默症的更大風險相關，而且不僅僅是一個副本，而是兩個 (*e4/e4*)，這意味著她罹患阿茲海默症的風險高達 12 倍比擁有兩個常見 *e3* 等位基因副本的人更重要。e2 版本的 APOE 似乎可以保護攜帶者免受阿茲海默症的侵害：e2/e3 患者的風險降低 10%，e2/e2 患者的風險降低約 20%。史蒂芬妮很不幸。

She was only the fourth patient I'd ever encountered with this quite uncommon genotype, shared by only about 2 to 3 percent of the population, and she had no idea she was at risk—although in hindsight, her mother's forgetfulness may have been a symptom of early Alzheimer's disease. Now I faced a double challenge: how to break the news to her, directly but gently; and even more tricky, how to explain what it meant and what it didn't mean.

她是我遇到的第四個患有這種非常罕見基因型的患者，這種基因型只佔人口的 2% 到 3%，而且她不知道自己處於危險之中——儘管事後看來，她母親的健忘可能是一個原因。早期阿茲海默症的症狀。現在我面臨著雙重挑戰：如何直接但溫和地向她透露這個消息；更棘手的是，如何解釋它的含義和不含義。

In circumstances like this I generally think it's best to get right to the point, so after we sat down, I said something like, "Stephanie, there is something we found in your blood test that may be of concern to me—not because anything is wrong now, but because of the risk it poses in twenty to thirty years or so. You have a combination of genes that increases your risk of developing

Alzheimer's disease. But it's also important that you understand that what we're about to discuss is only a marker for risk, not a fait accompli, and I am convinced that we can mitigate this risk going forward."

在這種情況下，我通常認為最好開門見山，所以在我們坐下後，我說了這樣的話，「史蒂芬妮，我們在你的血液檢查中發現了一些可能讓我擔心的東西——不是因為現在任何事情都是錯誤的，但因為它在二十到三十年後會帶來風險。您體內的多種基因組合會增加您罹患阿茲海默症的風險。但同樣重要的是，你要明白，我們將要討論的只是風險的標誌，而不是既成事實，我相信我們可以在未來減輕這種風險。」

Stephanie was devastated. She was dealing with a lot of stress to begin with: a divorce, a difficult work situation, and now this. It's tough to explain the nuances of genes and risk to somebody when their eyes are wide with fear and they are hearing only *I'm doomed*. It took several discussions over the course of many weeks before she began to understand the rest of the message, which was that she was not, in fact, doomed.

史蒂芬妮崩潰了。她一開始就承受著很大的壓力：離婚、困難的工作環境，以及現在的狀況。當人們因恐懼而睜大眼睛並且只聽到「我注定要失敗」時，很難向他們解釋基因和風險的細微差別。經過數週的多次討論，她才開始理解其餘的訊息，即她實際上並沒有註定要失敗。

Alzheimer's disease is perhaps the most difficult, most intractable of the Horsemen diseases. We have a much more limited understanding of how and why it begins, and how to slow or prevent it, than we do with atherosclerosis. Unlike with cancer, we currently have no way to treat it once symptoms begin. And unlike type 2 diabetes and metabolic dysfunction, it does not appear to be readily reversible (although the jury is still out on that). This is why, almost without exception, my patients fear dementia more than any other consequence of aging, including death. They would rather die from cancer or heart disease than lose their minds, their very selves.

阿茲海默症可能是騎士疾病中最困難、最難治的。與動脈粥狀硬化相比，我們對它如何發生、為何發生，以及如何減緩或預防它的了解要

有限得多。與癌症不同的是，一旦出現症狀，我們目前無法對其進行治療。與第 2 型糖尿病和代謝功能障礙不同，它似乎不容易逆轉（儘管目前尚無定論）。這就是為什麼我的病人幾乎無一例外地比任何其他衰老後果（包括死亡）更害怕癡呆症。他們寧願死於癌症或心臟病，也不願失去理智和自我。

Alzheimer's disease is the most common, but there are other neurodegenerative diseases that concern us. The most prevalent of these are Lewy body dementia and Parkinson's disease, which are actually different forms of a related disorder known (confusingly) as "dementia with Lewy bodies." The primary difference between them is that Lewy body dementia is primarily a dementing disorder, meaning it affects cognition, while Parkinson's disease is considered primarily (but not entirely) a movement disorder, although it does also result in cognitive decline. In the United States, about 6 million people are diagnosed with Alzheimer's disease, while about 1.4 million have Lewy body dementia, and 1 million have been diagnosed with Parkinson's, which is the fastest-growing neurodegenerative disease. Beyond that, there are a variety of less common but also serious neurodegenerative conditions such as amyotrophic lateral sclerosis (ALS, or Lou Gehrig's disease) and Huntington's disease.

阿茲海默症是最常見的疾病，但還有其他神經退化性疾病值得我們關注。其中最常見的是路易氏體失智症和帕金森氏症，它們實際上是一種相關疾病的不同形式，被稱為「路易氏體失智症」（令人困惑）。它們之間的主要區別在於，路易體癡呆主要是一種癡呆症，這意味著它會影響認知，而帕金森氏症被認為主要（但不完全）是一種運動障礙，儘管它也會導致認知能力下降。在美國，約有600 萬人被診斷出患有阿茲海默症，約140 萬人患有路易體癡呆症，100 萬人被診斷患有帕金森氏症，這是成長最快的神經退化性疾病。除此之外，還有各種不太常見但也很嚴重的神經退化性疾病，例如肌萎縮側索硬化症（ALS，或盧伽雷氏症）和亨丁頓舞蹈症。

All these result from some form of neurodegeneration, and as yet, there is no cure for any of them—despite the billions and billions of dollars that have been spent chasing these complex conditions. Maybe there will be a

breakthrough in the near future, but for now our best and only strategy is to try to prevent them. The only shred of good news here is that while these disorders have traditionally been considered as completely separate and distinct diseases, evolving evidence suggests that there is a larger continuum between them than has previously been recognized, which means that some of our prevention strategies could apply to more than one of them as well.

所有這些都是由某種形式的神經退化性疾病造成的，儘管已經花費了數十億美元來治療這些複雜的病症，但迄今為止，還沒有任何一種方法可以治癒它們。也許在不久的將來會有突破，但目前我們最好也是唯一的策略是盡力阻止它們。這裡唯一的好消息是，雖然這些疾病傳統上被認為是完全獨立和不同的疾病，但不斷發展的證據表明它們之間存在比以前認識到的更大的連續體，這意味著我們的一些預防策略可以適用也不只一個。

—

Many doctors shy away from *APOE* gene testing. The conventional wisdom holds that someone with the high-risk *e4* allele is all but guaranteed to develop Alzheimer's disease, and there is nothing we can do for them. So why burden the patient with this terrible knowledge?

許多醫生迴避 *APOE* 基因檢測。傳統觀點認為，攜帶高風險 *e4* 等位基因的人幾乎肯定會患上阿茲海默症，而我們對此無能為力。那為什麼要讓病人承受這些可怕的知識呢？

Because there are two types of bad news: that about things we can change, and about things that we can't. Assuming that a patient's *e4* status falls into the latter category is, in my opinion, a mistake. While it is true that over one-half of people with Alzheimer's disease have at least one copy of *e4*, merely possessing this risk gene is not the same as being diagnosed with dementia due to Alzheimer's disease. There are *e4/e4*-carrying centenarians without any signs of dementia, likely because they have other genes that protect them from *e4*; for example, a certain variant of the gene *Klotho* (*KL*), called *kl-vs*, seems to protect carriers of *e4* from developing dementia. And plenty of "normal"

e3/e3 carriers will still go on to develop Alzheimer's. Having the *e4* gene variant merely signals increased risk. It's not a done deal.

因為壞消息有兩種：一種是我們可以改變的事情，另一種是我們不能改變的事情。在我看來，假設患者的 *e4* 狀態屬於後者是錯誤的。雖然超過一半的阿茲海默症患者確實至少有一個 *e4* 拷貝，但僅僅擁有這個風險基因並不等同於被診斷出患有阿茲海默症引起的癡呆症。有些攜帶 *e4/e4* 的百歲老人沒有任何失智跡象，可能是因為他們有其他基因可以保護他們免受 *e4* 的影響；例如，*Klotho* (*KL*) 基因的某種變異（稱為 *kl-vs*）似乎可以保護 *e4* 攜帶者免於罹患失智症。許多「正常」的 *e3/e3* 攜帶者仍會患上阿茲海默症。擁有 *e4* 基因變異僅僅意味著風險增加。這還沒完成。

The other point I tried to make to Stephanie was that time was on her side. The disease rarely progresses to a clinical stage before about age sixty-five, even in patients with two copies of *e4*. That gives us about twenty-five years to try to prevent or delay her from developing this horrible illness with the tools currently at our disposal. In the interim, hopefully, researchers might come up with more effective treatments. It was a classic asymmetric situation, where doing nothing was actually the riskiest course of action.

我試圖向史蒂芬妮表達的另一點是，時間站在她這邊。即使在攜帶兩個 *e4* 拷貝的患者中，這種疾病也很少在 65 歲之前發展到臨床階段。這給了我們大約二十五年的時間，利用我們目前掌握的工具來嘗試預防或延緩她患上這種可怕的疾病。在此期間，希望研究人員能想出更有效的治療方法。這是一種典型的不對稱情況，什麼都不做實際上是最危險的行動方案。

Understanding Alzheimer's

了解阿茲海默症

Although Alzheimer's disease was first named in the early 1900s, the phenomenon of "senility" has been remarked on since ancient times. Plato

believed that because advancing age seemingly “gives rise to all manners of forgetfulness as well as stupidity,” older men were unsuited for leadership positions requiring acumen or judgment. William Shakespeare gave us an unforgettable portrayal of an old man struggling with his failing mind in *King Lear*.

雖然阿茲海默症早在1900年代初就被首次命名，但「衰老」現象自古以來就被人們所關注。柏拉圖認為，由於年齡的增長似乎“會導致各種健忘和愚蠢”，因此老年男性不適合擔任需要敏銳或判斷力的領導職位。威廉·莎士比亞在《李爾王》中為我們描繪了一個令人難忘的老人與自己失敗的思想作鬥爭的形象。

The notion that this might be a disease was first suggested by Dr. Alois Alzheimer, a psychiatrist who worked as medical director at the state asylum in Frankfurt, Germany. In 1906, while performing an autopsy on a patient named Auguste Deter, a woman in her midfifties who had suffered from memory loss, hallucinations, aggression, and confusion in her final years, he noticed that something was clearly wrong with her brain. Her neurons were entangled and spiderweb-like, coated with a strange white dental substance. He was so struck by their odd appearance that he made drawings of them.

這可能是一種疾病的想法是由阿洛伊斯·阿茲海默博士首先提出的，他是一位精神病學家，曾在德國法蘭克福國家精神病院擔任醫療主任。1906年，在對一位名叫奧古斯特·德特(Auguste Deter)的病人進行屍檢時，他注意到她的大腦明顯出了問題。奧古斯特·德特是一位五十多歲的女性，晚年有記憶喪失、幻覺、攻擊性和精神錯亂等症狀。她的神經元糾纏在一起，呈現蜘蛛網狀，上面覆蓋著一種奇怪的白色牙齒物質。他對它們奇怪的外表感到震驚，於是把它們畫下來。

Another colleague later dubbed this condition “Alzheimer’s disease,” but after Alzheimer himself died in 1915 (of complications from a cold, at fifty-one), the disease he had identified was more or less forgotten for fifty years, relegated to obscurity along with other less common neurological conditions such as Huntington’s and Parkinson’s diseases as well as Lewy body dementia. Patients with the kinds of symptoms that we now associate with these conditions, including mood changes, depression, memory loss, irritability, and

irrationality, were routinely institutionalized, as Auguste Deter had been. Plain old “senility,” meanwhile, was considered to be an inevitable part of aging, as it had been since Plato’s day.

另一位同事後來將這種病症稱為“阿茲海默症”，但在阿茲海默症本人於1915年去世（因感冒併發症，時年51歲）後，他所發現的這種疾病或多或少地被遺忘了50年，與其他疾病一起陷入了默默無聞的境地。其他不太常見的神經系統疾病，例如亨廷頓氏症和帕金森氏症以及路易氏體失智症。患有我們現在與這些疾病相關的各種症狀的患者，包括情緒變化、憂鬱、記憶喪失、易怒和不理性，通常都會被送入收容機構，就像奧古斯特·德特一樣。同時，普通的「衰老」被認為是衰老不可避免的一部分，從柏拉圖時代開始就是如此。

It wasn’t until the late 1960s that scientists began to accept that “senile dementia” was a disease state and not just a normal consequence of aging. Three British psychiatrists, Garry Blessed, Bernard Tomlinson, and Martin Roth, examined the brains of seventy patients who had died with dementia and found that many of them exhibited the same kinds of plaques and tangles that Alois Alzheimer had observed. Further studies revealed that a patient’s degree of cognitive impairment seemed to correlate with the extent of plaques found in his or her brain. These patients, they concluded, also had Alzheimer’s disease. A bit more than a decade later, in the early 1980s, other researchers identified the substance in the plaques as a peptide called amyloid-beta. Because it is often found at the scene of the crime, amyloid-beta was immediately suspected to be a primary cause of Alzheimer’s disease.

直到20世紀60年代末，科學家才開始接受「阿茲海默症」是一種疾病狀態，而不僅僅是衰老的正常後果。三位英國精神科醫生加里·布萊塞德（Garry Blessed）、伯納德·湯姆林森（Bernard Tomlinson）和馬丁·羅斯（Martin Roth）檢查了七十名死於癡呆症的患者的大腦，發現他們中的許多人都表現出與阿洛伊斯·阿茲海默（Alois Alzheimer）觀察到的相同類型的斑塊和纏結。進一步的研究表明，患者的認知障礙程度似乎與他或她大腦中發現的斑塊的程度有關。他們得出的結論是，這些患者也患有阿茲海默症。十多年後，在20世紀80年代初，其他研究人員鑑定出斑塊中的物質是一種稱為澱粉樣蛋白 - β 的勝肽。由於 β 澱

粉樣蛋白經常在犯罪現場被發現，因此立即被懷疑是阿茲海默症的主要原因。

Amyloid-beta is a by-product that is created when a normally occurring substance called amyloid precursor protein, or APP, a membrane protein that is found in neuronal synapses, is cleaved into three pieces. Normally, APP is split into two pieces, and everything is fine. But when APP is cut in thirds, one of the resulting fragments then becomes “misfolded,” meaning it loses its normal structure (and thus its function) and becomes chemically stickier, prone to aggregating in clumps. This is amyloid-beta, and it is clearly bad stuff. Laboratory mice that have been genetically engineered to accumulate amyloid-beta (they don’t naturally) have difficulty performing cognitive tasks that are normally easy, such as finding food in a simple maze. At the same time, amyloid also triggers the aggregation of another protein called tau, which in turn leads to neuronal inflammation and, ultimately, brain shrinkage. Tau was likely responsible for the neuronal “tangles” that Alois Alzheimer observed in Auguste Deter.

β 澱粉樣蛋白是一種副產品，是一種稱為澱粉樣前體蛋白（APP）的正常存在的物質（一種存在於神經元突觸中的膜蛋白）被切割成三塊時產生的副產品。通常情況下，APP被分成兩塊，一切都很好。但當APP被切成三分之一時，其中一個片段就會“錯誤折疊”，這意味著它失去了正常結構（從而失去了功能），並且化學性質變得更加粘稠，容易聚集成團。這是 β -澱粉樣蛋白，它顯然是個壞東西。經過基因改造以累積 β -澱粉樣蛋白的實驗室小鼠（它們不是天生的）很難執行通常很容易的認知任務，例如在簡單的迷宮中尋找食物。同時，澱粉樣蛋白還會引發另一種名為 tau 的蛋白質的聚集，進而導致神經元炎症，最終導致大腦萎縮。阿洛伊斯·阿茲海默 (Alois Albert) 在奧古斯特·德特 (Auguste Deter) 身上觀察到的神經元「纏結」可能與 Tau 蛋白有關。

Scientists have identified a handful of genetic mutations that promote very rapid amyloid-beta accumulation, all but ensuring that someone will develop the disease, often at a fairly young age. These mutations, the most common of which are called *APP*, *PSEN1*, and *PSEN2*, typically affect the APP cleavage.

In families carrying these genes, very-early-onset Alzheimer's disease is rampant, with family members often developing symptoms in their thirties and forties. Luckily, these mutations are very rare, but they occur in 10 percent of early-onset Alzheimer's cases (or about 1 percent of total cases). People with Down syndrome also tend to accumulate large amounts of amyloid plaques over time, because of genes related to APP cleavage that reside on chromosome 21.

科學家已經發現了一些基因突變，這些突變會促進 β -澱粉樣蛋白非常快速地積累，幾乎確保了某人會患上這種疾病，而且通常是在相當年輕的時候。這些突變（最常見的是 APP、PSEN1 和 PSEN2）通常會影響 APP 裂解。在攜帶這些基因的家庭中，早發性阿茲海默症十分猖獗，家庭成員常在三、四十歲時出現症狀。幸運的是，這些突變非常罕見，但它們發生在 10% 的早發性阿茲海默症病例中（或約佔總病例的 1%）。由於與 APP 裂解相關的基因位於 21 號染色體上，患有唐氏症的人也傾向於隨著時間的推移累積大量的澱粉樣斑塊。

It was not a huge leap to conclude, on the basis of available evidence, that Alzheimer's disease is caused directly by this accumulation of amyloid-beta in the brain. The "amyloid hypothesis," as it's called, has been the dominant theory of Alzheimer's disease since the 1980s, and it has driven the research priorities of the National Institutes of Health and the pharmaceutical industry alike. If you could eliminate the amyloid, the thinking has been, then you could halt or even reverse the progression of the disease. But it hasn't worked out that way. Several dozen drugs have been developed that target amyloid-beta in one way or another. But even when they succeed in clearing amyloid or slowing its production, these drugs have yet to show benefit in improving patients' cognitive function or slowing the progression of the disease. Every single one of them failed.

根據現有證據，得出阿茲海默症是由大腦中 β 澱粉樣蛋白累積直接引起的結論並不是一個巨大的飛躍。自 1980 年代以來，所謂的「澱粉樣蛋白假說」一直是阿茲海默症的主導理論，它推動了美國國立衛生研究院和製藥業的研究重點。人們一直認為，如果能夠消除澱粉樣蛋白，那麼就可以阻止甚至逆轉疾病的進展。但事實並非如此。已經開發出

數十種以某種方式靶向 β -澱粉樣蛋白的藥物。但即使它們成功清除澱粉樣蛋白或減緩其產生，這些藥物尚未顯示出在改善患者認知功能或減緩疾病進展方面的益處。他們每個人都失敗了。

One hypothesis that emerged, as these drugs were failing one after another, was that patients were being given the drugs too late, when the disease had already taken hold. It is well known that Alzheimer's develops slowly, over decades. What if we gave the drugs earlier? This promising hypothesis has been tested in large and well-publicized clinical trials involving people with an inherited mutation that basically predestines them to early-onset Alzheimer's, but those, too, failed in the end. A broader clinical trial was launched in 2022 by Roche and Genentech, testing early administration of an anti-amyloid compound in genetically normal people with verified amyloid accumulation in their brains but no clear symptoms of dementia; results are expected in 2026. Some researchers think that the disease process might be reversible at the point where amyloid is present but not tau, which appears later. That theory is being tested in yet another ongoing study.

隨著這些藥物相繼失效，出現了一種假設：當疾病已經發病時，患者服用藥物的時間太晚了。眾所周知，阿茲海默症的發展緩慢，需要數十年的時間。如果我們早點服藥會怎樣？這個有希望的假設已經在大型且廣為人知的臨床試驗中得到了檢驗，這些臨床試驗涉及具有遺傳突變的人，這種突變基本上註定了他們患有早發性阿茲海默症，但這些最終也失敗了。羅氏(Roche) 和基因泰克(Genentech) 於2022 年啟動了一項更廣泛的臨床試驗，測試在基因正常的人群中早期施用抗澱粉樣蛋白化合物，這些人群已證實大腦中有澱粉樣蛋白積累，但沒有明顯的癡呆症狀；預計將於 2026 年得出結果。一些研究人員認為，當澱粉樣蛋白出現但 tau 蛋白出現較晚時，疾病過程可能是可逆的。該理論正在另一項正在進行的研究中得到檢驗。

Meanwhile, in June of 2021, the FDA gave approval to an amyloid-targeting drug called aducanumab (Aduhelm). The drug's maker, Biogen, had submitted data for approval twice before and had been turned down. This was its third try. The agency's expert advisory panel recommended against approving the drug this time as well, saying the evidence of a benefit was

weak or conflicted, but the agency went ahead and approved it anyway. It has met a tepid reception in the marketplace, with Medicare and some insurers refusing to pay its \$28,000 annual cost unless it is being used in a clinical trial at a university.

同時，2021 年 6 月，FDA 批准了一種名為 aducanumab (Aduhelm) 的澱粉樣蛋白標靶藥物。該藥物的製造商百健 (Biogen) 此前曾兩次提交數據申請批准，但均被拒絕。這是它的第三次嘗試。該機構的專家顧問小組這次也建議不要批准該藥物，稱其益處的證據薄弱或相互矛盾，但該機構還是繼續批准了該藥物。它在市場上的反應不溫不火，醫療保險和一些保險公司拒絕支付其每年 28,000 美元的費用，除非它被用於大學的臨床試驗。

This cascade of drug failures has caused frustration and confusion in the Alzheimer's field, because amyloid has long been considered a signature of the disease. As Dr. Ronald Petersen, director of the Mayo Clinic Alzheimer's Disease Research Center, put it to *The New York Times* in 2020: "Amyloid and tau define the disease....To not attack amyloid doesn't make sense."

這一連串的藥物失敗引起了阿茲海默症領域的沮喪和困惑，因為澱粉樣蛋白長期以來一直被認為是這種疾病的特徵。正如 Mayo Clinic 阿茲海默症研究中心主任 Ronald Petersen 博士在 2020 年向《紐約時報》所說：「澱粉樣蛋白和 tau 蛋白定義了這種疾病...不攻擊澱粉樣蛋白是沒有意義的。」

But some scientists have begun to openly question the notion that amyloid causes *all* cases of Alzheimer's disease, citing these drug failures above all. Their doubts seemed to be validated in July of 2022, when *Science* published an article calling into question a widely cited 2006 study that had given new impetus to the amyloid theory, at a time when it had already seemed to be weakening. The 2006 study had pinpointed a particular subtype of amyloid that it claimed directly caused neurodegeneration. That in turn inspired numerous investigations into that subtype. But according to the *Science* article, key images in that study had been falsified.

但一些科學家開始公開質疑澱粉樣蛋白導致所有阿茲海默症的觀點，首先列舉了這些藥物的失敗。他們的懷疑似乎在2022年7月得到了證實，當時《科學》雜誌發表了一篇文章，對2006年一項被廣泛引用的研究提出了質疑，該研究為澱粉樣蛋白理論提供了新的推動力，而當時該理論似乎已經在減弱。2006年的研究指出了澱粉樣蛋白的一種特殊亞型，聲稱這種亞型直接導致神經退化。這反過來又激發了對此亞型的大量研究。但根據《科學》雜誌的文章，該研究中的關鍵圖像已被偽造。

There was already plenty of other evidence calling into question the causal relationship that has long been assumed between amyloid and neurodegeneration. Autopsy studies have found that more than 25 percent of cognitively normal people nevertheless had large deposits of amyloid in their brains when they died—some of them with the same degree of plaque buildup as patients who died with severe dementia. But for some reason, these people displayed no cognitive symptoms. This was not actually a new observation: Blessed, Tomlinson, and Roth noted back in 1968 that other researchers had observed “plaque formation and other changes [that] were sometimes just as intense in normal subjects as in cases of senile dementia.”

已經有大量其他證據對長期以來人們認為的澱粉樣蛋白和神經退化之間的因果關係提出了質疑。屍檢研究發現，超過25%的認知正常的人在死亡時大腦中仍然存在大量澱粉樣蛋白沉積，其中一些人的斑塊堆積程度與死於嚴重癡呆症的患者相同。但由於某些原因，這些人並沒有表現出認知症狀。這實際上並不是一個新的觀察結果：布萊塞德、湯姆林森和羅斯早在1968年就指出，其他研究人員觀察到「斑塊形成和其他變化有時在正常受試者中與老年癡呆症病例中一樣強烈」。

Some experts maintain that these patients actually did have the disease but that its symptoms had been slower to emerge, or that they had somehow masked or compensated for the damage to their brains. But more recent studies have found that the reverse can also be true: some patients with all the symptoms of Alzheimer’s disease, including significant cognitive decline, have little to no amyloid in their brains, according to amyloid PET scans and/or cerebrospinal fluid (CSF) biomarker testing, two common diagnostic

techniques. Researchers from the Memory and Aging Center at University of California San Francisco found via PET scans that close to one in three patients with mild to moderate dementia had no evidence of amyloid in their brains. Still other studies have found only a weak correlation between the degree of amyloid burden and the severity of disease. It appears, then, that the presence of amyloid-beta plaques may be neither necessary for the development of Alzheimer's disease nor sufficient to cause it.

一些專家堅持認為，這些患者確實患有這種疾病，但症狀出現得較慢，或者他們以某種方式掩蓋或補償了大腦的損傷。但最近的研究發現，相反的情況也可能成立：根據澱粉樣蛋白PET 掃描和/或腦脊髓液(CSF)，一些患有阿茲海默症所有症狀（包括顯著認知能力下降）的患者，其大腦中幾乎沒有澱粉樣蛋白。生物標記測試，兩種常見的診斷技術。加州大學舊金山分校記憶與老化中心的研究人員透過 PET 掃描發現，近三分之一的輕度至中度癡呆患者的大腦中沒有澱粉樣蛋白的證據。還有其他研究發現澱粉樣蛋白負荷程度與疾病嚴重程度之間的相關性很弱。那麼， β -澱粉樣蛋白斑塊的存在可能既不是阿茲海默症發生所必需的，也不足以引起此病。

This raises another possibility: that the condition that Alois Alzheimer observed in 1906 was not the same condition as the Alzheimer's disease that afflicts millions of people around the world. One major clue has to do with the age of onset. Typically, what we call Alzheimer's disease (or late-onset Alzheimer's disease) does not present in significant numbers until age sixty-five. But Dr. Alzheimer's own Patient Zero, Auguste Deter, showed severe symptoms by the time she was fifty, a trajectory more in line with early-onset Alzheimer's disease than with the dementia that slowly begins to afflict people in their late sixties, seventies, and eighties. A 2013 analysis of preserved tissue from Auguste Deter's brain found that she did in fact carry the *PSEN1* mutation, one of the early-onset dementia genes. (It affects the cleavage of the amyloid precursor protein, producing loads of amyloid.) She did have Alzheimer's disease, but a form of it that you get *only* because you have one of these highly deterministic genes. Our mistake might have been to assume

that the other 99 percent of Alzheimer's disease cases progress the way hers did.

這就提出了另一種可能性：阿洛伊斯·阿茲海默 (Alois Alzheimer) 在 1906 年觀察到的情況與困擾全世界數百萬人的阿茲海默症不同。一個主要線索與發病年齡有關。通常，我們所說的阿茲海默症（或遲發性阿茲海默症）直到六十五歲才會大量出現。但阿茲海默博士自己的零號病人奧古斯特·德特在五十歲的時候就表現出了嚴重的症狀，這一軌跡更符合早發性阿茲海默症，而不是慢慢開始困擾六、七十歲人群的癡呆症。八十年代。2013 年對奧古斯特·德特 (Auguste Deter) 大腦保存組織的分析發現，她實際上帶有 PSEN1 突變，這是早發性癡呆基因之一。（它會影響澱粉樣蛋白前體蛋白的裂解，產生大量澱粉樣蛋白。）她確實患有阿茲海默症，但這種疾病的一種形式只是因為你擁有這些高度確定性的基因之一。我們的錯誤可能在於假設其他 99% 的阿茲海默症病例的進展與她的情況相同。

This is not all that uncommon in medicine, where the index case for a particular disease turns out to be the exception rather than the rule; extrapolating from this one case can lead to problems and misunderstanding down the road. At the same time, if Auguste Deter's illness had appeared when she was seventy-five instead of fifty, then perhaps it might not have seemed remarkable at all.

這在醫學上並不少見，某種特定疾病的指示病例被證明是例外而不是規則。從這一案例進行推論可能會導致日後出現問題和誤解。同時，如果奧古斯特·德特的病是在她七十五歲而不是五十歲的時候出現的，那麼也許這看起來根本就不是什麼了不起的事情。

Just as Alzheimer's disease is defined (rightly or wrongly) by accumulations of amyloid and tau, Lewy body dementia and Parkinson's disease are associated with the accumulation of a neurotoxic protein called alpha-synuclein, which builds up in aggregates known as Lewy bodies (first observed by a colleague of Alois Alzheimer's named Friedrich Lewy). The *APOE e4* variant not only increases someone's risk for Alzheimer's but also significantly raises their risk of Lewy body dementia as well as Parkinson's

disease with dementia, further supporting the notion that these conditions are related on some level.

正如阿茲海默症的定義（正確或錯誤）是澱粉樣蛋白和tau 蛋白的積累一樣，路易體癡呆和帕金森氏症與一種稱為 α -突觸核蛋白的神經毒性蛋白的積累有關，這種蛋白以稱為路易氏體的聚集體形式累積（首先觀察到）由阿洛伊斯·阿茲海默症的同事弗里德里希·路易（Friedrich Lewy）提出）。APOE e4 變異體不僅會增加某人罹患阿茲海默症的風險，還會顯著增加路易氏體失智症以及帕金森氏症伴隨失智症的風險，這進一步支持了這些疾病在某種程度上相關的觀點。

All this places high-risk patients like Stephanie in a terrible predicament: they are at increased risk of developing a disorder or disorders whose causes we still do not fully understand, and for which we lack effective treatments. That means we need to focus on what until fairly recently was considered a taboo topic in neurodegenerative disease: prevention.

所有這些都使像史蒂芬妮這樣的高風險患者陷入可怕的困境：他們患上一種或多種疾病的風險增加，而這些疾病的原因我們仍然不完全了解，而且我們缺乏有效的治療方法。這意味著我們需要關注直到最近才被認為是神經退化性疾病的禁忌話題：預防。

Can Neurodegenerative Disease Be Prevented?

神經退化性疾病可以預防嗎？

Stephanie was terrified. I had treated other patients who had two copies of the *e4* gene, but none of them had responded with this much fear and anxiety. It took us four long discussions over a period of two months just to get her past the initial shock of the news. Then it was time to have a talk about what to do.

史蒂芬妮很害怕。我曾治療過其他有兩個 e4 基因拷貝的患者，但沒有一個人表現出如此強烈的恐懼和焦慮。我們在兩個月的時間裡進行了

四次長時間的討論，讓她擺脫了這個消息最初的震驚。然後是時候討論該做什麼了。

She had no obvious signs of cognitive impairment or memory loss. Yet. Just as a side note, some of my patients freak out because they lose their car keys or their phones from time to time. As I keep reminding them, that does not mean they have Alzheimer's disease. It generally only means that they are busy and distracted (ironically, often by the very same cell phones that they keep misplacing). Stephanie was different. Her risk was real, and now she knew it.

她沒有明顯的認知障礙或記憶喪失跡象。然而。順便說一句，我的一些病人因為時不時丟失車鑰匙或手機而感到驚慌。正如我不斷提醒他們的那樣，這並不意味著他們患有阿茲海默症。這通常只意味著他們很忙並且分心（諷刺的是，他們經常被他們不斷放錯地方的同一部手機所干擾）。史蒂芬妮則不同。她的風險是真實存在的，現在她知道了。

With my highest-risk patients, like Stephanie, I would at that time typically collaborate with Dr. Richard Isaacson, who opened the first Alzheimer's disease prevention clinic in the United States in 2013. Richard remembers that when he first interviewed with the dean of Weill Cornell Medical College and described his proposed venture, she seemed taken aback by his then-radical idea; the disease was not considered to be preventable. Also, at barely thirty, he did not look the part. "She was expecting Oliver Sacks," he told me. "Instead, she was sitting across the table from Doogie Howser."

對於像史蒂芬妮這樣風險最高的患者，我當時通常會與理查德·艾薩克森博士合作，他於2013 年在美國開設了第一家阿茲海默症預防診所。理查德記得當他第一次採訪威爾學院院長時康奈爾醫學院並描述了他提議的冒險活動，她似乎對他當時激進的想法感到驚訝；這種疾病不被認為是可以預防的。而且，他還不到三十歲，看起來也不像那個人。「她正在等奧利佛薩克斯，」他告訴我。“相反，她坐在杜吉·豪瑟的桌子對面。”

Isaacson had gone off to college at age seventeen, to a joint BA-MD program at the University of Missouri in Kansas City and had his medical degree in hand by the time he was twenty-three. He was motivated to learn as much as possible about Alzheimer's disease by the fear that it ran in his family.

艾薩克森十七歲時就開始上大學，在堪薩斯城的密蘇里大學攻讀學士-醫學博士聯合項目，並在二十三歲時獲得了醫學學位。由於擔心他的家族會遺傳這種疾病，他有動力盡可能多地了解阿茲海默症。

When he was growing up in Commack, Long Island, Richard had watched his favorite relative, his great-uncle Bob, succumb to Alzheimer's disease. When Richard was three, Uncle Bob had saved him from drowning in a swimming pool at a family party. But about a decade later, his beloved uncle had begun to change. He repeated his stories. His sense of humor faded. He developed a vacant stare and seemed to take longer to process what he was hearing around him. He was eventually diagnosed with Alzheimer's disease—but he was already gone. It was as if he had vanished.

當理查德在長島康馬克長大時，他目睹了他最喜歡的親戚，他的叔祖父鮑勃死於阿茲海默症。當理查三歲的時候，叔叔鮑伯在一次家庭聚會的游泳池裡救了他，使他免於溺水。但大約十年後，他深愛的叔叔開始改變。他重複了他的故事。他的幽默感消失了。他眼神空洞，似乎需要更長的時間來處理周圍聽到的聲音。他最終被診斷出患有阿茲海默症，但他已經去世了。他就像憑空消失了一樣。

Richard couldn't stand to watch his favorite uncle be reduced to nothing. He was also worried because he knew that Alzheimer's disease risk has a strong genetic component. Was he also at risk? Were his parents? Could the disease somehow be prevented?

理查德無法忍受看著他最喜歡的叔叔變得一無所有。他也很擔心，因為他知道阿茲海默症的風險有很強的遺傳因素。他也有危險嗎？是他的父母嗎？這種疾病可以透過某種方式預防嗎？

As he went into medical practice at the University of Miami, he began collecting every single study and recommendation he could find on possible

ways to reduce risk of Alzheimer's disease, gathering them into a photocopied sheaf that he would hand out to patients. He published the sheaf in 2010 as a book titled *Alzheimer's Treatment, Alzheimer's Prevention: A Patient and Family Guide*.

當他進入邁阿密大學從事醫療實踐時，他開始收集他能找到的關於降低阿茲海默症風險的可能方法的每一項研究和建議，並將它們收集成複印的一捆，然後分發給患者。2010年，他將這捆書出版為《阿茲海默症治療、阿茲海默症預防：病患與家屬指南》一書。

He soon found out that in Alzheimer's disease circles, the very word *prevention* was somewhat off limits. "The Alzheimer's Association said, you can't really say this," he remembers. That same year, a panel of experts assembled by the National Institutes of Health declared, "Currently, firm conclusions cannot be drawn about the association of any modifiable risk factor with cognitive decline or Alzheimer's disease."

他很快發現，在阿茲海默症圈子裡，「預防」這個詞在某種程度上是被禁止的。「阿茲海默症協會說，你不能真的這麼說，」他回憶道。同年，美國國立衛生研究院組建的專家小組宣布：“目前，無法就任何可改變的風險因素與認知能力下降或阿茲海默症之間的關係得出明確的結論。”

That led Isaacson to realize that the only way to show that a preventive approach could work, in a way that would be accepted by the broader medical community, was in a large academic setting. Cornell was willing to take a chance, and his clinic opened in 2013. It was the first of its kind in the country, but now there are half a dozen similar centers, including one in Puerto Rico. (Isaacson now works for a private company in New York; his colleague, Dr. Kellyann Niotis, has joined my practice, focusing on patients at risk for neurodegenerative diseases.)

這使得艾薩克森認識到，要證明預防性方法可以發揮作用，並且能夠被更廣泛的醫學界接受，唯一的方法就是在大型學術環境中。康奈爾願意冒險，他的診所於2013年開業。這是該國第一個此類中心，但現在有六個類似的中心，其中包括波多黎各的一家。（艾薩克森現在在

紐約的一家私人公司工作；他的同事凱莉安·尼奧蒂斯博士加入了我的診所，專注於有神經退化性疾病風險的患者。）

Meanwhile, the idea of preventing Alzheimer's disease began to gain scientific support. A two-year randomized controlled trial in Finland, published in 2015, found that interventions around nutrition, physical activity, and cognitive training helped maintain cognitive function and prevent cognitive decline among a group of more than 1,200 at-risk older adults. Two other large European trials have found that multidomain lifestyle-based interventions have improved cognitive performance among at-risk adults. So there were signs of hope.

同時，預防阿茲海默症的想法開始獲得科學支持。2015年在芬蘭發表的一項為期兩年的隨機對照試驗發現，圍繞營養、身體活動和認知訓練的干預措施有助於維持 1,200 多名高風險老年人的認知功能並防止認知能力下降。另外兩項大型歐洲試驗發現，基於生活方式的多領域干預措施可以改善高風險成年人的認知能力。所以出現了希望的跡象。

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To a typical doctor, Stephanie's case would have seemed pointless: She had no symptoms and she was still relatively young, in her early forties, a good two decades before any clinical dementia was likely to develop. Medicine 2.0 would say there was nothing for us to treat yet. In Medicine 3.0, this makes her an ideal patient, and her case an urgent one. If there were ever a disease that called for a Medicine 3.0 approach—where prevention is not only important but our *only option*—Alzheimer's disease and related neurodegenerative diseases are it.

對於典型的醫生來說，史蒂芬妮的病例似乎毫無意義：她沒有任何症狀，而且還相對年輕，四十歲出頭，比可能出現任何臨床癡呆症早了整整二十年。醫學2.0會說我們還沒有什麼可以治療的。在醫學 3.0 中，這使她成為理想的患者，而且她的病例也很緊急。如果有一種疾

病需要醫學 3.0 方法——預防不僅重要，而且是我們唯一的選擇——阿茲海默症和相關的神經退化性疾病就是它。

Frankly, it might seem odd for a practice as small as ours to employ a full-time preventive neurologist such as Kellyann Niotis. Why do we do this? Because we think we can really move the needle by starting early and being very rigorous in how we quantify and then try to address each patient's risk. Some patients, like Stephanie, are at obvious higher risk; but in a broader sense, all of us are at some risk of Alzheimer's disease and other neurodegenerative disease.

坦白說，對於像我們這樣的小診所來說，聘請凱莉安·尼奧蒂斯這樣的全職預防性神經科醫生似乎很奇怪。我們為什麼要做這個？因為我們認為，透過儘早開始並非常嚴格地量化然後嘗試解決每個患者的風險，我們確實可以取得進展。有些患者，如史蒂芬妮，面臨明顯更高的風險；但從更廣泛的意義上來說，我們所有人都面臨著阿茲海默症和其他神經退化性疾病的某種風險。

Viewed through the lens of prevention, the fact that Stephanie had the *APOE e4/e4* genotype was actually good news, in a way. Yes, she was at far higher risk than someone with *e3/e3*, but at least we knew the genes we were up against and the likely trajectory of the disease, if she developed it. It is more worrying when a patient presents with an overwhelming family history of dementia, or the early signs of cognitive decline, but does *not* carry any of the known Alzheimer's risk genes, such as *APOE e4* and a few others. That means that there could be some other risk genes in play, and we don't know what they might be. Stephanie was at least facing a known risk. This was a start.

從預防的角度來看，史蒂芬妮攜帶 *APOE e4/e4* 基因型的事實在某種程度上實際上是個好消息。是的，她的風險比患有 *e3/e3* 的人高得多，但至少我們知道我們所面對的基因以及如果她患有這種疾病的話，疾病可能的發展軌跡。當患者出現明顯的失智症家族史或認知能力下降的早期跡象，但不攜帶任何已知的阿茲海默症風險基因（例如 *APOE e4* 和其他一些基因）時，更令人擔憂。這意味著可能還有其他一些風

險基因在起作用，但我們不知道它們可能是什麼。史蒂芬妮至少面臨一個已知的風險。這是一個開始。

She had two additional risk factors that were out of her control: being Caucasian and being female. While those of African descent are at an overall increased risk of developing Alzheimer's disease, for unclear reasons, *APOE e4* seems to present *less* risk to them than to people of Caucasian, Asian, and Hispanic descent. Regardless of *APOE* genotype, however, Alzheimer's disease is almost twice as common in women than in men. It is tempting to attribute this to the fact that more women live to age eighty-five and above, where incidence of the disease pushes 40 percent. But that alone does not explain the differential. Some scientists believe there may be something about menopause, and the abrupt decline in hormonal signaling, that sharply increases the risk of neurodegeneration in older women. In particular, it appears that a rapid drop in estradiol in women with an *e4* allele is a driver of risk; that, in turn, suggests a possible role for perimenopausal hormone replacement therapy in these women.

她還有兩個無法控制的額外風險因素：白人身分和女性身分。雖然非洲後裔罹患阿茲海默症的風險總體較高，但由於不明原因，*APOE e4* 對他們的風險似乎低於白人、亞洲人和西班牙人後裔。然而，無論 *APOE* 基因型如何，阿茲海默症在女性中的發生率幾乎是男性的兩倍。人們很容易將此歸因於越來越多的女性活到 85 歲及以上的事實，而此時該疾病的發生率高達 40%。但僅憑這一點並不能解釋這種差異。一些科學家認為，更年期和荷爾蒙訊號突然下降可能會急劇增加老年女性神經退化性疾病的風險。特別是，攜帶 *e4* 等位基因的女性雌二醇迅速下降似乎是風險的驅動因素；這反過來表明圍絕經期荷爾蒙替代療法對這些女性可能發揮作用。

Menopause is not the only issue here. Other reproductive history factors, such as the number of children the woman has had, age of first menstruation, and exposure to oral contraceptives, may also have a significant impact on Alzheimer's risk and later life cognition. And new research suggests that women are more prone to accumulate tau, the neurotoxic protein we mentioned earlier. The end result is that women have a greater age-adjusted

risk of Alzheimer's, as well as faster rates of disease progression overall, regardless of age and educational level.

更年期並不是唯一的問題。其他生育史因素，例如女性生育的孩子數量、第一次月經的年齡以及口服避孕藥的使用情況，也可能對阿茲海默症的風險和晚年認知產生重大影響。新的研究表明，女性更容易累積 tau 蛋白，這是我們之前提到的神經毒性蛋白。最終結果是，無論年齡和教育程度如何，女性罹患阿茲海默症的年齡調整風險更大，而且整體疾病進展速度更快。

While female Alzheimer's patients outnumber men by two to one, the reverse holds true for Lewy body dementia and Parkinson's, both of which are twice as prevalent in men. Yet Parkinson's also appears to progress more rapidly in women than in men, for reasons that are not clear.

雖然女性阿茲海默症患者的數量比男性多為二比一，但路易氏體失智症和帕金森氏症的情況卻恰恰相反，這兩種疾病在男性中的盛行率是男性的兩倍。然而，女性帕金森氏症的進展似乎也比男性更快，原因尚不清楚。

Parkinson's is also tricky genetically: While we have identified several gene variants that increase risk for PD, such as *LRRK2* and *SNCA*, about 15 percent of patients diagnosed have some family history of the disease—and are therefore presumed to have a genetic component—but do not have any known risk genes or SNPs.

帕金森氏症在遺傳上也很棘手：雖然我們已經確定了幾種增加帕金森氏症風險的基因變異，例如LRRK2 和SNCA，但大約15% 的診斷患者有一些該疾病的家族史，因此被認為具有遺傳成分，但是沒有任何已知的風險基因或 SNP。

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Like the other Horsemen, dementia has an extremely long prologue. Its beginnings are so subtle that very often the disease isn't recognized until someone is well into its early stages. This is when their symptoms go beyond

occasional lapses and forgetfulness to noticeable memory problems such as forgetting common words and frequently losing important objects (forgetting passwords becomes a problem too). Friends and loved ones notice changes, and performance on cognitive tests begins to slip.

與其他騎士一樣，癡呆症也有一個極其漫長的序幕。它的開始非常微妙，以至於人們常常在早期階段才發現這種疾病。此時，他們的症狀不僅是偶爾的失誤和健忘，而是出現明顯的記憶問題，例如忘記常用單字和經常丟失重要物品（忘記密碼也成為一個問題）。朋友和親人注意到變化，認知測驗的表現開始下滑。

Medicine 2.0 has begun to recognize this early clinical stage of Alzheimer's, which is known as mild cognitive impairment (MCI). But MCI is not the first stage on the long road to dementia: a large 2011 analysis of data from the UK's Whitehall II cohort study found that subtler signs of cognitive changes often become apparent well before patients meet the criteria for MCI. This is called stage I preclinical Alzheimer's disease, and in the United States alone over forty-six million people are estimated to be in this stage, where the disease is slowly laying the pathological scaffolding in and around neurons but major symptoms are still largely absent. While it's not clear how many of these patients will go on to develop Alzheimer's, what is clear is that just as most of an iceberg lies beneath the surface of the ocean, dementia can progress unnoticed for years before any symptoms appear.

醫學 2.0 已經開始認識到阿茲海默症的這個早期臨床階段，即所謂的輕度認知障礙 (MCI)。但MCI 並不是通往癡呆症漫長道路上的第一階段：2011 年對英國Whitehall II 隊列研究數據進行的一項大型分析發現，認知變化的微妙跡象往往在患者達到MCI 標準之前就變得明顯。這被稱為第一階段臨床前阿茲海默症，僅在美國，估計就有超過四千六百萬人處於這一階段，該疾病正在神經元內部和周圍緩慢鋪設病理支架，但主要症狀仍然基本上不存在。雖然尚不清楚這些患者中有多少人會繼續患上阿茲海默症，但可以肯定的是，就像大部分冰山位於海面以下一樣，癡呆症可能會在出現任何症狀之前數年不被注意到。

The same is true of other neurodegenerative diseases, although they each have different early warning signs. Parkinson's may show up as subtle changes

in movement patterns, a frozen facial expression, stooped posture or shuffling gait, a mild tremor, or even changes in a person's handwriting (which may become small and cramped). Someone in the early stages of Lewy body dementia may exhibit similar physical symptoms, but with slight cognitive changes as well; both may exhibit alterations in mood, such as depression or anxiety. Something seems “off,” but it's hard for a layperson to pinpoint.

其他神經退化性疾病也是如此，儘管它們各自有不同的早期預警訊號。帕金森氏症可能表現為運動模式的微妙變化、臉部表情僵硬、彎腰或拖著步態、輕微的顫抖，甚至字蹟的變化（可能變得又小又局促）。路易氏體失智症早期階段的人可能會表現出類似的身體症狀，但也會有輕微的認知變化；兩者都可能表現出情緒的變化，例如憂鬱或焦慮。有些東西似乎“不對勁”，但外行人很難準確指出。

This is why an important first step with any patient who may have cognitive issues is to subject them to a grueling battery of tests. One reason I like to have a preventive neurologist on staff is that these tests are so complicated and difficult to administer that I feel they are best left to specialists. They are also critically important to a correct diagnosis—assessing whether the patient is already on the road to Alzheimer's disease or to another form of neurodegenerative dementia, and how far along they might be. These are clinically validated, highly complex tests that cover every domain of cognition and memory, including executive function, attention, processing speed, verbal fluency and memory (recalling a list of words), logical memory (recalling a phrase in the middle of a paragraph), associative memory (linking a name to a face), spatial memory (location of items in a room), and semantic memory (how many animals you can name in a minute, for example). My patients almost always come back complaining about the difficulty of the tests. I just smile and nod.

這就是為什麼對於任何可能有認知問題的患者來說，重要的第一步就是讓他們接受一系列嚴格的測試。我喜歡在工作人員中配備預防性神經科醫生的原因之一是，這些測試非常複雜且難以執行，因此我認為最好將其留給專家。它們對於正確的診斷也至關重要——評估患者是否已經患有阿茲海默症或另一種形式的神經退化性癡呆，以及可能進

展到什麼程度。這些是經過臨床驗證的高度複雜的測試，涵蓋認知和記憶的各個領域，包括執行功能、注意力、處理速度、言語流暢性和記憶（回憶單字清單）、邏輯記憶（回憶段落中間的短語）、聯想記憶（將名字與臉孔連結）、空間記憶（房間中物品的位置）和語意記憶（例如，您在一分鐘內可以說出多少種動物）。我的病人幾乎總是回來抱怨測試的困難。我只是微笑點頭。

The intricacies and nuances of the tests give us important clues about what might be happening inside the brains of patients who are still very early in the process of cognitive change that goes along with age. Most importantly, they enable us to distinguish between normal brain aging and changes that may lead to dementia. One important section of the cognitive testing evaluates the patient's sense of smell. Can they correctly identify scents such as coffee, for example? Olfactory neurons are among the first to be affected by Alzheimer's disease.

這些測試的複雜性和細微差別為我們提供了重要的線索，讓我們了解那些仍處於隨年齡增長而發生的認知變化過程中的早期患者的大腦內部可能發生的情況。最重要的是，它們使我們能夠區分正常的大腦老化和可能導致癡呆的變化。認知測試的一個重要部分是評估患者的嗅覺。例如，他們能正確辨識咖啡等氣味嗎？嗅覺神經元是最早受到阿茲海默症影響的神經元之一。

Specialists such as Richard and Kellyann also become attuned to other, less quantifiable changes in people on the road to Alzheimer's disease, including changes in gait, facial expressions during conversations, even visual tracking. These changes could be subtle and not recognizable to the average person, but someone more skilled can spot them.

理查德和凱利安等專家也開始關注人們在患有阿茲海默症過程中發生的其他難以量化的變化，包括步態、談話時面部表情的變化，甚至視覺追蹤的變化。這些變化可能很微妙，一般人無法識別，但技術更熟練的人可以發現它們。

The trickiest part of the testing is interpreting the results to distinguish among different types of neurodegenerative disease and dementia. Kellyann

dissects the test results to try and trace the likely location of the pathology in the brain, and the specific neurotransmitters that are involved; these determine the pathological features of the disease. Frontal and vascular dementias primarily affect the frontal lobe, a region of the brain responsible for executive functioning such as attention, organization, processing speed, and problem solving. So these forms of dementia rob an individual of such higher-order cognitive features. Alzheimer's disease, on the other hand, predominantly affects the temporal lobes, so the most distinct symptoms relate to memory, language, and auditory processing (forming and comprehending speech)—although researchers are beginning to identify different possible subtypes of Alzheimer's disease, based on which brain regions are most affected. Parkinson's is a bit different in that it manifests primarily as a movement disorder, resulting from (in part) a deficiency in producing dopamine, a key neurotransmitter. While Alzheimer's can be confirmed by testing for amyloid in the cerebrospinal fluid, these other forms of neurodegeneration are largely clinical diagnoses, based on testing and interpretation. Thus, they can be more subjective, but with all these conditions it is critical to identify them as soon as possible, to allow more time for preventive strategies to work.

測試中最棘手的部分是解釋結果以區分不同類型的神經退化性疾病和癡呆症。凱莉安剖析了測試結果，試圖追蹤大腦中病變的可能位置，以及所涉及的特定神經傳導物質；這些決定了疾病的病理特徵。額葉和血管性失智症主要影響額葉，額葉是大腦中負責注意力、組織、處理速度和解決問題等執行功能的區域。因此，這些形式的失智症剝奪了個體的這種高階認知特徵。另一方面，阿茲海默症主要影響顳葉，因此最明顯的症狀與記憶、語言和聽覺處理（形成和理解言語）有關——儘管研究人員開始根據以下數據識別阿茲海默症的不同可能亞型：哪些腦部區域受影響最嚴重。帕金森氏症有點不同，它主要表現為運動障礙，部分原因是缺乏多巴胺（一種關鍵的神經傳導物質）的產生。雖然阿茲海默症可以透過檢測腦脊髓液中的澱粉樣蛋白來確診，但這些其他形式的神經退化性疾病主要是基於檢測和解釋的臨床

診斷。因此，它們可能更加主觀，但鑑於所有這些情況，盡快識別它們至關重要，以便有更多時間讓預防策略發揮作用。

One reason why Alzheimer's and related dementias can be so tricky to diagnose is that our highly complex brains are adept at compensating for damage, in a way that conceals these early stages of neurodegeneration. When we have a thought or a perception, it's not just one neural network that is responsible for that insight, or that decision, but many individual networks working simultaneously on the same problem, according to Francisco Gonzalez-Lima, a behavioral neuroscientist at the University of Texas in Austin. These parallel networks can reach different conclusions, so when we use the expression "I am of two minds about something," that is not scientifically inaccurate. The brain then picks the most common response. There is redundancy built into the system.

阿茲海默症和相關癡呆症的診斷如此棘手的一個原因是，我們高度複雜的大腦善於補償損傷，從而掩蓋了神經退化性疾病的早期階段。該大學的行為神經科學家弗朗西斯科·岡薩雷斯-利馬表示，當我們有一種想法或一種感知時，不僅僅是一個神經網路負責這種洞察力或那種決定，而是許多單獨的網路同時處理同一問題德州奧斯汀。這些平行網路可以得出不同的結論，因此當我們使用「我對某事有兩種想法」這一表達方式時，這在科學上並不是不準確的。然後大腦會選擇最常見的反應。系統內建冗餘。

The more of these networks and subnetworks that we have built up over our lifetime, via education or experience, or by developing complex skills such as speaking a foreign language or playing a musical instrument, the more resistant to cognitive decline we will tend to be. The brain can continue functioning more or less normally, even as some of these networks begin to fail. This is called "cognitive reserve," and it has been shown to help some patients to resist the symptoms of Alzheimer's disease. It seems to take a longer time for the disease to affect their ability to function. "People that have Alzheimer's disease and are very cognitively engaged, and have a good backup pathway, they're not going to decline as quickly," Richard says.

我們在一生中透過教育或經驗，或透過發展說外語或演奏樂器等複雜

技能建立的這些網絡和子網絡越多，我們對認知能力下降的抵抗力就越強。即使其中一些網路開始出現故障，大腦仍可以或多或少地繼續正常運作。這被稱為“認知儲備”，已被證明可以幫助一些患者抵抗阿茲海默症的症狀。疾病似乎需要更長的時間才能影響他們的功能能力。理查德說：“患有阿茲海默症的人認知能力很強，並且有良好的後備途徑，他們的衰退不會那麼快。”

There is a parallel concept known as “movement reserve” that becomes relevant with Parkinson’s disease. People with better movement patterns, and a longer history of moving their bodies, such as trained or frequent athletes, tend to resist or slow the progression of the disease as compared to sedentary people. This is also why movement and exercise, not merely aerobic exercise but also more complex activities like boxing workouts, are a primary treatment/prevention strategy for Parkinson’s. Exercise is the only intervention shown to delay the progression of Parkinson’s.

有一個與帕金森氏症相關的平行概念，稱為「運動儲備」。與久坐的人相比，具有更好運動模式和較長身體運動歷史的人，例如訓練有素或經常運動的人，往往能抵抗或減緩疾病的進展。這也是為什麼運動和鍛煉，不僅僅是有氧運動，還包括拳擊訓練等更複雜的活動，是帕金森氏症的主要治療/預防策略。運動是唯一被證明可以延緩帕金森氏症進展的干預措施。

But it’s difficult to disentangle cognitive reserve from other factors, such as socioeconomic status and education, which are in turn linked to better metabolic health and other factors (also known as “healthy user bias”). Thus, the evidence on whether cognitive reserve can be “trained” or used as a preventive strategy, such as by learning to play a musical instrument or other forms of “brain training,” is highly conflicted and not conclusive—although neither of these can hurt, so why not?

但很難將認知儲備與其他因素分開，例如社會經濟地位和教育，而這些因素又與更好的代謝健康和其他因素（也稱為「健康使用者偏見」）有關。因此，關於認知儲備是否可以被「訓練」或用作預防策略（例如透過學習演奏樂器或其他形式的「大腦訓練」）的證據是高

度矛盾的並且不是結論性的——儘管這些都不能受傷了，那為什麼不呢？

The evidence suggests that tasks or activities that present more varied challenges, requiring more nimble thinking and processing, are more productive at building and maintaining cognitive reserve. Simply doing a crossword puzzle every day, on the other hand, seems only to make people better at doing crossword puzzles. The same goes for movement reserve: dancing appears to be more effective than walking at delaying symptoms of Parkinson's disease, possibly because it involves more complex movement.

有證據表明，提出更多不同挑戰、需要更靈活思維和處理的任務或活動在建立和維持認知儲備方面更有成效。另一方面，每天簡單地做填字遊戲似乎只會讓人們更擅長做填字遊戲。運動儲備也是如此：跳舞似乎比步行更能有效延緩帕金森氏症的症狀，可能是因為它涉及更複雜的運動。

This was one thing that Stephanie, a high-performing, well-educated professional, had in her favor. Her cognitive reserve was very robust, and her baseline scores were strong. This meant that we likely had plenty of time to devise a prevention strategy for her, perhaps decades—but given her increased genetic risk, we could not afford to delay. We needed to come up with a plan. What would that plan look like? How can this seemingly unstoppable disease be prevented?

史蒂芬妮是一位表現出色、受過良好教育的專業人士，這一點對她有利。她的認知儲備非常強大，基線分數也很高。這意味著我們可能有足夠的時間為她制定預防策略，也許是幾十年，但考慮到她的遺傳風險增加，我們不能再拖延了。我們需要製定一個計劃。該計劃會是什麼樣子？如何預防這種看似無法阻止的疾病？

We'll start by taking a closer look at changes that might be happening *inside* the brain of someone on the road to Alzheimer's. How are these changes contributing to the progression of the disease, and can we do anything to stop them or limit the damage?

首先，我們將仔細研究患有阿茲海默症的人的大腦內部可能發生的變化。這些變化如何導致疾病的進展，我們可以採取什麼措施來阻止它們或限制損害？

Once we begin looking at Alzheimer's disease outside the prism of the amyloid theory, we start to see certain other defining characteristics of dementia that might offer opportunities for prevention—weaknesses in our opponent's armor.

一旦我們開始在澱粉樣蛋白理論的棱鏡之外觀察阿茲海默症，我們就會開始看到癡呆症的某些其他定義特徵，這些特徵可能為預防提供機會——對手盔甲的弱點。

Alternatives to Amyloid

澱粉樣蛋白的替代品

For decades, almost in tandem with observations of plaques and tangles, researchers have also noted problems with cerebral blood flow, or “perfusion,” in patients with dementia. On autopsy, Alzheimer's brains often display marked calcification^[*] of the blood vessels and capillaries that feed them. This is not a new observation: In their seminal 1968 paper that defined Alzheimer's disease as a common age-related condition, Blessed, Tomlinson, and Roth had also noted severe vascular damage in the brains of their deceased study subjects. The phenomenon had been noted in passing for decades, as far back as 1927. But it was generally considered to be a consequence of neurodegeneration and not a potential cause.

幾十年來，幾乎在觀察斑塊和纏結的同時，研究人員也注意到癡呆症患者的腦血流或「灌注」問題。在屍檢中，阿茲海默症的大腦經常顯示出為其供血的血管和毛細血管的明顯鈣化[*]。這並不是一個新的觀察結果：Blessed、Tomlinson 和Roth 在1968 年發表的開創性論文中將阿茲海默症定義為一種常見的與年齡相關的疾病，他們還注意到已故研究對象的大腦中存在嚴重的血管損傷。早在 1927 年，這種現象幾十

年來就已被人們注意到。但人們普遍認為這是神經退化性變的結果，而不是潛在的原因。

In the early 1990s, a Case Western Reserve neurologist named Jack de la Torre was flying to Paris for a conference and thinking about the origins of Alzheimer's disease. The amyloid hypothesis was still fairly new, but it didn't sit well with de la Torre because of what he had observed in his own lab. On the flight, he had a eureka moment. "The evidence from dozens of rat experiments seemed to be screaming at me," he later wrote. In those experiments, he had restricted the amount of blood flowing to the rats' brains, and over time they had developed symptoms remarkably similar to those of Alzheimer's disease in humans: memory loss and severe atrophy of the cortex and hippocampus. Restoring blood flow could halt or reverse the damage to some extent, but it seemed to be more severe and more lasting in older animals than younger ones. The key insight was that robust blood flow seemed to be critical to maintaining brain health.

1990 年代初，凱斯西儲大學的一位名叫傑克·德拉托雷 (Jack de la Torre) 的神經學家飛往巴黎參加一個會議，思考阿茲海默症的起源。澱粉樣蛋白假說仍然是相當新的，但由於德拉托雷在自己的實驗室中觀察到的情況，它並不適合他。在飛機上，他突然靈光一現。「數十次老鼠實驗的證據似乎在向我尖叫，」他後來寫道。在這些實驗中，他限制了流向老鼠大腦的血液量，隨著時間的推移，它們出現了與人類阿茲海默症非常相似的症狀：記憶喪失以及皮質和海馬體的嚴重萎縮。恢復血流可以在一定程度上阻止或逆轉損傷，但老年動物的損傷似乎比年輕動物更嚴重、更持久。關鍵的見解是，強烈的血流似乎對維持大腦健康至關重要。

The brain is a greedy organ. It makes up just 2 percent of our body weight, yet it accounts for about 20 percent of our total energy expenditure. Its eighty-six billion neurons *each* have between one thousand and ten thousand synapses connecting them to other neurons or target cells, creating our thoughts, our personalities, our memories, and the reasoning behind both our good and bad decisions. There are computers that are bigger and faster, but no machine yet made by man can match the brain's ability to intuit and learn, much less feel

or create. No computer possesses anything approaching the multidimensionality of the human self. Where a computer is powered by electricity, the beautiful machine that is the human brain depends on a steady supply of glucose and oxygen, delivered via a huge and delicate network of blood vessels. Even slight disruptions to this vascular network can result in a crippling or even fatal stroke.

大腦是一個貪婪的器官。它只占我們體重的 2%，但卻占我們總能量消耗的 20% 左右。它有八百六十億個神經元，每個神經元都有一千到一萬個突觸，將它們與其他神經元或目標細胞連結起來，創造了我們的思想、我們的個性、我們的記憶，以及我們好的和壞的決定背後的推理。現在有更大、更快的計算機，但人類製造的任何機器都無法與大腦的直覺和學習能力相媲美，更不用說感覺或創造了。沒有電腦擁有任何接近人類自我的多維性。電腦是由電力驅動的，而人腦這台美麗的機器則依賴於透過巨大而脆弱的血管網絡提供穩定的葡萄糖和氧氣。即使血管網絡受到輕微破壞，也可能導致嚴重甚至致命的中風。

On top of this, brain cells metabolize glucose in a different way from the rest of the body; they do not depend on insulin, instead absorbing circulating glucose directly, via transporters that essentially open a gate in the cell membrane. This enables the brain to take top priority to fuel itself when blood glucose levels are low. If we lack new sources of glucose, the brain's preferred fuel, the liver converts our fat into ketone bodies, as an alternative energy source that can sustain us for a very long time, depending on the extent of our fat stores. (Unlike muscle or liver, the brain itself does not store energy.) When our fat runs out, we will begin to consume our own muscle tissue, then our other organs, and even bone, all in order to keep the brain running at all costs. The brain is the last thing to shut off.

最重要的是，腦細胞以與身體其他部位不同的方式代謝葡萄糖。它們不依賴胰島素，而是透過本質上打開細胞膜閘門的轉運蛋白直接吸收循環葡萄糖。當血糖水平較低時，這使得大腦能夠優先考慮為自己提供能量。如果我們缺乏新的葡萄糖來源（大腦首選的燃料），肝臟會將我們的脂肪轉化為酮體，作為一種替代能源，可以維持我們很長一段時間，這取決於我們脂肪儲存的程度。（與肌肉或肝臟不同，大腦

本身不會儲存能量。) 當我們的脂肪耗盡時，我們將開始消耗我們自己的肌肉組織，然後是我們的其他器官，甚至骨骼，所有這些都是為了保持大腦運轉成本。大腦是最後要關閉的東西。

As his plane crossed the Atlantic, de la Torre scribbled down his ideas on the only available writing surface, which happened to be an air-sickness bag. The flight attendants looked grim as he asked for another bag, and another. His “barf bag theory,” as he jokingly called it, was that Alzheimer’s disease is primarily a vascular disorder of the brain. The dementia symptoms that we see result from a gradual reduction in blood flow, which eventually creates what he calls a “neuronal energy crisis,” which in turn triggers a cascade of unfortunate events that harms the neurons and ultimately causes neurodegeneration. The amyloid plaques and tangles come later, as a consequence rather than a cause. “We believed, and still do, that amyloid-beta is an important pathological *product* of neurodegeneration,” de la Torre wrote recently, “...[but] it is not the cause of Alzheimer’s disease.”

當他的飛機飛越大西洋時，德拉托雷在唯一可用的書寫表面上寫下了他的想法，而這個書寫表面恰好是一個暈機袋。當他要一個又一個行李時，空服員表情嚴肅。他開玩笑地稱之為“嘔吐袋理論”，即阿茲海默症主要是一種大腦血管疾病。我們看到的癡呆症症狀是由於血流量逐漸減少造成的，這最終會造成他所說的“神經元能量危機”，進而引發一系列不幸事件，損害神經元並最終導致神經變性。澱粉樣斑塊和纏結隨後出現，是結果而不是原因。“我們相信，並且仍然相信， β 澱粉樣蛋白是神經退化的重要病理產物，”德拉托雷最近寫道，“.....[但]它不是阿茲海默症的原因。”

There was already evidence to support his theory. Alzheimer’s is more likely to be diagnosed in patients who have suffered a stroke, which typically results from a sudden blockage of blood flow in specific regions of the brain. In these cases, symptoms emerge abruptly, as if a switch has been flipped. Additionally, it has been established that people with a history of cardiovascular disease are at a higher risk of developing Alzheimer’s disease. Evidence also demonstrates a linear relationship between cognitive decline and increased intimal media thickness in the carotid artery, a major blood

vessel that feeds the brain. Cerebral blood flow already declines naturally during the aging process, and this arterial thickening, a measure of arterial aging, could cause a further reduction in cerebral blood supply. Vascular disease is not the only culprit here either. In all, some two dozen known risk factors for Alzheimer's disease also happen to reduce blood flow, including high blood pressure, smoking, head injury, and depression, among others. The circumstantial evidence is strong.

已經有證據支持他的理論。中風的患者更有可能診斷出阿茲海默症，中風通常是由於大腦特定區域的血流突然阻塞造成的。在這些情況下，症狀會突然出現，就像開關被打開一樣。此外，已經確定有心血管疾病史的人患阿茲海默症的風險更高。證據還表明，認知能力下降與頸動脈內膜中層厚度增加之間存在線性關係，頸動脈是為大腦供血的主要血管。在老化過程中，腦血流量已經自然下降，而這種動脈增厚（動脈老化的衡量標準）可能會導致腦部供血進一步減少。血管疾病也不是唯一的罪魁禍首。總之，大約有兩打已知的阿茲海默症危險因子也會減少血流量，包括高血壓、吸菸、頭部受傷和憂鬱症等。間接證據是有力的。

Improved neuroimaging techniques have confirmed not only that cerebral perfusion is decreased in brains affected by Alzheimer's disease but also that a drop in blood flow seems to predict *when* a person will transition from preclinical Alzheimer's disease to MCI, and on to full-fledged dementia. Although vascular dementia is currently considered distinct from dementia due to Alzheimer's, making up roughly 15 to 20 percent of dementia diagnoses in North America and Europe, and up to 30 percent in Asia and developing countries, its symptoms and pathology overlap so significantly that de la Torre considers them different manifestations of the same basic condition.

改進的神經影像技術不僅證實了受阿茲海默症影響的大腦中的腦灌注減少，而且血流量的下降似乎可以預測一個人何時會從臨床前阿茲海默症轉變為輕度認知障礙，進而轉變為全面的癡呆症。儘管血管性癡呆目前被認為與阿茲海默症引起的癡呆不同，在北美和歐洲約佔癡呆診斷的15% 至20%，在亞洲和發展中國家高達30%，但其症狀和病理

學重疊程度如此之大，以至於de la托雷認為它們是同一基本條件的不同表現。

Another compelling and perhaps parallel theory of Alzheimer's disease says that it stems from abnormal glucose metabolism in the brain. Scientists and physicians have long noted a connection between Alzheimer's disease and metabolic dysfunction. Having type 2 diabetes doubles or triples your risk of developing Alzheimer's disease, about the same as having one copy of the *APOE e4* gene. On a purely mechanistic level, chronically elevated blood glucose, as seen in type 2 diabetes and prediabetes/insulin resistance, can directly damage the vasculature of the brain. But insulin resistance alone is enough to elevate one's risk

另一個令人信服且可能平行的阿茲海默症理論認為，該疾病源自於大腦中的葡萄糖代謝異常。科學家和醫生長期以來一直注意到阿茲海默症與代謝功能障礙之間的關聯。患有第 2 型糖尿病會使您罹患阿茲海默症的風險增加一倍或三倍，這與攜帶一份 *APOE e4* 基因副本的風險大致相同。從純粹的機械層面來看，慢性血糖升高（如第 2 型糖尿病和糖尿病前期/胰島素抗性）會直接損害大腦的脈管系統。但光是胰島素抗性就足以增加一個人的風險

Insulin seems to play a key role in memory function. Insulin receptors are highly concentrated in the hippocampus, the memory center of the brain. Several studies have found that spraying insulin right into subjects' noses—administering it as directly as possible into their brains—quickly improves cognitive performance and memory, even in people who have already been diagnosed with Alzheimer's disease. One study found that intranasal insulin helped preserve brain volume in Alzheimer's patients. Clearly, it is helpful to get glucose into neurons; insulin resistance blocks this. As the authors wrote, "Several lines of evidence converge to suggest that central insulin resistance plays a causal role in the development and progression of Alzheimer's disease."

胰島素似乎在記憶功能中發揮關鍵作用。胰島素受體高度集中在海馬體，即大腦的記憶中心。幾項研究發現，將胰島素直接噴入受試者的鼻子（盡可能直接將其注射到他們的大腦中）可以快速改善認知能力

和記憶力，即使對於已經被診斷患有阿茲海默症的人也是如此。一項研究發現，鼻內胰島素有助於保護阿茲海默症患者的腦容量。顯然，讓葡萄糖進入神經元是有幫助的。胰島素阻抗會阻止這一點。正如作者所寫，“多條證據集中表明，中樞胰島素阻抗在阿茲海默症的發生和進展中起著因果作用。”

The signal event here (again) appears to be a drop in energy delivery to the brain, similar to what is seen in the onset of vascular dementia. Brain imaging studies reveal lower brain glucose metabolism, decades before the onset of other symptoms of vascular dementia. Intriguingly, this reduction appears to be especially dramatic in brain regions that are also affected in Alzheimer's disease, including the parietal lobe, which is important for processing and integrating sensory information; and the hippocampus of the temporal lobe, which is critical to memory. Just like reduced blood flow, reduced glucose metabolism essentially starves these neurons of energy, provoking a cascade of responses that include inflammation, increased oxidative stress, mitochondrial dysfunction—and ultimately neurodegeneration itself.

這裡的訊號事件（再次）似乎是大腦能量輸送的下降，類似於血管性失智症發作時所看到的情況。腦部影像研究表明，大腦葡萄糖代謝較低，比血管性失智症的其他症狀早了幾十年。有趣的是，這種減少似乎在也受到阿茲海默症影響的大腦區域尤其顯著，包括頂葉，它對於處理和整合感覺訊息很重要；以及顳葉的海馬體，對記憶至關重要。就像血流量減少一樣，葡萄糖代謝減少本質上會導致這些神經元缺乏能量，引發一系列反應，包括發炎、氧化壓力增加、粒線體功能障礙，最終導致神經退化。

The Role of **APOE e4**

APOE e4 的作用

It is still not completely clear how or why, but *e4* seems to accelerate other risk factors and driver mechanisms for Alzheimer's—particularly metabolic

factors such as reduced brain glucose metabolism, which we've just discussed. Simply put, it appears to make everything worse, including the Alzheimer's gender gap: a woman with one copy of *e4* is four times more likely to develop the disease than a man with the same genotype.

目前尚不完全清楚如何或為何，但 *e4* 似乎會加速阿茲海默症的其他危險因子和驅動機制，特別是代謝因素，例如我們剛剛討論過的腦葡萄糖代謝降低。簡而言之，這似乎讓一切變得更糟，包括阿茲海默症的性別差距：擁有一份 *e4* 拷貝的女性患這種疾病的可能性是擁有相同基因型的男性的四倍。

The protein for which it codes, APOE (apolipoprotein E), plays an important role in both cholesterol transport and glucose metabolism. It serves as the main cholesterol carrier in the brain, moving cholesterol across the blood-brain barrier to supply the neurons with the large amounts of it they require. Hussain Yassine, a neuroscientist at the University of Southern California who studies the role of APOE in Alzheimer's disease, compares its role to that of an orchestra conductor. For some reason, he says, people with the *e4* allele appear to have defects in both cholesterol transport and glucose metabolism, to a degree not seen in those with *e2* or *e3*. Even though the higher risk APOE *e4* protein differs from the harmless *e3* one by just one amino acid, it appears to be less efficient at moving cholesterol into and especially out of the brain. There is also some evidence that the APOE *e4* protein may also cause early breakdown of the blood-brain barrier itself, making the brain more susceptible to injury and eventual degeneration.

它編碼的蛋白質 APOE（載脂蛋白 E）在膽固醇轉運和葡萄糖代謝中發揮重要作用。它是大腦中主要的膽固醇載體，使膽固醇穿過血腦屏障，為神經元提供所需的大量膽固醇。南加州大學的神經科學家侯賽因·亞辛 (Hussain Yassine) 研究 APOE 在阿茲海默症中的作用，他將其作用與管弦樂團指揮的作用進行了比較。他說，出於某種原因，帶有 *e4* 等位基因的人似乎在膽固醇轉運和葡萄糖代謝方面都存在缺陷，其程度在帶有 *e2* 或 *e3* 的人中沒有發現。儘管風險較高的 APOE *e4* 蛋白與無害的 *e3* 蛋白只有一個胺基酸不同，但它在將膽固醇移入大腦、尤其是移出大腦方面似乎效率較低。還有一些證據表明，APOE *e4* 蛋白

也可能導致血腦屏障本身的早期破壞，使大腦更容易受傷並最終退化。

Curiously, *APOE e4* was not always a bad actor. For millions of years, *all* our post-primate ancestors were *e4/e4*. It was the original human allele. The *e3* mutation showed up about 225,000 years ago, while *e2* is a relative latecomer, arriving only in the last 10,000 years. Data from present-day populations with a high prevalence of *e4* suggest that it may have been helpful for survival in environments with high levels of infectious disease: children carrying *APOE e4* in Brazilian favelas are more resistant to diarrhea and have stronger cognitive development, for example. In environments where infectious disease was a leading cause of death, *APOE e4* carriers may have been the lucky ones, in terms of longevity.

奇怪的是，*APOE e4* 並不總是一個壞演員。數百萬年來，我們所有的後靈長類祖先都是 *e4/e4*。這是最初的人類等位基因。*e3*突變大約在225,000年前出現，而*e2*突變相對較晚，直到最近10,000年才出現。來自當今*e4* 患病率較高的人群的數據表明，它可能有助於在傳染病高發環境中生存：例如，巴西貧民窟攜帶*APOE e4* 的兒童對腹瀉的抵抗力更強，認知能力發展也更強。在傳染病是主要死亡原因的環境中，*APOE e4* 攜帶者在長壽方面可能是幸運的。

This survival benefit may have been due to the role of *APOE e4* in promoting inflammation, which can be beneficial in some situations (e.g., fighting infection) but harmful in others (e.g., modern life). As we saw in chapter 7, inflammation promotes atherosclerotic damage to our blood vessels, setting the stage for Alzheimer's disease and dementia. People with Alzheimer's disease often have high levels of inflammatory cytokines such as TNF-alpha and IL-6 in their brains, and studies have also found higher levels of neuroinflammation in *e4* carriers. None of these, obviously, are good for our long-term brain health; as noted earlier, *e4* just seems to make every risk factor for Alzheimer's disease worse.

這種生存益處可能是由於 *APOE e4* 在促進發炎方面的作用，這在某些情況下（例如對抗感染）可能是有益的，但在其他情況下（例如現代生活）則是有害的。正如我們在第七章中所看到的，發炎會促進血管

的動脈粥狀硬化損傷，為阿茲海默症和失智症奠定基礎。阿茲海默症患者的大腦中通常存在高水平的發炎細胞因子，例如 TNF- α 和 IL-6，研究也發現 e4 攜帶者的神經發炎水平較高。顯然，這些都不利於我們的長期大腦健康。如前所述，e4 似乎只會使阿茲海默症的所有危險因子變得更糟。

The *e4* variant also seems to be maladaptive in other ways, such as in dealing with our modern diets. Not only are *e4* carriers more likely to develop metabolic syndrome in the first place, but the APOE *e4* protein may be partially responsible for this, by disrupting the brain's ability to regulate insulin levels and maintain glucose homeostasis in the body. This phenomenon becomes apparent when these patients are on continuous glucose monitoring, or CGM (which we'll discuss in more detail in chapter 15). Even young patients with *e4* show dramatic blood glucose spikes after eating carbohydrate-rich foods, although the clinical significance of this is unclear.

e4 變體似乎在其他方面也存在適應不良，例如在處理我們的現代飲食方面。e4 攜帶者不僅更容易患上代謝綜合徵，而且 APOE e4 蛋白可能是造成這種情況的部分原因，因為它破壞了大腦調節胰島素水平和維持體內葡萄糖穩態的能力。當這些患者接受連續血糖監測或 CGM（我們將在第 15 章中更詳細地討論）時，這種現象變得明顯。即使患有 e4 的年輕患者在食用富含碳水化合物的食物後也會出現劇烈的血糖峰值，儘管其臨床意義尚不清楚。

Thus, *e4* itself could help drive the very same metabolic dysfunction that also increases risk of dementia. At the same time, it appears to intensify the damage done to the brain by metabolic dysfunction. Researchers have found that in high-glucose environments, the aberrant form of the APOE protein encoded by *APOE e4* works to block insulin receptors in the brain, forming sticky clumps or aggregates that prevent neurons from taking in energy.

因此，e4 本身可以幫助驅動同樣的代謝功能障礙，這也會增加罹患失智症的風險。同時，它似乎也會加劇代謝功能障礙對大腦造成的損害。研究人員發現，在高葡萄糖環境中，APOE e4 編碼的 APOE 蛋白的異常形式會阻斷大腦中的胰島素受體，形成黏性團塊或聚集體，阻止神經元吸收能量。

But not everyone with the *APOE e4* genotype is affected by it in the same way. Its effects on disease risk and the course of disease are highly variable. Factors like biological sex, ethnicity, and lifestyle clearly play a role, but it is now believed that Alzheimer's risk and the effect of *APOE* are also powerfully dependent on *other* Alzheimer's-risk-related genes that a person might carry, such as *Klotho*, the protective gene we mentioned earlier. This could explain, for example, why some people with *e4* may never go on to develop Alzheimer's disease, while others do so quickly.

但並非所有攜帶 APOE e4 基因型的人都會受到相同的影響。它對疾病風險和病程的影響變化很大。生物性別、種族和生活方式等因素顯然起著一定的作用，但現在人們相信，阿茲海默症的風險和APOE 的影響也很大程度上取決於一個人可能攜帶的其他與阿茲海默症病風險相關的基因，例如Klotho，我們前面提到的保護基因。例如，這可以解釋為什麼一些患有 e4 的人可能永遠不會繼續患有阿茲海默症，而另一些人則很快就會患上阿茲海默症。

All this suggests that metabolic and vascular causes of dementia may be somewhat overlapping, just as patients with insulin resistance are also prone to vascular disease. And it tells us that with high-risk patients like Stephanie, we need to pay special attention to their metabolic health.

所有這些都表明，癡呆症的代謝和血管原因可能有些重疊，就像胰島素抗性患者也容易患血管疾病一樣。它告訴我們，對於像史蒂芬妮這樣的高風險患者，我們需要特別關注他們的代謝健康。

The Preventive Plan

預防計劃

In spite of everything, I remain cautiously optimistic for patients like Stephanie, even with her highly elevated genetic risk. The very concept of Alzheimer's prevention is still relatively new; we have only begun to scratch the surface of what might be accomplished here. As we better understand the

disease, our treatments and interventions can become more sophisticated and hopefully effective.

儘管如此，我對像史蒂芬妮這樣的患者仍然保持謹慎樂觀，即使她的遺傳風險很高。預防阿茲海默症的概念也相對較新。我們才剛開始觸及這裡可能完成的工作的皮毛。隨著我們更了解這種疾病，我們的治療和介入措施可以變得更加複雜並且有望有效。

I actually think we know more about preventing Alzheimer's than we do about preventing cancer. Our primary tool for preventing cancer is to not smoke and to keep our metabolic health on track, but that's a very broad-brush approach that only takes us so far. We still need to screen aggressively and hope we somehow manage to find any cancers that do develop before it's too late. With Alzheimer's disease, we have a much larger preventive tool kit at our disposal, and much better diagnostic methods as well. It's relatively easy to spot cognitive decline in its early stages, if we're looking carefully. And we're learning more about genetic factors as well, including those that at least partially offset high-risk genes like *APOE e4*.

事實上，我認為我們對預防阿茲海默症的了解比對預防癌症的了解更多。我們預防癌症的主要方法是不吸煙並保持代謝健康正常，但這是一種非常粗略的方法，只能幫助我們到目前為止。我們仍然需要積極篩檢，並希望能夠在為時已晚之前找到任何確實發生的癌症。對於阿茲海默症，我們擁有更強大的預防工具包，以及更好的診斷方法。如果我們仔細觀察的話，在早期階段就相對容易發現認知能力下降。我們也在更了解遺傳因素，包括那些至少部分抵消 *APOE e4* 等高風險基因的因素。

Because metabolism plays such an outsize role with at-risk *e4* patients like Stephanie, our first step is to address any metabolic issues they may have. Our goal is to improve glucose metabolism, inflammation, and oxidative stress. One possible recommendation for someone like her would be to switch to a Mediterranean-style diet, relying on more monounsaturated fats and fewer refined carbohydrates, in addition to regular consumption of fatty fish. There is some evidence that supplementation with the omega-3 fatty acid DHA, found in fish oil, may help maintain brain health, especially in *e4/e4* carriers.

Higher doses of DHA may be required because of *e4*-induced metabolic changes and dysfunction of the blood-brain barrier.

由於新陳代謝對於像 Stephanie 這樣的高危險 *e4* 患者有著至關重要的作用，因此我們的第一步是解決他們可能存在的任何代謝問題。我們的目標是改善葡萄糖代謝、發炎和氧化壓力。對於像她這樣的人來說，一個可能的建議是改用地中海式飲食，除了經常食用富含脂肪的魚外，還依賴更多的單元不飽和脂肪和更少的精製碳水化合物。有證據表明，補充魚油中的 omega-3 脂肪酸 DHA 可能有助於維持大腦健康，尤其是 *e4/e4* 攜帶者的大腦健康。由於 *e4* 誘導的代謝變化和血腦屏障功能障礙，可能需要更高劑量的 DHA。

This is also one area where a ketogenic diet may offer a real functional advantage: when someone is in ketosis, their brain relies on a mix of ketones and glucose for fuel. Studies in Alzheimer's patients find that while their brains become less able to utilize glucose, their ability to metabolize ketones does not decline. So it may make sense to try to diversify the brain's fuel source from only glucose to both glucose and ketones. A systematic review of randomized controlled trials found that ketogenic therapies improved general cognition and memory in subjects with mild cognitive impairment and early-stage Alzheimer's disease. Think of it as a flex-fuel strategy.

這也是生酮飲食可能提供真正功能優勢的一個領域：當某人處於酮症狀態時，他們的大腦依賴酮和葡萄糖的混合物作為燃料。對阿茲海默症患者的研究發現，雖然他們的大腦利用葡萄糖的能力下降，但他們代謝酮的能力並沒有下降。因此，嘗試將大腦的燃料來源從僅葡萄糖轉變為葡萄糖和酮可能是有意義的。對隨機對照試驗的系統性回顧發現，生酮療法可以改善患有輕度認知障礙和早期阿茲海默症的受試者的一般認知和記憶。將其視為靈活燃料策略。

In Stephanie's case, she cut out not only added sugar and highly refined carbohydrates but also alcohol. The precise role of alcohol in relation to Alzheimer's disease remains somewhat controversial: some evidence suggests that alcohol may be slightly protective against Alzheimer's, while other evidence shows that heavier drinking is itself a risk factor for the disease, and

e4 carriers may be more susceptible to alcohol's deleterious effects. I'm inclined to err on the side of caution, and so is Stephanie.

就史蒂芬妮而言，她不僅戒掉了添加糖和高度精製的碳水化合物，還戒掉了酒精。酒精與阿茲海默症相關的確切作用仍存在一定爭議：一些證據表明，酒精可能對阿茲海默症有輕微的保護作用，而其他證據表明，大量飲酒本身就是該疾病的危險因素，而*e4* 攜帶者可能更容易患上阿茲海默症。酒精的有害影響。我傾向於謹慎行事，史蒂芬妮也是如此。

The single most powerful item in our preventive tool kit is exercise, which has a two-pronged impact on Alzheimer's disease risk: it helps maintain glucose homeostasis, and it improves the health of our vasculature. So along with changing Stephanie's diet, we put her back on a regular exercise program, focusing on steady endurance exercise to improve her mitochondrial efficiency. This had a side benefit in that it helped manage her off-the-charts high cortisol levels, due to stress; stress and anxiety-related risk seem more significant in females. As we'll see in chapter 11, endurance exercise produces factors that directly target regions of the brain responsible for cognition and memory. It also helps lower inflammation and oxidative stress.

我們的預防工具箱中最強大的一項是運動，它對阿茲海默症風險有兩個方面的影響：它有助於維持葡萄糖穩態，並改善我們脈管系統的健康。因此，在改變史蒂芬妮的飲食的同時，我們讓她重新開始定期鍛煉計劃，重點是穩定的耐力鍛煉，以提高她的粒線體效率。這還有一個附帶的好處，因為它有助於控制她因壓力而出現的異常高的皮質醇水平。與壓力和焦慮相關的風險似乎在女性身上更為顯著。正如我們將在第 11 章中看到的，耐力運動會產生直接針對負責認知和記憶的大腦區域的因子。它還有助於降低發炎和氧化壓力。

Strength training is likely just as important. A study looking at nearly half a million patients in the United Kingdom found that grip strength, an excellent proxy for overall strength, was strongly and inversely associated with the incidence of dementia (see figure 8). People in the lowest quartile of grip strength (i.e., the weakest) had a 72 percent higher incidence of dementia, compared to those in the top quartile. The authors found that this association

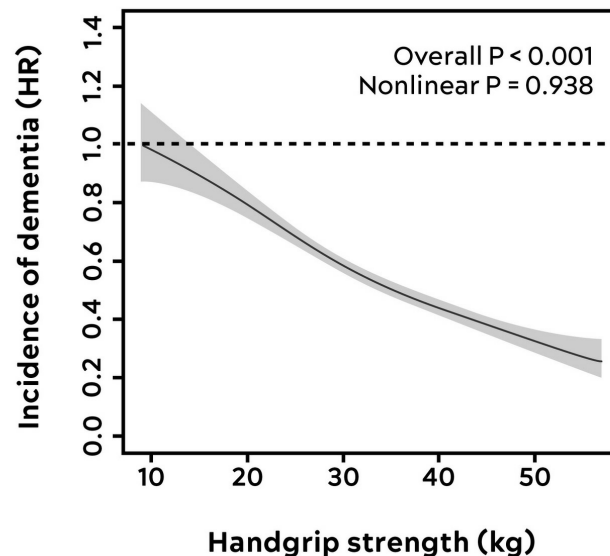
held up even after adjusting for the usual confounders such as age, sex, socioeconomic status, diseases such as diabetes and cancer, smoking, and lifestyle factors such as sleep patterns, walking pace, and time spent watching TV. And there appeared to be no upper limit or “plateau” to this relationship; the greater someone’s grip strength, the lower their risk of dementia.

肌力訓練可能同樣重要。一項針對英國近 50 萬名患者進行的研究發現，握力是整體力量的一個很好的指標，與失智症的發生率呈現強烈的負相關（見圖 8）。與握力最高四分之一的人相比，握力最低四分位數（即最弱）的人罹患失智症的幾率高出 72%。作者發現，即使在調整了常見的混雜因素（例如年齡、性別、社會經濟地位、糖尿病和癌症等疾病、吸煙以及睡眠模式、步行速度和看電視時間等生活方式因素）後，這種關聯仍然存在。這種關係似乎沒有上限或「穩定期」。一個人的握力越大，罹患失智症的風險就越低。

It’s tempting to dismiss findings like these for the same reasons we should be skeptical of epidemiology. But unlike epidemiology in nutrition (much more on that in chapter 14), the epidemiology linking strength and cardiorespiratory fitness to lower risk for neurodegeneration is so uniform in its direction and magnitude that my own skepticism of the power of exercise, circa 2012, has slowly melted away. I now tell patients that exercise is, full stop and hands down, the best tool we have in the neurodegeneration prevention tool kit. (We’ll explore the ins and outs of this in great detail in chapters 11 and 12.)

基於同樣的原因，我們很容易忽略這些發現，就像我們應該對流行病學持懷疑態度一樣。但與營養學中的流行病學不同（第14章中有更多介紹），將力量和心肺健康與降低神經退化性變風險聯繫起來的流行病學在方向和幅度上是如此一致，以至於我自己在2012年左右對運動的力量的懷疑慢慢地消失了。融化了。我現在告訴患者，運動是我們神經退化性疾病預防工具箱中最好的工具。（我們將在第11章和第12章中詳細探討其細節。）

Figure 8. Association of Handgrip Strength with Dementia Incidence



Source: Esteban-Cornejo et al. (2022).

來源：Esteban-Cornejo 等人。（2022）。

This graph shows how the incidence of dementia declines with increasing handgrip strength. Note that data are presented as hazard ratios in comparison with the weakest group; e.g., 0.4 = 40 percent. Thus someone with 40 kg grip strength has about 40 percent as much risk of dementia as someone with 10 kg.

此圖顯示了失智症的發生率如何隨著握力的增加而下降。請注意，數據以與最弱組相比的風險比表示；例如，0.4 = 40%。因此，握力為 40 公斤的人罹患失智症的風險比握力為 10 公斤的人高約 40%。

Sleep is also a very powerful tool against Alzheimer's disease, as we'll see in chapter 16. Sleep is when our brain heals itself; while we are in deep sleep our brains are essentially "cleaning house," sweeping away intracellular waste that can build up between our neurons. Sleep disruptions and poor sleep are potential drivers of increased risk of dementia. If poor sleep is accompanied by high stress and elevated cortisol levels, as in Stephanie's case, that acts almost as a multiplier of risk, as it contributes to insulin resistance and damaging the hippocampus at the same time. Furthermore, hypercortisolemia (excess cortisol due to stress) impairs the release of melatonin, the hormone that normally signals to our brains that it is time to go to sleep (and that may

also help prevent neuronal loss and cognitive impairment). Addressing Stephanie's difficulties with sleep was therefore urgent. Her divorce and her work situation were making it almost impossible for her to get more than four hours of uninterrupted sleep on any given night.

正如我們將在第 16 章中看到的，睡眠也是對抗阿茲海默症的一個非常強大的工具。當我們處於深度睡眠時，我們的大腦本質上是在“打掃房間”，清除神經元之間積聚的細胞內廢物。睡眠中斷和睡眠品質差是失智症風險增加的潛在驅動因素。如果睡眠品質不佳伴隨著高壓力和皮質醇水平升高，就像史蒂芬妮的情況一樣，那麼這幾乎會增加風險，因為它會導致胰島素阻抗，同時損害海馬體。此外，高皮質醇血症（由於壓力導致皮質醇過多）會損害褪黑激素的釋放，褪黑激素通常會向我們的大腦發出該睡覺的信號（這也可能有助於防止神經元損失和認知障礙）。因此，解決史蒂芬妮的睡眠困難刻不容緩。離婚和工作狀況使她幾乎不可能在任何一個晚上獲得超過四個小時不間斷的睡眠。

Another somewhat surprising risk factor that has emerged is hearing loss. Studies have found that hearing loss is clearly associated with Alzheimer's disease, but it's not a direct symptom. Rather, it seems hearing loss may be causally linked to cognitive decline, because folks with hearing loss tend to pull back and withdraw from interactions with others. When the brain is deprived of inputs—in this case auditory inputs—it withers. Patients with hearing loss miss out on socializing, intellectual stimulation, and feeling connected; prescribing them hearing aids may help relieve some symptoms. This is just a hypothesis for the moment, but it is being tested right now in a clinical trial called ACHIEVE (Aging and Cognitive Health Evaluation in Elders) that is currently ongoing.

另一個令人驚訝的風險因素是聽力損失。研究發現，聽力損失顯然與阿茲海默症有關，但它並不是直接症狀。相反，聽力損失似乎可能與認知能力下降有因果關係，因為聽力損失的人往往會退縮並退出與他人的互動。當大腦失去輸入（在本例中為聽覺輸入）時，它就會萎縮。聽力損失患者會錯過社交、智力刺激和連結感；給他們開助聽器可能有助於緩解一些症狀。目前這只是一個假設，但目前正在一項名

為 ACHIEVE（老年人老化和認知健康評估）的臨床試驗中進行測試，該試驗目前正在進行中。

While depression is also associated with Alzheimer's disease, it appears to be more of a symptom than a risk factor or driver of the disease. Nevertheless, treating depression in patients with MCI or early Alzheimer's disease does appear to help reduce some other symptoms of cognitive decline.

雖然憂鬱症也與阿茲海默症有關，但它似乎更多的是一種症狀，而不是疾病的危險因子或驅動因素。儘管如此，治療輕度認知障礙或早期阿茲海默症患者的憂鬱症似乎確實有助於減輕認知能力下降的其他一些症狀。

Another surprising intervention that may help reduce systemic inflammation, and possibly Alzheimer's disease risk, is brushing *and* flossing one's teeth. (You heard me: *Floss*.) There is a growing body of research linking oral health, particularly the state of one's gum tissue, with overall health. Researchers have found that one pathogen in particular, a microbe called *P. gingivalis* that commonly causes gum disease, is responsible for large increases in levels of inflammatory markers such as IL-6. Even stranger, *P. gingivalis* has also shown up inside the brains of patients with Alzheimer's disease, although scientists are not certain that this bacterium is directly causing dementia, notes Dr. Patricia Corby, a professor of dental health at New York University. Nevertheless, the association is too strong to be ignored. (Also, better oral health correlates strongly with better overall health, particularly in terms of cardiovascular disease risk, so I pay much more attention to flossing and gum health than I used to.)

另一種令人驚訝的干預措施可能有助於減少全身炎症，並可能有助於減少阿茲海默症的風險，那就是刷牙和使用牙線。（你聽到我說的：牙線。）越來越多的研究將口腔健康，特別是牙齦組織的狀態與整體健康聯繫起來。研究人員發現，一種病原體，一種稱為牙齦卟啉單胞菌的微生物，通常會導致牙齦疾病，它會導致 IL-6 等發炎標記物水平大幅升高。紐約大學牙科健康教授派翠西亞·科比博士指出，更奇怪的是，牙齦卟啉單胞菌也出現在阿茲海默症患者的大腦中，儘管科學家不確定這種細菌是否直接導致癡呆症。然而，這種關聯太強大，不容

忽視。（此外，更好的口腔健康與更好的整體健康密切相關，特別是在心血管疾病風險方面，因此我比以前更加關注牙線和牙齦健康。）

One other somewhat recent addition to my thinking on dementia (and ASCVD while we're at it) prevention is the use of dry saunas. Until about 2019 I was very skeptical of the data linking sauna use to brain and heart health. However, the more time I spend buried in this literature, the more I become convinced by the magnitude of the benefit, the uniformity of the studies, and the mechanisms providing plausibility. I'm not quite as confident that regular sauna use will reduce your risk of Alzheimer's disease as I am that exercise will do so, but I am much more confident than I was at the outset of my journey. The best interpretation I can draw from the literature suggests that at least four sessions per week, of at least twenty minutes per session, at 179 degrees Fahrenheit (82 degrees Celsius) or hotter seems to be the sweet spot to reduce the risk of Alzheimer's by about 65 percent (and the risk of ASCVD by 50 percent).

我最近對預防癡呆症（以及 ASCVD）的想法的另一個補充是使用乾桑拿。直到 2019 年左右，我對將桑拿使用與大腦和心臟健康聯繫起來的數據非常懷疑。然而，我花在這些文獻上的時間越多，我就越相信其益處的大小、研究的一致性以及提供合理性的機制。我不太相信經常使用桑拿會降低阿茲海默症的風險，但我比我開始旅程時更有信心。我從文獻中得出的最佳解釋表明，每周至少進行四次療程，每次至少二十分鐘，在 179 華氏度（82 攝氏度）或更高的溫度下進行鍛煉似乎是降低阿爾茨海默病風險的最佳點。約 65%（ASCVD 風險降低 50%）。

Other potential interventions that have shown some promise in studies include lowering homocysteine with B vitamins, while optimizing omega-3 fatty acids. Higher vitamin D levels have been correlated with better memory in *e4/e4* patients but it's difficult to know from the current literature if this means supplementing with vitamin D will reduce risk of AD. And as mentioned earlier, hormone replacement therapy for women during the transition from perimenopause to menopause seems promising, especially for women with at least one copy of *e4*.

研究中顯示出一些前景的其他潛在幹預措施包括用 B 群維生素降低同型半胱氨酸，同時優化 omega-3 脂肪酸。e4/e4 患者的維生素 D 水平較高與記憶力較好相關，但從現有文獻中很難得知這是否意味著補充維生素 D 會降低 AD 風險。如同前面所提到的，在從圍絕經期到更年期的過渡期間，荷爾蒙替代療法似乎很有前途，尤其是對於至少擁有一份 e4 拷貝的女性。

—

The scariest aspect of Alzheimer's disease boils down to this: Medicine 2.0 cannot help us. At all. The point at which Medicine 2.0 steps in, the point of diagnosis, is also likely near the point of no return for most Alzheimer's patients, beyond which little or nothing can be done. Once dementia is diagnosed, it is extremely difficult to slow and maybe impossible to reverse (though we're not certain of that). So we are forced to leave the familiar territory of the medicine that we know, with its promise of certainty, and embrace the Medicine 3.0 concepts of prevention and risk reduction.

阿茲海默症最可怕的地方可以歸結為：醫學2.0無法幫助我們。完全沒有。對於大多數阿茲海默症患者來說，醫學 2.0 介入的時間點（即診斷時間點）也可能接近「不可逆轉」的程度，除此之外幾乎無能為力。一旦診斷出癡呆症，就很難減緩，甚至不可能逆轉（儘管我們不確定這一點）。因此，我們被迫離開我們所熟悉的醫學領域及其確定性的承諾，並接受預防和降低風險的醫學 3.0 概念。

As it stands now, Alzheimer's disease is the last of the Horsemen that we must bypass on our way to becoming centenarians; it's the last obstacle we face. Typically, it is diagnosed later in life—and centenarians develop it *much* later in life, if at all. The longer we can go without developing dementia, the better our odds of living longer, and living in better health. (Remember, cognition is one of the three key vectors of healthspan.) But until science comes up with more effective treatments, prevention is our only option. Therefore, we need to adopt a very early and comprehensive approach to preventing Alzheimer's and other forms of neurodegenerative disease.

就目前情況而言，阿茲海默症是我們在成為百歲老人的道路上必須繞過的最後一位騎士。這是我們面臨的最後一個障礙。通常情況下，這種疾病是在晚年才被診斷出來的，而百歲老人即使有這種病，也是在晚年才被診斷出來的。我們不罹患失智症的時間越長，我們活得更久、活得更健康的幾率就越大。（請記住，認知是健康壽命的三個關鍵向量之一。）但在科學找到更有效的治療方法之前，預防是我們唯一的選擇。因此，我們需要採取非常早期和全面的方法來預防阿茲海默症和其他形式的神經退化性疾病。

Broadly, our strategy should be based on the following principles:

總的來說，我們的策略應基於以下原則：

1. **WHAT'S GOOD FOR THE HEART IS GOOD FOR THE BRAIN. That is, vascular health (meaning low apoB, low inflammation, and low oxidative stress) is crucial to brain health.**

對心臟有益的東西對大腦也有好處。也就是說，血管健康（意味著低 apoB、低發炎和低氧化壓力）對大腦健康至關重要。

2. **WHAT'S GOOD FOR THE LIVER (AND PANCREAS) IS GOOD FOR THE BRAIN. Metabolic health is crucial to brain health.**

對肝臟（和胰臟）有益的東西對大腦也有好處。代謝健康對大腦健康至關重要。

3. **TIME IS KEY. We need to think about prevention early, and the more the deck is stacked against you genetically, the harder you need to work and the sooner you need to start. As with cardiovascular disease, we need to play a very long game.**

時間是關鍵。我們需要及早考慮預防，基因對你不利的因素越多，你就越需要努力工作，也需要越早開始。就像心血管疾病一樣，我們需要打一場持久戰。

4. **OUR MOST POWERFUL TOOL FOR PREVENTING COGNITIVE DECLINE IS EXERCISE. We've talked a lot about diet and metabolism, but exercise appears to act**

in multiple ways (vascular, metabolic) to preserve brain health; we'll get into more detail in Part III, but exercise—lots of it—is a foundation of our Alzheimer's-prevention program.

預防認知能力下降最有力的工具就是運動。我們已經談論了很多關於飲食和新陳代謝的話題，但運動似乎可以透過多種方式（血管、代謝）來保護大腦健康。我們將在第三部分中詳細介紹，但是大量的運動是我們預防阿茲海默症計畫的基礎。

I have great hope that in the future we will learn much more about how to prevent and treat all forms of dementia. But it's going to take hard work and creative thinking from scientists researching the disease, a significant investment in new theories and approaches, much more attention to strategies of prevention, and courage on the part of patients such as Stephanie who must face down this most feared and least understood of all the Horsemen.

我非常希望將來我們能更了解如何預防和治療各種形式的癡呆症。但這需要研究這種疾病的科學家們付出辛勤的努力和創造性思維，對新理論和方法進行大量投資，對預防策略給予更多關注，以及像斯蒂芬妮這樣必鬚面對這種最可怕的疾病的患者的勇氣。也是所有騎士中最不被理解的。

[SKIP NOTES](#)

[跳過註釋](#)

* You may recall from chapter 7 that calcification is part of the repair process for blood vessels damaged by the forces of atherosclerosis.

* 您可能還記得第 7 章中提到的，鈣化是動脈粥狀硬化損傷血管修復過程的一部分。

PART III

第三部分

CHAPTER 10

第10章

Thinking Tactically

戰術思考

Building a Framework of Principles That Work for
You

建立適合您的原則框架

Absorb what is useful, discard what is useless, and add
what is specifically your own.

吸收有用的東西，丟棄無用的東西，添加屬於自
己的東西。

—BRUCE LEE

-李小龍

In the mid-nineteenth century, a French physician named Stanislas Tanchou observed that cancer was becoming ever more prevalent in the fast-growing cities of Europe. The Industrial Revolution was charging ahead at full speed, changing society in unimaginable ways. He saw a connection between the two: “Cancer, like insanity, seems to increase with the progress of civilization.”

十九世紀中葉，一位名叫斯坦尼斯拉斯·坦楚（Stanislas Tanchou）的法國醫生觀察到，癌症在歐洲快速發展的城市中變得越來越普遍。工業革命正全速前進，以難以想像的方式改變社會。他看到了兩者之間的聯繫：“癌症就像精神錯亂一樣，似乎隨著文明的進步而增加。”

He was prescient. Eventually cancer, as well as heart disease, type 2 diabetes, and dementia (along with a few others), became collectively known as “diseases of civilization,” because they seemed to have spread in lockstep with the industrialization and urbanization of Europe and the United States.

他很有先見之明。最終，癌症以及心臟病、2型糖尿病和癡呆症（以及其他一些疾病）被統稱為“文明疾病”，因為它們似乎與歐洲和歐洲的工業化和城市化同步傳播。美國。

This doesn't mean that civilization is somehow “bad” and that we all need to return to a hunter-gatherer lifestyle. I would much rather live in our modern world, where I worry about losing my iPhone or missing a plane flight, than endure the rampant disease, random violence, and lawlessness that our ancestors suffered through for millennia (and that people in some parts of our world still experience). But even as modern life has helped extend our lifespans and improve living standards, it has also created conditions that conspire to *limit* our longevity in certain ways.

這並不意味著文明在某種程度上是“壞的”，我們都需要回歸狩獵採集的生活方式。我寧願生活在現代世界，擔心失去 iPhone 或錯過航班，也不願忍受我們的祖先幾千年來所遭受的猖獗的疾病、隨機的暴力和無法無天的生活（以及我們某些地區的人們）世界仍經歷）。但即使現代生活有助於延長我們的壽命並提高生活水平，它也創造了在某些方面限制我們壽命的條件。

The conundrum we face is that our environment has changed dramatically over the last century or two, in almost every imaginable way—our food supply and eating habits, our activity levels, and the structure of our social networks—while our genes have scarcely changed at all. We saw a classic example of this in chapter 6, with the changing role that fructose has played in our diet. Long ago, when we consumed fructose mainly in the form of fruit and honey, it enabled us to store energy as fat to survive cold winters and periods of scarcity. Fructose was our friend. Now fructose is vastly overabundant in our diet, too much of it in liquid form, which disrupts our metabolism and our overall energy balance. We can easily take in far more fructose calories than our bodies can safely handle.

我們面臨的難題是，我們的環境在過去一兩個世紀裡發生了巨大的變化，幾乎以所有可以想像的方式發生了巨大的變化——我們的食物供應和飲食習慣、我們的活動水平以及我們的社交網絡的結構——而我們的基因幾乎沒有改變。全部。我們在第六章中看到了一個典型的例子，果糖在我們的飲食中所扮演的角色正在改變。很久以前，當我們主要以水果和蜂蜜的形式攝取果糖時，它使我們能夠以脂肪的形式儲存能量，以度過寒冷的冬天和匱乏時期。果糖是我們的朋友。現在，我們的飲食中果糖含量嚴重過剩，其中太多是液體形式，這破壞了我們的新陳代謝和整體能量平衡。我們很容易攝取的果糖熱量遠遠超過我們的身體可以安全處理的量。

This new environment we have created is potentially toxic with respect to what we eat (chronically, not acutely),^[*] how we move (or don't move), how we sleep (or don't sleep), and its overall effect on our emotional health (just spend a few hours on social media). It's as foreign to our evolved genome as an airport would have been to, say, Hippocrates. That, coupled with our newfound ability to survive epidemics, injuries, and illnesses that formerly killed us, has added up to almost a defiance of natural selection. Our genes no longer match our environment. Thus, we must be cunning in our tactics if we are to adapt and thrive in this new and hazardous world.

我們創造的這個新環境對於我們吃的東西（長期的，而不是劇烈的）、[*]我們如何移動（或不移動）、我們如何睡覺（或不睡覺）及

其整體來說具有潛在的毒性.對我們情緒健康的影響（只需在社交媒體上花幾個小時）。它對我們進化的基因組來說是陌生的，就像機場對希波克拉底來說一樣陌生。再加上我們新發現的生存能力，能夠在以前殺死我們的流行病、傷害和疾病中生存，幾乎是對自然選擇的蔑視。我們的基因不再與我們的環境相符。因此，如果我們想適應這個充滿危險的新世界並取得發展，就必須採取狡猾的策略。

This is why we have navigated through the preceding two hundred pages about our objective and our strategy. To figure out what to do, we need to know our adversary inside and out, the way Ali knew Foreman. By now, we should understand our strategy fairly well. Hopefully, I have at least given you some understanding of the biological mechanisms that help predispose us to certain diseases, and how those diseases progress.

這就是為什麼我們瀏覽了前面兩百頁關於我們的目標和策略的原因。為了弄清楚該怎麼做，我們需要徹底了解我們的對手，就像阿里了解福爾曼一樣。到現在為止，我們應該相當了解我們的策略了。希望我至少讓您對有助於我們易患某些疾病的生物機制以及這些疾病如何進展有一些了解。

Now it's time to explore our tactics, the means and methods by which we will try to navigate this strange and sometimes perilous new environment. How are we going to outlive our old expectations and live our best Bonus Decades? What concrete actions can we take to reduce our risk of disease and death and improve the quality of our lives as we age?

現在是時候探索我們的策略、手段和方法了，我們將嘗試在這個奇怪的、有時甚至是危險的新環境中航行。我們如何超越我們過去的期望並度過我們最好的紅利十年？隨著年齡的增長，我們可以採取哪些具體行動來降低疾病和死亡風險並提高生活品質？

In Medicine 3.0, we have five tactical domains that we can address in order to alter someone's health. The first is *exercise*, which I consider to be by far the most potent domain in terms of its impact on both lifespan and healthspan. Of course, exercise is not just one thing, so I break it down into its components of aerobic efficiency, maximum aerobic output (VO₂ max),

strength, and stability, all of which we'll discuss in more detail. Next is diet or nutrition—or as I prefer to call it, *nutritional biochemistry*. The third domain is *sleep*, which has gone underappreciated by Medicine 2.0 until relatively recently. The fourth domain encompasses a set of tools and techniques to manage and improve *emotional health*. Our fifth and final domain consists of the various drugs, supplements, and hormones that doctors learn about in medical school and beyond. I lump these into one bucket called *exogenous molecules*, meaning molecules we ingest that come from outside the body.

在醫學 3.0 中，我們可以透過五個戰術領域來改變某人的健康狀況。首先是運動，就其對壽命和健康的影響而言，我認為這是迄今為止最有效的領域。當然，運動不僅僅是一件事，所以我將其分解為有氧效率、最大有氧輸出 ($VO_2 \text{ max}$)、力量和穩定性等組成部分，所有這些我們都將在更多詳情。接下來是飲食或營養——或者我更喜歡稱之為營養生物化學。第三個領域是睡眠，直到最近，醫學 2.0 還沒有充分認識到睡眠。第四個領域包括一套管理和改善情緒健康的工具和技術。我們的第五個也是最後一個領域包括醫生在醫學院及其他地方學到的各種藥物、補充劑和荷爾蒙。我將它們歸入一個稱為外源性分子的桶中，這意味著我們攝取的來自體外的分子。

In this section I will not be talking much about exogenous molecules, beyond those that I have already mentioned specifically (e.g., lipid-lowering drugs, rapamycin, and metformin, the diabetes drug that is being tested for possible longevity effects). Instead, I want to focus on the other four domains, none of which were really covered, or even mentioned, in medical school or residency. We learned next to nothing about exercise, nutrition, sleep, or emotional health. That may be changing, slowly, but if some doctors understand these things today, and are actually able to help you, it's likely because they have sought out that information on their own.

在本節中，除了我已經具體提到的那些外源性分子（例如降血脂藥、雷帕黴素和二甲雙胍，一種正在測試可能的長壽效果的糖尿病藥物）之外，我不會過多談論外源性分子。相反，我想重點關注其他四個領域，這些領域在醫學院或住院醫師實習中都沒有真正涵蓋，甚至沒有提及。我們對運動、營養、睡眠或情緒健康幾乎一無所知。這種情況

可能正在慢慢改變，但如果今天有些醫生了解這些事情，並且實際上能夠幫助您，很可能是因為他們自己找到了這些資訊。

At first glance, some of our tactics might seem a bit obvious. Exercise. Nutrition. Sleep. Emotional health. Of course, we want to optimize all of these. But the devil (or, to me, the delight) is in the details. *In what way(s)* should we be exercising? *How* are we going to improve our diet? *How* can we sleep longer and better?

乍一看，我們的一些策略可能看起來有點明顯。鍛煉。營養。睡覺。情緒健康。當然，我們希望優化所有這些。但魔鬼（或者，對我來說，快樂）在於細節。我們應該以什麼方式鍛鍊？我們要如何改善飲食呢？怎樣才能睡得更久、睡得更好呢？

In each of these cases, while the broad-brush goals are clear, the specifics and the nuances are not. Our options are almost infinite. This requires us to really drill down and figure out how to come up with an effective tactical game plan—and to be able to change course as needed. We have to dig deeper to get beyond the obvious.

在每種情況下，雖然粗略目標都很明確，但具體細節和細微差別卻並不明確。我們的選擇幾乎是無限的。這要求我們真正深入研究並找出如何制定有效的戰術計劃，並能夠根據需要改變路線。我們必須深入挖掘才能超越顯而易見的事實。

What constitutes an effective tactic?

什麼是有效的策略？

One way I like to explain this is through the example of car accidents, which also happen to be a minor obsession of mine. They kill far too many people across all age groups—one person every twelve minutes, according to the National Highway Traffic Safety Administration—yet I believe that a fair number of these deaths could be prevented, with the proper tactics.

我喜歡解釋這一點的一種方式是透過車禍的例子，這也恰好是我的一個小困擾。它們殺死了太多各個年齡層的人——根據國家公路交通安

全管理局的數據，每十二分鐘就有了一個人——但我相信，透過適當的策略，可以避免相當數量的死亡。

What can we do to reduce our risk of dying behind the wheel? Is it even possible to avoid car accidents, when they seem so random?

我們可以做些什麼來降低駕駛死亡的風險？當車禍看起來如此隨機時，是否有可能避免它們？

The obvious tactics we already know about: wear a seat belt, don't text and drive (seemingly difficult for many people), and don't drink and drive, since alcohol is a factor in up to a third of fatalities. Automotive fatality statistics also reveal that almost 30 percent of deaths involve excessive speed. These are helpful reminders, but not really surprising or insightful.

我們已經知道的明顯策略是：繫上安全帶，開車時不要發短信（對很多人來說似乎很困難），不要酒後開車，因為酒精是導致高達三分之一死亡的因素之一。汽車死亡統計數據也顯示，近 30% 的死亡與超速有關。這些都是有用的提醒，但並不令人驚訝或富有洞察力。

Recognizing the danger points is the first step in developing good tactics. I had almost automatically assumed that freeways would prove to be the deadliest place to drive because of the high speeds involved. But decades' worth of auto accident data reveal that, in fact, a very high proportion of fatalities occur at intersections. The most common way to be killed, as a driver, is by another car that hits yours from the left, on the driver's side, having run a red light or traveling at high speed. It's typically a T-bone or broadside crash, and often the driver who dies is not the one at fault.

認識危險點是製定良好戰術的第一步。我幾乎自然而然地認為高速公路將被證明是最致命的駕駛場所，因為速度很高。但數十年的車禍數據表明，事實上，很大一部分死亡事故發生在十字路口。作為一名司機，最常見的死亡方式是被另一輛車從左側撞到你的車，在司機一側，闖紅燈或高速行駛。這通常是丁字事故或側面事故，而且死亡的司機通常不是過失方。

The good news is that at intersections we have choices. We have agency. We can decide whether and when to drive into the crossroads. This gives us an

opportunity to develop specific tactics to try to avoid getting hit in an intersection. We are most concerned about cars coming from our left, toward our driver's side door, so we should pay special attention to that side. At busy intersections, it makes sense to look left, then right, then left again, in case we missed something the first time. A high school friend who is now a long-haul truck driver agrees: before entering *any* intersection, even if he has the right of way (i.e., a green light), he *always* looks left first, then right, specifically to avoid this type of crash. And keep in mind, he's in a huge truck.

好消息是，在十字路口我們有選擇。我們有代理商。我們可以決定是否以及何時駛入十字路口。這使我們有機會制定具體策略，盡量避免在十字路口被撞。我們最關心的是從我們左邊駛向駕駛員側門的汽車，因此我們應該特別注意那一側。在繁忙的十字路口，最好先向左看，然後向右看，然後再向左看，以防我們第一次錯過一些東西。一位現在是長途卡車司機的高中朋友同意：在進入任何路口之前，即使他有路權（即綠燈），他總是先向左看，然後向右看，專門為了避免這種情況崩潰。請記住，他在一輛大卡車裡。

Now we have a *specific, actionable* tactic that we can employ every time we drive. Even if it can't guarantee that we are 100 percent safe, it reduces our risk in a small but demonstrable way. Better yet, our tactic has leverage: a relatively minor effort yields a potentially significant risk reduction.

現在我們有了一個具體的、可操作的策略，我們可以在每次開車時使用。即使它不能保證我們 100% 安全，它也會以微小但明顯的方式降低我們的風險。更好的是，我們的策略具有槓桿作用：相對較小的努力可能會顯著降低風險。

We approach our tactics the same way, zooming in from the vague and general to the specific and targeted. We use data and intuition to figure out where to focus our efforts, and feedback to determine what is and isn't working. And seemingly small tweaks can yield a significant advantage if compounded over time.

我們以同樣的方式處理我們的策略，從模糊和籠統放大到具體和有針對性。我們利用數據和直覺來確定我們的工作重點，並利用回饋來確

定什麼是有效的，什麼是無效的。如果隨著時間的推移，看似微小的調整可以產生顯著的優勢。

My car accident analogy may seem like a bit of a tangent, but it's really not that dissimilar from the situation we face in our quest for longevity. The automobile is ubiquitous in our society, an environmental hazard that we need to learn to live with. Similarly, in order to stay healthy as we grow older, we must learn to navigate a world that is filled with ever more hazards and risks to our health. In this third and final section of the book, we will explore various methods by which we can mitigate or eliminate those risks, and improve and increase our healthspan—and how to apply them to each unique patient.

我的車禍比喻可能看起來有點離題，但它與我們追求長壽時所面臨的情況確實沒有什麼不同。汽車在我們的社會中無所不在，這是我們需要學會忍受的環境危害。同樣，為了隨著年齡的增長保持健康，我們必須學會駕馭這個充滿健康危害和風險的世界。在本書的第三部分，也是最後一部分，我們將探索各種方法來減輕或消除這些風險，改善和延長我們的健康壽命，以及如何將它們應用於每個獨特的患者。

—

Our two most complex tactical domains are nutrition and exercise, and I find that most people need to make changes in both—rarely just one or the other. When I evaluate new patients, I'm always asking three key questions:

我們兩個最複雜的戰術領域是營養和鍛煉，我發現大多數人都需要在這兩方面做出改變——很少只是其中之一。當我評估新患者時，我總是會問三個關鍵問題：

a. Are they overnourished or undernourished? That is, are they taking in too many or too few calories?

A. 他們是營養過剩還是營養不良？也就是說，他們攝取的卡路里過多還是過少？

b. Are they undermuscle or adequately muscle?

b.他們肌肉不足還是肌肉充足？

c. Are they metabolically healthy or not?

C.他們的新陳代謝是否健康？

Not surprisingly, there is a high degree of overlap between the overnourished camp and those with poor metabolic health, but I've taken care of many thin patients with metabolic problems as well. Almost always, though, poor metabolic health goes along with being undermuscle, which speaks to the interplay between nutrition and exercise.

毫不奇怪，營養過剩的陣營和代謝健康狀況不佳的陣營之間存在高度重疊，但我也照顧過許多患有代謝問題的瘦弱患者。然而，新陳代謝健康狀況不佳幾乎總是伴隨著肌肉不足，這說明了營養和運動之間的相互作用。

We will talk about all these different situations in much more detail, but briefly, this is why it's important to coordinate between *all* the different tactical interventions we employ. For example, with a patient who is overnourished, we want to find a way to reduce their caloric intake (there are three ways to do this, as you'll see in chapter 15). But if they are also undermuscle, which is common, we want to be careful to make sure they are still getting enough protein, since the goal is not weight loss but fat loss coupled with muscle gain. It can get complicated.

我們將更詳細地討論所有這些不同的情況，但簡單地說，這就是為什麼在我們採用的所有不同的戰術幹預之間進行協調很重要。例如，對於營養過剩的患者，我們希望找到一種方法來減少他們的熱量攝取

（有三種方法可以做到這一點，正如您將在第 15 章中看到的）。但如果他們也肌肉不足（這種情況很常見），我們要小心確保他們仍然攝取足夠的蛋白質，因為我們的目標不是減肥，而是減脂和增肌。它可能會變得複雜。

None of our tactical domains is fully separate from the others. In chapter 16, for example, we will see how sleep has a tremendous effect on our insulin sensitivity and our exercise performance (and our emotional well-being, as well). That said, with most patients I devote a great deal of attention to their fitness and their nutrition, which are closely linked. We rely heavily on data in our decision-making and developing our tactics, including static biomarkers such as triglycerides and liver function tests, as well as dynamic biomarkers such as oral glucose tolerance tests, along with anthropometric measures such as data on body composition, visceral adipose tissue, bone density, and lean mass.

我們的戰術領域沒有一個是完全獨立於其他領域的。例如，在第 16 章中，我們將看到睡眠如何對我們的胰島素敏感性和運動表現（以及我們的情緒健康）產生巨大影響。也就是說，對於大多數患者，我非常關注他們的健康和營養，這是密切相關的。我們在決策和製定策略時嚴重依賴數據，包括甘油三酯和肝功能測試等靜態生物標誌物，以及口服葡萄糖耐量測試等動態生物標誌物，以及身體組成、內臟數據等人體測量指標。脂肪組織、骨密度和瘦體重。

Much of what you are about to read mirrors the discussions I have with my patients every single day. We talk about their objectives, and the science underpinning our strategy. When it comes to specific tactics, I give them direction to help them create their own playbook. I almost never write out a prescription for them to follow blindly. My goal is to empower them to take action to fix their fitness, nutrition, sleep, and emotional help. (Note that for most of these things, I don't actually even *need* a prescription pad.) But the *action* part is their responsibility; not much of this stuff is easy. It requires them to change their habits and do the work.

您將要閱讀的大部分內容都反映了我每天與患者進行的討論。我們討論他們的目標以及支撐我們策略的科學基礎。當談到具體策略時，我會給他們指導，幫助他們創建自己的戰術手冊。我幾乎從不開處方讓他們盲目遵循。我的目標是讓他們能夠採取行動來改善他們的健康、營養、睡眠和情緒幫助。（請注意，對於大多數這些事情，我實際上

甚至不需要處方簿。）但行動部分是他們的責任；這些東西並不容易。它要求他們改變習慣並做好工作。

What follows is not a step-by-step plan to be followed blindly. There is no blanket solution for every person. Providing very granular exercise, dietary, or lifestyle advice requires individual feedback and iteration, something I can't safely or accurately accomplish in a book. Rather, I hope you will learn a framework for managing your movement, nutrition, sleep, and emotional health that will take you much further than any broad prescription for how many grams of this or that macronutrient every single person on earth must eat. I believe this represents the best we can do right now, on the basis of our current understanding of the relevant science and my own clinical experience (which is where the “art” comes in). I'm constantly tinkering, experimenting, switching things up in my own regimen and in that of my patients. And my patients themselves are constantly changing.

接下來的內容並不是一個可以盲目遵循的逐步計劃。沒有適合每個人的解決方案。提供非常細緻的運動、飲食或生活方式建議需要個人回饋和迭代，這是我無法在書中安全或準確地完成的。相反，我希望你能學習一個管理你的運動、營養、睡眠和情緒健康的框架，這比任何關於地球上每個人必須吃多少克這種或那種大量營養素的寬泛處方更能讓你走得更遠。我相信，根據我們目前對相關科學的理解和我自己的臨床經驗（這就是「藝術」的來源），這代表了我們現在能做的最好的事情。我不斷地修補、試驗、改變我自己和病人的治療方案。我的病人本身也在不斷改變。

We are not bound by any specific ideology or school of thought, or labels of any kind. We are not “keto” or “low-fat,” and we do not emphasize aerobic training at the expense of strength, or vice versa. We range widely and pick and choose and test tactics that will hopefully work for us. We are open to changing our minds. For example, I used to recommend long periods of water-only fasting for some of my patients—and practiced it myself. But I no longer do so, because I've become convinced that the drawbacks (mostly having to do with muscle loss and undernourishment) outweigh its metabolic benefits in all

but my most overnourished patients. We adapt our tactics on the basis of our changing needs and our changing understanding of the best science out there.

我們不受任何特定意識形態或思想流派或任何類型的標籤的約束。我們不是“生酮”或“低脂”，我們不會以犧牲力量為代價來強調有氧訓練，反之亦然。我們範圍廣泛，挑選並測試希望對我們有用的策略。我們願意改變想法。例如，我曾經建議我的一些患者長時間只喝水，並且自己也實踐過。但我不再這樣做了，因為我已經確信，除了我最營養過剩的患者之外，它的缺點（主要與肌肉損失和營養不良有關）超過了它對代謝的益處。我們根據不斷變化的需求以及對現有最佳科學不斷變化的理解來調整我們的策略。

Our only goal is to live longer and live better—to *outlive*. To do that, we must rewrite the narrative of decline that so many others before us have endured and figure out a plan to make each decade better than the one before.

我們唯一的目標是活得更長、活得更好——活得更長久。為此，我們必須重寫我們之前許多人所經歷的衰落敘述，並製定一項計劃，使每個十年都比前一個十年更好。

[SKIP NOTES](#)

[跳過註釋](#)

* Acutely, our food supply is safer than ever thanks to refrigeration and advances in food processing, and regulations that prevent toxic substances from being used in food. Chronically, not so much (see chapter 15).

* 顯然，由於冷藏和食品加工的進步以及防止食品中使用有毒物質的法規，我們的食品供應比以往任何時候都更加安全。長期來看，沒有那麼多（見第15章）。

CHAPTER 11

第11章

Exercise

鍛鍊

The Most Powerful Longevity Drug

最強效的長壽藥

I never won a fight in the ring; I always won in
preparation.

我在拳擊場上從來沒有贏過；我總是在準備中獲
勝。

—MUHAMMAD ALI

-穆罕默德阿里

Several years ago, my friend John Griffin pinged me with a question about how he should be exercising: Should he be doing more cardio or more weights? What did I think?

幾年前，我的朋友約翰·格里芬向我詢問他應該如何鍛鍊：他應該做更多的有氧運動還是更多的舉重運動？我怎麼想的？

“I’m really confused by all the contradictory stuff I’m seeing out there,” he wrote.

「我對所看到的所有矛盾的東西感到非常困惑，」他寫道。

Behind his seemingly simple question, I heard a plea for help. John is a smart guy with an incisive mind, and yet even he was frustrated by all the conflicting advice from “experts” touting this or that workout as the sure path to perfect health. He couldn’t figure out what he needed to be doing in the gym or why.

在他看似簡單的問題背後，我聽見了求助的聲音。約翰是個聰明人，頭腦敏銳，但即使是他也對「專家」提出的相互矛盾的建議感到沮喪，這些建議聲稱這種或那種運動是通往完美健康的必經之路。他不知道自己需要在健身房做什麼，也不知道為什麼。

This was before I had gotten back into the full-time practice of medicine. At the time, I was immersed in the world of nutrition research, which if anything is even *more* confounding than exercise science, rife with contradictory findings and passionately held dogmas backed by flimsy data. Are eggs bad or good? What about coffee? It was driving me nuts too.

那是在我重新全職從事醫學工作之前。當時，我沉浸在營養研究的世界中，如果說有什麼比運動科學更令人困惑的話，它充滿了相互矛盾的發現和由脆弱數據支持的狂熱教條。雞蛋是好是壞？咖啡呢？這也讓我發瘋。

I started typing out a reply and kept on writing. By the time I hit SEND, I had written close to two thousand words, way more than he asked for. The poor guy just wanted a quick answer, not a memo. I didn’t stop there either. I

later expanded that email into a ten-thousand-word manifesto on longevity, which eventually grew into the book you are holding in your hands.^[*1]

我開始打出回覆並繼續寫作。當我點擊“發送”時，我已經寫了近兩千字，比他要求的多得多。這個可憐的傢伙只是想要一個快速答案，而不是一份備忘錄。我也沒有就此止步。後來我把那封電子郵件擴展成了一篇關於長壽的萬字宣言，它最終變成了你手上的這本書。[*1]

Clearly, something about John's question triggered me. It's not that I was a passionate devotee of strength training over endurance, or vice versa; I'd done plenty of both. I was reacting to the binary nature of his question. In case you haven't figured it out by now, I'm not fond of the way we reduce these complex, nuanced, vitally important questions down to simple either-ors. Cardio or weights? Low-carb or plant-based? Olive oil or beef tallow?

顯然，約翰的問題觸動了我。這並不是說我熱衷於肌力訓練而非耐力訓練，反之亦然。這兩件事我都做了很多。我正在對他問題的二元性做出反應。如果你現在還沒有弄清楚，我不喜歡我們將這些複雜、微妙、極其重要的問題簡化為簡單的非此即彼的方式。有氧運動還是舉重？低碳水化合物還是植物性的？橄欖油還是奶油？

I don't know. Must we really take sides?

我不知道。我們真的必須選邊站嗎？

The problem, and we will see this again in the nutrition chapters, is that we have this need to turn everything into a kind of religious war over which is the One True Church. Some experts insist that strength training is superior to cardio, while an equal number assert the opposite. The debate is as endless as it is pointless, sacrificing science on the altar of advocacy. The problem is that we are looking at these hugely important domains of life—exercise, but also nutrition—through a far too narrow lens. It's not about which side of the gym you prefer. It's so much more essential than that.

我們將在營養章節中再次看到的問題是，我們需要將一切變成一場宗教戰爭，爭奪唯一真正的教會。一些專家堅持認為肌力訓練優於有氧運動，而同樣數量的專家則持相反觀點。這場爭論無休無止，毫無意義，為了宣傳而犧牲了科學。問題在於，我們透過過於狹隘的視角來

看待生活中這些極其重要的領域——鍛煉，還有營養。這與您喜歡健身房的哪一側無關。它比這重要得多。

More than any other tactical domain we discuss in this book, exercise has the greatest power to determine how you will live out the rest of your life. There are reams of data supporting the notion that even a fairly minimal amount of exercise can lengthen your life by several years. It delays the onset of chronic diseases, pretty much across the board, but it is also amazingly effective at extending and improving healthspan. Not only does it reverse physical decline, which I suppose is somewhat obvious, but it can slow or reverse cognitive decline as well. (It also has benefits in terms of emotional health, although those are harder to quantify.)

與我們在本書中討論的任何其他策略領域相比，運動最能決定你將如何度過餘生。有大量數據支持這一觀點：即使是相當少量的運動也可以延長您的壽命數年。它幾乎全面推遲了慢性疾病的發作，但它在延長和改善健康壽命方面也非常有效。它不僅可以逆轉身體衰退（我認為這有點明顯），而且還可以減緩或逆轉認知衰退。（它在情緒健康方面也有好處，儘管這些好處很難量化。）

So if you adopt only one new set of habits based on reading this book, it *must* be in the realm of exercise. If you currently exercise, you will likely want to rethink and modify your program. And if exercise is not a part of your life at the moment, you are not alone—77 percent of the US population is like you. Now is the time to change that. Right now. Even a little bit of daily activity is much better than nothing. Going from zero weekly exercise to just ninety minutes per week can reduce your risk of dying from all causes by 14 percent. It's very hard to find a drug that can do that.

因此，如果你在閱讀本書的基礎上只養成了一套新習慣，那麼它一定是在運動的範圍內。如果您目前正在鍛煉，您可能需要重新考慮並修改您的計劃。如果運動目前還不是您生活的一部分，那麼您並不孤單——77% 的美國人和您一樣。現在是改變這種狀況的時候了。現在。即使是一點點的日常活動也比沒有好得多。從每週零鍛鍊到每週僅運動 90 分鐘可以將您因各種原因死亡的風險降低 14%。很難找到一種藥物可以做到這一點。

Thus, my answer to questions like the one my friend John Griffin asked me is yes and yes. Yes, you should be doing more cardio. And yes, you should be lifting more weights.

因此，對於我的朋友約翰·格里芬問我的問題，我的回答是肯定的。是的，你應該多做有氧運動。是的，你應該舉起更多的重量。

At the other end of the spectrum, if you're someone like me who has been exercising since kindergarten, I promise you these chapters will offer you insights about how to better structure your program—not to achieve a faster marathon time or bragging rights at your gym, but to live a longer and better life, and most important, a life in which you can continue enjoying physical activity well into your later years.

另一方面，如果你像我一樣從幼兒園就開始鍛煉，我向你保證，這些章節將為你提供有關如何更好地構建你的計劃的見解，而不是為了實現更快的馬拉松時間或吹噓的權利您的健身房，但為了活得更長久、更好，最重要的是，您可以在晚年繼續享受體育活動。

—

It's obviously not a revelation that exercise is good for you; so is chicken soup if you have a sore throat. But not many people realize how profound its effects really are. Study after study has found that regular exercisers live as much as a *decade* longer than sedentary people. Not only do habitual runners and cyclists tend to live longer, but they stay in better health, with less morbidity from causes related to metabolic dysfunction. For those who are not habitual exercisers (yet), you're in luck: The benefits of exercise begin with any amount of activity north of zero—even brisk walking—and go up from there. Just as almost any diet represents a vast improvement over eating only fast food, almost any exercise is better than remaining sedentary.

顯然，這並不是說運動對你有好處；而是說運動對你有好處。如果你喉嚨痛，雞湯也是。但沒有多少人意識到它的影響到底有多深遠。一項又一項的研究發現，經常運動的人比久坐的人壽命要長十年。經常

跑步和騎自行車的人不僅壽命更長，而且保持更好的健康狀況，與代謝功能障礙相關的發病率也更低。對於那些還沒有習慣運動的人來說，您很幸運：運動的好處始於零以上的任何活動量（甚至是快走），然後從那裡開始增加。正如幾乎任何飲食都比只吃快餐有巨大改善一樣，幾乎任何運動都比久坐更好。

Although my medical school classmates and I learned almost zilch about exercise, let alone how to “prescribe” it to patients, Medicine 2.0 does at least recognize its value. Unfortunately, the advice rarely goes beyond generic recommendations to move more and sit less. The US government’s physical activity guidelines suggest that “active adults” engage in at least 30 minutes of “moderate-intensity aerobic activity,” five times per week (or 150 minutes in total). This is to be supplemented with two days of strength training, targeting “all major muscle groups.”

儘管我和我的醫學院同學對運動幾乎一無所知，更不用說如何給病人「開處方」了，但醫學2.0至少認識到了它的價值。不幸的是，這些建議很少超越過動少坐的一般建議。美國政府的身體活動指南建議，“活躍的成年人”至少進行 30 分鐘的“中等強度有氧運動”，每週 5 次（或總共 150 分鐘）。除此之外，還需要進行兩天的肌力訓練，針對「所有主要肌肉群」。

Imagine if doctors were this vague about cancer treatment:

想像一下，如果醫生對癌症治療如此模糊：

DOCTOR: Ms. Smith, I’m sorry to have to tell you this, but you have colon cancer.

醫生：史密斯女士，我很抱歉必須告訴您這一點，但您患有結腸癌。

MS. SMITH: That’s terrible news, Doctor. What should I do?

多發性硬化症。史密斯：這是個可怕的消息，醫生。我該怎麼辦？

DOCTOR: You need chemotherapy treatment.

醫生：你需要化療。

MS. SMITH: What kind of chemotherapy? What dose? How often? For how long? What about the side effects?

多發性硬化症。史密斯：什麼樣的化療？什麼劑量？多常？多長時間？那麼副作用呢？

DOCTOR: _(ツ)_/

醫生： _(ツ)_/

We need more specific guidance to help us achieve our goals, and to do so in a way that is efficient but also safe. But first, I want to spend some time exploring *why* exercise is so important, because I find the data around it to be so persuasive. When I share these data with my patients, they are rarely surprised by the fact that high aerobic fitness and strength are associated with longer lifespan and healthspan—but they are always amazed by the *magnitude* of the benefit. The data on exercise tell us, with great clarity, that the more we do, the better off we will be.

我們需要更具體的指導來幫助我們實現目標，並以高效且安全的方式實現這一目標。但首先，我想花一些時間探索為什麼運動如此重要，因為我發現圍繞著運動的數據非常有說服力。當我與患者分享這些數據時，他們很少對高有氧運動和力量與更長的壽命和健康壽命相關這一事實感到驚訝，但他們總是對益處的程度感到驚訝。運動數據非常清楚地告訴我們，運動越多，我們的生活就會越好。

Let's start with cardiorespiratory or aerobic fitness. This means how efficiently your body can deliver oxygen to your muscles, and how efficiently your muscles can extract that oxygen, enabling you to run (or walk) or cycle or swim long distances. It also comes into play in daily life, manifesting as physical stamina. The more aerobically fit you are, the more energy you will have for whatever you enjoy doing—even if your favorite activity is shopping.

讓我們從心肺或有氧健身開始。這意味著您的身體向肌肉輸送氧氣的效率，以及肌肉提取氧氣的效率，使您能夠長距離跑步（或步行）、

騎自行車或游泳。它也在日常生活中發揮作用，表現為身體耐力。您的有氧運動越健康，您就越有精力去做您喜歡做的事情——即使您最喜歡的活動是購物。

It turns out that peak aerobic cardiorespiratory fitness, measured in terms of $\text{VO}_2 \text{ max}$, is perhaps the single most powerful marker for longevity. $\text{VO}_2 \text{ max}$ represents the maximum rate at which a person can utilize oxygen. This is measured, naturally, while a person is exercising at essentially their upper limit of effort. (If you've ever had this test done, you will know just how unpleasant it is.) The more oxygen your body is able to use, the higher your $\text{VO}_2 \text{ max}$.

事實證明，以最大攝氧量 $\text{VO}_2 \text{ max}$ 衡量的有氧心肺健康高峰可能是長壽的最有力標誌。 $\text{VO}_2 \text{ max}$ 表示一個人可以利用氧氣的最大速率。當然，這是在一個人基本上以自己的努力上限進行鍛鍊時測量的。（如果您曾經做過此測試，您就會知道它是多麼令人不快。）您的身體能夠使用的氧氣越多，您的最大攝氧量 $\text{VO}_2 \text{ max}$ 就越高。

Our human body has an amazing ability to respond to the demands placed on it. Let's say I'm just sitting on the couch, watching a movie. At rest, someone my size might require about 300 ml of oxygen per minute in order to generate enough ATP, the chemical "fuel" that powers our cells, to perform all the physiological functions necessary to stay alive and watch the movie. This is a pretty low level of energy demand, but if I go outside and jog around my neighborhood, the energy demands ramp up. My breathing quickens, and my heart rate accelerates to help me extract and utilize ever more oxygen from the air I breathe, in order to keep my muscles working. At this level of intensity, someone my size might require 2,500 to 3,000 ml of oxygen per minute, an eight- to tenfold increase from when I was sitting on the couch. Now, if I start running up a hill as fast as I can, my body's oxygen demand will increase from there: 4,000 ml, 4,500 ml, even 5,000 ml or more depending on the pace and my fitness level. The fitter I am, the more oxygen I can consume to make ATP, and the faster I can run up that hill.

我們的人體具有驚人的能力來回應對其提出的要求。假設我只是坐在沙發上看電影。在休息時，我這個體型的人每分鐘可能需要大約300毫升的氧氣才能產生足夠的ATP（為我們的細胞提供動力的化學「燃料」），以執行維持生命和觀看電影所需的所有生理功能。這是一個相當低的能源需求水平，但如果我出去在附近慢跑，能源需求就會增加。我的呼吸加快，心率加快，幫助我從呼吸的空氣中提取和利用更多的氧氣，以保持我的肌肉工作。在這種強度水平下，我這個體型的人每分鐘可能需要 2,500 到 3,000 毫升的氧氣，比我坐在沙發上時增加了八到十倍。現在，如果我開始盡可能快地跑上山，我身體的需氧量將從那裡開始增加：4,000 毫升、4,500 毫升，甚至 5,000 毫升或更多，具體取決於配速和我的健身水平。我身體越健康，生成 ATP 所需的氧氣就越多，爬上山坡的速度就越快。

Eventually, I will reach the point at which I just can't produce any more energy via oxygen-dependent pathways, and I'll be forced to switch over to less efficient, less sustainable ways of producing power, such as those used in sprinting. The amount of oxygen that I am using at this level of effort represents my VO_2 max. (And not long after that, I will "fail," meaning I am no longer able to continue running up the hill at that pace.) VO_2 max is typically expressed in terms of the volume of oxygen a person can use, per kilogram of body weight, per minute. An average forty-five-year-old man will have a VO_2 max around 40 ml/kg/min, while an elite endurance athlete will likely score in the high 60s and above. An unfit person in their thirties or forties, on the other hand, might score only in the high 20s on a VO_2 max test, according to Mike Joyner, an exercise physiologist and researcher at the Mayo Clinic. They simply won't be able to run up that hill at all.^[*2] The higher someone's VO_2 max, the more oxygen they can consume to make ATP, and the faster they can ride or run—in short, the more they can do.

最終，我將達到無法透過依賴氧氣的途徑產生更多能量的地步，我將被迫轉向效率較低、可持續性較差的發電方式，例如短跑中使用的方式。我在此努力程度下使用的氧氣量代表我的最大攝氧量₂。（不久之後，我就會“失敗”，這意味著我無法再以那樣的速度繼續跑上

山。) 最大攝氧量 $\dot{V}O_2$ 通常用氧氣的體積來表示人每分鐘每公斤體重可以使用。平均 45 歲男性的最大攝氧量 $\dot{V}O_2$ 約為 40 毫升/公斤/分鐘，而精英耐力運動員的得分可能在 60 多分及以上。另一方面，梅奧診所的運動生理學家兼研究員邁克·喬伊納(Mike Joyner) 表示，另一方面，一個三四十歲不健康的人在最大攝氧量 $\dot{V}O_2$ 測試中可能只能獲得20 多分。他們根本無法跑上那座山。[*2] 某人的最大攝氧量 $\dot{V}O_2$ 越高，他們可以消耗更多的氧氣來製造ATP，他們騎車或跑步的速度就越快，簡而言之，他們能做的事情就越多。

This number is not just relevant to athletes; it turns out to be highly correlated with longevity. A 2018 study in *JAMA* that followed more than 120,000 people found that higher $\dot{V}O_2$ max (measured via a treadmill test) was associated with lower mortality across the board. The fittest people had the lowest mortality rates—by a surprising margin. Consider this: A person who smokes has a 40 percent greater risk of all-cause mortality (that is, risk of dying at any moment) than someone who does not smoke, representing a hazard ratio or (HR) of 1.40. This study found that someone of below-average $\dot{V}O_2$ max for their age and sex (that is, between the 25th and 50th percentiles) is at *double* the risk of all-cause mortality compared to someone in the top quartile (75th to 97.6th percentiles). Thus, poor cardiorespiratory fitness carries a greater relative risk of death than smoking.

這個數字不僅與運動員有關，而且與運動員有關。事實證明，它與壽命高度相關。《美國醫學會雜誌》2018 年對超過 12 萬人進行的一項研究發現，較高的最大攝氧量 $\dot{V}O_2$ （透過跑步機測試測量）與較低的死亡率相關。最健康的人死亡率最低，幅度驚人。想想看：吸菸者的全因死亡風險（即隨時死亡的風險）比不吸菸者高 40%，風險比或 (HR) 為 1.40。這項研究發現，與年齡和性別相比，攝氧量 $\dot{V}O_2$ 最大低於平均值（即第25 和第50 個百分位之間）的人的全因死亡風險是最高的人的兩倍四分位數（第 75 到 97.6 個百分位數）。因此，心肺健康狀況不佳比吸菸有更大的相對死亡風險。

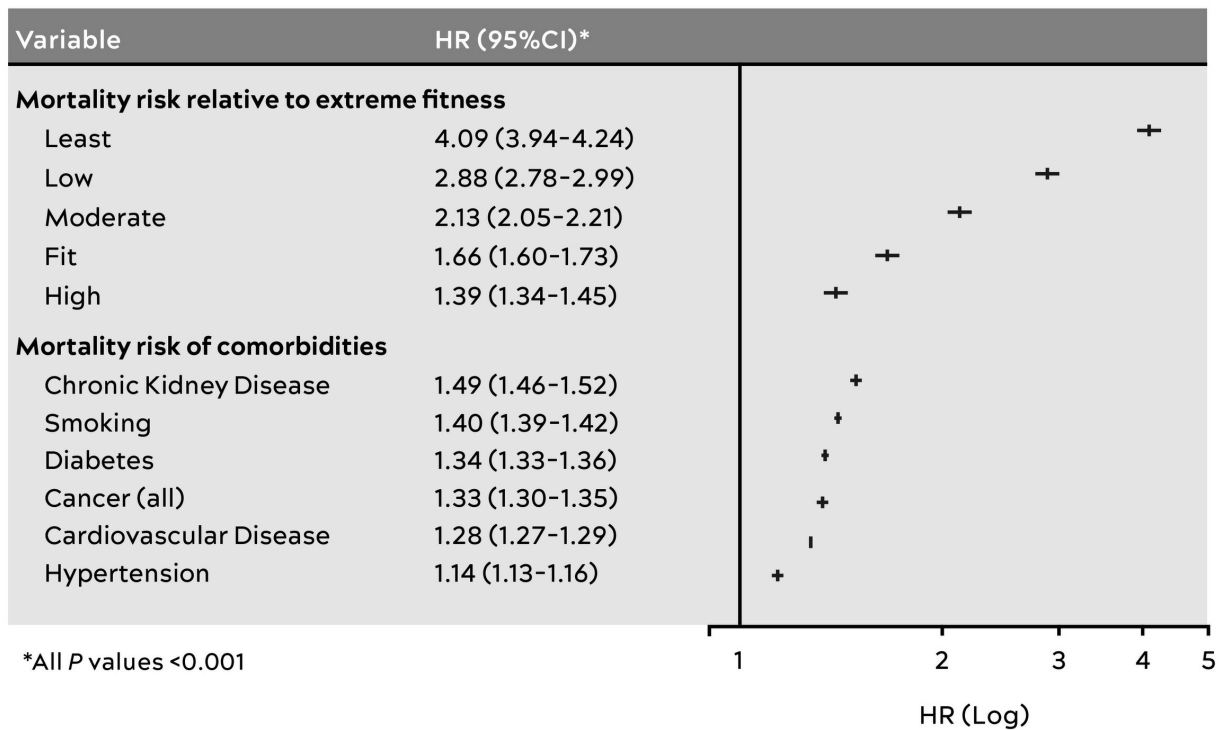
That's only the beginning. Someone in the bottom quartile of $\dot{V}O_2$ max for their age group (i.e., the least fit 25 percent) is nearly four times likelier to die

than someone in the top quartile—and five times likelier to die than a person with elite-level (top 2.3 percent) VO_2 max. That's stunning. These benefits are not limited to the very fittest people either; even just climbing from the bottom 25 percent into the 25th to 50th percentile (e.g., least fit to below average) means you have cut your risk of death nearly in half, according to this study.

這只是開始。處於其年齡組的最大攝氧量 VO_2 底部四分之一的人（即最不适合的25%），其死亡可能性幾乎是頂部四分之一的人的四倍，而死亡的可能性是其他人的五倍。具有精英級別（前 2.3%） VO_2 最大的人太棒了。這些好處不僅限於最健康的人；根據這項研究，即使只是從最低的 25% 上升到第 25 至 50 個百分位（例如，最不适合到低於平均水平），也意味著您的死亡風險已降低了近一半。

These results were confirmed by a much larger and more recent study, published in 2022 in the *Journal of the American College of Cardiology*, looking at data from 750,000 US veterans ages thirty to ninety-five (see figure 9). This was a completely different population that encompassed both sexes and all races, yet the researchers found a nearly identical result: someone in the least fit 20 percent has a 4.09 times greater risk of dying than a person in the top 2 percent of their age and sex category. Even someone of moderate fitness (40th to 60th percentile) is still at more than double the risk of all-cause mortality than the fittest group, this study found. “Being unfit carried a greater risk than any of the cardiac risk factors examined,” the authors concluded.

這些結果得到了2022 年發表在《美國心臟病學會雜誌》上的一項更大規模、更近期的研究的證實，該研究研究了75 萬名30 至95 歲美國退伍軍人的數據（見圖9 ）。這是一個完全不同的人群，包括性別和所有種族，但研究人員發現了幾乎相同的結果：最不健康的 20% 的人的死亡風險是同齡人中前 2% 的人的 4.09 倍，性別類別。這項研究發現，即使是中等健康程度的人（第 40 至 60 個百分點），全因死亡的風險仍然是最健康族群的兩倍以上。作者總結道：“身體不適所帶來的風險比所檢查的任何心臟風險因素都要大。”

Figure 9. Mortality Risk For Non-Elite Fitness and Select Comorbidities

Source: Kokkinos et al. (2022).

來源：Kokkinos 等人。（2022）。

This table expresses all-cause mortality risk for different fitness levels compared to individuals in the top 2% of VO_2 max for their age and sex (“extreme fitness”) [TOP] and for various comorbidities—that is, people with versus without each illness. [BOTTOM] Fitness groups are divided by percentile: Least (<20th percentile); Low (21st to 40th percentile); Moderate (41st to 60th percentile); Fit (61st to 80th percentile); High (81st to 97th percentile).

表格顯示了不同健康程度的全因死亡風險，與年齡和性別（「極端健康」）[TOP] 最大攝氧量₂ 前2% 的個體相比，以及各種合併症的風險 -也就是說，患有每種疾病的人和沒有每種疾病的人。[底部] 健身組依百分位數：最少（<第 20 百分位）；低（21% 至 40%）；中（第 41 至第 60 個百分位）；適合（第 61 至 80 個百分位）；高（第 81 至 97 個百分位）。

Of course, there are almost certainly confounders here, just as with all observational study, including that of nutrition. But at least five factors^[*3] increase my confidence in at least the partial causality of this relationship. First, the *magnitude* of the effect size is very large. Second, the data are consistent and *reproducible* across many studies of disparate populations.

Third, there is a *dose-dependent response* (the fitter you are, the longer you live). Fourth, there is great *biologic plausibility* to this effect, via the known mechanisms of action of exercise on lifespan and healthspan. And fifth, virtually all *experimental data* on exercise in humans suggest that it supports improved health.

當然，就像所有觀察性研究（包括營養學研究）一樣，這裡幾乎肯定存在混雜因素。但至少有五個因素 [*3] 增強了我對這段關係至少部分因果關係的信心。首先，效應量的大小非常大。其次，針對不同族群的許多研究中的數據是一致且可重複的。第三，存在劑量依賴性反應（你越健康，你的壽命就越長）。第四，透過運動對壽命和健康壽命的已知作用機制，這種效應具有很大的生物學合理性。第五，幾乎所有關於人類運動的實驗數據都顯示運動有助於改善健康。

As the authors of the *JAMA* study concluded, “Cardiorespiratory fitness is inversely associated with long-term mortality *with no observed upper limit of benefit* [emphasis mine]. Extremely high aerobic fitness was associated with the greatest survival.”

正如《美國醫學會雜誌》研究的作者所總結的那樣，「心肺健康與長期死亡率呈負相關，但沒有觀察到益處的上限[強調我的]。極高的有氧運動與最大的生存率有關。」

I can't tell you, from these data, that simply having a high VO_2 max will offset your high blood pressure or your smoking habit, as much as these hazard ratios suggest it might. Without a randomized controlled trial, we can't know for sure, but I kind of doubt it. But I can say with a very high degree of certainty that having a higher VO_2 max is better for your overall health and longevity than having a lower VO_2 max. Period.

根據這些數據，我無法告訴您，僅僅擁有高攝氧量 VO_2 最大就能抵消您的高血壓或吸煙習慣，正如這些風險比所表明的那樣。如果沒有隨機對照試驗，我們無法確定，但我對此表示懷疑。但我可以非常肯定地說，較高的攝氧量 VO_2 最大值比較低的攝氧量 VO_2 最大值更有利於您的整體健康和壽命。時期。

Even better news, for our purposes, is that VO_2 max can be increased via training. We can move the needle a lot on this measure of fitness, as we'll see.

就我們的目的而言，更好的消息是最大攝氧量 VO_2 可以透過訓練來增加。正如我們將看到的，我們可以在這個健康指標上做出很大的改變。

—

The strong association between cardiorespiratory fitness and longevity has long been known. It might surprise you, as it did me, to learn that muscle may be almost as powerfully correlated with living longer. A ten-year observational study of roughly 4,500 subjects ages fifty and older found that those with low muscle mass were at 40 to 50 percent greater risk of mortality than controls, over the study period. Further analysis revealed that it's not the mere muscle *mass* that matters but the *strength* of those muscles, their ability to generate force. It's not enough to build up big pecs or biceps in the gym—those muscles also have to be strong. They have to be capable of creating force. Subjects with low muscle strength were at double the risk of death, while those with low muscle mass and/or low muscle strength, plus metabolic syndrome, had a 3 to 3.33 times greater risk of all-cause mortality.

心肺健康與長壽之間的密切聯繫早已眾所周知。你可能會感到驚訝，就像我一樣，得知肌肉可能與長壽幾乎同樣密切相關。一項針對約 4,500 名 50 歲及以上受試者的為期 10 年的觀察性研究發現，在研究期間，肌肉質量較低的人的死亡風險比對照組高 40% 至 50%。進一步的分析表明，重要的不僅僅是肌肉質量，還有這些肌肉的力量及其產生力量的能力。在健身房裡僅僅鍛鍊出大胸肌或二頭肌是不夠的——這些肌肉還必須強壯。他們必須有能力創造力量。肌肉力量低的受試者死亡風險增加一倍，而肌肉質量低和/或肌肉強度低加上代謝症候群的受試者全因死亡風險增加 3 至 3.33 倍。

Strength may even trump cardiorespiratory fitness, at least one study suggests. Researchers following a group of approximately 1,500 men over forty with hypertension, for an average of about eighteen years, found that

even if a man was in the bottom half of cardiorespiratory fitness, his risk of all-cause mortality was still almost 48 percent lower if he was in the top third of the group in terms of strength versus the bottom third.^[*4]

至少一項研究表明，力量甚至可能勝過心肺健康。研究人員對大約 1,500 名 40 歲以上患有高血壓的男性進行了平均約 18 年的跟踪研究，結果發現，即使一名男性的心肺健康狀況處於最低水平，如果滿足以下條件，他的全因死亡風險仍會降低近 48%：就力量而言，他排在小組前三分之一，而小組中墊底三分之一。^[*4]

It's pretty much the same story we saw with VO_2 max: The fitter you are, the lower your risk of death. Again, there is no other intervention, drug or otherwise, that can rival this magnitude of benefit. Exercise is so effective against diseases of aging—the Horsemen—that it has often been compared to medicine.

這與我們在 VO_2 max 上看到的情況幾乎相同：您的健康狀況越好，死亡風險就越低。同樣，沒有任何其他幹預措施（無論是藥物還是其他方式）可以與這種程度的益處相媲美。運動對於對抗老化疾病（「騎士」）非常有效，以至於人們經常將其與藥物進行比較。

John Ioannidis, a Stanford scientist with a penchant for asking provocative questions, decided to test this metaphor literally, running a side-by-side comparison of exercise studies versus drug studies. He found that in numerous randomized clinical trials, exercise-based interventions performed as well as *or better than* multiple classes of pharmaceutical drugs at reducing mortality from coronary heart disease,^[*5] prediabetes or diabetes, and stroke.

史丹佛大學科學家約翰·約安尼迪斯 (John Ioannidis) 喜歡提出挑釁性的問題，他決定從字面上檢驗這個比喻，對運動研究和藥物研究進行並列比較。他發現，在大量隨機臨床試驗中，基於運動的干預措施在降低冠心病、^[*5] 糖尿病前期或糖尿病和中風死亡率方面與多種藥物一樣好，甚至更好。

Even better: You don't need a doctor to prescribe exercise for you.

更好的是：您不需要醫生為您開運動處方。

Much of this effect, I think, likely has to do with improved mechanics: exercise strengthens the heart and helps maintain the circulatory system. As we'll see later in this chapter, it also improves the health of the mitochondria, the crucial little organelles that produce energy in our cells (among other things). That, in turn, improves our ability to metabolize both glucose and fat. Having more muscle mass and stronger muscles helps support and protect the body—and also maintains metabolic health, because those muscles consume energy efficiently. The list goes on and on, but simply put, exercise helps the human “machine” perform far better for longer.

我認為，這種效果很大程度上可能與力學的改進有關：運動可以增強心臟功能，有助於維持循環系統。正如我們將在本章後面看到的，它還可以改善粒線體的健康，粒線體是在我們的細胞中產生能量的重要小細胞器（除其他外）。這反過來又提高了我們代謝葡萄糖和脂肪的能力。擁有更多的肌肉質量和更強的肌肉有助於支持和保護身體，還可以維持代謝健康，因為這些肌肉可以有效地消耗能量。這樣的例子不勝枚舉，但簡單地說，運動可以幫助人類「機器」在更長時間內表現得更好。

At a deeper biochemical level, exercise really does act like a drug. To be more precise, it prompts the body to produce its own, endogenous drug-like chemicals. When we are exercising, our muscles generate molecules known as cytokines that send signals to other parts of our bodies, helping to strengthen our immune system and stimulate the growth of new muscle and stronger bones. Endurance exercise such as running or cycling helps generate another potent molecule called brain-derived neurotrophic factor, or BDNF, that improves the health and function of the hippocampus, a part of the brain that plays an essential role in memory. Exercise helps keep the brain vasculature healthy, and it may also help preserve brain volume. This is why I view exercise as a particularly important part of the tool kit for patients at risk of developing Alzheimer's disease—such as Stephanie, the woman with the high-risk Alzheimer's genes whom we met in chapter 9.

從更深層的生化層面來看，運動確實扮演了藥物的角色。更準確地說，它促使身體產生自己的內源性藥物樣化學物質。當我們鍛鍊時，

我們的肌肉會產生被稱為細胞因子的分子，這些分子會向我們身體的其他部位發送訊號，幫助增強我們的免疫系統並刺激新肌肉和更強壯骨骼的生長。跑步或騎自行車等耐力運動有助於產生另一種有效分子，稱為腦源性神經營養因子（BDNF），它可以改善海馬體的健康和功能，海馬體是大腦的一部分，在記憶中發揮著重要作用。運動有助於保持大腦脈管系統健康，也可能有助於維持腦容量。這就是為什麼我認為運動對於有阿茲海默症風險的患者來說是一個特別重要的工具包——比如斯蒂芬妮，我們在第9章遇到的帶有高危險阿茲海默症基因的女性。

The data demonstrating the effectiveness of exercise on lifespan are as close to irrefutable as one can find in all human biology. Yet if anything, I think exercise is even *more* effective at preserving healthspan than extending lifespan. There is less hard evidence here, but I believe that this is where exercise really works its magic when applied correctly. I tell my patients that even if exercise *shortened* your life by a year (which it clearly does not), it would still be worthwhile purely for the healthspan benefits, especially in middle age and beyond.

證明運動對壽命的有效性的數據幾乎是人類生物學中無可辯駁的。但如果有的話，我認為運動在保持健康方面比延長壽命更有效。雖然缺乏確鑿的證據，但我相信，如果運用得當，這就是鍛鍊真正發揮其魔力的地方。我告訴我的病人，即使運動會使你的壽命縮短一年（顯然事實並非如此），純粹為了健康壽命的好處，它仍然是值得的，尤其是在中年及以後。

One of the prime hallmarks of aging is that our physical capacity erodes. Our cardiorespiratory fitness declines for various reasons that begin with lower cardiac output, primarily due to reduced maximum heart rate. We lose strength and muscle mass with each passing decade, our bones grow fragile and our joints stiffen, and our balance falters, a fact that many men and women discover the hard way, by falling off a ladder or while stepping off a curb.

老化的主要標誌之一是我們的體能退化。我們的心肺健康因各種原因而下降，首先是心輸出量降低，主要是因為最大心率降低。每過十

年，我們就會失去力量和肌肉質量，我們的骨骼變得脆弱，關節變得僵硬，我們的平衡會變得不穩定，這是許多男人和女人從梯子上摔下來或走下路邊時經歷的慘痛經驗才發現的事實。

To paraphrase Hemingway, this process happens in two ways: gradually, and then suddenly. The reality of the situation is that old age can be really tough on our bodies. Longitudinal and cross-sectional studies find that fat-free mass (meaning mostly muscle mass) and activity levels remain relatively consistent as people age from their twenties and thirties into middle age. But both physical activity levels *and* muscle mass decline steeply after about age sixty-five, and then even more steeply after about seventy-five. It's as if people just fall off a cliff sometime in their mid-seventies.

用海明威的話來說，這個過程以兩種方式發生：逐漸發生，然後突然發生。現實情況是，老年對我們的身體來說確實很艱難。縱向和橫斷面研究發現，隨著人們從二、三十歲進入中年，去脂質量（主要是肌肉質量）和活動水平保持相對一致。但身體活動量和肌肉量在六十五歲左右後急劇下降，在七十五歲左右後下降幅度甚至更大。就好像人們在七十多歲的時候從懸崖上掉下來一樣。

By age eighty, the average person will have lost eight kilograms of muscle, or about eighteen pounds, from their peak. But people who maintain higher activity levels lose much less muscle, more like three to four kilograms on average. While it's not clear which direction the causation flows here, I suspect it's probably both ways: people are less active because they are weaker, and they are weaker because they are less active.

到八十歲時，一般人會比巔峰時期減少八公斤肌肉，即約十八磅。但維持較高活動量的人損失的肌肉要少得多，平均約三到四公斤。雖然尚不清楚因果關係朝哪個方向發展，但我懷疑這可能是雙向的：人們不那麼活躍是因為他們更弱，而他們更弱是因為他們不那麼活躍。

Continued muscle loss and inactivity literally puts our lives at risk. Seniors with the least muscle mass (also known as lean mass) are at the greatest risk of dying from all causes. One Chilean study looked at about one thousand men and four hundred women, with an average age of seventy-four at enrollment.

The researchers divided the subjects into quartiles, based on their appendicular lean mass index (technically, the muscle mass of their extremities, arms and legs, normalized to height), and followed them over time. After twelve years, approximately 50 percent of those in the lowest quartile were dead, compared to only 20 percent of those in the highest quartile for lean mass. While we can't establish causality here, the strength and reproducibility of findings like this suggest this is more than just a correlation. Muscle helps us survive old age.

持續的肌肉損失和不活動確實會讓我們的生命處於危險之中。肌肉質量（也稱為瘦體重）最少的老年人死於各種原因的風險最大。智利的一項研究調查了大約 1000 名男性和 400 名女性，入組時的平均年齡為 74 歲。研究人員根據受試者的四肢瘦肉質量指數（從技術上講，是四肢、手臂和腿部的肌肉質量，標準化為身高）將受試者分為四分位數，並隨著時間的推移對他們進行跟蹤。十二年後，處於最低四分位數的人中約有 50% 死亡，而處於瘦體重最高四分位數的人中只有 20% 死亡。雖然我們無法在這裡確定因果關係，但此類研究結果的強度和可重複性表明這不僅僅是一種相關性。肌肉幫助我們度過晚年。

This is another area where lifespan and healthspan overlap to a great extent. That is, I suspect that having more muscle mass delays death precisely *because* it also preserves healthspan. This is why I place so much emphasis on maintaining our musculoskeletal structure—which I call the “exoskeleton,” à la *Terminator*, for lack of a better term.

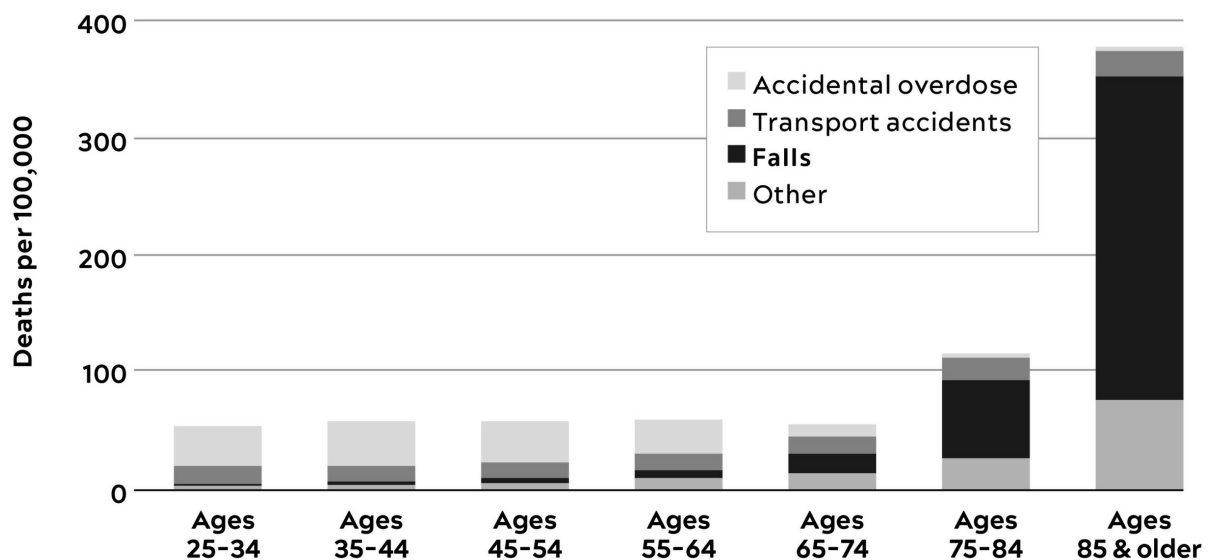
這是壽命和健康壽命在很大程度上重疊的另一個領域。也就是說，我懷疑擁有更多的肌肉量可以延遲死亡，因為它還能維持健康壽命。這就是為什麼我如此強調維持我們的肌肉骨骼結構——我稱之為“外骨骼”，就像《魔鬼終結者》一樣，因為沒有更好的術語了。

Your exoskeleton (muscle) is what keeps your actual skeleton (bones) upright and intact. Having more muscle mass on your exoskeleton appears to protect you from all kinds of trouble, even adverse outcomes following surgery—but most important, it is highly correlated with a lower risk of falling, a leading but oft-ignored cause of death and disability in the elderly. As figure 10 reveals, falls are by *far* the leading cause of accidental deaths in

those ages sixty-five and older—and this is without even counting the people who die three or six or twelve months after their nonfatal but still serious fall pushed them into a long and painful decline. Eight hundred thousand older people are hospitalized for falls each year, according to the CDC.

您的外骨骼（肌肉）使您的實際骨骼（骨骼）保持直立和完整。外骨骼上擁有更多的肌肉似乎可以保護您免受各種麻煩，甚至是手術後的不良後果，但最重要的是，它與較低的跌倒風險高度相關，跌倒是導致死亡和殘疾的主要原因，但常被忽視。老年人。如圖10 所示，迄今為止，跌倒是65 歲及以上老年人意外死亡的主要原因，這甚至沒有計算在非致命但仍然嚴重的跌倒導致他們陷入困境後三、六個月或十二個月死亡的人數。漫長而痛苦的衰退。據疾病預防控制中心稱，每年有八十萬名老年人因跌倒而住院。

Figure 10. Accidental Deaths in the United States



Source: CDC (2021).

資料來源：疾病預防控制中心 (2021)。

I believe this association likely works both ways: someone with more muscle mass is less likely to fall and injure themselves, while those who are less likely to fall for other reasons (better balance, more body awareness) will also have an easier time maintaining muscle mass. Conversely, muscle atrophy

and sarcopenia (age-related muscle loss) increase our risk of falling and possibly requiring surgery—while at the same time worsening our odds of surviving said surgery without complications. Just as with VO_2 max, it is important to maintain muscle mass at all costs.

我相信這種關聯可能是雙向的：肌肉量較多的人摔倒和受傷的可能性較小，而那些因其他原因（更好的平衡、更多的身體意識）而不太可能摔倒的人也將更容易保持肌肉大量的。相反，肌肉萎縮和肌少症（與年齡相關的肌肉損失）會增加我們跌倒並可能需要手術的風險，同時也會降低我們在手術中沒有併發症的生存幾率。正如最大攝氧量₂一樣，不惜一切代價維持肌肉質量非常重要。

Exercise in all its forms is our most powerful tool for fighting this misery and reducing our risk of death across the board. It slows the decline, not just physically but across all three vectors of healthspan, including cognitive and emotional health. A recent study of older British adults found that those with sarcopenia at baseline were nearly *six times* likelier to report having a low quality of life a decade later than those who had maintained more muscle mass.

各種形式的運動是我們對抗這種痛苦和全面降低死亡風險的最有力工具。它不僅可以減緩身體的衰退，還可以減緩健康壽命的所有三個面向的衰退，包括認知和情緒健康。最近一項針對英國老年人的研究發現，基線患有肌少症的人十年後報告生活品質低下的可能性比那些保持更多肌肉質量的人高出近六倍。

This is what we want to avoid. We can avoid it with the help of this powerful “drug” called exercise that miraculously extends lifespan and improves healthspan. The difference is that it requires much more work and knowledge than simply taking a pill. But the more effort you’re willing to put in now, the more benefit you’ll reap in the future.

這是我們想要避免的。我們可以藉助這種名為運動的強大「藥物」來避免這種情況，它可以奇蹟般地延長壽命並改善健康狀況。不同之處在於，它比簡單地吃藥需要更多的工作和知識。但你現在願意付出的努力越多，未來你獲得的收穫就越多。

This is why I place such an emphasis on weight training—and doing it now, no matter your age. It is never too late to start; my mom did not begin lifting weights until she was sixty-seven, and it has changed her life. There are dozens of studies showing that strength training programs can significantly improve the mobility and physical function of subjects who are obese, or recovering from cancer treatment, even those who are already elderly and frail. Therefore, I will find a way to lift heavy weights in some way, shape, or form four times per week, no matter what else I am doing or where I might be traveling.

這就是為什麼我如此重視重量訓練——無論你的年齡如何，現在就做。任何時候開始都不晚；我媽媽直到六十七歲才開始舉重，改變了她的人生。有數十項研究表明，肌力訓練計畫可以顯著改善肥胖者或從癌症治療中恢復的受試者的活動能力和身體功能，甚至是那些已經年老體弱的受試者。因此，我會找到一種方法，以某種方式、形狀或形式每週舉起重物四次，無論我在做什麼或在哪裡旅行。

But exercise gets little more than lip service from Medicine 2.0. When was the last time your doctor tested your grip strength or asked you a detailed question about your strength training? Does your doctor know your VO_2 max? Or have they offered training suggestions for how to improve it? I'm guessing that has happened precisely never—because none of what we're covering here or in the nutrition chapters is even considered to rise to the level of “healthcare,” at least in our system. Some insurance companies offer discounts or incentives for members to go to the gym, but the kind of focused attention that I think we all need (including me) is well beyond the purview of most physicians.

但醫學 2.0 中的運動只不過是口頭說說而已。您的醫生最後一次測試您的握力或詢問您有關肌力訓練的詳細問題是什麼時候？您的醫師知道您的最大攝氧量 VO_2 嗎？或者他們是否提供瞭如何改進的培訓建議？我猜這種情況從來沒有發生過——因為我們在這裡或營養章節中介紹的任何內容都沒有被認為上升到“醫療保健”的水平，至少在我們的系統中是這樣。一些保險公司為會員去健身房提供折扣或獎勵，但我認

為我們所有人（包括我）都需要的那種集中注意力遠遠超出了大多數醫生的職權範圍。

It's only *after* we get injured or become so weak that we are in danger of losing our independence, that we are deemed eligible for physical therapy and rehabilitation. So think of what follows as “prehab”—physical therapy *before* you need it.

只有當我們受傷或變得如此虛弱以至於我們面臨失去獨立的危險時，我們才被認為有資格接受物理治療和康復。因此，請考慮接下來的「預復健」——在您需要之前進行物理治療。

—

When I talk with my patients about exercise, I often bring them back to the story of Sophie, my friend Becky's mother, whom we met in chapter 3. She had actually been relatively active, even in retirement. She played golf once or twice a week and worked most days in her garden. It wasn't a structured “exercise” program; she was just doing the things she loved. But then she injured her shoulder, and then her knee, requiring surgery for both. Even after surgery, she was never able to recover fully. Her activity level dropped off almost to zero. As Becky related to me, her mother mostly sat around the house, feeling depressed. Her cognitive decline fairly quickly ensued.

當我和我的病人談論運動時，我經常讓他們回想起我朋友貝基的母親索菲的故事，我們在第三章中認識了她。她實際上一直相對活躍，即使在退休時也是如此。她每週打一兩次高爾夫球，大部分時間都在花園工作。這不是一個結構化的「鍛鍊」計劃；而是一個計劃。她只是在做她喜歡的事。但隨後她的肩膀和膝蓋都受傷了，需要手術治療。即使手術後，她也未能完全康復。她的活動水準幾乎下降到零。正如貝琪告訴我的那樣，她的母親大部分時間都坐在房子裡，感到沮喪。她的認知能力很快就下降了。

This made me incredibly sad as I sat there in the pew at her funeral. Yet her story was all too familiar. We have all seen older friends and relatives go through a similar ordeal, slowly (or not slowly) weakening until they can no

longer find enjoyment in the things they once loved to do. What could have been done, I wondered, to change Sophie's fate?

當我坐在她葬禮上的長椅上時，這讓我非常悲傷。然而她的故事卻太熟悉了。我們都曾經看過年長的朋友和親戚經歷過類似的磨難，慢慢地（或不是慢慢地）衰弱，直到他們不再能從他們曾經喜歡做的事情中找到樂趣。我想知道，可以做些什麼來改變蘇菲的命運呢？

Had she simply needed to “exercise more”? Go to the gym and use the elliptical? Would that have saved her somehow?

她只是需要「多運動」嗎？去健身房使用橢圓機？這會以某種方式拯救她嗎？

It wasn't clear that the answer was that simple. I had done plenty of exercise in my own life, but by the time of Sophie's funeral I was nursing a handful of my own pet injuries that I'd accumulated over the years. Fit as I was, it wasn't clear that I was on a better path than Sophie had been.

目前尚不清楚答案是否那麼簡單。我一生中進行了大量的鍛煉，但到了索菲的葬禮時，我正在護理自己多年來積累的一些寵物傷口。儘管我很健康，但我並不清楚我是否走上了比蘇菲更好的道路。

For most of my life, I've been obsessive with respect to fitness, always focusing on one particular sport—and inevitably taking it to an extreme. After I had burned myself out on boxing, then running, and finally long-distance open-water swimming, I turned to cycling. I went all in: My primary aim in life was to win the local cycling time-trial series, a twenty-kilometer individual race against the clock that almost nobody else cared about. I spent hours analyzing power-meter data and calculating my coefficient of aerodynamic drag, looking to shave precious seconds from my times using dorky models that I built in Excel.

在我生命的大部分時間裡，我一直著迷於健身，總是專注於一項特定的運動——並且不可避免地把它發揮到極致。當我在拳擊、跑步、最後長距離開放水域游泳中精疲力盡後，我轉向騎自行車。我全力以赴：我人生的首要目標是贏得當地自行車計時賽系列賽，這是一項幾乎沒有人關心的與時間賽跑的二十公里個人賽。我花了幾個小時分析

功率計數據併計算空氣動力阻力係數，希望使用我在 Excel 中建立的愚蠢模型來節省寶貴的時間。

The truth was that I had become pretty useless at everything *except* pedaling my road bike as fast as possible for twenty kilometers. I possessed a high VO_2 max and I could produce a lot of power through the pedals, but I was not truly strong or flexible, and I did not have great balance or stability. I was a one-dimensional athlete, and if I had kept it up, I might have ended up with my spine fused into my time-trial tuck, still able to ride my bike but unable to do anything else useful, especially with my upper body. I eventually quit competitive cycling because it became clear that at a certain point this obsessive approach becomes unsustainable in virtually any activity. How many old marathon runners do you know who are still racing? Probably not many.

事實上，除了盡可能快地騎公路自行車二十公里之外，我對一切都變得毫無用處。我擁有較高的最大攝氧量 VO_2 ，並且可以透過踏板產生大量動力，但我並不真正強壯或靈活，而且我沒有很好的平衡或穩定性。I was a one-dimensional athlete, and if I had kept it up, I might have ended up with my spine fused into my time-trial tuck, still able to ride my bike but unable to do anything else useful, especially with my upper 身體。我最終退出了競技自行車運動，因為很明顯，在某種程度上，這種強迫性的方法幾乎在任何活動中都變得不可持續。你知道有多少仍在參加比賽的老馬拉松選手嗎？可能不多。

After that, I fell into this kind of directionless limbo where I bounced around between different fitness activities. I tried to get back into running. I went to Pilates classes with my wife. I did Barry's Bootcamp for a time. You name it, I tried it. Then I joined a boutique fitness chain that specializes in high-intensity interval training, or HIIT. I enjoyed the fast-paced workouts they offered, like treadmill sprints and thirty-second Burpee blocks, and it took a fraction of the time that cycling did, so I was happy about that. But I didn't have a goal other than "exercising."

從那以後，我就陷入了這種沒有方向的困境，在不同的健身活動之間跳來跳去。我試著重新開始跑步。我和妻子一起去上普拉提課。我參

加過一次巴里的訓練營。你說得出來，我試過了。然後我加入了一家專門從事高強度間歇訓練（HIIT）的精品健身連鎖店。我很喜歡他們提供的快節奏鍛煉，例如跑步機衝刺和三十秒波比跳，而且它所花費的時間只是騎自行車的一小部分，所以我對此感到很高興。但除了「鍛鍊」之外，我沒有其他目標。

All this changed as I sat in the pew of the church at Sophie's funeral. Officially, she had died from pneumonia, but what had really killed her, I realized, was the slow gravitational pull of aging on her body. That had not begun in the last year or even the last decade of her life. It had been working against her, pulling her down, since before I had met her—for decades. And it was killing the rest of us, too: her daughter, Becky, along with my patients, myself, and everyone reading this book is likely headed for the same steep decline.

當我坐在蘇菲葬禮上教堂的長椅上時，這一切都改變了。根據官方說法，她死於肺炎，但我意識到，真正殺死她的是她身體上緩慢的衰老引力。這並不是從她生命的最後一年甚至最後十年開始的。自從我遇見她之前，幾十年來，它就一直對她不利，把她拖垮。它也殺死了我們其他人：她的女兒貝琪、我的病人、我自己，以及讀這本書的每個人都可能走向同樣的急劇下降。

That thought saddened me to my core. But then it hit me: the only way that we would be able to fight this was to adopt the philosophy of a decathlete—and apply it to aging.

這個想法讓我內心深處感到悲傷。但後來我突然想到：我們能夠對抗這個問題的唯一方法就是採用十項全能的理念，並將其應用於老化。

Of all Olympic athletes, the decathletes are most revered. The male and female winners of the gold medal are declared the “World's Greatest Athletes.” Yet they are not the best at any of the ten individual events in which they compete; they likely would not even medal. But they are still considered the greatest because they are remarkably good at so many different events. They are true generalists—yet they train like specialists.

在所有奧運選手中，十項全能運動員最受尊敬。男女金牌得主被宣佈為“世界上最偉大的運動員”。然而，他們在參加的十個個人項目中都不是最好的；他們甚至可能不會獲得獎牌。但他們仍然被認為是最偉大的，因為他們在許多不同的項目上都非常擅長。他們是真正的多面手，但他們卻像專家一樣接受訓練。

We need to adopt a similar approach to aging, I decided: each of us needs to be training for the Centenarian Decathlon.

我決定，我們需要採取類似的方法來應對老化：我們每個人都需要接受百歲十項全能的訓練。

The Centenarian Decathlon

百歲十項全能

What in the world is the Centenarian Decathlon?

百歲十項全能到底是什麼？

I'm not talking about an actual competition among hundred-year-olds, although similar events do already exist: the National Senior Games, held every other year, brings together remarkable older athletes, some of them in their nineties and beyond. The record for the hundred-meter dash for women ages one hundred and up is about forty-one seconds.

我說的不是百歲老人之間的實際比賽，儘管類似的賽事確實存在：每隔一年舉行一次的全國老年運動會，聚集了傑出的老年運動員，其中一些已經九十多歲了。百歲以上女性百公尺短跑的紀錄約四十一秒。

The Centenarian Decathlon is a framework I use to organize my patients' physical aspirations for the later decades of their lives, especially their Marginal Decade. I know, it's a somewhat morbid topic, thinking about our own physical decline. But not thinking about it won't make it any less inevitable.

百歲十項全能是我用來組織患者在生命的後幾十年，尤其是他們的邊緣十年的身體願望的一個框架。我知道，這是一個有點病態的話題，思考我們自己的身體衰退。但不去想它並不會讓它變得不那麼不可避免。

Think of the Centenarian Decathlon as the ten most important physical tasks you will want to be able to do for the rest of your life. Some of the items on the list resemble actual athletic events, while some are closer to activities of daily living, and still others might reflect your own personal interests. I find it useful because it helps us visualize, with great precision, exactly what kind of fitness we need to build and maintain as we get older. It creates a template for our training.

將百歲十項全能視為您在餘生中希望能夠完成的十項最重要的體能任務。清單中的一些項目類似於實際的體育賽事，而一些更接近日常生活活動，還有一些可能反映您自己的個人興趣。我發現它很有用，因為它可以幫助我們非常精確地想像隨著年齡的增長，我們需要建立和維持什麼樣的健康狀況。它為我們的培訓創建了一個模板。

I start by presenting my patients with a long list of physical tasks that might include some of the following:

我首先向患者展示一長串身體任務，其中可能包括以下一些內容：

1. Hike 1.5 miles on a hilly trail.

在山路上徒步 1.5 英里。

2. Get up off the floor under your own power, using a maximum of one arm for support.

用自己的力量從地板上站起來，最多使用一隻手臂作為支撐。

3. Pick up a young child from the floor.

從地板上抱起一個小孩。

4. Carry two five-pound bags of groceries for five blocks.

攜帶兩袋五磅重的食品雜貨走五個街區。

5. Lift a twenty-pound suitcase into the overhead compartment of a plane.
將二十磅重的行李箱抬進飛機的頭頂行李艙。
6. Balance on one leg for thirty seconds, eyes open. (Bonus points: eyes closed, fifteen seconds.)
單腳保持平衡三十秒，睜開眼睛。（加分：閉眼十五秒。）
7. Have sex.
發生性關係。
8. Climb four flights of stairs in three minutes.
三分鐘內爬四層樓梯。
9. Open a jar.
打開一個罐子。
10. Do thirty consecutive jump-rope skips.
連續跳繩三十次。

The full list is much longer, with more than fifty different items, but you get the idea. Once they've read it I ask them to please select which of these tasks they want to be able to perform in their ninth, or better yet tenth, decade. Which ones do they choose?

完整的清單要長得多，有五十多個不同的項目，但你明白了。他們讀完後，我會要求他們選擇他們希望在第九個、甚至第十個十年中能夠執行的任務中的哪些。他們選擇哪些？

All of them, typically. They want to be able to hike a mile and a half, or carry their own groceries, or pick up a great-grandchild, or get up if they fall down. Or play eighteen holes of golf, or open a jar, or fly somewhere on a plane. Of course they do.

通常，他們都是。他們希望能夠徒步一英里半，或者自己攜帶雜貨，或者抱起曾孫，或者在跌倒時站起來。或打十八洞高爾夫球，或打開罐子，或搭飛機飛往某個地方。當然有。

That's great, I say. You'll make that kid's day when you pick her up like that. But now let's do a little math. Let's say the kid weighs twenty-five or thirty pounds. That's basically the same as doing a squat while holding a thirty-pound dumbbell in front of you (i.e., a goblet squat). Can you do that now, at age forty? Most likely. But now let's look into the future. Over the next thirty or forty years, your muscle strength will decline by about 8 to 17 percent per decade—accelerating as time goes on. So if you want to pick up that thirty-pound grandkid or great-grandkid when you're eighty, you're going to have to be able to lift about fifty to fifty-five pounds now. Without hurting yourself. Can you do that?

太好了，我說。當你像那樣去接她時，你就會度過那個孩子的一天。但現在讓我們來做一些數學計算。假設這個孩子重二十五或三十磅。這基本上與在你面前拿著一個三十磅的啞鈴進行深蹲（即高腳杯深蹲）相同。四十歲的你現在還能做到嗎？最有可能的。但現在讓我們展望未來。在接下來的三十或四十年裡，您的肌肉力量每十年就會下降約 8% 到 17%，而且隨著時間的推移，速度會加速下降。因此，如果你想在八十歲時接起那個三十磅重的孫子或曾孫，那麼你現在必須能夠舉起大約五十到五十五磅的重量。在不傷害自己的情況下。你能做到嗎？

I press the issue. You also want to be able to hike on a hilly trail? To do that comfortably requires a VO_2 max of roughly 30 ml/kg/min. Let's take a look at the results of your latest VO_2 max test—and guess what, you only scored a 30. You're average for your age, but I'm afraid that's not good enough, because your VO_2 max is also going to decline. So we're going to have to go ahead and cross that hike off your list. You can pull it off now, but you likely won't be able to do it when you're older.

我按這個問題。您還想能夠在丘陵小徑上健行嗎？要舒適地做到這一點，最大攝氧量 \dot{V}_O_2 大約為 30 毫升/公斤/分鐘。讓我們來看看您最新的 VO_2 最大測試結果 - 你猜怎麼著，您只得到了 30 分。就您的年齡而言，您處於平均水平，但恐怕這還不夠好，因為您的最大攝氧量 \dot{V}_O_2 也

會下降。所以我們必須繼續前進，把這次徒步旅行從你的清單上劃掉。你現在可以做到，但當你老了的時候你可能就做不到了。

On it goes. To lift that twenty-pound suitcase overhead when you are older means doing so with forty or fifty pounds now. To be able to climb four flights of stairs in your eighties means you should be able to pretty much sprint up those same stairs today. In every case, you need to be doing *much more now*, to armor yourself against the natural and precipitous decline in strength and aerobic capacity that you will undergo as you age.

繼續。當你年紀大了，要把那個二十磅的行李箱舉過頭頂，現在就代表要用四十到五十磅。在八十多歲時能夠爬四層樓梯意味著您今天應該能夠幾乎衝刺相同的樓梯。在任何情況下，您現在都需要做更多的事情，以保護自己免受隨著年齡的增長而自然而急劇地下降的力量和有氧能力的影響。

Eventually, my patients get it. Together, we come up with a list of ten or fifteen events in their personal Centenarian Decathlon, representing their goals for their later decades. This then determines how they should be training.

最終，我的病人明白了。我們共同列出了他們個人百歲十項全能中的十到十五個項目的清單，代表了他們晚年的目標。這決定了他們應該如何訓練。

The beauty of the Centenarian Decathlon is that it is broad yet unique to each individual. Nor is it limited to ten events; for most people it ends up being more, depending on their goals. My version of the Decathlon is tailored to my own particular interests, such as swimming and archery. It's also fairly aggressive, I admit, reflecting the importance of a high level of fitness in my life. So I would probably add in some of the following events:

百歲十項全能的美妙之處在於它範圍廣泛，但對每個人來說都是獨特的。也不限於十項活動；對於大多數人來說，最終會更多，這取決於他們的目標。我的迪卡儂版本是根據我自己的特殊興趣量身定制的，例如游泳和射箭。我承認，這也相當具有侵略性，反映了高水平健身在我生活中的重要性。所以我可能會添加以下一些事件：

11. Swim half a mile in twenty minutes.
二十分鐘遊半英里。
12. Walk with a thirty-pound dumbbell in each hand for one minute.
每隻手拿著三十磅的啞鈴行走一分鐘。
13. Draw back and fire a fifty-pound compound bow.
退後並發射五十磅的複合弓。
14. Do five pull-ups.
做五個引體向上。
15. Climb ninety steps in two minutes ($\text{VO}_2 \text{ max} = 32$).
兩分鐘內爬九十階（最大攝氧量₂ = 32）。
16. Dead-hang for one minute.
靜止一分鐘。
17. Drive a race car within 5 to 8 percent of the pace I can do so today.
以我今天能達到的速度 5% 到 8% 的速度駕駛賽車。
18. Hike with a twenty-pound backpack for an hour.
背著二十磅重的背包健行一個小時。
19. Carry my own luggage.
我自己拎著行李。
20. Walk up a steep hill.
走上一座陡峭的山坡。

In the end, most people's Centenarian Decathlons will probably overlap to a degree. Someone who enjoys stand-up paddleboarding, for example, would perhaps choose "events" focused around building core and cross-body strength. But she will likely be training the same muscle groups as I am doing for archery, and maintaining a similar degree of stamina and balance.

最終，大多數人的百歲十項全能可能會在某種程度上重疊。例如，喜歡立槳板運動的人可能會選擇專注於增強核心力量和跨身體力量的「活動」。但她可能會訓練與我射箭相同的肌肉群，並保持相似程度的耐力和平衡。

The Centenarian Decathlon is ambitious, no question. A ninety-year-old who is even able to board a plane under her own power, let alone hoist a carry-on bag, is doing extremely well. But there is a method to the madness. These individual tasks are not out of reach. There are octogenarians, nonagenarians, and even centenarians right now who are running marathons, racing bicycles, lifting weights, flying airplanes, jumping *out* of airplanes, skiing the Rocky Mountains, competing in actual decathlons, and doing all sorts of other amazing things. So all these events are within the realm of possibility.

毫無疑問，百歲十項全能是雄心勃勃的。一個九十多歲的老人，連自己的力量都能登上飛機，更不用說拎起隨身攜帶的包了，已經是非常出色了。但有一種方法可以達到瘋狂的目的。這些單獨的任務並非遙不可及。現在有八十多歲的老人、九十多歲的老人，甚至還有百歲老人，他們在跑馬拉松、騎自行車、舉重、駕駛飛機、從飛機上跳下來、在洛磯山脈滑雪、參加真正的十項全能比賽，以及做各種其他令人驚奇的事。因此，所有這些事件都是有可能發生的。

One purpose of the Centenarian Decathlon, in fact, is to help us redefine what is possible in our later years and wipe away the default assumption that most people will be weak and incapable at that point in their lives. We need to abolish that decrepit stereotype and create a new narrative—perhaps modeled after the old-school fitness guru Jack LaLanne, who kept doing his usual rigorous daily workout right up until his death at age ninety-six. Unlike most very long-lived individuals, he didn't just get there by accident or luck. He built and maintained a high level of fitness throughout his life, beginning in the 1930s, when very few people exercised regularly and “fitness centers” did not yet exist. As he got older, he set out very deliberately to defy the stereotype of aging as a period of misery and decline. He did the work, and he succeeded, giving us a glimpse of what an older person is truly capable of achieving.

事實上，百歲十項全能的目的之一是幫助我們重新定義晚年的可能性，並消除大多數人在生命的那個階段將變得軟弱和無能的默認假設。我們需要廢除這種陳舊的刻板印象，創造一種新的敘述方式——也許可以效仿老派健身大師傑克·拉蘭尼（Jack LaLanne），他每天都堅持嚴格的鍛煉，直到九十六歲去世。與大多數長壽者不同，他的到達並非偶然或幸運。從 20 世紀 30 年代開始，他一生都建立並保持了高水平的健康水平，當時很少有人定期鍛煉，而且「健身中心」還不存在。隨著年齡的增長，他開始非常有意識地打破「衰老是一段痛苦和衰落時期」的刻板印象。他做了這項工作，而且成功了，讓我們看到了老年人真正有能力實現什麼目標。

If we are to follow in LaLanne's footsteps, we must stop pointlessly "exercising," just because we think we are supposed to, banging away on the elliptical trainer at lunch hour. I promise, you can do better. I suggest you join me and start *training*, with a very specific purpose, which is to be kick-ass one-hundred-year-olds. When my patients say they are more interested in being kick-ass fifty-year-olds than Centenarian Decathletes, I reply that there is no better way to make that happen than to set a trajectory toward being vibrant at one hundred (or ninety, or eighty) just as an archer who trains at 100 yards will be more accurate at 50. By fixing our aim on the Centenarian Decathlon, we can make every decade between now and then better as well.

如果我們要追隨拉蘭的腳步，我們就必須停止毫無意義的“鍛煉”，僅僅因為我們認為我們應該在午餐時間敲擊橢圓機。我保證，你可以做得更好。我建議你和我一起開始訓練，有一個非常明確的目標，就是成為百歲老人。當我的病人說他們更感興趣的是成為五十歲的強者，而不是百歲十項全能運動員時，我回答說，要實現這一目標，沒有比設定一條在一百歲（或九十歲，或80）就像弓箭手在100 碼處訓練一樣，在50 碼處訓練會更加準確。透過將我們的目標定為百歲十項全能，我們也可以讓從現在到那時的每一個十年都變得更好。

With the Centenarian Decathlon as my goal, I now work out with the focus that I once directed exclusively toward cycling, swimming, or boxing. It's not about being great at any one pursuit, but about being pretty good at just about everything. As Centenarian Decathletes, we are no longer training for a

specific event, but to become a different sort of athlete altogether: an athlete of life.

以百歲十項全能作為我的目標，我現在的運動重點是以前專門針對自行車、游泳或拳擊的。這並不是要在任何一項追求上都表現出色，而是要在所有事情上都表現出色。身為百歲十項全能運動員，我們不再是為了某個特定的項目而訓練，而是為了成為完全不同類型的運動員：生活的運動員。

[SKIP NOTES](#)

[跳過註釋](#)

[*1](#) So if you like this book, please thank John Griffin. If you don't, blame me.

*1 如果您喜歡這本書，請感謝約翰·格里芬。如果你不這樣做，那就怪我吧。

[*2](#) Most of the top riders in the Tour de France will have a VO_2 max in the high 70s or low 80s. The highest VO_2 max ever recorded was an absolutely mind-bending 97.5 ml/kg/min.

*2 環法自行車賽中的大多數頂級車手的最大攝氧量₂都在70多歲或80多歲以下。有史以來記錄的最高攝氧量₂最大值絕對是令人費解的97.5毫升/公斤/分鐘。

[*3](#) These factors represent five of the nine criteria defined in the 1930s by Austin Bradford Hill, one of the godfathers of scientific methodology, as a tool for evaluating epidemiological and laboratory findings. We will meet Bradford Hill again in the chapters on nutrition.

*3 這些因素代表了科學方法論教父之一奧斯汀·布拉德福德·希爾(Austin Bradford Hill)在20世紀30年代定義的九個標準中的五個，作為評估流行病學和實驗室結果的工具。我們將在營養章節中再次見到布拉德福德·希爾。

[*4](#) Cardiorespiratory fitness was measured on a treadmill using a modified Balke Protocol, and strength was measured by one-rep max in bench press and leg extension.

*4 心肺健康是在跑步機上使用修改後的巴爾克方案測量的，力量是透過臥推和腿部伸展的最大一次次數來測量的。

[*5](#) The exception, in Ioannidis's analysis, was heart failure, which responded more favorably to treatment with diuretic drugs than to exercise-based interventions.

*5 在Ioannidis的分析中，例外情況是心臟衰竭，利尿藥物治療的反應比基於運動的干預措施更有利。

CHAPTER 12

第12章

Training 101

培訓101

How to Prepare for the Centenarian Decathlon

如何為百歲十項全能做準備

It is impossible to produce superior performance unless
you do something different from the majority.

除非你做一些與大多數人不同的事情，否則不可
能產生卓越的表現。

—SIR JOHN TEMPLETON

——約翰·坦普爾頓爵士

Most treatments of exercise are either very specific (e.g., how to train for your first marathon) or overly vague (e.g., “Just keep moving!”). Or they emphasize “cardio” over “weights,” or vice versa. In this chapter, we are seeking to optimize our exercise regimen around the principle of longevity. What combination of modalities will help us delay the onset of chronic disease and death, while simultaneously maintaining healthspan for as long as possible?

大多數運動療法要么非常具體（例如，如何為你的第一次馬拉松進行訓練），要么過於模糊（例如，「繼續前進！」）。或者他們強調“有氧運動”而不是“重量”，反之亦然。在本章中，我們將圍繞長壽原則尋求優化我們的鍛鍊方案。哪一種方式組合可以幫助我們延緩慢性病的發作和死亡，同時盡可能長時間地維持健康壽命？

This question turns out to be more complicated than how to lower your risk of cardiovascular disease, because there are more variables, and more choices within each variable. It is not a one-dimensional problem but more of a three-dimensional one. The three dimensions in which we want to optimize our fitness are aerobic endurance and efficiency (aka cardio), strength, and stability. All three of these are key to maintaining your health and strength as you age. (And as we’ve seen, they also extend lifespan.) But both cardio and strength are far more nuanced than most people realize—and stability may be the least understood component of all.

事實證明，這個問題比如何降低心血管疾病的風險更複雜，因為變數更多，每個變數中的選擇也更多。這不是一個一維的問題，而是一個立體的問題。我們想要優化健身的三個維度是有氧耐力和效率（又稱有氧運動）、力量和穩定性。隨著年齡的增長，這三者都是保持健康和體力的關鍵。（正如我們所看到的，它們還可以延長壽命。）但是有氧運動和力量訓練都比大多數人意識到的要微妙得多，而穩定性可能是其中最不為人所知的組成部分。

When we say “cardio,” we are talking about not one thing, but a physiologic continuum, ranging from an easy walk to an all-out sprint. The various levels of intensity all count as cardio but are fueled by multiple

different energy systems. For our purposes, we are interested in two particular regions of this continuum: long, steady endurance work, such as jogging or cycling or swimming, where we are training in what physiologists call zone 2, and maximal aerobic efforts, where $\text{VO}_2 \text{ max}$ comes into play.

當我們說「有氧運動」時，我們談論的不是一件事，而是一個生理連續體，從輕鬆步行到全力衝刺。各種強度等級都算是有氧運動，但由多種不同的能量系統提供動力。就我們的目的而言，我們對這個連續體的兩個特定區域感興趣：長期、穩定的耐力運動，例如慢跑、騎自行車或游泳，我們在生理學家所說的第2區進行訓練，以及最大有氧運動，其中 $\text{VO}_2 \text{ max}$ 發揮作用。

The strength side of the equation seems simpler, at first: if you use your muscles to counter some resistance, in the form of weights or other forces (e.g., gravity, or elastic bands), they will adapt and grow stronger. That's how muscle works, and it's really quite wonderful. There are a few specific movements that I consider to be foundational, but here our most important goal is not only to build strength and muscle mass. It's equally important that we avoid injury in the process.

首先，等式的力量方面似乎更簡單：如果你用肌肉來抵抗一些阻力，以重量或其他力（例如重力或鬆緊帶）的形式，它們就會適應並變得更強。這就是肌肉的運作方式，真的很美妙。我認為有一些特定的動作是基礎性的，但在這裡我們最重要的目標不僅僅是增強力量和肌肉質量。同樣重要的是我們在過程中避免受傷。

This is where stability comes in. We will talk about it in much more detail in the next chapter, but I consider stability to be just as important as aerobic fitness and strength. It's a bit hard to define, but I think of stability as the solid foundation that enables us to do everything else that we do, without getting injured. Stability makes us bulletproof. Sophie was relatively fit for her age, but she likely lacked stability, making her vulnerable to injury. Many people are in the same boat without even realizing it—even me, in my twenties. It almost doesn't matter how fit you are; you can still be at risk. This is why our approach to exercise must increase not only our conventional measures of

fitness, such as our VO_2 max and our muscular strength, but above all our resistance to injury.

這就是穩定性的用武之地。我們將在下一章中更詳細地討論它，但我認為穩定性與有氧健身和力量同樣重要。這有點難以定義，但我認為穩定性是堅實的基礎，使我們能夠在不受傷的情況下完成我們所做的所有其他事情。穩定使我們刀槍不入。蘇菲的身體狀況相對適合她的年齡，但她可能缺乏穩定性，這使得她很容易受傷。很多人都在同一條船上，甚至沒有意識到這一點——甚至是我，二十多歲的人。你的健康狀況幾乎不重要；您仍然可能面臨風險。這就是為什麼我們的運動方法不僅必須提高傳統的健身指標，例如最大攝氧量 VO_2 和肌肉力量，最重要的是提高我們對傷害的抵抗力。

In the sections to follow, we will be building a framework around each of these, to help you craft your training program for your own Centenarian Decathlon.

在接下來的部分中，我們將圍繞每個方面建立一個框架，以幫助您為自己的百歲十項全能製定培訓計劃。

Aerobic Efficiency: Zone 2

有氧效率：2 區

Notice that one word has been missing in our discussion of exercise thus far: *calories*. Most people think that one of the primary benefits of exercise, if not the primary benefit, is that it “burns calories.” And it does, but we are more interested in a finer distinction—not calories, but *fuels*. How we utilize different fuels, glucose and fatty acids, is critical not only to our fitness but also to our metabolic and overall health. Aerobic exercise, done in a very specific way, improves our ability to utilize glucose and especially fat as fuel.

請注意，到目前為止，我們對運動的討論中缺少一個字：卡路里。大多數人認為運動的主要好處之一（如果不是主要好處的話）是它「燃燒卡路里」。確實如此，但我們更感興趣的是更精細的區別——不是

卡路里，而是燃料。我們如何利用不同的燃料、葡萄糖和脂肪酸，不僅對我們的健康至關重要，而且對我們的新陳代謝和整體健康也至關重要。以非常特定的方式進行的有氧運動可以提高我們利用葡萄糖，特別是脂肪作為燃料的能力。

The key here are the mitochondria, those tiny little intracellular organelles that produce much of our energy. These cellular “engines” can burn both glucose and fat, and thus they are fundamental to our metabolic health. Healthy mitochondria are also important to maintaining the health of our brain, and to controlling potential bad actors like oxidative stress and inflammation. I am convinced that it is impossible to be healthy without also having healthy mitochondria, which is why I place a great deal of emphasis on long, steady endurance training in zone 2.

這裡的關鍵是粒線體，這些微小的細胞內細胞器可以產生我們大量的能量。這些細胞「引擎」可以燃燒葡萄糖和脂肪，因此它們對於我們的代謝健康至關重要。健康的粒線體對於維持大腦的健康以及控制氧化壓力和發炎等潛在的不良因素也很重要。我堅信，如果沒有健康的粒線體，就不可能保持健康，這就是為什麼我非常重視第 2 區的長期、穩定的耐力訓練。

Zone 2 is one of five levels of intensity used by coaches and trainers in endurance sports to structure their athletes' training programs. It can get confusing, because some coaches define training zones in terms of heart rate, while others focus on different levels of power output; adding to the confusion, some models have five zones, but others have six or seven. Typically, zone 1 is a walk in the park and zone 5 (or 6, or 7) is an all-out sprint. Zone 2 is more or less the same in all training models: going at a speed slow enough that one can still maintain a conversation but fast enough that the conversation might be a little strained. It translates to aerobic activity at a pace somewhere between easy and moderate.

2 區是耐力運動中教練和訓練員用來制定運動員訓練計畫的五個強度之一。這可能會讓人感到困惑，因為有些教練會根據心率定義訓練區域，而有些教練則專注於不同程度的功率輸出；更令人困惑的是，有些型號有五個區域，但其他型號有六個或七個區域。通常，1 區是在

公園散步，5 區（或 6 或 7）是全力衝刺。區域 2 在所有訓練模型中或多或少都是相同的：速度足夠慢，人們仍然可以保持對話，但又足夠快，以至於對話可能會有點緊張。它指的是節奏介於輕鬆和中等之間的有氧運動。

I had done plenty of zone 2 workouts in my cycling days; this type of training is foundational for any endurance sport. But I had never fully grasped the importance of zone 2 training to our overall health until I happened to meet a very bright exercise scientist named Iñigo San Millán in 2018. I had flown to the United Arab Emirates for a meeting, and shortly after landing, at 11 p.m. on a cool December evening, I was introduced to San Millán, an assistant professor at the University of Colorado School of Medicine who had recently been hired as director of performance for the UAE Team Emirates professional cycling team. He was there to do preseason testing of some of the UAE team riders, and when he found out I was a former cyclist, he put me on a stationary bike right then and there, in the middle of the night, to do a VO_2 max test. My kind of guy.

在我騎自行車的日子裡，我進行了大量的 2 區訓練；這種類型的訓練是任何耐力運動的基礎。但我從未完全理解 2 區訓練對我們整體健康的重要性，直到 2018 年我碰巧遇到了一位非常聰明的運動科學家，名叫伊尼戈·聖米蘭(Iñigo San Millán)。我飛往阿拉伯聯合酋長國參加一個會議，落地後不久，晚上 11 點 12 月一個涼爽的夜晚，我被介紹給聖米蘭 (San Millán)，他是科羅拉多大學醫學院的助理教授，最近被聘為阿聯酋阿聯酋航空職業自行車隊的表現總監。他在那裡對阿聯酋隊的一些車手進行季前測試，當他發現我是一名前自行車手時，他立即讓我騎上一輛固定自行車，在半夜，做一個 VO_2 最大測試。我這種人。

A native of Spain and a former professional cyclist himself, San Millán has worked with all kinds of athletes and coaches in many sports, including hundreds of top professional cyclists. He is also the personal coach of 2020 and 2021 Tour de France champion (and 2022 runner-up) Tadej Pogačar. Despite his impressive sports résumé, San Millán's true passion is studying the relationship between exercise, mitochondrial health, and diseases such as

cancer and type 2 diabetes. As he explained, he hopes to use his insights into the fittest people on the planet, professional cyclists and other elite endurance athletes, in order to help the very least fit people—the one-third to one-half of the population with metabolic diseases or derangements.

聖米蘭是西班牙人，曾是職業自行車手，他曾與許多運動項目的各類運動員和教練合作過，其中包括數百名頂級職業自行車手。他也是 2020 年和 2021 年環法自行車賽冠軍（以及 2022 年亞軍）塔德傑·波加查 (Tadej Pogačar) 的私人教練。儘管聖米蘭有著令人印象深刻的體育履歷，但他真正的熱情是研究運動、粒線體健康以及癌症和 2 型糖尿病等疾病之間的關係。正如他解釋的那樣，他希望利用自己對地球上最健康的人、職業自行車手和其他精英耐力運動員的洞察，來幫助最不健康的人——三分之一到二分之一患有代謝疾病的人或精神錯亂。

In San Millán's view, healthy mitochondria are key to both athletic performance *and* metabolic health. Our mitochondria can convert both glucose and fatty acids to energy—but while glucose can be metabolized in multiple different ways, fatty acids can be converted to energy *only* in the mitochondria. Typically, someone working at a lower relative intensity will be burning more fat, while at higher intensities they would rely more on glucose. The healthier and more efficient your mitochondria, the greater your ability to utilize fat, which is by far the body's most efficient and abundant fuel source. This ability to use both fuels, fat and glucose, is called “metabolic flexibility,” and it is what we want: in chapters 6 and 7, we saw how the relentless accumulation and spillover of fat drives conditions such as diabetes and cardiovascular disease. Healthy mitochondria (fostered by zone 2 training) help us keep this fat accumulation in check.

在聖米蘭看來，健康的粒線體對於運動表現和代謝健康都至關重要。我們的粒線體可以將葡萄糖和脂肪酸轉化為能量，但雖然葡萄糖可以透過多種不同的方式代謝，但脂肪酸只能在粒線體中轉化為能量。通常，相對強度較低的人會燃燒更多的脂肪，而相對強度較高的人會更依賴葡萄糖。粒線體越健康、越高效，您利用脂肪的能力就越強，而脂肪是迄今為止人體最有效、最豐富的燃料來源。這種同時使用脂肪和葡萄糖這兩種燃料的能力被稱為“代謝靈活性”，這正是我們想要

的：在第6章和第7章中，我們看到了脂肪的不斷積累和溢出如何導致糖尿病和心血管疾病等疾病。健康的粒線體（由2區訓練促進）幫助我們控制脂肪堆積。

A few years ago, San Millán and his colleague George Brooks published a fascinating study that helps illustrate this point. They compared three groups of subjects: professional cyclists, moderately active healthy males, and sedentary men who met the criteria for the metabolic syndrome, meaning essentially that they were insulin resistant. They had each group ride a stationary bicycle at a given level of intensity relative to their fitness (about 80 percent of their maximum heart rate), while the scientists analyzed the amount of oxygen they consumed and the CO₂ they exhaled in order to determine how efficiently they produced power—and what primary fuels they were using. The differences they found were striking. The professional cyclists could zoom along, producing a huge amount of power while still burning primarily fat. But the subjects with metabolic syndrome relied almost entirely on glucose for their fuel source, even from the first pedal stroke. They had virtually zero ability to tap into their fat stores, meaning they were metabolically *inflexible*: able to use only glucose but not fat.

幾年前，聖米蘭和他的同事喬治布魯克斯發表了一項有趣的研究，有助於說明這一點。他們比較了三組受試者：職業自行車手、適度活躍的健康男性和符合代謝症候群標準的久坐男性，這意味著他們本質上有胰島素抗性。他們讓每組人以相對於他們的健康水平的給定強度（大約是最大心率的80%）騎固定自行車，同時科學家們分析了他們消耗的氧氣量和二氧化碳₂呼氣以確定它們發電的效率以及它們使用的主要燃料。他們發現的差異是驚人的。職業自行車手可以快速前進，產生巨大的動力，同時仍然主要燃燒脂肪。但患有代謝症候群的受試者幾乎完全依賴葡萄糖作為燃料來源，甚至從第一次踩踏開始。他們利用脂肪儲備的能力幾乎為零，這意味著他們的代謝不靈活：只能利用葡萄糖，而不能利用脂肪。

Obviously, these two groups—professional athletes and sedentary, unhealthy people—were as dissimilar as could be. San Millán's insight was that the sedentary subjects needed to be training in a manner similar to the

Tour de France-bound cyclists he worked with. A professional cyclist might spend thirty to thirty-five hours a week training on his or her bike, and 80 percent of that time in zone 2. For an athlete, this builds a foundation for all their other, more intense training. (The catch is that a professional rider's zone 2 output feels like zone 5 for most people.)

顯然，這兩個群體——職業運動員和久坐、不健康的人——有著天壤之別。聖米蘭的見解是，久坐的受試者需要以類似於他合作的環法自行車賽運動員的方式進行訓練。職業自行車手可能每週花 30 到 35 小時在自行車上訓練，其中 80% 的時間在第 2 區。對於運動員來說，這為他們所有其他更激烈的訓練奠定了基礎。（問題是，對大多數人來說，職業騎士的 2 區輸出感覺就像 5 區。）

As fundamental as zone 2 training is for professional cyclists, however, San Millán believes that it's even *more* important for nonathletes, for two reasons. First, it builds a base of endurance for anything else you do in life, whether that is riding your bike in a one-hundred-mile century ride or playing with your kids or grandkids. The other reason is that he believes it plays a crucial role in preventing chronic disease by improving the health and efficiency of your mitochondria, which is why training aerobic endurance and efficiency (i.e., zone 2 work) is the first element of my Centenarian Decathlon training program.

然而，2 區訓練對於職業自行車手來說至關重要，但聖米蘭認為，對於非運動員來說，這更為重要，原因有二。首先，它為你在生活中所做的任何其他事情奠定了耐力的基礎，無論是騎自行車進行一百英里世紀的騎行，還是與你的孩子或孫子一起玩耍。The other reason is that he believes it plays a crucial role in preventing chronic disease by improving the health and efficiency of your mitochondria, which is why training aerobic endurance and efficiency (i.e., zone 2 work) is the first element of my Centenarian Decathlon training程式。

When we are exercising in zone 2, most of the work is being done by our type 1, or “slow-twitch,” muscle fibers. These are extremely dense with mitochondria and thus well-suited for slow-paced, efficient endurance work. We can go for a long time without feeling fatigued. If we pick up the pace, we

begin to recruit more type 2 (“fast-twitch”) muscle fibers, which are less efficient but more forceful. They also generate more lactate in the process, because of the way they create ATP. Lactate itself is not bad; trained athletes are able to recycle it as a type of fuel. The problem is that lactate becomes lactic acid when paired with hydrogen ions, which is what causes that acute burning you feel in your muscles^[*1] during a hard effort.

當我們在 2 區運動時，大部分的工作是由 1 型或「慢肌纖維」完成。它們含有極其密集的粒線體，因此非常適合慢節奏、高效的耐力訓練。我們可以走很久而不感到疲倦。如果我們加快步伐，我們就會開始募集更多的 2 型（「快肌」）肌纖維，這些纖維效率較低，但更有力。由於它們產生 ATP 的方式，它們也會在過程中產生更多的乳酸。乳酸本身並不壞；訓練有素的運動員能夠將其作為燃料進行回收。問題在於，當乳酸鹽與氫離子結合時會變成乳酸，這就是導致您在努力訓練時感到肌肉劇烈燃燒的原因^[*1]。

In technical terms, San Millán describes zone 2 as the maximum level of effort that we can maintain without accumulating lactate. We still produce it, but we’re able to match production with clearance. The more efficient our mitochondrial “engine,” the more rapidly we can clear lactate, and the greater effort we can sustain while remaining in zone 2. If we are “feeling the burn” in this type of workout, then we are likely going too hard, creating more lactate than we can eliminate.

用技術術語來說，San Millán 將 2 區描述為我們在不累積乳酸的情況下可以維持的最大努力程度。我們仍然生產它，但我們能夠將生產與清除相匹配。我們的粒線體“引擎”越高效，我們清除乳酸的速度就越快，並且在保持在第 2 區的同時我們就能保持更大的努力。如果我們在這種類型的鍛煉中“感到燃燒”，那麼我們很可能也會繼續很難，產生的乳酸多於我們能夠消除的乳酸。

Because I am a numbers guy and I love biomarkers and feedback, I often test my own lactate while I am working out this way, using a small handheld lactate monitor, to make sure my pacing is correct. The goal is to keep lactate levels constant, ideally between 1.7 and 2.0 millimoles. This is the zone 2 threshold for most people. If I’m working too hard, lactate levels will rise, so

I'll slow down. (It's sometimes tempting to go too hard in zone 2, because the workout feels relatively “easy” on good days.) I make a point of this because lactate is literally what defines zone 2. It's all about keeping lactate levels steady in this range, and the effort sustainable.

因為我是一個數位迷，而且我喜歡生物標記和回饋，所以我經常在以這種方式運動時使用小型手持式乳酸監測儀測試自己的乳酸，以確保我的節奏正確。目標是保持乳酸水平恆定，最好在 1.7 至 2.0 毫摩爾之間。這是大多數人的 2 區閾值。如果我工作太辛苦，乳酸水平就會升高，所以我會放慢速度。（有時在第2 區太用力是很誘人的，因為在好的日子裡鍛煉感覺相對“容易”。）我之所以強調這一點，是因為乳酸實際上就是定義第2 區的。一切都是為了將乳酸水平保持在這個範圍內穩定，並且努力可持續。

If you don't happen to have a portable lactate meter on hand, like most people, there are other ways to estimate your zone 2 range that are reasonably accurate. If you know your maximum heart rate—not estimated, but your actual maximum, the highest number you've ever seen on a heart rate monitor—your zone 2 will correspond to between approximately 70 and 85 percent of that peak number, depending on your fitness levels. That's a big range, so when starting people out, I prefer they rely on their rate of perceived exertion, or RPE, also known as the “talk test.” How hard are you working? How easy is it to speak? If you're at the top of zone 2, you should be able to talk but not particularly interested in holding a conversation. If you can't speak in complete sentences at all, you're likely into zone 3, which means you're going too hard, but if you can comfortably converse, you're likely in zone 1, which is too easy.

如果您像大多數人一樣手邊沒有便攜式乳酸計，則還有其他方法可以相當準確地估計您的 2 區範圍。如果您知道您的最大心率（不是估計值，而是您的實際最大值，即您在心率監測器上見過的最高數字），您的區域2 將對應於該峰值數字的大約70%到85%，取決於您的心率健身水平。這是一個很大的範圍，所以當人們開始訓練時，我更喜歡他們依靠他們的感知用力率（RPE），也稱為「談話測試」。你工作有多努力？說話談何容易？如果您位於第 2 區的頂部，您應該能夠說

話，但對進行對話不是特別感興趣。如果你根本無法說出完整的句子，那麼你可能會進入第 3 區，這意味著你太難了，但如果你可以輕鬆地交談，你可能會進入第 1 區，這太容易了。

Zone 2 output is highly variable, depending on one's fitness. In San Millán and Brooks's study, the professional cyclists produced about three hundred watts of power in zone 2, while the sedentary, metabolically unhealthy subjects could generate only about one hundred watts at the same relative level of intensity. That's a huge difference. If we express this output in terms of watts per kilogram of body weight, the difference becomes even more stark: The seventy-kilogram cyclists put out more than four watts per kilogram of body weight, while the one-hundred-plus kilogram sedentary subjects could only manage about one watt per kilogram.

2 區輸出變化很大，取決於個人的健康狀況。在 San Millán 和 Brooks 的研究中，職業自行車手在 2 區產生約 300 瓦的功率，而久坐、代謝不健康的受試者在相同的相對強度水平下只能產生約 100 瓦的功率。這是一個巨大的差異。如果我們用每公斤體重的瓦特數來表示這個輸出，那麼差異就變得更加明顯：七十公斤的騎自行車者每公斤體重輸出超過四瓦特，而一百多公斤的久坐者則可以每公斤只能管理約一瓦特。

This pronounced difference comes back to the fact that the unhealthy subjects' mitochondria—their engine(s)—were much less efficient than those of the athletes, so they very quickly switched over from aerobic respiration, burning fat and glucose in the mitochondria with oxygen, to the much less efficient glycolysis, an energy-producing pathway that consumes only glucose and produces loads of lactate (similar to the way cancer cells produce energy, via the Warburg effect). Once we start producing energy this way, lactate accumulates and our effort quickly becomes unsustainable. There are other (fortunately rare) genetic diseases that target the mitochondria and produce far more severe sequelae, but in terms of mass-acquired chronic conditions, type 2 diabetes does a real number on the mitochondria, and San Millán's data very elegantly demonstrate the disability that it creates.

這種明顯的差異源於這樣一個事實：不健康受試者的粒線體（他們的

引擎)比運動員的效率低得多，因此他們很快就從有氧呼吸轉變為用氧氣燃燒粒線體中的脂肪和葡萄糖。，到效率低得多的糖酵解，這是一種僅消耗葡萄糖並產生大量乳酸的能量產生途徑（類似於癌細胞通過瓦爾堡效應產生能量的方式）。一旦我們開始以這種方式產生能量，乳酸就會積累，我們的努力很快就會變得不可持續。還有其他（幸運的是罕見）遺傳性疾病以粒線體為目標並產生更嚴重的後遺症，但就大規模獲得性慢性病而言，2 型糖尿病對粒線體的影響確實很大，而San Millán 的數據非常優雅地證明了這種殘疾它創造的。

Even when we are at rest, our lactate levels tell us much about our metabolic health. People with obesity or other metabolic problems will tend to have much higher resting lactate levels, a clear sign that their mitochondria are not functioning optimally, because they are already working too hard just to maintain baseline energy levels. This means that they are relying almost totally on glucose (or glycogen) for all their energy needs—and that they are totally unable to access their fat stores. It seems unjust, but the people who most need to burn their fat, the people with the most of it, are unable to unlock virtually *any* of that fat to use as energy, while the lean, well-trained professional athletes are able to do so easily because they possess greater metabolic flexibility (and healthier mitochondria).[*2]

即使我們在休息時，乳酸水平也能告訴我們很多關於代謝健康的資訊。患有肥胖或其他代謝問題的人往往有更高的靜止乳酸水平，這是他們的粒線體無法發揮最佳功能的明顯跡象，因為他們已經為了維持基線能量水平而過度努力工作。這意味著他們幾乎完全依賴葡萄糖（或肝醣）來滿足所有能量需求，並且他們完全無法獲得脂肪儲存。這似乎不公平，但最需要燃燒脂肪的人，脂肪最多的人，幾乎無法釋放任何脂肪來用作能量，而精瘦、訓練有素的職業運動員卻能夠做到這一點如此容易，因為它們具有更大的代謝靈活性（和更健康的粒線體）。[*2]

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Mitochondrial health becomes especially important as we grow older, because one of the most significant hallmarks of aging is a decline in the number and quality of our mitochondria. But the decline is not necessarily a one-way street. Mitochondria are incredibly plastic, and when we do aerobic exercise, it stimulates the creation of many new and more efficient mitochondria through a process called mitochondrial biogenesis, while eliminating ones that have become dysfunctional via a recycling process called mitophagy (which is like autophagy, touched on in chapter 5, but for mitochondria). A person who exercises frequently in zone 2 is improving their mitochondria with every run, swim, or bike ride. But if you don't use them, you lose them.

隨著年齡的增長，粒線體健康變得尤為重要，因為老化最顯著的標誌之一是粒線體數量和品質的下降。但衰退不一定是一條單行道。粒線體具有令人難以置信的可塑性，當我們進行有氧運動時，它會透過稱為粒線體生物發生的過程刺激許多新的、更有效的粒線體的產生，同時消除透過稱為粒線體自噬的回收過程（類似於自噬，觸摸）而變得功能失調的粒線體。在第 5 章中，但針對粒線體）。經常在 2 區運動的人每次跑步、游泳或騎自行車都會改善粒線體。但如果你不使用它們，你就會失去它們。

This is another reason why zone 2 is such a powerful mediator of metabolic health and glucose homeostasis. Muscle is the largest glycogen storage sink in the body, and as we create more mitochondria, we greatly increase our capacity for disposing of that stored fuel, rather than having it end up as fat or remaining in our plasma. Chronic blood glucose elevations damage organs from our heart to our brain to our kidneys and nearly everything in between—even contributing to erectile dysfunction in men. Studies have found that while we are exercising, our overall glucose uptake increases as much as one-hundred-fold compared to when we are at rest. What's interesting is that this glucose uptake occurs via multiple pathways. There is the usual, insulin-signaled way that we're familiar with, but exercise also activates other pathways, including one called non-insulin-mediated glucose uptake, or NIMGU, where glucose is transported directly across the cell membrane without insulin being involved at all.

這是 2 區成為代謝健康和葡萄糖穩態的強大調節劑的另一個原因。肌肉是體內最大的肝醣儲存庫，當我們產生更多的粒線體時，我們就大大增加了處理儲存的燃料的能力，而不是讓它最終變成脂肪或留在我們的血漿中。慢性血糖升高會損害從心臟到大腦再到腎臟的所有器官，甚至會導致男性勃起功能障礙。研究發現，當我們運動時，我們的整體葡萄糖攝取量比我們休息時增加了一百倍。有趣的是，這種葡萄糖攝取是透過多種途徑發生的。有我們熟悉的常見胰島素信號傳導方式，但運動也會激活其他途徑，包括一種稱為非胰島素介導的葡萄糖攝取（NIMGU）的途徑，其中葡萄糖直接穿過細胞膜轉運，無需胰島素參與根本不。

This in turn explains why exercise, especially in zone 2, can be so effective in managing both type 1 and type 2 diabetes: It enables the body to essentially bypass insulin resistance in the muscles to draw down blood glucose levels. I have one patient with type 1 diabetes, meaning he produces zero insulin, who keeps his glucose in check almost entirely by walking briskly for six to ten miles every day, and sometimes more. As he walks, his muscle cells are vacuuming glucose out of his bloodstream via NIMGU. He still needs to inject himself with insulin, but only a tiny fraction of the amount that he would otherwise require.

這反過來解釋了為什麼運動，尤其是 2 區運動，可以如此有效地控制第 1 型和第 2 型糖尿病：它使身體能夠從根本上繞過肌肉中的胰島素阻抗，從而降低血糖水平。我有一位患有第 1 型糖尿病的患者，這意味著他產生的胰島素為零，他幾乎完全透過每天快走六到十英里（有時甚至更多）來控制血糖。當他行走時，他的肌肉細胞會透過 NIMGU 將葡萄糖從血液中吸出。他仍然需要給自己注射胰島素，但只需要注射胰島素的一小部分。

One other plus of zone 2 is that it is very easy to do, even for someone who has been sedentary. For some people, a brisk walk might get them into zone 2; for those in better condition, zone 2 means walking uphill. There are many different ways to do it: you can ride a stationary bicycle at the gym, or walk or jog or run around the track at the local high school, or swim some laps in the pool. The key is to find an activity that fits into your lifestyle, that you

enjoy doing, and that enables you to work at a steady pace that meets the zone 2 test: You're able to talk in full sentences, but just barely.

2 區的另一個優點是，即使對於久坐的人來說，也很容易做到。對某些人來說，快走可能會讓他們進入第 2 區；對於條件較好的人來說，2 區意味著步行上坡。有很多不同的方法可以做到這一點：您可以在健身房騎固定自行車，或在當地高中的跑道上散步、慢跑或跑步，或在游泳池裡遊幾圈。關鍵是找到一項適合您的生活方式、您喜歡做的活動，並且使您能夠以穩定的節奏工作，以滿足 2 區測試：您能夠用完整的句子說話，但只是勉強。

How much zone 2 training you need depends on who you are. Someone who is just being introduced to this type of training will derive enormous benefit from even two 30-minute sessions per week to start with. Based on multiple discussions with San Millán and other exercise physiologists, it seems that about three hours per week of zone 2, or four 45-minute sessions, is the minimum required for most people to derive a benefit and make improvements, once you get over the initial hump of trying it for the first time. (People who are training for major endurance events, such as running a marathon, obviously need to do more than this.) I am so persuaded of the benefits of zone 2 that it has become a cornerstone of my training plan. Four times a week, I will spend about an hour riding my stationary bike at my zone 2 threshold.

您需要多少 2 區訓練取決於您的身分。剛開始接觸此類訓練的人即使從每週兩次 30 分鐘的課程中也會受益匪淺。根據與San Millán 和其他運動生理學家的多次討論，對於大多數人來說，每周大約3 小時的2 區訓練，或者4 次45 分鐘的訓練，一旦超過了這個範圍，就可以獲得益處並做出改進。第一次嘗試時的最初困難。（正在訓練重大耐力賽事（例如跑馬拉松）的人顯然需要做的不只這些。）我對 2 區的好處深信不疑，它已成為我訓練計畫的基石。每週四次，我會花大約一個小時在 2 區閾值騎固定自行車。

One way to track your progression in zone 2 is to measure your output in watts at this level of intensity. (Many stationary bikes can measure your wattage as you ride.) You take your average wattage output for a zone 2

session and divide it by your weight to get your watts per kilogram, which is the number we care about. So if you weigh 60 kilos (about 132 pounds) and can generate 125 watts in zone 2, that works out to a bit more than 2 watts/kg, which is about what one would expect from a reasonably fit person. These are rough benchmarks, but someone who is very fit will be able to produce 3 watts/kg, while professional cyclists put out 4 watts/kg and up. It's not the number that matters, but how much you are improving over time. (If you're a runner or a walker, the same principle applies: As you improve, your zone 2 pace will get faster.)

追蹤第 2 區進展的一種方法是測量在此強度等級下的輸出（以瓦為單位）。（許多固定自行車可以在您騎行時測量您的瓦數。）您將 2 區訓練的平均瓦數輸出除以您的體重，即可得到每公斤的瓦數，這就是我們關心的數字。因此，如果您的體重為 60 公斤（約 132 磅），並且可以在 2 區產生 125 瓦的功率，則計算結果略高於 2 瓦/公斤，這大約是一個身體健康的人所期望的功率。這些是粗略的基準，但非常健康的人將能夠產生 3 瓦/公斤的能量，而專業自行車手則可以產生 4 瓦/公斤甚至更高的能量。重要的不是數字，而是隨著時間的推移你進步了多少。（如果您是跑步者或步行者，同樣的原則也適用：隨著您的進步，您的 2 區配速會變得更快。）

Zone 2 can be a bit boring on its own, so I typically use the time to listen to podcasts or audiobooks, or just think about issues that I'm working on—a side benefit of zone 2 is that it also helps with cognition, by increasing cerebral blood flow and by stimulating the production of BDNF, brain-derived neurotrophic factor, which we touched on earlier. This is another reason why zone 2 is such an important part of our Alzheimer's disease prevention program.

區域 2 本身可能有點無聊，所以我通常會利用時間聽播客或有聲讀物，或者只是思考我正在研究的問題 - 區域 2 的一個附帶好處是它也有助於認知，透過增加腦血流量和刺激BDNF（我們之前提到的腦源性神經營養因子）的產生。這是 2 區成為我們阿茲海默症預防計畫如此重要的一部分的另一個原因。

I think of zone 2 as akin to building a foundation for a house. Most people

will never see it, but it is nevertheless important work that helps support virtually everything else we do, in our exercise regimen and in our lives.

我認為 2 區類似於為房屋打地基。大多數人永遠不會看到它，但它仍然是一項重要的工作，它幾乎幫助支持我們所做的所有其他事情，包括我們的運動方案和我們的生活。

Maximum Aerobic Output: VO_2 Max

最大有氧輸出： VO_2 Max

If zone 2 represents a steady state, where you are kind of cruising along at a sustainable pace, VO_2 max efforts are almost the opposite. This is a much higher level of intensity—a hard, minutes-long effort, but still well short of an all-out sprint. At VO_2 max, we are using a combination of aerobic and anaerobic pathways to produce energy, but we are at our maximum rate of oxygen consumption. Oxygen consumption is the key.

如果區域 2 代表穩定狀態，即您以可持續的速度巡航，則 VO_2 最大努力幾乎相反。這是一個更高程度的強度——需要長達數分鐘的艱苦努力，但仍遠未達到全力衝刺的程度。在最大攝氧量 $\dot{V}\text{O}_{2\text{max}}$ 時，我們使用有氧和無氧途徑的組合來產生能量，但我們處於最大耗氧率。耗氧量是關鍵。

Besides improving mitochondrial health and glucose uptake and metabolic flexibility, and all those other good things, zone 2 training also increases your VO_2 max somewhat. But if you really want to raise your VO_2 max, you need to train this zone more specifically. Typically, for patients who are new to exercising, we introduce VO_2 max training after about five or six months of steady zone 2 work.

除了改善粒線體健康、葡萄糖攝取和代謝靈活性以及所有其他好處之外，2 區訓練還會在一定程度上增加您的最大攝氧量 $\dot{V}\text{O}_{2\text{max}}$ 。但如果您確實想提高 VO_2 最大攝氧量，則需要更具體地訓練該區域。通常，對於

剛開始運動的患者，我們會在進行大約五到六個月的穩定 2 區訓練後引入最大攝氧量₂訓練。

One reason why I emphasize this so much is that this measure of peak aerobic capacity is powerfully correlated with longevity, as we saw in chapter 11. I have all my patients undergo VO₂ max testing and then train to improve their score. Even if you are not competing in high-level endurance sports, your VO₂ max is an important number that you can and should know.

我如此強調這一點的原因之一是，正如我們在第11章中看到的那樣，這種峰值有氧能力的衡量標準與壽命密切相關。我讓所有患者都接受最大攝氧量₂測試，然後進行訓練以提高他們的分數。即使您不參與高水平耐力運動，您的最大攝氧量₂也是您可以而且應該知道的重要數字。

Testing is widely available, even from some of the larger fitness chains. The bad news is that the VO₂ max test is an unpleasant affair that entails riding an exercise bike or running on a treadmill at ever greater intensity, while wearing a mask designed to measure oxygen consumption and CO₂ production. The peak amount of oxygen you consume, typically close to the point at which you “fail,” meaning the point where you just can’t keep going, yields your VO₂ max. We have all our patients do the test at least annually, and they almost all hate it. We then compare their results, normalized by weight, to the population of their age and sex.

測試廣泛存在，甚至來自一些較大的健身連鎖店。壞消息是，最大攝氧量₂測試是一件令人不愉快的事情，需要以更高的強度騎健身車或在跑步機上跑步，同時戴著旨在測量耗氧量和CO₂生產。您消耗的氧氣峰值量（通常接近您「失敗」的點，即您無法繼續前進的點）產生您的最大攝氧量₂。我們讓所有患者至少每年進行一次測試，他們幾乎都討厭它。然後，我們將按體重標準化的結果與同齡和性別的人群進行比較。

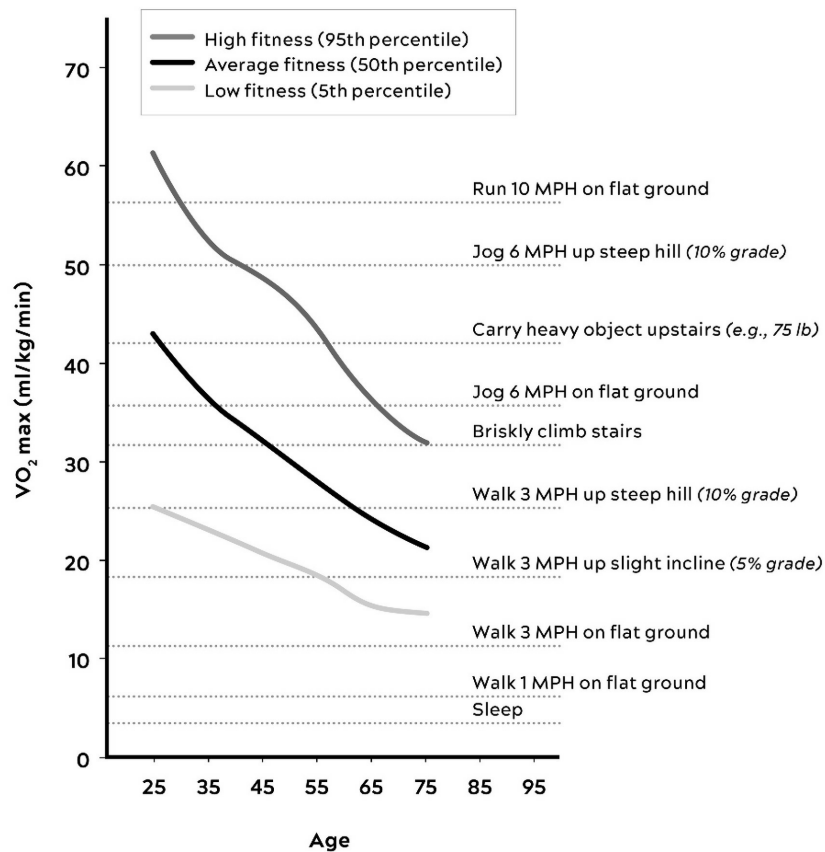
Why is this important? Because our VO₂ max is a pretty good proxy measure of our physical capability. It tells us what we can do—and what we

cannot do. Take a look at figure 11, which charts low, average, and high VO_2 max levels by age. Two things stand out. First, there's a huge gap in fitness between the top and bottom 5 percent of each age group (the upper vs. lower lines). Second, it's striking how steeply VO_2 max declines with age, and how this decline corresponds to diminished functional capacity. The lower it goes, the less you can do.

為什麼這很重要？因為我們的最大攝氧量 VO_2 是衡量我們身體能力的一個很好的代理指標。它告訴我們什麼可以做，什麼不能做。請看圖 11，其中按年齡列出了低、平均和高 VO_2 最大水準。有兩件事很突出。首先，每個年齡層的前 5% 和後 5%（上線與下線）之間的健康狀況存在巨大差距。其次，令人驚訝的是，最大攝氧量 VO_2 隨著年齡的增長而急劇下降，以及這種下降與功能能力的下降是如何對應的。它越低，你能做的就越少。

For example, a thirty-five-year-old man with average fitness for his age—a VO_2 max in the mid-30s—should be able to run at a ten-minute mile pace (6 mph). But by age seventy, only the very fittest 5 percent of people will still be able to manage this. Similarly, an average forty-five- to fifty-year-old will be able to climb stairs briskly (VO_2 max = 32), but at seventy-five, such a feat demands that a person be in the top tier of their age group. Activities that are easy when we are young or middle-aged become difficult if not impossible as we get older. This explains why so many people are miserable in their Marginal Decade. They simply can't *do* much of anything.

例如，一名 35 歲男性，其年齡處於平均健康水平（最大攝氧量 VO_2 在 30 多歲左右）應該能夠以 10 分鐘英里的配速（6 英里/小時）跑步）。但到了七十歲，只有最健康的 5% 的人仍然能夠做到這一點。同樣，平均四十五到五十歲的人能夠輕快地爬樓梯（ VO_2 max = 32），但到了七十五歲，這樣的壯舉要求一個人在他們年齡組中的頂尖水平。當我們年輕或中年時很容易的活動隨著年齡的增長而變得困難，甚至不可能。這就解釋了為什麼這麼多人在他們的邊緣十年裡過得很痛苦。他們根本無能為力。

Figure 11. How VO₂ Max Declines with Age

Source: Graph by Jayson Gifford, Brigham Young University, based on data from Ligouri (2020).

資料來源：楊百翰大學 Jayson Gifford 根據 Ligouri (2020) 的數據繪製的圖表。

I push my patients to train for as high a VO₂ max as possible, so that they can maintain a high level of physical function as they age. Ideally, I want them to target the “elite” range for their age and sex (roughly the top 2 percent). If they achieve that level, I say good job—now let’s reach for the elite level for your sex, but *two decades younger*. This may seem like an extreme goal, but I like to aim high, in case you haven’t noticed.

我督促我的患者進行盡可能高的最大攝氧量 VO_2 訓練，以便他們能夠隨著年齡的增長而保持高水平的身體機能。理想情況下，我希望他們的目標是年齡和性別的「菁英」範圍（大約是前 2%）。如果他們達到了這個水平，我會說乾得好——現在讓我們達到你們性別的精英水平，

但要年輕二十歲。這可能看起來是一個極端的目標，但我喜歡設定更高的目標，以防你沒有註意到。

There is a logic to it. Let's say you are a fifty-year-old woman, and you enjoy hiking in the mountains; that's how you want to spend your retirement. That kind of activity would require a VO_2 max of about 30, give or take. Let's also assume, for the sake of argument, that you're in the 50th percentile for your age; that puts you at about 32 ml/kg/min. You can do that hike now!

這是有邏輯的。假設您是一位五十歲的女性，喜歡在山上健行；這就是您想要的退休生活。此類活動需要 VO_2 max 約為 30，無論給予或接受。為了方便討論，我們也假設您處於年齡的第 50 個百分位；這意味著您的流量約為 32 毫升/公斤/分鐘。你現在就可以進行徒步旅行了！

That seems like good news—but it's really the bad news. Studies suggest that your VO_2 max will decline by roughly 10 percent per decade—and up to 15 percent per decade after the age of fifty. So simply having average or even above-average VO_2 max now just won't cut it. We are planning for you to live for another thirty years, or forty. If you are only starting at 32 ml/kg/min now, at fifty, you can expect to be closer to 21 ml/kg/min at age eighty. These are not abstract numbers; they represent a profound decline in function. It's the difference between walking easily up a flight of stairs versus struggling to even walk on an inclined surface. It's a far cry from hiking in the Dolomites. To arrive in her ninth decade with a sufficient level of fitness to achieve her goal, our fifty-year-old would need to have a VO_2 max of about 45 to 49 right now. This is the top tier for her sex, but two decades younger.

這看起來是個好消息，但其實是個壞消息。研究表明，您的最大攝氧量 VO_2 每十年大約下降 10%，50 歲後每十年下降高達 15%。因此，現在僅僅擁有平均甚至高於平均 VO_2 max 是不夠的。我們計劃讓你再活三十年，或四十年。如果您現在 50 歲時僅開始攝取 32 毫升/公斤/分鐘，那麼您在 80 歲時預計會接近 21 毫升/公斤/分鐘。這些不是抽象的數字；而是抽象的數字。它們代表著功能的嚴重衰退。這就像輕鬆爬上一段樓梯和在傾斜的表面上艱難行走之間的差異。這與在多洛米蒂山

徒步旅行相差甚遠。為了在九十歲時擁有足夠的健康水平來實現她的目標，我們這位五十歲的女士現在需要有大約 45 到 49 的最大攝氧量₂。這是她同性別中的頂級水平，但比她年輕二十歲。

It is important that your goals reflect your own priorities—the activities that you enjoy, and what you want to be able to accomplish in your later decades. The more active you want or plan to be as you age, the more you need to train for it now.

重要的是，你的目標要反映你自己的優先事項——你喜歡的活動，以及你希望在以後的幾十年中能夠完成的事情。隨著年齡的增長，您想要或計劃越活躍，您現在就越需要為此進行訓練。

Keep in mind, increasing your VO_2 max *by any amount* is going to improve your life, not only in terms of how long you live but also how well you live, today and in the future. Improving your VO_2 max from the very bottom quartile to the quartile above (i.e., below average) is associated with almost a 50 percent reduction in all-cause mortality, as we saw earlier. I believe that almost anyone is capable of achieving this—and they should, because the alternative is so unacceptable. Once maximal oxygen consumption or VO_2 max drops below a certain level (typically about 18 ml/kg/min in men, and 15 in women), it begins to threaten your ability to live on your own. Your engine is beginning to fail.

請記住，增加您的最大攝氧量₂ 任何數量都會改善您的生活，不僅會改善您的壽命，還會改善您今天和未來的生活品質。如我們先前所見，將最大攝氧量₂ 從最低四分位數提高到上方四分位數（即低於平均）與全因死亡率降低近 50% 相關。我相信幾乎任何人都有能力實現這一目標——而且他們應該這樣做，因為替代方案是如此不可接受。一旦最大耗氧量或最大攝氧量₂ 低於一定水平（通常男性約為18 毫升/公斤/分鐘，女性約為15 毫升/公斤/分鐘），它就會開始威脅您獨立生活的能力。你的引擎開始故障。

This is why it's so essential to train VO_2 max in addition to zone 2. It's a key to maintaining a fulfilling, independent life as you age. But it takes hard

work over a long period of time to build it up and keep it up.

這就是為什麼除了第 2 區之外還訓練最大攝氧量 $\dot{V}O_2$ 如此重要的原因。這是隨著年齡的增長保持充實、獨立生活的關鍵。但它需要長期的艱苦努力才能建立並維持它。

How trainable is $\dot{V}O_2$ max? The conventional wisdom, reflecting the bulk of the literature, suggests that it's possible to improve elderly subjects' aerobic capacity by about 13 percent over eight to ten weeks of training, and by 17 percent after twenty-four to fifty-two weeks, according to one review. That's a good start, but I think it represents only the beginning of what is possible; as usual with Medicine 2.0, these studies are almost always too short. We are talking about a lifelong training program, not one that lasts only eight weeks. Everyone is different, in terms of their fitness potential and their response to training, but Mike Joyner believes that longer and more focused training can yield much larger gains over extended periods of time—periods measured in years, not weeks. I tell my patients that this is not a two-month project; it's a two-year project.

最大攝氧量 $\dot{V}O_2$ 的可訓練性如何？根據大量文獻，傳統觀點表明，在八到十週的訓練中，老年受試者的有氧能力可以提高約 13%，在二十四到五十二週後可以提高 17%。一篇評論。這是一個好的開始，但我認為這只是可能的開始；與醫學 2.0 一樣，這些研究幾乎總是太短。我們談論的是一項終身培訓計劃，而不是只持續八週的培訓計劃。每個人的健身潛力和對訓練的反應都是不同的，但邁克·喬伊納(Mike Joyner) 相信，更長時間、更有針對性的訓練可以在較長的時間內（以數年而不是數週來衡量）產生更大的收益。我告訴我的病人，這不是一個為期兩個月的計畫；而是一個為期兩個月的計畫。這是一個為期兩年的計畫。

It is not clear how much upside it is possible to achieve, but the literature suggests that sustained, diligent training can pay off. A small study of nine well-trained octogenarian endurance athletes (cross-country skiers) found that their average $\dot{V}O_2$ max was 38, versus 21 for a control group of untrained octogenarian men, a difference of more than 80 percent. That's huge. The

athletes had the aerobic capacity of people decades younger than them,^[*3] while the men in the control group had declined so far that they were on the verge of losing their ability to live independently. True, the study subjects were lifelong athletes—but that’s also part of the point here. Our goal is to become elite athletes of aging.

目前尚不清楚可以實現多少提升，但文獻顯示持續、勤奮的培訓可以獲得回報。一項針對9 名訓練有素的八十多歲耐力運動員（越野滑雪運動員）的小型研究發現，他們的平均攝氧量 $\dot{V}O_2$ 最大為38，而未經訓練的八十多歲男性對照組為21，相差超過80百分。那是巨大的。運動員的有氧能力與比他們年輕幾十年的人相當[*3]，而對照組的男性則大幅下降，以至於他們瀕臨失去獨立生活的能力。誠然，研究對像是終身運動員——但這也是本文的重點之一。我們的目標是成為老化精英運動員。

The payoff is that increasing your $\dot{V}O_2$ max makes you functionally younger. One study found that boosting elderly subjects’ $\dot{V}O_2$ max by 6 ml/kg/min, or about 25 percent, was equivalent to subtracting twelve years from their age. If you are a man in your sixties and you are starting with a $\dot{V}O_2$ max of 30, you are more or less average for your age group (see figure 12). (Women typically have a somewhat lower average $\dot{V}O_2$ max by age, because of various factors, so an “average” woman in her sixties would be at about 25 ml/kg/min.) If you can boost that up to 35 via training, you will be squarely in the top 25 percent of your age group. Nice work. Now, here’s another way to look at it: In your sixties, you will have achieved the aerobic fitness of an average man in his fifties, a decade younger than you. If you can get it still higher, to 38 or 39, you will be the aerobic equivalent of an average thirty-something. This means you will have bought yourself a phase shift, like we talked about with the centenarians: you now have the fitness of someone decades younger than you. So give yourself a pat on the back; you’ve earned it.

回報是增加您的最大攝氧量 $\dot{V}O_2$ 讓您在功能上更年輕。一項研究發現，將老年受試者的最大攝氧量 $\dot{V}O_2$ 提高 6 毫升/公斤/分鐘，約 25%，相當於年齡減去 12 歲。如果您是一位 60 多歲的男性，而您的初始攝氧量 $\dot{V}O_2$

最大值為 30，那麼您或多或少處於您所在年齡段的平均值（見圖 12）。（由於各種因素，女性的平均攝氧量 $\dot{V}O_2$ 隨著年齡的增長通常會稍低一些，因此六十多歲的「平均」女性約為 25 毫升/公斤/分鐘。）透過訓練，直到 35 歲，您將完全躋身同齡組的前 25%。幹得好。現在，我們可以用另一種方式來看待它：在你六十多歲的時候，你將達到一個比你年輕十歲的五十多歲的普通男人的有氧健身水平。如果你能達到更高的水平，達到 38 或 39，那麼你的有氧運動水平就相當於 30 多歲的平均水平。這意味著你將為自己購買一個相移，就像我們與百歲老人談論的那樣：你現在擁有比你年輕數十歲的人的健康狀況。因此，請拍拍自己的背；這是你應得的。

The beauty of this is that $\dot{V}O_2$ max can *always* be improved by training, no matter how old you are. Don't believe me? Then let me introduce you to an amazing Frenchman named Robert Marchand, who set an age-group world record in 2012 by cycling 24.25 kilometers in an hour, at the age of 101. Apparently, he wasn't satisfied with that performance, so he decided he needed to train harder. Following a strict program designed by top coaches and physiologists, he managed to boost his $\dot{V}O_2$ max from an already-impressive 31 ml/kg/min up to 35 ml/kg/min, which would put him in the elite 2.5 percent of men in their eighties. Two years later, now 103, he came back and broke his own record, riding almost twenty-seven kilometers in an hour. That's impressive, and it shows that it's never too late to improve your $\dot{V}O_2$ max.

這樣做的好處是，無論您多大，最大攝氧量 $\dot{V}O_2$ 總是可以透過訓練來提高。不相信我？那麼我為大家介紹一位了不起的法國人，名叫羅伯特·馬爾尚（Robert Marchand），他在 2012 年以 101 歲高齡創下了每小時騎行 24.25 公里的年齡組世界紀錄。顯然，他對這樣的表現並不滿意，所以他決定他需要更努力地訓練。遵循頂級教練和生理學家設計的嚴格計劃，他成功地將最大攝氧量 $\dot{V}O_2$ 從已經令人印象深刻的 31 毫升/公斤/分鐘提高到 35 毫升/公斤/分鐘，這將使他進入 80 多歲男性的精英佔 2.5%。兩年後，現年 103 歲的他回來了，打破了自己的紀錄，每小時

騎了近 27 公里。這令人印象深刻，它表明提高您的最大攝氧量 $\dot{V}O_2$ 永遠不會太晚。

Even if we are not out to set world records, the way we train $\dot{V}O_2$ max is pretty similar to the way elite athletes do it: by supplementing our zone 2 work with one or two $\dot{V}O_2$ max workouts per week.

即使我們不是要創造世界紀錄，我們訓練最大攝氧量 $\dot{V}O_2$ 的方式也與精英運動員的方式非常相似：用一到兩個攝氧量 $\dot{V}O_2$

Where HIIT intervals are very short, typically measured in seconds, $\dot{V}O_2$ max intervals are a bit longer, ranging from three to eight minutes—and a notch less intense. I do these workouts on my road bike, mounted to a stationary trainer, or on a rowing machine, but running on a treadmill (or a track) could also work. The tried-and-true formula for these intervals is to go four minutes at the maximum pace you can sustain for this amount of time—not an all-out sprint, but still a very hard effort. Then ride or jog four minutes easy, which should be enough time for your heart rate to come back down to below about one hundred beats per minute. Repeat this four to six times and cool down.^[*4]

HIIT 間隔非常短，通常以秒為單位，而 $\dot{V}O_2$ 最大間隔則稍長一些，從三到八分鐘不等，強度也稍低一些。我在公路自行車上進行這些鍛煉，安裝在固定訓練器上，或在划船機上，但在跑步機（或跑道）上跑步也可以。這些間隔的經過驗證的公式是，以您在這段時間內可以維持的最大配速跑四分鐘，這不是全力衝刺，但仍然是一項非常艱苦的努力。然後輕鬆騎行或慢跑四分鐘，這應該足以讓您的心率降至每分鐘一百次以下。重複此四到六次並冷卻。^[*4]

Figure 12. VO₂ Max by Age, Sex, Fitness

| Age | Performance Group by VO ₂ max (ml/kg/min) | | | | |
|--------------|--|---------------|---------------|-------|-------|
| | Low | Below Average | Above Average | High | Elite |
| Women | | | | | |
| 18-19 | < 35 | 35-39 | 40-45 | 40-52 | ≥ 53 |
| 20-29 | < 28 | 28-35 | 36-40 | 41-50 | ≥ 51 |
| 30-39 | < 27 | 27-33 | 34-38 | 39-48 | ≥ 49 |
| 40-49 | < 26 | 26-31 | 32-36 | 37-46 | ≥ 47 |
| 50-59 | < 25 | 25-28 | 29-35 | 36-45 | ≥ 46 |
| 60-69 | < 21 | 21-24 | 25-29 | 30-38 | ≥ 40 |
| 70-79 | < 18 | 18-21 | 22-24 | 25-35 | ≥ 36 |
| ≥ 80 | < 15 | 15-19 | 20-22 | 23-29 | ≥ 30 |
| Men | | | | | |
| 18-19 | < 38 | 38-45 | 46-49 | 50-57 | ≥ 58 |
| 20-29 | < 36 | 36-42 | 43-48 | 49-55 | ≥ 56 |
| 30-39 | < 35 | 35-39 | 40-45 | 46-52 | ≥ 53 |
| 40-49 | < 34 | 34-38 | 39-43 | 44-51 | ≥ 52 |
| 50-59 | < 29 | 29-35 | 36-40 | 41-49 | ≥ 50 |
| 60-69 | < 25 | 25-29 | 30-35 | 36-45 | ≥ 46 |
| 70-79 | < 21 | 21-24 | 25-29 | 30-40 | ≥ 41 |
| ≥ 80 | < 18 | 18-22 | 23-25 | 26-35 | ≥ 36 |

Source: Mandsager et al. (2018).

資料來源：Mandsager 等人。（2018）。

Group comparisons for VO₂ max are Low (bottom 25%), Below Average (26th to 50th percentile), Above Average (51st to 75th percentile), High (75th to 97.6th percentile), and Elite (top 2.3%).

最大攝氧量的組別比較分為低（最低25%）、低於平均值（第26至50個百分位數）、高於平均值（第51至75個百分位數）、高（第75至97.6個百分位數）和菁英（最高2.3%）。

You want to make sure that you get as close to fully recovered as possible before beginning the next set. If you fail to recover sufficiently between sets, you will not be able to reach your peak effort in the working sets and you'll

consequently miss the desired adaptation. Also, be sure to give yourself enough time to warm up and then cool down from this intense effort.

在開始下一組之前，您需要確保自己盡可能接近完全恢復。如果你在組間未能充分恢復，你將無法在工作組中達到最大努力程度，從而錯過所需的適應。另外，一定要給自己足夠的時間熱身，然後從這種激烈的努力中冷靜下來。

The good news, I suppose, is that you don't need to spend very much time in the pain cave. Unless you are training to be competitive in elite endurance sports like cycling, swimming, running, triathlon, or cross-country skiing, a single workout per week in this zone will generally suffice. You'll pretty quickly find that it boosts your performance across the rest of your exercise program as well—and, more importantly, in the rest of your life.

我想，好消息是你不需要在痛苦的洞穴裡花太多時間。除非您正在訓練自行車、游泳、跑步、鐵人三項或越野滑雪等精英耐力運動的競爭力，否則每週在該區域進行一次鍛鍊通常就足夠了。您很快就會發現它也可以提高您在其餘鍛鍊計劃中的表現，更重要的是，在您的餘生中。

I learned this lesson very vividly not long ago, when my wife and I had a very tight connection at Heathrow Airport in London. Anyone who has connected there knows that getting from Terminal 5 to Terminal 3 is basically a trip within a trip. The only way we were going to catch our connecting flight was to run the equivalent of a mile in less than eight minutes, while each carrying a twenty-pound suitcase. This was not going to be a zone 2 effort; we were going to have to go much harder than that, for eight straight minutes. We needed to be able to produce a burst of power that was much closer to our VO_2 max than to zone 2.

不久前，當我和妻子在倫敦希思羅機場有非常緊密的聯繫時，我非常生動地學到了這個教訓。坐過那裡的人都知道，從 5 號航站樓到 3 號航站樓基本上是一次行程中的行程。我們要趕上轉機航班的唯一方法就是在八分鐘內跑完一英里，同時每人攜帶一個二十磅的手提箱。這

不會是 2 區的工作；我們必須比這更努力，連續八分鐘。我們需要能夠產生更接近 VO_2 最大攝氧量而不是區域 2 的爆發功率。

In that moment, we were in a situation not all that different from what our hunter-gatherer ancestors frequently faced (apart from the setting, obviously). Besides being much more fun than traveling through airports, hunting requires 95 percent slow and steady effort, and 5 percent all-out intensity. If you were going to have a chance to kill the antelope or mammoth or whatever else you were tracking, you really needed that extra power to close the deal.

在那一刻，我們所處的情況與我們的狩獵採集祖先經常面臨的情況並沒有什麼不同（顯然，除了環境之外）。除了比在機場旅行更有趣之外，狩獵還需要 95% 的緩慢而穩定的努力，以及 5% 的全力以赴的強度。如果你有機會殺死羚羊或猛獁像或任何你正在追蹤的其他動物，你確實需要額外的力量來完成交易。

My point is that if you really stop to consider the kind of aerobic fitness that most people actually *need* in the course of their lives, it basically boils down to being really good at going slow for a long time, but also able to go hard and fast when needed. Training and maintaining a high level of aerobic fitness, and doing it now, is essential to preserving this range of function in your later years.

我的觀點是，如果你真的停下來考慮大多數人在一生中真正需要的有氧健身方式，那麼它基本上可以歸結為非常擅長長時間慢速運動，但也能夠努力並堅持下去。需要時快速。訓練和保持高水準的有氧運動，現在就進行，對於在晚年保持這些功能至關重要。

In a way, maximum aerobic output is like guitarist Nigel Tufnel's special amplifier, in the classic film *This Is Spinal Tap*: Where most amps only let you turn the volume up to 10, his went up to 11. As he memorably explained, "It's one higher."

在某種程度上，最大有氧輸出就像經典電影《This Is Spinal Tap》中吉他手Nigel Tufnel 的特殊擴音器：大多數擴音器只允許您將音量調至 10，而他的則調至 11。正如他令人難忘地解釋的那樣，“這是更高一點。”

Every once in a while, it's nice to have that range. We made our flight with a few seconds to spare.

每隔一段時間，擁有這個範圍就很好。我們起飛時還剩幾秒鐘。

Strength

力量

Weight training has been a touchstone for me since I was fourteen years old and my best friend John and I, both wannabe prizefighters, first wandered into the gym at the Scarborough campus of the University of Toronto. It was a smelly dungeon two floors underground, inhabited by very sweaty dudes who absolutely lived to lift heavy metal weights. It had no heat, no windows, and no AC, so winters were freezing and summers were so hot it was not uncommon for someone to pass out after a max-effort set. We loved it. It was as mythical to us as Gold's Gym at Venice Beach.

從我十四歲起，舉重訓練就一直是我的試金石，我和我最好的朋友約翰，我們都想成為職業拳擊手，第一次走進多倫多大學士嘉堡校區的健身房。那是一座地下兩層、散發著惡臭的地牢，裡面住著滿頭大汗的傢伙，他們絕對是為了舉起重金屬而活。這裡沒有暖氣，沒有窗戶，也沒有空調，因此冬天寒冷，夏天炎熱，有人在盡最大努力後昏倒的情況並不少見。我們喜歡它。它對我們來說就像威尼斯海灘的黃金健身房一樣神秘。

Back then, I went to the gym to pursue my boxing ambitions. I literally had no thought of what my life would look like after about age twenty-three. Now that I'm a middle-aged guy myself, I finally understand the seriousness with which those older guys approached their training. I am chasing a different dream—the Centenarian Decathlon, in case you forgot—but I suspect that I'm on the same page as them now.

那時，我去健身房追求我的拳擊夢想。我確實沒有想過二十三歲以後我的生活會是什麼樣子。現在我自己也已經是中年人了，我終於明白

那些老傢伙們對訓練的認真態度了。我正在追逐一個不同的夢想——百歲十項全能，以防你忘記了——但我懷疑我現在和他們站在同一立場上。

The sad fact is that our muscle mass begins to decline as early as our thirties. An eighty-year-old man will have about 40 percent less muscle tissue (as measured by cross section of the *vastus lateralis*, aka the “quad” muscle of the thigh) than he did at twenty-five. But muscle mass may be the least important metric here. According to Andy Galpin, a professor of kinesiology at California State University, Fullerton, and one of the foremost authorities on strength and performance, we lose muscle strength about two to three times more quickly than we lose muscle mass. And we lose power (strength x speed) two to three times faster than we lose strength. This is because the biggest single change in the aging muscle is the atrophy of our fast twitch or type 2 muscle fibers. Ergo, our training must be geared towards improving these with heavy resistance training. Daily life and zone 2 endurance work may be enough to prevent atrophy of type 1 fibers—but unless you are working against significant resistance, your type 2 muscle fibers will wither away.

可悲的事實是，我們的肌肉質量早在三十多歲就開始下降。一名 80 歲的男性的肌肉組織（透過股外側肌（又稱大腿「股四頭肌」肌肉）的橫斷面測量）比 25 歲時少約 40%。但肌肉質量可能是這裡最不重要的指標。加州州立大學富勒頓分校運動機能學教授、力量和表現方面最權威的權威之一安迪·加爾平(Andy Galpin) 表示，我們失去肌肉力量的速度比失去肌肉質量的速度快兩到三倍。我們失去力量（力量 x 速度）的速度比失去力量的速度快兩到三倍。這是因為老化肌肉中最大的單一變化是快肌纖維或 2 型肌纖維的萎縮。因此，我們的訓練必須旨在透過高強度阻力訓練來改善這些。日常生活和 2 區耐力訓練可能足以防止 1 型肌纖維萎縮，但除非您在很大的阻力下進行訓練，否則您的 2 型肌纖維將會萎縮。

It takes much less time to lose muscle mass and strength than to gain it, particularly if we are sedentary. Even if someone has been training diligently, a short period of inactivity can erase many of those gains. If that inactivity stems from a fall or a broken bone, and lasts longer than a few days, it can

often kick off a steep decline from which we may never fully recover, which is pretty much what happened with Sophie. A study of twelve healthy volunteers with an average age of sixty-seven found that after just ten days of bed rest, which is about what a person would experience from a major illness or orthopedic injury, study participants lost an average of 3.3 pounds of lean mass (muscle). That's substantial, and it shows just how dangerous inactivity can be. If someone is sedentary and consuming excess calories, muscle loss accelerates, because one of the primary destinations of fat spillover is into muscle.

失去肌肉質量和力量所需的時間比獲得肌肉質量和力量所需的時間要少得多，特別是當我們久坐時。即使有人一直在努力訓練，短暫的不活動也會抹去許多這些收穫。如果這種不活動的原因是跌倒或骨折，而且持續時間超過幾天，它通常會導致我們的身體急劇下降，而我們可能永遠無法完全恢復，這與索菲的情況差不多。一項針對12名平均年齡67歲的健康志願者進行的研究發現，僅臥床休息10天（大約是一個人因重大疾病或骨科損傷所經歷的情況）後，研究參與者平均減掉了3.3磅的瘦肉量（肌肉）。這是很重要的，它顯示不活動是多麼危險。如果一個人久坐並消耗過多的熱量，肌肉流失就會加速，因為脂肪溢出的主要目的地之一是肌肉。

In its most extreme form, this muscle loss is called sarcopenia, as noted in chapter 11. Someone with sarcopenia will have low energy, feelings of weakness, and problems with balance. Sarcopenia is a prime marker for a broader clinical condition called frailty, where a person meets three of these five criteria: unintended weight loss; exhaustion or low energy; low physical activity; slowness in walking; and weak grip strength (about which more soon). It can become difficult to stand or walk, and they are at huge risk of falling and breaking bones.

在最極端的形式中，這種肌肉損失被稱為肌少症，如第11章所述。患有肌少症的人會出現精力低下、虛弱感和平衡問題。肌少症是一種更廣泛的臨床病症（稱為虛弱）的主要標誌，即一個人滿足這五個標準中的三個：意外體重減輕；精疲力竭或精力不足；體力活動量低；行

走緩慢；握力較弱（稍後會詳細介紹）。他們可能會變得難以站立或行走，並且面臨跌倒和骨折的巨大風險。

Regaining that muscle, once we've gotten to this state, is no easy task. One study looked at sixty-two frail seniors (average age seventy-eight) who engaged in a program of strength training and found that even after six months of pure strength training, half of the subjects did not gain *any* muscle mass. They also didn't lose any muscle mass, likely thanks to the weight training, but the upshot is, it is very difficult to put on muscle mass later in life.

一旦我們達到這種狀態，恢復肌肉就不是一件容易的事了。一項研究對 62 名體弱老年人（平均年齡 78 歲）進行了力量訓練，結果發現，即使經過六個月的純粹力量訓練，一半的受試者也沒有獲得任何肌肉質量。他們也沒有失去任何肌肉質量，這可能是由於重量訓練，但結果是，在以後的生活中很難增加肌肉質量。

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Another metric that we track closely in our patients is their bone density (technically, bone mineral density or BMD). We measure BMD in every patient, every year, looking at both of their hips and their lumbar spine using DEXA. This also measures body fat and lean mass, so it's a useful tool across all of the body-composition domains that we care about.

我們密切追蹤患者的另一個指標是他們的骨密度（技術上是骨礦物質密度或 BMD）。我們每年都會使用 DEXA 測量每位患者的臀部和腰椎 BMD。它還可以測量身體脂肪和瘦體重，因此它是我們關心的所有身體組成領域的有用工具。

These three bone regions are typically used to make a diagnosis of osteopenia or osteoporosis. The standard guidelines only recommend screening in women at age sixty-five or men at age seventy—which is classic Medicine 2.0, waiting until someone may be staring danger in the eye before doing anything. We think it's important to get a handle on this much earlier, before any problems arise.

這三個骨骼區域通常用於診斷骨質減少或骨質疏鬆症。標準指南僅建議在 65 歲的女性或 70 歲的男性中進行篩檢——這是經典的醫學 2.0，等到有人可能注視著危險才採取任何行動。我們認為，在出現任何問題之前儘早解決這個問題非常重要。

The fact is that bone density diminishes on a parallel trajectory to muscle mass, peaking as early as our late twenties before beginning a slow, steady decline. For women, this decline happens much more quickly once they hit menopause, if they are not on HRT (yet another reason we heavily favor HRT), because estrogen is essential for bone strength—in both men and women. Other risk factors for low bone density include genetics (family history), a history of smoking, long use of corticosteroids (e.g., for asthma or autoimmune conditions), drugs that block estrogen (e.g., women taking such drugs for breast cancer), low muscle mass (again), and being undernourished.

事實上，骨密度的減少與肌肉質量的減少是平行的，早在二十多歲時就達到峰值，然後開始緩慢、穩定的下降。對於女性來說，一旦進入更年期，如果不接受荷爾蒙替代療法（這也是我們大力支持荷爾蒙替代療法的另一個原因），這種衰退會發生得更快，因為雌激素對於男性和女性的骨骼強度都至關重要。其他骨密度低的危險因子包括遺傳（家族史）、吸菸史、長期使用皮質類固醇（例如，治療氣喘或自體免疫疾病）、阻斷雌激素的藥物（例如，服用此類藥物治療乳癌的女性）、低骨密度。肌肉質量（再次），且營養不良。

Why do we care so much? Just as with muscle, it comes down to protection. We want to slow this decline, armoring ourselves against injury and physical frailty. The mortality from a hip or femur fracture is staggering once you hit about the age of sixty-five. It varies by study, but ranges from 15 to 36 percent in one year—meaning that up to one-third of people over sixty-five who fracture their hip are dead within a year. Even if a person does not die from the injury, the setback can be the functional equivalent of death in terms of how much muscle mass and, hence, physical capacity is lost during the period of bed rest (recall how quickly people over sixty-five lose muscle mass when bedridden).

為什麼我們如此關心？就像肌肉一樣，它歸結為保護。我們希望減緩這種衰退，保護自己免受傷害和身體虛弱。一旦你到了六十五歲左右，髖部或股骨骨折的死亡率就會令人震驚。具體情況因研究而異，但一年內發生率從 15% 到 36% 不等，這意味著 65 歲以上髖部骨折的人中有多達三分之一會在一年內死亡。即使一個人沒有因受傷而死亡，就肌肉質量和身體能力在臥床休息期間的損失程度而言，這種挫折可能相當於死亡（回想一下，六十五歲以上的人損失的速度有多快）臥床不起時會失去肌肉量）。

Our goal is to try to spot this issue, if it arises, decades before a potential fracture might occur. When we detect low or rapidly declining BMD in a middle-aged person, we use the following four strategies:

我們的目標是在潛在骨折發生幾十年前嘗試發現這個問題（如果出現）。當我們發現中年人類骨密度低或快速下降時，我們會使用以下四種策略：

1. Optimize nutrition, focusing on protein and total energy needs (see nutrition chapters).

優化營養，重點關注蛋白質和總能量需求（請參閱營養章節）。

2. Heavy loading-bearing activity. Strength training, especially with heavy weights, stimulates the growth of bone—more than impact sports such as running (though running is better than swimming/cycling). Bones respond to mechanical tension and estrogen is the key hormone in mediating the mechanical signal (weight bearing) to a chemical one telling the body to lay down more bone.

重負荷活動。肌力訓練，尤其是大重量訓練，比跑步等衝擊性運動更能刺激骨骼生長（儘管跑步比游泳/騎自行車更好）。骨骼會對機械張力做出反應，而雌激素是將機械訊號（負重）傳遞給化學訊號的關鍵激素，告訴身體釋放更多的骨骼。

3. HRT, if indicated.

HRT（如果有指示）。

4. Drugs to increase BMD, if indicated.

如有需要，可使用增加 BMD 的藥物。

Ideally, we can solve the problem with the first two, but are not afraid to use the second two methods where appropriate. The takeaway for readers here is that your BMD is important, demanding at least as much attention as muscle mass, so you should at least check your BMD every few years. (Particularly if your primary sports are nonweight-bearing, like cycling or swimming.)

理想情況下，我們可以用前兩種方法解決問題，但不要害怕在適當的情況下使用後兩種方法。讀者的要點是，您的 BMD 很重要，至少需要與肌肉質量一樣多的關注，因此您至少應該每隔幾年檢查一次您的 BMD。（特別是如果您的主要運動是非負重運動，例如騎自行車或游泳。）

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I think of strength training as a form of retirement saving. Just as we want to retire with enough money saved up to sustain us for the rest of our lives, we want to reach older age with enough of a “reserve” of muscle (and bone density) to protect us from injury and allow us to continue to pursue the activities that we enjoy. It is much better to save and invest and plan ahead, letting your wealth build gradually over decades, than to scramble to try to scrape together an individual retirement account in your late fifties and hope and pray that the stock market gods help you out. Like investing, strength training is also cumulative, its benefits compounding. The more of a reserve you build up, early on, the better off you will be over the long term.

我認為肌力訓練是退休儲蓄的一種形式。正如我們希望在退休時存下足夠的錢來維持我們的餘生一樣，我們希望在老年時擁有足夠的肌肉「儲備」（和骨密度）來保護我們免受傷害，並讓我們能夠繼續從事我們喜歡的活動。儲蓄、投資和提前計劃，讓你的財富在幾十年內逐漸積累，比在五十多歲的時候努力拼湊個人退休帳戶並希望和祈禱股

市之神幫助你要好得多。與投資一樣，肌力訓練也是累積的，其好處是複合的。您儘早建立的儲備越多，長遠來看就會越好。

Yet unlike some guys in the gym, I'm less concerned with how big my biceps are or how much I can bench press. Those might matter if you're a bodybuilder or a powerlifter, but I'd argue they matter less in the Centenarian Decathlon (or in real life). A far more important measure of strength, I've concluded, is how much heavy stuff you can carry. I say this on the basis of my intuition but also research into hunter-gatherers and human evolution. Carrying is our superpower as a species. It's one reason why we have thumbs, as well as long legs (and arms). No other animal is capable of carrying large objects from one place to another with any efficiency. (And the ones that can, like horses and other livestock, do so only because we bred and trained and harnessed them.) This frames how I view strength training in general. It's largely about improving your ability to carry things.

然而，與健身房裡的一些人不同，我不太關心我的二頭肌有多大，或者我可以臥推多少。如果你是健美運動員或舉重運動員，這些可能很重要，但我認為它們在百歲十項全能（或現實生活中）中不太重要。我得出的結論是，衡量力量的一個更重要的標準是你可以搬運多少重物。我這樣說是基於我的直覺，也是基於對狩獵採集者和人類進化的研究。攜帶是我們作為一個物種的超能力。這就是我們擁有拇指和長腿（和手臂）的原因之一。沒有其他動物能夠有效率地將大型物體從一個地方運送到另一個地方。（那些能夠做到這一點的動物，例如馬和其他牲畜，只是因為我們飼養、訓練和駕馭它們。）這概括了我對力量訓練的看法。這主要是為了提高你搬運東西的能力。

I've always been a fan of carrying heavy objects with my hands. As a teenager working on a construction site over the summers, I always volunteered to haul tools and materials across the site, and today I still incorporate some kind of carrying, typically with dumbbells, kettlebells, or sandbags, into most of my workouts. I've also become semiobsessed with an activity called *rucking*, which basically means hiking or walking at a fast pace with a loaded pack on your back. Three or four days a week, I'll spend an hour rucking around my neighborhood, up and down hills, typically climbing and

descending several hundred feet over the course of three or four miles. The fifty- to sixty-pound pack on my back makes it quite challenging, so I'm strengthening my legs and my trunk while also getting in a solid cardiovascular session. The best part is that I never take my phone on these outings; it's just me, in nature, or maybe with a friend or a family member or a houseguest (for whom rucking is mandatory; I keep two extra rucksacks in the garage).

我一直都喜歡用手搬運重物。當我還是個夏天在建築工地工作的青少年時，我總是自願在工地上搬運工具和材料，如今我仍然將某種搬運方式（通常是啞鈴、壺鈴或沙袋）納入我的大部分鍛煉中。我還對一種叫做 rucking 的活動半著迷，這基本上意味著背著負重的背包徒步旅行或快步行走。每週三到四天，我會花一個小時在我的社區周圍閒逛，上下山，通常在三四英里的路程中爬升和下降數百英尺。我背上五十到六十磅的重物讓這件事變得相當具有挑戰性，所以我在加強我的腿部和軀幹的同時，也進行了紮實的心血管訓練。最好的一點是，我在外出時從不帶手機。只有我，在大自然中，或者可能和朋友、家人或房客一起（對他們來說，翻滾是強制性的；我在車庫裡放了兩個額外的背包）。

I was introduced to this pastime by Michael Easter in his eye-opening book *The Comfort Crisis*. His intriguing thesis is that because we have removed all discomfort of any kind from modern life, we have lost touch with the fundamental skills (not to mention the frequent suffering) that once defined what it meant to be human. Carrying stuff over long distances is one of these skills; our ancestors likely had to range far and wide to hunt food for their families and then carry their kills back to camp to feed everyone. But it's so effective that the military has incorporated it into their training.

伊斯特（Michael Easter）在令人大開眼界的書《舒適危機》中向我介紹了這項消遣。他有趣的論點是，因為我們已經消除了現代生活中任何形式的不適，所以我們已經失去了曾經定義人類意義的基本技能（更不用說頻繁的痛苦）。長距離搬運物品就是這些技能之一。我們的祖先可能必須長途跋涉為家人尋找食物，然後將獵物帶回營地來養活每個人。但它非常有效，以至於軍方已將其納入訓練中。

“Carrying shaped our species,” he says. “Our ancestors carried often. It

gave them robust functional strength and endurance that was likely very protective. But we've engineered carrying out of our lives, just as we have many other forms of discomfort. Rucking is a practical way to add carrying back into our lives.”

「攜帶塑造了我們的物種，」他說。「我們的祖先經常攜帶。它賦予了它們強大的功能力量和耐力，這可能非常有保護作用。但正如我們有許多其他形式的不適一樣，我們也設計了自己的生活。拉動是一種讓攜帶物品重新回到我們生活中的實用方法。」

The main difference is that instead of carrying sixty pounds of antelope meat in my pack, I'm typically hauling heavy metal weights, which are admittedly less appetizing. One thing I specifically focus on when rucking is the hills. Going uphill gives me a chance to push my VO_2 max energy system; first-time ruckers are amazed at how taxing it is to walk up a 15 percent grade with even twenty pounds on your back—and then walk back down. (A good goal is to be able to carry one-quarter to one-third of your body weight once you develop enough strength and stamina. My daughter and wife routinely carry this much when they join me.)

主要的區別在於，我的背包裡不是攜帶六十磅的羚羊肉，而是通常拖著重金屬重物，這無疑不太令人胃口大開。越野時我特別關注的一件事是山丘。上坡讓我有機會推動我的 VO_2 最大能量系統；第一次玩滑板的人會驚訝地發現，背著 20 磅的重量爬上 15% 的坡度，然後再走下來是多麼費力。（一個好的目標是，一旦你有足夠的力量和耐力，就能夠承擔你體重的四分之一到三分之一。我的女兒和妻子加入我時通常會承擔這麼多。）

As great as rucking is, it's not the only thing I rely on to build my strength. Fundamentally I structure my training around exercises that improve the following:

儘管拉力很偉大，但它並不是我增強力量的唯一依靠。從根本上來說，我圍繞著改善以下方面的練習來建立我的訓練：

1. *Grip strength*, how hard you can grip with your hands, which involves everything from your hands to your lats (the large muscles on your back). Almost all actions begin with the grip.

握力，即用手抓握的力度，涉及從手到背闊肌（背部的大肌肉）的各個部分。幾乎所有的動作都是從握力開始的。

2. Attention to both *concentric* and *eccentric loading* for all movements, meaning when our muscles are shortening (concentric) *and* when they are lengthening (eccentric). In other words, we need to be able to lift the weight up and put it back down, slowly and with control. Rucking down hills is a great way to work on eccentric strength, because it forces you to put on the “brakes.”

注意所有運動的同心和偏心負荷，這意味著我們的肌肉何時縮短（同心）和何時延長（偏心）。換句話說，我們需要能夠緩慢且有控制地舉起重物並放下。下山是鍛鍊離心力量的好方法，因為它會迫使你踩「煞車」。

3. *Pulling motions*, at all angles from overhead to in front of you, which also requires grip strength (e.g., pull-ups and rows).

從頭頂到身前各個角度的拉動動作，也需要握力（例如引體向上和划船）。

4. *Hip-hinging movements*, such as the deadlift and squat, but also step-ups, hip-thrusters, and countless single-leg variants of exercises that strengthen the legs, glutes, and lower back.

髖部鉸鏈運動，例如硬舉和深蹲，還有踏步、髖部推進器以及無數單腳練習，可以增強腿部、臀部和下背部的力量。

I focus on these four foundational elements of strength because they are the most relevant to our Centenarian Decathlon—and also to living a fulfilling and active life in our later decades. If you can grip strongly, you can open a jar with ease. If you can pull, you can carry groceries and lift heavy objects. If

you can do a hip-hinge correctly, you can get up out of a chair with no problem. You're setting yourself up to age well. It's not about how much weight you can deadlift now, but how well you will function in twenty or thirty or forty years.

我關注力量的這四個基本要素，因為它們與我們的百歲十項全能最相關，也與我們在晚年過著充實和積極的生活最相關。如果你能有力地抓住，你就能輕鬆地打開罐子。如果你會拉，你就可以搬運雜貨和舉起重物。如果你能正確地完成髖部鉸鏈，你就可以毫無問題地從椅子上站起來。你正在為自己做好準備，以適應年齡的增長。重要的不是你現在能硬舉多少重量，而是你二十年、三十年或四十年後的表現如何。

I put grip strength first because it's something that most people don't really think about. Even I was surprised to discover that there is an enormous body of literature linking better grip strength in midlife and beyond to decreased risk of overall mortality.^[*5] The data are as robust as for VO_2 max and muscle mass, in fact. Many studies suggest that grip strength—literally, how hard you can squeeze something with one hand—predicts how long you are likely to live, while low grip strength in the elderly is considered to be a symptom of sarcopenia, the age-related muscle atrophy we just discussed. In these studies, grip strength is likely acting as a proxy for overall muscle strength, but it is also a broader indicator of general robustness *and* the ability to protect yourself if you slip or lose balance. If you have the strength to grab a railing, or a branch, and hold on, you might avoid a fall.

我把握力放在第一位，因為大多數人並沒有真正考慮到這一點。就連我也驚訝地發現，有大量文獻將中年及以後更好的握力與整體死亡率風險降低聯繫起來。[*5] 事實上，這些數據與最大攝氧量₂和肌肉質量一樣可靠。許多研究表明，握力（字面意思是用一隻手擠壓某物的力度）可以預測您的壽命，而老年人的握力較低被認為是肌肉減少症（一種與年齡相關的肌肉萎縮症）的症狀我們剛討論過。在這些研究中，握力可能是整體肌肉力量的指標，但它也是整體穩健性以及滑倒或失去平衡時保護自己的能力更廣泛指標。如果您有力量抓住欄桿或樹枝並堅持住，您可能會避免跌倒。

Surprisingly, given the extent to which fitness and gym-going have become so commonplace in our culture in the last few decades, American adults actually seem to have far weaker grip strength—and thus less muscle mass—than they did even a generation ago. In 1985, men ages twenty to twenty-four had an average right-handed grip strength of 121 pounds, while in 2015, men of the same age averaged just 101 pounds. This suggests that people now in their thirties are entering midlife with much less strength than their parents, which could lead to problems as they get older.

令人驚訝的是，考慮到過去幾十年來健身和去健身房在我們的文化中變得如此普遍，美國成年人的握力實際上似乎比上一代人要弱得多，因此肌肉質量也更少。1985年，20至24歲的男性平均右手握力為121磅，而2015年，同年齡層男性的平均握力僅101磅。這表明，現在三十多歲的人進入中年時，體力比他們的父母要弱得多，這可能會隨著年齡的增長而出現問題。

Grip strength is important at all ages. Every interaction that we have begins with our hands (or feet, as we'll discuss later). Our grip is our primary point of contact in almost any physical task, from swinging a golf club to chopping wood; it is our interface with the world. If our grip is weak, then everything else is compromised.

握力對於所有年齡層都很重要。我們的每一次互動都是從我們的手（或腳，我們將在後面討論）開始的。幾乎在所有體力任務中，從揮動高爾夫球桿到劈柴，我們的握力都是主要接觸點；它是我們與世界的介面。如果我們的抓地力較弱，那麼其他一切都會受到影響。

Training grip strength is not overly complicated. One of my favorite ways to do it is the classic farmer's carry, where you walk for a minute or so with a loaded hex bar or a dumbbell or kettlebell in each hand. (Bonus points: Hold the kettlebell up vertically, keeping your wrist perfectly straight and elbow cocked at ninety degrees, as though you were carrying it through a crowded room.) One of the standards we ask of our male patients is that they can carry half their body weight in each hand (so full body weight in total) for at least one minute, and for our female patients we push for 75 percent of that weight.

This is, obviously, a lofty goal—please don't try to do it on your next visit to the gym. Some of our patients need as much as a year of training before they can even attempt this test.

訓練握力不會太複雜。我最喜歡的方法之一是經典的農夫背法，即每隻手拿著一個負重的六角桿或啞鈴或壺鈴行走一分鐘左右。（加分點：垂直舉起壺鈴，保持手腕完全伸直，肘部翹起九十度，就好像你拿著壺鈴穿過擁擠的房間一樣。）我們對男性患者提出的標準之一是，他們可以攜帶一半的壺鈴。她們的體重每隻手上（所以整個體重）至少一分鐘，對於我們的女性患者，我們力爭達到該體重的75%。顯然，這是一個崇高的目標——請不要在下次去健身房時嘗試這樣做。我們的一些患者需要長達一年的訓練才能嘗試這項測試。

In general, we urge our new patients to begin with far *less* weight than they have lifted in the past, sometimes even dropping down to body weight exercises at first. As we will see in the next chapter, on stability, it is far more important to learn and practice ideal movement patterns than to be pounding heavy weights all the time. That said, a farmer's carry is pretty straightforward (weight in each hand, arms at sides, walk). The most important tip is to keep your shoulder blades down and back, not pulled up or hunched forward. If you are new to strength training, start with light weights, even as low as ten to fifteen pounds, and work up from there.

一般來說，我們敦促新患者一開始的重量遠低於過去的重量，有時甚至一開始就進行自重練習。正如我們將在下一章中看到的，關於穩定性，學習和練習理想的運動模式比一直敲擊大重量要重要得多。也就是說，農民的搬運非常簡單（每隻手負重，手臂放在兩側，步行）。最重要的提示是保持肩胛骨向下和向後，而不是向上拉或向前彎腰。如果您是力量訓練新手，請從輕重量開始，甚至低至十到十五磅，然後逐漸增加。

Another way to test your grip is by dead-hanging from a pull-up bar for as long as you can. (This is not an everyday exercise; rather, it's a once-in-a-while test set.) You grab the bar and just hang there, supporting your body weight. This is a simple but sneakily difficult exercise that also helps strengthen the critically important scapular (shoulder) stabilizer muscles, which we will talk

about in the next chapter. Here we like to see men hang for at least two minutes and women for at least ninety seconds at the age of forty. (We reduce the goal slightly for each decade past forty.)

另一種測試握力的方法是盡可能長時間地在引體向上桿上懸掛。（這不是日常練習；相反，這是一次偶爾的測試。）您抓住槓鈴並懸掛在那裡，支撐您的體重。這是一項簡單但難度較高的練習，也有助於增強至關重要的肩胛（肩部）穩定肌，我們將在下一章中討論這一點。在這裡，我們希望看到四十歲的男人被絞死至少兩分鐘，女人被絞死至少九十分鐘。（四十歲以後每十年我們都會稍微降低目標。）

No discussion of strength is complete without mentioning *concentric* and especially *eccentric* loading. Again, eccentric loading means loading the muscle as it is lengthening, such as when you lower a bicep curl. It's more intuitive when lifting something to focus on the concentric phase, such as curling the dumbbell with your biceps. This is the strength of a muscle getting shorter. One of the tests we have our patients perform is stepping onto and off an eighteen-inch block and taking three full seconds to reach the ground (a forward step down, like descending a very tall step). The stepping up part is comparatively easy, but most people initially struggle with a controlled three-second descent. That requires eccentric strength and control. (I'll talk about step-ups and step-downs in detail at the end of chapter 13.)

如果不提及同心載荷，尤其是偏心載荷，對強度的討論就不完整。同樣，偏心負載意味著在肌肉拉長時加載肌肉，例如當您降低二頭肌彎舉時。當舉起某物以專注於同心階段時，例如用二頭肌彎舉啞鈴，會更直觀。這是肌肉變短的力量。我們讓患者進行的一項測試是踏上和踏下十八英寸的木塊，並花費整整三秒的時間才能到達地面（向前邁出一步，就像走下一個很高的台階一樣）。上坡部分相對容易，但大多數人一開始就很難控制住三秒的下坡。這需要偏心的力量和控制力。（我將在第 13 章末尾詳細討論升壓和降壓。）

In life, especially as we age, eccentric strength is where many people falter. Eccentric strength in the quads is what gives us the control we need when we are moving down an incline or walking down a set of stairs. It's really important to keep us safe from falls and from orthopedic injuries. When we

can eccentrically load our muscles, it also prevents our joints from taking excess stress, especially our knees. Think about creeping slowly down a very steep hill versus running down in an uncontrolled manner. The difference in force transmission to your knees is dramatic (as is the difference in likely outcomes—safe descent versus faceplant and likely knee injury).

在生活中，尤其是隨著年齡的增長，古怪的力量是許多人動搖的地方。當我們下斜坡或走下樓梯時，股四頭肌的偏心力量可以為我們提供所需的控制力。確保我們免受跌倒和骨科傷害非常重要。當我們可以對肌肉進行偏心負荷時，它還可以防止我們的關節承受過多的壓力，尤其是膝蓋。想像一下緩慢地爬下一座非常陡峭的山坡，而不是不受控制地跑下山坡。傳遞到膝蓋的力的差異是巨大的（可能的結果也存在差異——安全下降與面朝下以及可能的膝蓋受傷）。

Training eccentric strength is relatively simple. Big picture, it means focusing on the “down” phase of lifts ranging from pull-ups or pull-downs to deadlifts to rows; rucking downhill, carrying a weighted pack, is a great way to build both eccentric strength as well as spatial awareness and control, which are important parts of stability training (next chapter). It also helps protect against knee pain. You don’t need to do this for every rep of every set. Sometimes you just want to focus on moving the weight quickly or moving a heavier load, but make sure at some point in each workout that you are taking the time to cue the eccentric phase of your lifts.

訓練偏心力量比較簡單。從大局來看，這意味著專注於舉重的「向下」階段，從引體向上或下拉到硬舉再到划船；背著負重背包下坡，是增強離心力量以及空間意識和控制力的好方法，而這些是穩定性訓練的重要組成部分（下一章）。它還有助於防止膝蓋疼痛。你不需要對每組的每一次重複都這樣做。有時您只想專注於快速移動重量或移動較重的負載，但請確保在每次鍛鍊的某個時刻您花時間提示舉重的偏心階段。

Next is pulling, which is closely related to grip strength. Pulling motions are how we exert our will on the world, whether we are hoisting a bag of groceries out of the car trunk or climbing El Capitan. It is an anchor movement. In the gym, it typically takes the form of rows, where you’re

pulling the weight toward your body, or pull-ups. A rowing machine, something I love to use for VO_2 max training, is another simple and effective way to work on pulling strength.

其次是拉力，與握力密切相關。拉動動作是我們向世界施加意志的方式，無論我們是從汽車後備箱中提起一袋雜貨還是攀登酋長岩。這是一個錨定運動。在健身房裡，通常採取划船的形式，將重量拉向身體，或引體向上。我喜歡用划船機進行最大攝氧量 VO_2 訓練，它是另一種簡單而有效的鍛鍊拉力的方法。

The final foundational element of strength is hip-hinging, which is what it sounds like: You bend at the hips—*not* the spine—to harness your body's largest muscles, the gluteus maximus and the hamstrings. (I repeat: Do not bend your spine.) It is a very powerful move that is essential to life. Whether you are launching off an Olympic ski jump, picking up a lucky penny off the sidewalk, or simply getting up out of a chair, you are hip-hinging.

力量的最後一個基本要素是髋部鉸鏈，顧名思義：你彎曲臀部，而不是脊柱，以利用你身體最大的肌肉，臀大肌和腿筋。（我再說一次：不要彎曲你的脊椎。）這是一個非常有力的舉動，對生命至關重要。無論你是要參加奧運跳台滑雪、在人行道上撿到一枚幸運硬幣，還是只是從椅子上站起來，你都在扭屁股。

Hip-hinging under high axial load, as with a heavy deadlift or squat, should be approached with care because of the risk of injury to the spine. This is why we have our patients work up to weighted hip-hinging very slowly, typically beginning with single-leg step-ups (see description below) and split-stance Romanian deadlift, either without weights or with only very light weights held in the hands.

在高軸向負荷下進行髋部鉸鏈（如大重量硬舉或深蹲）時應小心謹慎，因為有脊椎受傷的風險。這就是為什麼我們讓患者非常緩慢地進行負重髋部鉸鏈訓練，通常從單腿上台階（見下面的描述）和分離式羅馬尼亞硬舉開始，要么不舉重，要么只舉起非常輕的重量。。

Normally, this would be the section where I would write a lengthy treatise on the finer points of how to do pull-ups and hip-hinges. I've come to the

conclusion that they can't actually be done right without dozens of pictures and thousands of words, in a book that is already too long. There are two reasons why I have decided not to give the details. One, I believe that this type of content is best learned in person, from someone who knows how to cue the movements. For example, the "hard" part about teaching a proper hip-hinge is not illustrating the correct position of the spine relative to the femur and lower leg, or the angle of the hips, in a diagram. The hard part is knowing how to eccentrically load the glutes and hamstrings *before* you hinge, and how to feel your feet pushing into the floor evenly across the full surface of your foot.

通常情況下，我會在這一部分寫一篇長篇論文，討論如何做引體向上和髖關節鉸鏈的細節。我得出的結論是，在一本太長的書中，如果沒有數十張圖片和數千個文字，實際上就無法完成它們。我決定不透露細節有兩個原因。第一，我認為這種類型的內容最好是親自從知道如何提示動作的人那裡學習。例如，關於教導正確的臀部鉸鏈的「困難」部分並沒有在圖表中說明脊椎相對於股骨和小腿的正確位置，或臀部的角度。困難的部分是知道如何在鉸接之前對臀肌和腿筋施加偏心負荷，以及如何感覺雙腳在整個腳表面均勻地推入地板。

If this is hard to follow, you see exactly why I've come to the conclusion that the best way to communicate this information to you, in a way that is actionable, is to show you, as opposed to telling you. And the best way I can show you, shy of working out with you, is having you watch me do these exercises over video, with my colleague Beth Lewis cuing me. (I've placed a link to these videos, and a brief description, at the end of the next chapter.)

如果這很難理解，那麼您就會明白為什麼我得出這樣的結論：以可行的方式向您傳達此訊息的最佳方式是向您展示，而不是告訴您。我可以向您展示的最好方法是讓您透過影片觀看我做這些練習，並由我的同事貝絲·劉易斯（Beth Lewis）指導我，因為我不敢與您一起鍛鍊。（我在下一章的末尾放置了這些影片的連結和簡要說明。）

The second reason I've opted not to describe all these exercises in detail is that when new patients come to us, we typically have them *stop* strength training, at least with heavy weights. Our first step is to put them through a series of strength and movement tests designed to assess not only their

physical condition but also their degree of stability. So before you do anything in the gym, I would urge you to read the next chapter, to begin to understand the crucial and complex concept of stability.

我選擇不詳細描述所有這些練習的第二個原因是，當新患者來找我們時，我們通常會讓他們停止力量訓練，至少是大重量訓練。我們的第一步是讓他們接受一系列的力量和運動測試，旨在評估他們的身體狀況和穩定性。因此，在你在健身房做任何事情之前，我強烈建議你先閱讀下一章，開始理解穩定性這個關鍵而複雜的概念。

[SKIP NOTES](#)

[跳過註釋](#)

[*1](#) This is because the hydrogen ion does not allow the actin and myosin filaments in your muscles to relax, causing pain and stiffness in the muscle.

*1 這是因為氫離子不允許肌肉中的肌動蛋白和肌球蛋白絲放鬆，導致肌肉疼痛和僵硬。

[*2](#) Patients on chemotherapy treatment for cancer often seem to be similarly compromised in terms of mitochondrial efficiency. There is also speculation, with some evidence, that this afflicts patients with so-called “long COVID.”

*2 接受癌症化療的患者在粒線體效率方面似乎也常常受到同樣的損害。也有一些證據表明，這種情況會影響所謂的「長期新冠病毒」患者。

[*3](#) Two of the aging athletes posted VO_2 max scores greater than 40, and the oldest subject, a ninety-one-year-old former Olympian, came very close to that, at 36, which would put them in the top quarter of men in their sixties.

*3 兩位老年運動員的 VO_2 最大得分超過 40，而最年長的受試者（一位 91 歲的前奧運選手）非常接近這個分數，36 歲，這將使他們在六十多歲的男性中名列前茅。

[*4](#) In practice, I've found that my ideal VO_2 max pace works out to about 33 percent more power than my zone 2 pace, if I'm doing four-on/four-off intervals. So if your zone 2 pace represents an output of 150 watts, your VO_2 max training pace should be about 200 watts for four minutes, followed by four minutes of rest. Better yet, if you know your functional threshold power (FTP), which is the highest power you can sustain for sixty minutes, you should target 120 percent of this for three-minute intervals and 106 percent of this for eight-minute intervals and adjust for everything in between.

*4 在實踐中，我發現，如果我進行四次/四次間歇訓練，我理想的 VO_2 最大配速比我的 2 區配速高出約 33% 的功率。因此，如果您的 2 區配速代表 150 瓦的輸出，則您的 VO_2 最大訓練配速應為 200 瓦左右，持續四分鐘，然後休息四分鐘。更好的是，如果您知道您的功能閾

值功率 (FTP)，即您可以維持 60 分鐘的最高功率，您應該以三分鐘間隔為 120%，以八分鐘間隔為 106%，並進行調整對於介於兩者之間的一切。

[*5](#) The consensus definition of sarcopenia requires the presence of low skeletal muscle mass and either low muscle strength (e.g., handgrip strength) or low physical performance (e.g., walking speed).

*5 肌少症的共識定義要求存在低骨骼肌質量和低肌肉力量（例如握力）或低身體表現（例如步行速度）。

CHAPTER 13

第13章

The Gospel of Stability

穩定的福音

Relearning How to Move to Prevent Injury

重新學習如何移動以防止受傷

The loftier the building, the deeper the foundation must
be laid.

大樓越高，地基必須打越深。

—THOMAS À KEMPIS

——托馬斯肯皮斯

By now it should be clear that it is important to stay in good physical condition as we age. But now consider another, related question: Why don't

more people actually pull this off?

到目前為止，我們應該清楚，隨著年齡的增長，保持良好的身體狀況非常重要。但現在考慮另一個相關問題：為什麼沒有更多的人真正實現這個目標？

A typical seventy-year-old will do less than half as much “moderate to vigorous” physical activity as she did at age forty—and after age seventy the decline accelerates. The fit people in their seventies and eighties are the exception, not the rule.

一個典型的七十歲老人所進行的「中等至劇烈」體力活動量還不到四十歲時的一半，而七十歲以後，這種下降速度會加速。七、八十歲健康的人是例外，而不是普遍現象。

It is tempting to attribute this to aging itself, the aches and pains that accumulate in middle age and beyond, not to mention the steady loss of aerobic capacity and strength. Other factors such as weight gain and poor sleep can also leave one feeling wiped out. But I think the missing X factor that explains *why* so many people just stop moving is something else: injury. That is, older people tend to exercise less, or not at all, because they simply can't. They have hurt themselves in some way, at some point in their lives, and they just never got back on the horse. So they continued to decline.

人們很容易將其歸因於老化本身，即中年及以後累積的疼痛，更不用說有氧能力和力量的不斷喪失。其他因素，例如體重增加和睡眠品質不佳，也會讓一種感覺消失殆盡。但我認為，解釋為什麼這麼多人停止運動的缺失 X 因素是另一個因素：受傷。也就是說，老年人往往運動較少，或根本不運動，因為他們根本做不到。他們在生命中的某個時刻以某種方式傷害了自己，但他們卻再也沒有回到馬背上。所以他們繼續下降。

This was certainly true of Sophie, my friend Becky's mother, but I too could have easily gone down that path. In my twenties, when I was in medical school and still training hard, lifting weights almost daily, I experienced a mysterious back injury that required two separate surgeries (one of which was botched), followed by a long and very difficult recovery. For several months I

was almost unable to function, surviving on large amounts of painkillers. I couldn't even brush my teeth without excruciating back pain, and I spent most of the day just lying on the floor. It got so bad that my mom had to fly out to Palo Alto and take care of me. The thing is, people think it's terrible when someone in their twenties has to go through this (and it is), yet they almost expect it for someone Sophie's age.

我朋友貝琪的母親蘇菲確實是這樣，但我也可以輕鬆地走上這條路。在我二十多歲的時候，當我在醫學院學習時，仍然刻苦訓練，幾乎每天舉重，我經歷了一次神秘的背部受傷，需要兩次單獨的手術（其中一次失敗），隨後是漫長而艱難的恢復。幾個月來，我幾乎無法活動，靠著大量止痛藥生存。我甚至無法刷牙而不感到背部疼痛，一天的大部分時間我都躺在地板上。情況變得如此糟糕，我媽媽不得不飛往帕洛阿爾托照顧我。問題是，人們認為二十多歲的人必須經歷這樣的事情是很可怕的（事實確實如此），但他們幾乎期望蘇菲這個年紀的人會經歷這樣的事情。

Sophie and I were not unique: this type of injury and chronic pain is shockingly widespread. According to the CDC, more than 27 percent of Americans over the age of forty-five report suffering from chronic pain, and about 10 to 12 percent say that pain has limited their activities on “most days or every day” during the previous six months. Most days or every day! Back pain, in particular, is a huge driver of opioid prescriptions and surgical procedures that are often of dubious value. It is a leading cause of disability around the world, and in the United States alone it drains off an estimated \$635 billion-with-a-B per year in medical costs and lost productivity.

蘇菲和我並不是獨一無二的：這種類型的傷害和慢性疼痛非常普遍。據 CDC 稱，超過 27% 的 45 歲以上美國人患有慢性疼痛，約 10% 至 12% 的人表示，在過去六個月中，疼痛限制了他們「大部分時間或每天」的活動。大多數日子或每天！尤其是背痛，是阿片類藥物處方和外科手術的重要推動因素，而這些處方和外科手術的價值往往令人懷疑。它是世界各地造成殘疾的主要原因，僅在美國，每年就因醫療費用和生產力損失而消耗約 6,350 億美元。

As I learned, all the aerobic fitness or strength in the world won't help you

if you get hurt and have to stop exercising for several months—or forever. Studies of college-age athletes who experience injury in their careers find that they report consistently lower quality of life at middle and older ages. Their injuries continue to affect them not only physically but psychologically as well, for decades into their lives. During my long ordeal, I came to appreciate how important our ability to function physically is to our overall well-being.

據我所知，如果您受傷並且必須停止運動幾個月甚至永遠，那麼世界上所有的有氧健身或力量都不會幫助您。一項針對在職業生涯中經歷過傷害的大學年齡層運動員的研究發現，他們在中年和老年時期的生活品質一直較低。在他們生命的幾十年裡，傷害不僅持續影響著他們的身體，也影響著他們的心理。在我漫長的磨難中，我開始意識到我們的身體機能對我們的整體健康有多重要。

All of the above, the research and my own experience, support my first commandment of fitness: *First, do thyself no harm.*

所有上述內容、研究和我自己的經驗，都支持我的健身第一誡：首先，不要傷害自己。

How do we do this? I think stability is the key ingredient. But it also requires a change in our mindset. We have to break out of the mentality that we must crush all our workouts every single time we go to the gym—doing the most reps, with the heaviest weights, day after day. As I learned, pushing oneself so hard all the time, without adequate stability, almost inevitably leads to injury. If you are struggling to get through your workout, then you are likely resorting to your body's own “cheats,” your ingrained but potentially dangerous movement patterns.

我們如何做到這一點？我認為穩定性是關鍵因素。但這也需要我們心態的改變。我們必須打破每次去健身房都必須完成所有運動的心態——日復一日地用最大的重量做最多的次數。據我所知，如果沒有足夠的穩定性，一直把自己逼得太緊，幾乎不可避免地會導致受傷。如果您在運動中遇到困難，那麼您可能會訴諸身體自身的“作弊”，即根深蒂固但具有潛在危險的運動模式。

Instead, we need to change our approach so that we are focused on doing things *right*, cultivating safe, ideal movement patterns that allow our bodies to work as designed and reduce our risk of injury. Better to work smart than to work too hard. But as I would see for myself, relearning these movement patterns is no simple task.

相反，我們需要改變我們的方法，以便我們專注於做正確的事情，培養安全、理想的運動模式，使我們的身體能夠按設計工作並降低受傷的風險。聰明地工作比過度努力工作更好。但正如我自己所看到的，重新學習這些運動模式並不是一件簡單的任務。

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Stability is often conflated with “core,” but there is much more to it than having strong abdominal muscles (which isn’t what “core” means anyway). In my view, stability is essential to any kind of movement, particularly if our goal is to be able to keep doing that movement for years or decades. It is the foundation on which our twin pillars of cardiovascular fitness and strength must rest. Without it, as we used to say in Canada, you are hosed. Maybe not immediately, but sooner or later you will likely experience an injury that limits your movement, kiboshes your daily activities as you age, and possibly knocks you out of the Centenarian Decathlon for good.

穩定性常常與「核心」混為一談，但它不僅僅是擁有強壯的腹部肌肉（無論如何，這不是「核心」的意思）。在我看來，穩定性對於任何類型的運動都是至關重要的，特別是如果我們的目標是能夠持續進行這種運動數年或數十年。它是我們心血管健康和力量兩大支柱必須依賴的基礎。沒有它，正如我們在加拿大常說的那樣，你就會被淹沒。也許不會立即發生，但遲早您可能會受到傷害，從而限制您的活動，隨著年齡的增長而影響您的日常活動，並可能使您永遠退出百歲十項全能。

One thing that stability training has taught me is that most “acute” injuries, such as a torn ACL or a hamstring tear, are rarely sudden. While their onset may be rapid—instantaneous back or neck or knee pain—there was likely a

chronic weakness or lack of stability at the foundation of the joint that was the true culprit. This is the real iceberg in the water. The “acute” injury is just the part you see, the manifestation of the underlying weakness. So if we are to complete the goals we have set in our own Centenarian Decathlon, we need to be able to anticipate and avoid any potential injuries that lie in our path, like icebergs at sea. This means understanding stability and incorporating it into our routine.

穩定性訓練教會我的一件事是，大多數「急性」傷害，例如前十字韌帶撕裂或腿筋撕裂，很少是突然的。雖然它們的發作可能很快——即時的背部、頸部或膝蓋疼痛——但真正的罪魁禍首很可能是關節基礎的慢性虛弱或缺乏穩定性。這才是真正的水中冰山。「急性」傷害只是你所看到的部分，是潛在弱點的表現。因此，如果我們要完成我們在百歲十項全能中設定的目標，我們需要能夠預測並避免我們道路上的任何潛在傷害，就像海上的冰山一樣。這意味著了解穩定性並將其納入我們的日常生活中。

Stability is tricky to define precisely, but we intuitively know what it is. A technical definition might be: stability is the subconscious ability to harness, decelerate, or stop force. A stable person can react to internal or external stimuli to adjust position and muscular tension appropriately without a tremendous amount of conscious thought.

穩定性很難精確定義，但我們直覺知道它是什麼。技術定義可能是：穩定性是潛意識中駕馭、減速或阻止力量的能力。一個穩定的人可以對內部或外部刺激做出反應，從而適當地調整位置和肌肉張力，而無需大量有意識的思考。

I like to explain stability using an analogy from my favorite sport, auto racing. A few years ago I drove to a racetrack in Southern California to spend a couple of days training with my coach. To warm up, I took a few “sedan laps” in my street car at the time, a modified BMW M3 coupe with a powerful 460+ HP engine. After months of creeping along on clogged Southern California freeways, it was hugely fun to dive into the corners and fly down the straightaways.

我喜歡用我最喜歡的運動賽車來類比來解釋穩定性。幾年前，我開車去南加州的一個賽馬場，和我的教練一起訓練了幾天。為了熱身，我開著當時的街車跑了幾圈，這是一輛經過改裝的 BMW M3 轎跑車，配備強大的 460+ 馬力引擎。在堵塞的南加州高速公路上爬行了幾個月後，衝入角落並沿著直道飛翔是非常有趣的。

Then I switched to the track car we had rented, basically a stripped-down, race-worthy version of the popular BMW 325i. Although this vehicle's engine produced only about one-third as much power (165 HP) as my street car, my lap times in it were several seconds faster, which is an eternity in auto racing. What made the difference? The track car's 20 percent lighter weight played a part, but far more important were its tighter chassis and its stickier, race-grade tires. Together, these transmitted more of the engine's force to the road, allowing this car to go much faster through the corners. Though my street car was quicker in the long straights, it was much slower overall because it could not corner as efficiently. The track car was faster because it had better stability.

然後我換上了我們租來的賽道車，基本上是流行的 BMW 325i 的精簡版、適合比賽的版本。雖然這輛車的引擎產生的功率只有我的街車的三分之一左右（165馬力），但我駕駛它的單圈時間快了幾秒鐘，這在賽車運動中是永恆的。是什麼造成了差異？賽道車的重量減輕了 20%，但更重要的是其更緊湊的底盤和更黏的比賽級輪胎。這些共同將更多的引擎動力傳遞到路面，使這輛車能夠更快地通過彎道。雖然我的街車在長直道上速度更快，但總體上要慢得多，因為它無法有效地轉彎。軌道車速度更快，因為它具有更好的穩定性。

Without stability, my street car's more powerful engine was not much use. If I attempted to drive it through the curves as fast as I drove the track car, I'd end up spinning into the dirt. In the context of the gym, my street car is the guy with huge muscles who loads the bar with plates but who always seems to be getting injured (and can't do much else *besides* lift weights in the gym). The track car is the unassuming-looking dude who can deadlift twice his body weight, hit a fast serve in tennis, and then go run up a mountain the next day. He doesn't necessarily look strong. But because he has trained for stability as

well as strength, his muscles can transmit much more force across his entire body, from his shoulders to his feet, while protecting his vulnerable back and knee joints. He is like a track-ready race car: strong, fast, stable—and healthy, because his superior stability allows him to do all these things while rarely, if ever, getting injured.

如果沒有穩定性，我的街車更強大的引擎就沒多大用處。如果我試圖以駕駛軌道車的速度駕駛它通過彎道，我最終會旋轉到泥土中。在健身房裡，我的街車是一個肌肉發達的傢伙，他在槓鈴上裝滿了盤子，但似乎總是受傷（除了在健身房舉重之外，他不能做太多其他事情）。賽道車是個看起來不起眼的傢伙，他可以硬舉兩倍於自己體重的東西，在網球中快速發球，然後第二天就去爬山。他看起來不一定很堅強。但由於他接受過穩定性和力量訓練，他的肌肉可以將更多的力量傳遞到整個身體，從肩膀到腳，同時保護他脆弱的背部和膝關節。他就像一輛準備在賽道上行駛的賽車：強大、快速、穩定而且健康，因為他卓越的穩定性使他能夠完成所有這些事情，同時很少（如果有的話）受傷。

Obviously, my street car would be much more comfortable for a long road trip; no analogy is perfect. But this street car/race car comparison works because it forces us to consider stability in the dynamic setting. Unfortunately, the words *stable* and *stability* are too often lumped in with static terms like *strong* and *in balance*. A tree is more stable than a sapling. A Jenga tower cannot stand without stability. But in the exercise context, we're not as interested in how rigid something is. Instead, we want to think about how efficiently and safely force can be transmitted *through* something.

顯然，我的街車對於長途公路旅行來說會舒適得多；沒有任何類比是完美的。但這種街車/賽車的比較之所以有效，是因為它迫使我們考慮動態環境中的穩定性。不幸的是，「穩定」和「穩定」這兩個詞經常與「強大」和「平衡」等靜態術語混為一談。一棵樹比一棵樹苗更穩定。如果沒有穩定性，疊疊樂塔就無法站立。但在練習環境中，我們對事物的剛性就沒那麼感興趣。相反，我們想考慮如何有效且安全地透過某物傳遞力。

The key word is *safely*. When stability is lacking, all that extra force has to

go somewhere. If my street car's powerful engine is transmitting only part of its power to the road through the tires, the remainder of that energy is leaking out, lost to friction and nonproductive motion, primarily. Parts of the car that should not be moving relative to each other are doing just that. As fun as it might be to drift a car around a corner, that lost energy is ravaging the tires and taking a toll on the suspension. Neither will last long. When this happens in our bodies, this force dissipation (as it's called) leaks out via the path of least resistance—typically via joints like knees, elbows, and shoulders, and/or the spine, any or all of which will give out at some point. Joint injuries are almost always the result of this kind of energy leak.

關鍵字是安全。當缺乏穩定性時，所有額外的力量都必須流向某個地方。如果我的街車的強大引擎僅透過輪胎將部分動力傳輸到道路，則其餘能量就會洩漏，主要損失在摩擦和非生產性運動中。汽車上不應該相對移動的部件正在這樣做。儘管讓汽車漂移過彎可能很有趣，但損失的能量會破壞輪胎並損害懸吊。兩者都不會持續很長時間。當這種情況發生在我們的身體中時，這種力量的消散（正如它所說的）會通過阻力最小的路徑洩漏出去——通常是通過膝蓋、肘部、肩膀和/或脊柱等關節，其中任何一個或全部都會在某個點。關節損傷幾乎都是這種能量洩漏的結果。

In sum, stability lets us create the most force in the safest manner possible, connecting our body's different muscle groups with much less risk of injury to our joints, our soft tissue, and especially our vulnerable spine. The goal is to be strong, fluid, flexible, and agile as you move through your world.

總之，穩定性讓我們能夠以最安全的方式產生最大的力量，連接我們身體的不同肌肉群，同時大幅降低我們的關節、軟組織，尤其是脆弱的脊椎受傷的風險。我們的目標是在你的世界中移動時保持強壯、流暢、靈活和敏捷。

In action, stability can be magnificent to behold. Stability lets a skinny pitcher throw a blazing fastball. Stability allows Kai Lenny to surf towering waves at Jaws. But stability is also what enables a seventy-five-year-old woman to continue playing tennis injury-free. Stability is what keeps an eighty-year-old grandmother from falling when she steps off a curb that is

unexpectedly high. Stability gives a ninety-five-year-old man the confidence to go walk his beloved dog in the park. It lets us keep doing what we love to do. And when you don't have stability, bad things will inevitably happen—as they did to me, and to Sophie, and to millions of other formerly fit people.

在行動中，穩定性是令人驚嘆的。穩定性可以讓瘦弱的投手投出熾熱的快球。穩定性讓凱·萊尼 (Kai Lenny) 能夠在大白鯊 (Jaws) 的巨浪中衝浪。但穩定性也能讓一位 75 歲的女性繼續打網球而不會受傷。穩定性是一位八十歲的祖母在走下意外高的路緣時不會摔倒的原因。穩定讓一位九十五歲的老人有信心去公園遛他心愛的狗。它讓我們繼續做我們喜歡做的事情。當你不穩定時，不好的事情將不可避免地發生——就像它們對我、蘇菲以及數百萬其他以前健康的人所做的那樣。

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My painful lower-back episode was only the beginning of my injury history. I completed one of my Catalina swims with a torn labrum that was almost certainly exacerbated by spending four hours a day training in the pool and ocean, and continuing to do so even after I started feeling pain.^[*1] I still needed surgery to fix the problem more than fifteen years later. That was the price I paid for overdoing it in one specific sport. But it took me another couple of decades to really begin to understand *why* I had injured my back.

我痛苦的腰部發作只是我受傷史的開始。我完成了一次卡塔琳娜游泳，但盂唇撕裂了，幾乎可以肯定的是，由於每天在泳池和海洋中訓練四個小時，而且即使在我開始感到疼痛後仍繼續這樣做，這種撕裂幾乎肯定會加劇。[*1] 十五年後我仍然需要手術來解決這個問題。這就是我在一項特定運動中過度使用所付出的代價。但我又花了幾十年才真正開始理解為什麼我的背部受傷了。

This knowledge came courtesy of Beth Lewis, a former professional dancer and powerlifter turned trainer and all-around movement genius who was then based in New York. (I've since talked her into moving to Austin.) We had barely even said hello before she ordered me to take off my shirt and squat. I obeyed, and she was not impressed. I was crestfallen. I had always

thought of myself as someone who knew what he was doing in the gym. Now I was being told that I couldn't even do a simple squat correctly.

這些知識來自貝絲·劉易斯 (Beth Lewis)，她曾是一名職業舞者和舉重運動員，後來成為教練和全能運動天才，當時居住在紐約。（後來我說服她搬到奧斯汀。）我們還沒打招呼，她就命令我脫掉襯衫蹲下。我服從了，她沒有留下深刻的印象。我垂頭喪氣。我一直認為自己是個知道自己在健身房做什麼的人。現在我被告知我甚至無法正確地做一個簡單的深蹲。

Figure 13.



Her iPhone video told a sorry tale, as you can see from the “before” photo on the left (see figure 13): As I loaded my hips and sank down, I automatically shifted my entire body to the right. I look like I’m about to topple over. My problem, as these photos make painfully clear, was that I lacked stability. It even hurts to look at it now, because it reminds me of the thousands of atrocious, strain-inducing squats I’d committed in this awkward position.

她的iPhone 影片講述了一個令人遺憾的故事，正如您從左邊的「之前」照片中看到的那樣（見圖13）：當我加載臀部並下沉時，我自動將整個身體向右移動。我看起來快要翻倒了。正如這些照片痛苦地表明的那樣，我的問題是我缺乏穩定性。現在看它甚至讓人心痛，因為它讓我想起了我在這個尷尬的姿勢下所做的數以千計的殘暴、緊張的深蹲。

I was not even aware that I was doing this, but I was likely compensating for various injuries and weaknesses that I had accumulated over the years. This is how it works, as I would learn: We try to cheat or work around our existing injuries and limitations and end up creating new problems. This rightward tilt may even explain my back injury when I was only in my twenties; even at that point, I had already been lifting heavy weights for years. Fixing the situation turned out to be a nine-month process, but it ultimately straightened me out, as you can see in the “after” photo on the right. It required retraining not only my body but my brain.

我甚至沒有意識到我在這樣做，但我很可能是在彌補多年來累積的各種傷害和弱點。這就是它的運作方式，正如我所了解的：我們試圖欺騙或解決現有的傷害和限制，最終會產生新的問題。這種向右傾斜甚至可以解釋我二十多歲時背部受傷的原因；即使在那時，我已經舉重很多年了。解決這個問題花了九個月的時間，但它最終讓我理清了思路，正如你在右側的“之後”照片中看到的那樣。它不僅需要重新訓練我的身體，還需要重新訓練我的大腦。

—

Both Beth and Michael Stromsness, a trainer with whom I'd worked in California and who had introduced me to Beth, were familiar with something I had never heard of called DNS. Short for *dynamic neuromuscular stabilization*, DNS sounds complicated, but it is based on the simplest, most natural movements we make: the way we moved when we were babies.

貝絲(Beth) 和邁克爾·斯特羅姆斯內斯(Michael Stromsness)（我在加利福尼亞州共事過的一位培訓師，也是他把我介紹給貝絲的）都熟悉我

從未聽說過的DNS 概念。 DNS 是動態神經肌肉穩定的縮寫，聽起來很複雜，但它是基於我們所做的最簡單、最自然的運動：我們嬰兒時的運動方式。

The theory behind DNS is that the sequence of movements that young children undergo on their way to learning how to walk is not random or accidental but part of a program of neuromuscular development that is essential to our ability to move correctly. As we go through this sequence of motions, our brain learns how to control our body and develop ideal patterns of movement.

DNS 背後的理論是，幼兒在學習如何走路的過程中所經歷的運動順序不是隨機或偶然的，而是神經肌肉發育程序的一部分，這對於我們正確運動的能力至關重要。當我們經歷這一系列的運動時，我們的大腦會學習如何控制我們的身體並形成理想的運動模式。

DNS originated with a group of Czech neurologists who were working with young children with cerebral palsy in a hospital in Prague in the 1960s. They noticed that because of their illness, these kids did *not* go through the normal infant stages of rolling, crawling, and so forth. Thus they had movement problems throughout their lives. But when the children with cerebral palsy were put through a “training” program consisting of a certain sequence of movements, replicating the usual stages of learning to crawl, sit up, and eventually stand, their symptoms improved and they were better able to control their motions as they matured. The researchers realized that as we grow up, most healthy people actually go through an opposite process—we lose these natural, healthy, almost ingrained movement patterns.

DNS 起源於一群捷克神經科醫生，他們於 20 世紀 60 年代在布拉格一家醫院治療患有腦性麻痺的幼兒。他們注意到，由於生病，這些孩子沒有經歷正常的嬰兒階段，例如打滾、爬行等。因此，他們一生都存在運動問題。但是，當腦性麻痺兒童接受由一定順序的動作組成的「訓練」計劃，複製學習爬行、坐起來和最終站立的通常階段時，他們的症狀得到改善，並且能夠更好地控制自己的行為。當他們成熟時的動作。研究人員意識到，隨著我們的成長，大多數健康的人實際上

會經歷相反的過程——我們失去了這些自然、健康、幾乎根深蒂固的運動模式。

Thus my youngest son, Ayrton, can execute a perfect ass-to-grass squat, dropping his little butt down practically to the ground, bending sharply at the knees yet remaining totally balanced and powerful. It's just a perfect hip-hinge, and it blows my mind every time. He is an absolute master. Yet when I attempted the same movement, I ended up tilted over in the ridiculous half-canted position in the “before” photo, one hip pointed down at the ground, my shoulders askew, my feet rolled outward. My toddler can squat, but apparently I couldn't.

因此，我最小的兒子艾爾頓（Ayrton）可以完成完美的屁股到草地的深蹲，將他的小屁股幾乎放在地上，膝蓋急劇彎曲，但仍保持完全平衡和力量。這只是一個完美的臀部鉸鏈，每次都讓我大吃一驚。他是絕對的大師。然而，當我嘗試同樣的動作時，我最終以“之前”照片中可笑的半傾斜姿勢傾斜，一個臀部朝下指向地面，我的肩膀歪斜，我的腳向外滾動。我的孩子可以蹲下，但顯然我不能。

And neither could my fourteen-year-old daughter, Olivia (before Beth got to work on her, too). Flexible as Gumby, skinny but whip-strong, she should be able to squat just as well as, if not better than, her youngest brother. But she couldn't, because even at her young age she had already spent two-thirds of her life in school, mostly sitting in chairs. The ideal movement patterns that she learned as an infant and toddler were erased before she was able to develop the hip stability needed to squat properly. If she spends the next thirty, forty, or fifty years primarily sitting in chairs, as is likely, then she'll be in the same boat as many of my patients, and myself as well: we have essentially forgotten how to move our bodies.

我十四歲的女兒奧莉維亞也不能（在貝絲也開始為她工作之前）。她像岡比一樣靈活，骨瘦如柴，但力量十足，她的蹲姿應該和她最小的弟弟一樣好，甚至更好。但她不能，因為即使在她很小的時候，她的人生就有三分之二的時間是在學校裡度過的，大部分時間都是坐在椅子上。在她能夠發展正確深蹲所需的臀部穩定性之前，她在嬰兒和幼兒時期學到的理想運動模式就被抹去了。如果她在接下來的三十年、

四十年或五十年裡主要坐在椅子上（這是有可能的），那麼她將和我的許多患者以及我自己處於同一條船上：我們基本上已經忘記瞭如何移動我們的身體。

Most adults can't squat correctly, even without any added weight. The only way many of us can come close to matching a toddler's form is to lie on our backs, as Michael Stromsness demonstrated with me in one of our early sessions. Then it becomes much easier to raise our knees into a perfect squat position, with the correct degree of curvature throughout the spine from the base of the skull to the tailbone. This tells us that range of motion per se is not what's stopping most adults from squatting well; it's that when the average adult is under a load, even as little as their own bodyweight, the job of stabilizing his or her own torso becomes too much.

即使沒有增加任何重量，大多數成年人也無法正確深蹲。我們中的許多人能夠接近幼兒姿勢的唯一方法就是仰臥，正如邁克爾·斯特羅姆內斯在我們早期的一次訓練中向我展示的那樣。然後，我們就可以更輕鬆地將膝蓋抬高到完美的蹲姿，從頭骨底部到尾骨的整個脊椎具有正確的彎曲度。這告訴我們，運動幅度本身並不是阻止大多數成年人深蹲的原因。問題在於，當一般成年人承受一定的負荷時，即使負荷只有自己的體重，穩定自己軀幹的工作也會變得太多。

The point of DNS is to retrain our bodies—and our brains—in those patterns of perfect movement that we learned as little kids. As Michael Rintala, a leading American practitioner of DNS, puts it, “DNS beautifully integrates with all the good work you are already doing—it's like a software upgrade for anything you are doing.”

DNS 的目的是要按照我們小時候學到的完美運動模式來重新訓練我們的身體和大腦。正如美國 DNS 領先實踐者 Michael Rintala 所說，“DNS 與您已經在做的所有出色工作完美地集成在一起，就像您正在做的任何事情的軟體升級一樣。”

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My own software was in serious need of an upgrade.

我自己的軟體急需升級。

The details of my own journey are too involved to lay out at length here, but in the rest of this chapter I will try to explain at least some of the basic principles that underlie stability training. These may seem a bit strange at first, and if you came to this chapter expecting a high-powered workout program, you may be disappointed. That is part of the point: in my practice, we don't like to push much strength training, including many of the assessments I've discussed, such as dead hangs and weighted step-ups, until we have established some modicum of stability. We don't think it's worth the risk. Just as in engineering, it's worth the extra time to build a solid foundation, even if it delays the project a few months.

我自己的旅程的細節太複雜，無法在這裡詳細闡述，但在本章的其餘部分中，我將嘗試解釋至少一些穩定性訓練的基本原則。這些一開始可能看起來有點奇怪，如果你來到本章期待一個高強度的運動計劃，你可能會失望。這就是要點的一部分：在我的實踐中，我們不喜歡進行太多的力量訓練，包括我討論過的許多評估，例如懸垂和負重踏步，直到我們建立了一定的穩定性。我們認為不值得冒這個風險。就像在工程領域一樣，花額外的時間來打下堅實的基礎是值得的，即使這會導致專案延遲幾個月。

A quick caveat: while strength training and aerobic conditioning are relatively straightforward, everyone has very different issues with regard to stability. Thus, it's impossible to give a one-size-fits-all prescription for everyone. My goal in the rest of this chapter is to give you some basic concepts to think about and try out, to help you learn and understand how your own body interacts with the world—which, in the end, is what stability is really about. If you'd like to know more after you've read this chapter, I suggest visiting the websites for DNS (www.rehabps.com) and the Postural Restoration Institute (PRI) (www.posturalrestoration.com), the two leading exponents of what I'm talking about here. Stability is an integral part of my training program. Twice a week, I spend an hour doing dedicated stability training, based on the principles of DNS, PRI, and other practices, with ten to fifteen minutes per day on the other days.

快速警告：雖然肌力訓練和有氧調節相對簡單，但每個人在穩定性方面都有不同的問題。因此，不可能為所有人提供一刀切的處方。本章其餘部分的目標是為您提供一些需要思考和嘗試的基本概念，幫助您學習和理解自己的身體如何與世界互動——最終，這才是穩定性的真正意義。如果您在讀完本章後想了解更多資訊，我建議您訪問 [DNS \(www.rehabps.com\)](http://www.rehabps.com) 和姿勢恢復研究所 (PRI) (www.posturalrestoration.com) 的網站，這兩個領先的指數我在這裡談論的內容。穩定性是我訓練計畫的一個組成部分。每週兩次，我會根據 DNS、PRI 和其他實踐的原則，花一個小時進行專門的穩定性訓練，其他日子每天進行 10 到 15 分鐘。



Stability training begins at the most basic level, with the breath.

穩定性訓練從最基本的層面開始，即呼吸。

Breathing is about much more than simple gas exchange or even cardiorespiratory fitness. We exhale and inhale more than twenty thousand times per day, and the way in which we do so has tremendous influence on how we move our body, and even our mental state. How we breathe, as Beth puts it, is who we are.

呼吸不僅僅是簡單的氣體交換甚至心肺健康。我們每天呼氣和吸氣超過兩萬次，我們呼氣和吸氣的方式對我們身體運動的方式，甚至我們的精神狀態有著巨大的影響。正如貝絲所說，我們的呼吸方式決定了我們是誰。

The link between the body, the mind, and the breath is not new to anyone who has done more than a few Pilates or yoga classes or practiced meditation. In these practices, the breath is our anchor, our touchstone, our timekeeper. It both reflects our mental state and affects it. If our breathing is off, it can disrupt our mental equilibrium, creating anxiety and apprehension; but anxiety can also worsen any breathing issues we might have. This is because deep, steady breathing activates the calming parasympathetic nervous system, while

rapid or ragged breathing triggers its opposite, the sympathetic nervous system, part of the fight-or-flight response.

對於參加過幾次普拉提或瑜伽課程或練習冥想的人來說，身體、思想和呼吸之間的聯繫並不新鮮。在這些練習中，呼吸是我們的錨、我們的試金石、我們的計時員。它既反映了我們的精神狀態，也影響著我們的精神狀態。如果我們的呼吸停止，就會破壞我們的心理平衡，產生焦慮和憂慮；但焦慮也會加劇我們可能有的呼吸問題。這是因為深而穩定的呼吸會激活鎮靜的副交感神經系統，而快速或不規則的呼吸會觸發其相反的交感神經系統，這是戰鬥或逃跑反應的一部分。

Yet breathing is also important to stability and movement, and even to strength. Poor or disordered breathing can affect our motor control and make us susceptible to injury, studies have found. In one experiment, researchers found that combining a breathing challenge (reducing the amount of oxygen available to study subjects) with a weight challenge reduced the subjects' ability to stabilize their spine. In real-world terms, this means that someone who is breathing hard (and poorly) while shoveling snow is putting themselves at increased risk of a back injury.

然而，呼吸對於穩定性和運動，甚至力量也很重要。研究發現，呼吸不良或紊亂會影響我們的運動控制，並使我們容易受傷。在一項實驗中，研究人員發現，將呼吸挑戰（減少研究對象可用的氧氣量）與體重挑戰結合起來會降低物體穩定脊椎的能力。在現實世界中，這意味著鏟雪時呼吸困難（且呼吸困難）的人會增加背部受傷的風險。

It's extremely subtle, but the way in which someone breathes gives tremendous insight to how they move their body and, more importantly, how they stabilize their movements. We run our patients through a series of respiration and movement tests to get the full picture of their respiration strategy and how it relates to their strength and stability issues.

這是非常微妙的，但是一個人的呼吸方式可以讓我們深入了解他們如何移動身體，更重要的是，他們如何穩定他們的動作。我們對患者進行一系列呼吸和運動測試，以全面了解他們的呼吸策略以及它與他們的力量和穩定性問題的關係。

One simple test that we ask of everyone, early on, looks like this: lie on your back, with one hand on your belly and the other on your chest, and just breathe normally, without putting any effort or thought into it. Notice which hand is rising and falling—is it the one on your chest, or your belly, or both (or neither)? Some people tend to flare their ribs and expand the chest on the inhale, while the belly is flat or even goes down. This creates tightness in the upper body and midline, and if the ribs stay flared, it's difficult to achieve a full exhalation. Others breathe primarily “into” the belly, which tilts the pelvis forward. Still others are compressed, meaning they have difficulty moving air in and out altogether, because they cannot expand the rib cage with each inhalation.

我們一開始就要求每個人進行一項簡單的測試，如下所示：仰臥，一隻手放在腹部，另一隻手放在胸部，正常呼吸，無需付出任何努力或思考。注意哪隻手在上升和下降——是放在你胸前的那隻手，還是放在你的肚子上，還是兩隻手都放在上面（或者都不放在上面）？有些人在吸氣時往往會張開肋骨、擴張胸部，而腹部卻是平坦的，甚至是下垂的。這會導致上半身和中線緊張，如果肋骨保持張開狀態，就很難實現完全呼氣。其他人主要將呼吸「吸入」腹部，從而使骨盆向前傾斜。還有一些人受到壓縮，這意味著他們很難將空氣完全吸入和排出，因為他們無法在每次吸氣時擴張胸腔。

Beth identifies three types of breathing styles and associated phenotypes, which she jokingly calls “Mr. Stay Puft,” the “Sad Guy,” and the “Yogini”—each corresponding to a different set of stability strategies:

貝絲（Beth）識別了三種類型的呼吸方式和相關的表型，她開玩笑地稱之為「呼吸先生」。「Stay Puft」、「Sad Guy」和「Yogini」——每一個都對應於一組不同的穩定策略：

Mr. Stay Puft

呆待先生

HYPERINFLATED. This person is an upper-chest breather who tends to pull up into spinal extension for both respiration and stability. Their lumbar spine is in hyperextension, while their pelvis lives in anterior (forward) tilt, meaning their butt sticks out. They are always pulling up into themselves, trying to look like they are in charge. They have a limited sense of grounding in the feet, and limited ability to pronate to absorb shock (the feet turn outward, or supinate). All of the above makes them quite susceptible to lower back pain, as well as tightness in their calves and hips.

過度膨脹。這個人是上胸部呼吸者，為了呼吸和穩定性，傾向於向上拉脊椎伸展。他們的腰椎處於過度伸展狀態，而他們的骨盆處於前傾狀態，這意味著他們的屁股伸出來。他們總是竭盡全力，努力讓自己看起來像是掌控一切。他們的足部著地感有限，內旋吸收衝擊的能力也有限（足部向外轉動，或外旋）。所有這些使他們容易受到腰痛以及小腿和臀部緊繃的影響。

Sad Guy

悲傷的傢伙

COMPRESSED. Everything about them is sort of scrunched down and tight. Their head juts forward, and so do their shoulders, which kind of roll to the front because they are always pulling forward to try and take in more air. Their midback rolls in an overly flexed or hyperkyphotic posture, and they have limited neck and upper limb motion. Sometimes their lower legs externally rotate, and the feet overpronate. Gravity is weighing them down.

壓縮。他們的一切都有點皺縮和緊張。他們的頭向前突出，肩膀也向前突出，因為他們總是向前拉，試圖吸入更多空氣。他們的中背部以過度彎曲或後凸的姿勢滾動，並且頸部和上肢的運動受到限制。有時，他們的小腿會向外旋轉，腳會過度內旋。重力正在壓垮他們。

Yogini

瑜珈士

UNCONTROLLED. These folks have extreme passive range of motion (i.e., flexibility)—and extremely limited ability to control it. They can often do a toe touch and put their palms flat on the floor, but because of their lack of control, these people are quite prone to joint injuries. They are always trying to find themselves in space, fidgeting and twitching; they compensate for their excessive flexibility by trying to stabilize primarily with their neck and jaw. It is very hard for them to put on lean mass (muscle). Sometimes they have very high anxiety, and possibly also a breathing pattern disorder.

不受控制。這些人的運動範圍極為被動（即靈活性），而且控制它的能力極為有限。他們經常可以用腳趾觸碰並將手掌平放在地板上，但由於缺乏控制，這些人很容易出現關節受傷。他們總是試圖在太空中找到自己，坐立不安、抽搐；他們透過嘗試主要用頸部和下巴來穩定身體，以彌補過度的靈活性。他們很難增加瘦體重（肌肉）。有時他們有非常高的焦慮，並且可能還有呼吸模式障礙。

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Not everyone fits exactly into one of these three types, but many of us will recognize at least some of these traits in ourselves. There is some overlap as well; it's possible to be a Sad Guy or Mr. Stay Puft and a Yogini at the same time, for example, because the Yogini type is really more about a lack of muscular control.

並不是每個人都完全符合這三種類型中的一種，但我們中的許多人至少會認識到自己身上的一些特徵。也有一些重疊；例如，有可能同時是一個悲傷的傢伙或保持沉默先生和瑜珈士，因為瑜珈士類型實際上更多的是缺乏肌肉控制。

I was a hyperinflated Mr. Stay Puft, according to Beth: When I inhaled, my ribs would flare out and up, like a rooster thrusting out his chest. This got air into my lungs, but it also pulled my center of mass forward. To balance, my spine would curve into kyphosis, and my butt would stick out (Beth called

it “duck butt”). This hyperextended my hamstrings, effectively disconnecting them from the rest of my body, so I was unable to access these muscles. For all those years, before I realized this, I was deadlifting using *only* my back and glutes, with virtually no help from my powerful hamstrings. In terms of breath training, I needed to think about getting air *out*, the exhale—while someone who tends more toward the Sad Guy type should work on getting air *in*, inhaling via the nose rather than the mouth.

貝絲說，我是一個過度充氣的「呆呆先生」：當我吸氣時，我的肋骨會向外張開並向上張開，就像一隻公雞伸出胸膛。這讓空氣進入我的肺部，但也將我的重心向前拉。為了平衡，我的脊椎會彎曲成後凸，我的屁股會伸出（貝絲稱之為「鴨屁股」）。這使我的腿筋過度伸展，有效地將它們與身體的其他部分斷開，因此我無法接觸到這些肌肉。多年來，在我意識到這一點之前，我只使用背部和臀部進行硬拉，幾乎沒有強大的腿筋的幫助。在呼吸訓練方面，我需要考慮將空氣排出，即呼氣，而更傾向於「悲傷的傢伙」類型的人應該努力吸入空氣，透過鼻子而不是嘴巴吸氣。

The idea behind breath training is that proper breathing affects so many other physical parameters: rib position, neck extension, the shape of the spine, even the position of our feet on the ground. The way in which we breathe reflects how we interact with the world. “Making sure that your breath can be wide and three-dimensional and easy is vital for creating good, efficient, coordinated movement,” Beth says.

呼吸訓練背後的想法是，正確的呼吸會影響許多其他身體參數：肋骨位置、頸部伸展、脊椎形狀，甚至腳在地面上的位置。我們呼吸的方式反映了我們與世界互動的方式。「確保你的呼吸寬廣、三維且輕鬆，對於創造良好、高效、協調的運動至關重要，」貝絲說。

Beth likes to start with an exercise that builds awareness of the breath and strengthens the diaphragm, which not only is important to breathing but is an important stabilizer in the body. She has the patient lie on their back with legs up on a bench or chair, and asks them to inhale as quietly as possible, with the least amount of movement possible. An ideal inhalation expands the entire rib cage—front, sides, and back—while the belly expands at the same time,

allowing the respiratory and pelvic diaphragm to descend. The telltale is that it is quiet. A noisy inhale looks and feels more dramatic, as the neck, chest, or belly will move first, and the diaphragm cannot descend freely, making it more difficult to get air in.

貝絲喜歡從增強呼吸意識和增強橫膈膜的運動開始，這不僅對呼吸很重要，而且是身體的重要穩定劑。她讓病人仰臥，雙腿放在長凳或椅子上，並要求他們盡可能安靜地吸氣，並盡可能減少運動量。理想的吸氣會擴張整個胸腔（前部、兩側和後部），同時腹部也會擴張，使呼吸隔膜和骨盆隔膜下降。說明情況是它很安靜。吵雜的吸氣看起來和感覺起來都更戲劇化，因為頸部、胸部或腹部會先移動，而橫膈膜無法自由下降，更難以吸入空氣。

Now, exhale fully through pursed lips for maximum compression and air resistance, to strengthen the diaphragm. Blow all that air out, fully emptying yourself before your shoulders round or your face or jaw gets tense. Very soon, you will see how a full exhale prepares you for a good inhale, and vice versa. Repeat the process for five breaths and do two to three sets. Be sure to pause after each exhale for at least two counts to hold the isometric contraction—this is key, in DNS.

現在，透過嘟起的嘴唇充分呼氣，以獲得最大的壓縮和空氣阻力，以強化橫膈膜。在你的肩膀變圓或你的臉或下巴變得緊張之前，把所有的空氣都吹出來，徹底清空自己。很快，您就會看到充分的呼氣如何為良好的吸氣做好準備，反之亦然。重複這個過程五次呼吸並做兩到三組。確保每次呼氣後暫停至少兩次以保持等長收縮——這在 DNS 中是關鍵。

In DNS, you learn to think of the abdomen as a cylinder, surrounded by a wall of muscle, with the diaphragm on top and the pelvic floor below. When the cylinder is inflated, what you're feeling is called *intra-abdominal pressure*, or IAP. It's critical to true core activation and foundational to DNS training. Learning to fully pressurize the cylinder, by creating IAP, is important to safe movement because the cylinder effectively stabilizes the spine.

在 DNS 中，您將學習將腹部視為圓柱體，周圍環繞著肌肉壁，橫膈膜位於頂部，骨盆底位於下方。當氣缸充氣時，您所感受到的壓力稱為腹內壓（IAP）。它對於真正的核心啟動至關重要，也是 DNS 訓練的基礎。學習透過產生 IAP 來完全加壓氣缸對於安全運動非常重要，因為氣缸可以有效地穩定脊椎。

Here's another quick exercise to help you understand how to create IAP: breathe all the way in, so you feel as if you are inflating the cylinder on all sides and pulling air all the way down into your pelvic floor, the bottom of the cylinder. You're not actually "breathing" there, in the sense that air is actually entering your pelvis; you're seeking maximal lung expansion, which in turn sort of pushes your diaphragm down. With every inhale, focus on expanding the cylinder around its whole diameter and not merely raising the belly. If you do this correctly, you will feel the entire circumference of your shorts expand evenly around your waist, even in the back, not just in the front. When you exhale, the diaphragm comes back up, and the ribs should rotate inward again as your waistband contracts.

這是另一個快速練習，可以幫助您了解如何創建 IAP：一直吸氣，這樣您就會感覺好像正在向氣缸的各個側面充氣，並將空氣一直吸入骨盆底（氣缸的底部）。從空氣實際上進入骨盆的意義上來說，您實際上並沒有在那裡「呼吸」；您實際上並沒有在那裡「呼吸」。你正在尋求最大限度的肺部擴張，這反過來又會將你的橫膈膜向下推。每次吸氣時，專注於將圓柱體擴大到其整個直徑，而不僅僅是抬高腹部。如果你做得正確，你會感覺到短褲的整個週長在腰部均勻地擴張，甚至在後面，而不僅僅是前面。當你呼氣時，橫膈膜會恢復原樣，當你的腰帶收縮時，肋骨會再次向內旋轉。

This inhale develops tension, and as you exhale, pushing out air, you *keep* that muscular tension all around your cylinder wall. This intra-abdominal pressure is the basic foundation for everything that we do in stability training—a deadlift, squats, anything. It's as if you have a plastic bottle: with the cap off, you can crush the bottle in one hand; with the cap on, there is too much pressure (i.e., stability) and the bottle can't be crushed. I practice this 360-

degree abdominal breathing every day, not only in the gym but also while I am at my desk.^[*2]

吸氣會產生張力，當你呼氣時，排出空氣，你會在氣缸壁周圍保持肌肉張力。這種腹內壓力是我們在穩定性訓練中所做的一切的基礎——硬舉、深蹲等等。就好像你有一個塑膠瓶：打開蓋子，你可以用一隻手捏碎瓶子；蓋上蓋子後，壓力太大（即穩定性），瓶子就不會被壓碎。我每天都會練習這種 360 度腹式呼吸，不僅在健身房裡，而且在辦公桌前也是如此。^[*2]

Your “type” also indicates how you should work out, to some extent. The Stay Puft people tend to need more grounding through the feet and more work with weight in front of them so as to pull their shoulders and hips into a more neutral position. Beth typically has someone like me hold a weight in front of my body, a few inches in front of the sternum. This forces my center of mass back, more over my hips. Try it with a light dumbbell or even a milk carton, and you’ll see what I mean. It’s a subtle but noticeable change of position.

您的「類型」在某種程度上也表明您應該如何鍛鍊。保持普夫特的人往往需要更多的腳部接地和更多的重物在他們面前的工作，以便將他們的肩膀和臀部拉到更中立的位置。貝絲通常會讓像我這樣的人在我的身體前面、胸骨前面幾英寸處舉起一個重物。這迫使我的重心向後移動，更多位於臀部上方。用輕啞鈴甚至牛奶盒嘗試一下，你就會明白我的意思。這是一個微妙但明顯的位置變化。

With the Sad Guys and Gals, Beth tends to work more on cross-body rotation, having them swing the arms across the body to open up the chest and shoulders. She is cautious about loading the back and shoulders, preferring to begin with body weight exercises and split-leg work, such as a walking lunge with a reach, either across the body or to the ceiling, on each step.

對於悲傷的男女，貝絲傾向於更多地進行跨身體旋轉，讓他們在身體上擺動手臂以打開胸部和肩膀。她對背部和肩部的負荷持謹慎態度，更喜歡從自重練習和分腿練習開始，例如弓步行走，每一步都可以跨過身體或到達天花板。

For the Yoginis, Beth recommends doing “closed-chain” exercises such as push-ups, using the floor or wall for support, as well as using exercise machines with a well-defined and limited range of motion, given their lack of joint control. Machines are important for these folks, and also for people who have not lifted much or at all, because machines keep their movements within safe boundaries. For the Yoginis, as well as for newbies in general, it’s important to become more aware of where they are in space, and where they are relative to their range of motion.

對於瑜珈愛好者，貝絲建議進行「閉鏈」練習，例如俯臥撐，使用地板或牆壁作為支撐，以及使用具有明確且有限的運動範圍的健身器材，因為它們缺乏關節控制。機器對這些人來說很重要，對於那些沒有舉起太多或根本沒有舉起的人來說也很重要，因為機器將他們的運動保持在安全範圍內。對於瑜珈士以及一般新手來說，重要的是要更加了解他們在空間中的位置以及相對於他們的運動範圍的位置。

The larger point is that someone’s breathing style gives us insight into their broader stability strategy, the set of patterns that they have evolved over the years to help them get by in the physical world. All of us have these strategies, and 95 percent of the time, in the course of daily life, they work fine. But once you add different stressors, such as speed, weight, and novelty or unfamiliarity (e.g., stepping off a stair in the dark), then those strategies, those instinctive physical reactions, can create problems. And if our respiration is also taxed, those other problems will be magnified.

更重要的一點是，某人的呼吸方式讓我們深入了解他們更廣泛的穩定策略，即他們多年來進化出的一套模式，以幫助他們在現實世界中度過難關。我們所有人都有這些策略，並且在日常生活中 95% 的情況下，它們都能發揮良好作用。但是，一旦你加入了不同的壓力源，例如速度、重量、新奇或不熟悉的事物（例如，在黑暗中走下樓梯），那麼這些策略、那些本能的身體反應就會產生問題。如果我們的呼吸也受到負擔，那麼其他問題就會被放大。

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If the road to stability begins with the breath, it travels through the feet—the most fundamental point of contact between our bodies and the world. Our feet are literally the foundation for any movement we might make. Whether we're lifting something heavy, walking or running (or rucking), climbing stairs, or standing waiting for a bus, we're always channeling force through our feet. Unfortunately, too many of us have lost basic strength and awareness of our feet, thanks to too much time spent in shoes, especially big shoes with thick soles.

如果通往穩定的道路從呼吸開始，那麼它會透過雙腳——我們的身體和世界之間最基本的接觸點。我們的腳實際上是我們進行任何運動的基礎。無論我們是在舉重物、步行或跑步（或搬運）、爬樓梯，還是站著等公車，我們總是透過腳傳遞力量。不幸的是，由於花太多時間穿鞋，尤其是厚底的大鞋，我們中的太多人已經失去了腳的基本力量和意識。

Going back to my race car analogy, our feet are like the tires, the only point of contact between the car and the road. The force of the engine, the stability and stiffness of the chassis, the skill of the driver—all of it is useless if the tires are not firmly gripping the track surface. I would argue that our feet are even more important to us than tires are to a car, as they also play a crucial role in dampening force before it reaches the knees, the hips, and the back (at least a car has suspension rods for that). Failing to pay attention to your feet, as most of us do, is like buying a McLaren Senna (my dream car) and then going to Walmart and getting the cheapest tires you can find. That's what spending years in mushy shoes does to us.

回到我的賽車比喻，我們的腳就像輪胎，是汽車和道路之間的唯一接觸點。如果輪胎不能牢牢地抓住賽道表面，引擎的力量、底盤的穩定性和剛性、車手的技術——所有這些都是毫無用處的。我認為，我們的腳對我們來說比輪胎對汽車更重要，因為它們在力到達膝蓋、臀部和背部之前起著至關重要的阻尼作用（至少汽車有懸吊桿）那）。沒有像我們大多數人那樣注意自己的腳，就像購買麥克拉倫塞納（我的夢想車），然後去沃爾瑪買你能找到的最便宜的輪胎一樣。這就是長年穿著軟鞋對我們造成的影響。

Take another look at my “before” squat. Yes, my hips are obviously askew, but look more closely at my feet. Are they flat on the floor? No, they are not. As you can clearly see, they are rolled out on their outside edges —“supinated,” in physiologist-speak. They should be flat, grounded, stable, and strong, to support my weight. But instead they are rolled over and wobbly. No wonder my squat looks so bad.

再看看我的「之前」深蹲。是的，我的臀部明顯歪斜，但仔細看看我的腳。它們平放在地板上嗎？不，他們不是。正如你可以清楚地看到的，它們的外邊緣被捲起來——用生理學家的話來說就是「旋後」。它們應該平坦、接地、穩定且堅固，以支撐我的重量。但相反，它們會翻滾並搖搖欲墜。難怪我的深蹲看起來那麼糟。

To help reacquaint us with our feet, Beth Lewis likes to put me, and our patients, through a routine she calls “toe yoga.” Toe yoga (which I hate, by the way) is a series of exercises intended to improve the dexterity and intrinsic strength of our toes, as well as our ability to control them with our mind. Toe strength may not be something you think about when you go to the gym, but it should be: Our toes are crucial to walking, running, lifting, and, most importantly, decelerating or lowering. The big toe especially is necessary for the push-off in every stride. Lack of big-toe extension can cause gait dysfunction and can even be a limiting factor in getting up off the floor unassisted as we age. If toe strength is compromised, everything up the chain is more vulnerable—ankle, knee, hip, spine.

為了幫助我們重新熟悉我們的腳，貝絲·劉易斯喜歡讓我和我們的病人進行她稱之為“腳趾瑜伽”的例行活動。腳趾瑜珈（順便說一句，我討厭它）是一系列練習，旨在提高腳趾的靈活性和內在力量，以及我們用意念控制腳趾的能力。當你去健身房時，你可能不會考慮腳趾的力量，但它應該是：我們的腳趾對於行走、跑步、舉重，最重要的是減速或降低至關重要。大腳趾對於每一步的推出尤其重要。大腳趾伸展不足會導致步態功能障礙，甚至可能成為隨著年齡的增長而無法在無人幫助的情況下從地板上站起來的限制因素。如果腳趾的力量受到損害，那麼鏈條上的所有部位都會變得更加脆弱——腳踝、膝蓋、臀部、脊椎。

Toe yoga is a lot harder than it sounds, which is why I've posted a video demonstration of this and other exercises at www.peterattiamd.com/outlive/videos. First, Beth tells her students to think of their feet as having four corners, each of which needs to be rooted firmly on the ground at all times, like the legs of a chair. As you stand there, try to feel each “corner” of each foot pressing into the ground: the base of your big toe, the base of your pinky toe, the inside and outside of your heel. This is easy, and revelatory; when was the last time you felt that grounded?

腳趾瑜珈比聽起來要難得多，這就是為什麼我在 www.peterattiamd.com/outlive/videos 上發布了此練習和其他練習的影片示範。首先，貝絲告訴她的學生，把他們的腳想像成有四個角，每個角都需要始終牢牢地紮根在地面上，就像椅子的腿一樣。當你站在那裡時，試著感受每隻腳的每個「角」壓入地面：大腳趾的根部、小腳趾的根部、腳跟的內側和外側。這很簡單，也很有啟發性；你上一次感到踏實是什麼時候？

Try to lift all ten toes off the ground and spread them as wide as you can. Now try to put just your big toe back on the floor, while keeping your other toes lifted. Trickier than you'd think, right? Now do the opposite: keep four toes on the floor and lift only your big toe. Then lift all five toes, and try to drop them one by one, starting with your big toe. (You get the idea.)[*3]

試著將所有十個腳趾抬離地面，並盡可能地展開它們。現在嘗試將大腳趾放回地板上，同時保持其他腳趾抬起。比你想像的更棘手，對吧？現在做相反的事情：將四個腳趾放在地板上，只抬起大腳趾。然後抬起所有五個腳趾，並嘗試從大腳趾開始一個一個放下。（你明白了。）[*3]

If you can do this at all, it likely takes a concerted mental effort, your brain *telling* that big toe to drop or rise—which is exactly the point. One of the goals of stability training is to regain mental control, conscious or not, over key muscles and body parts. Because our feet spend so much time crammed into shoes that may or may not fit properly, and likely have a lot of padding in their soles, many of us have lost touch with our feet, or have worked them into unhelpful contortions over time.

如果你能做到這一點，可能需要齊心協力，你的大腦告訴大腳趾放下或抬起——這正是重點。穩定性訓練的目標之一是重新獲得對關鍵肌肉和身體部位的精神控制，無論是否有意識。因為我們的腳花了很多時間塞在可能合腳或不合腳的鞋子裡，而且鞋底可能有很多襯墊，所以我們中的許多人已經失去了與腳的接觸，或者隨著時間的推移使腳變得無益的扭曲。

In my “before” squatting photo, as noted above, both of my feet are rolled out to the outside, or supinated, a common phenotype. Another common foot strategy is to “pronate” or fold the feet inward—a term you’re probably familiar with if you’ve ever bought running shoes. Beth compares pronation to driving a car with too little air in the tires, meaning you kind of slosh through your movements, unable to transfer force efficiently to the ground. Supination, on the other hand, is like having overinflated tires, so you skid and bounce around. Your feet are unable to absorb shock, and all that bouncing and jarring gets transferred straight to the ankles, hips, knees, and lower back. Both syndromes, pronation and supination, also expose us to risk of plantar fasciitis and knee injury, among other issues. We must be able to move in and out of both supination and pronation to locomote efficiently. Now when I squat, or do any standing lift, my first step is to ground my feet, to be aware of all four “corners,” and distribute weight equally. (Also important: I prefer to lift barefoot or in minimal shoes, with little to no cushioning in the soles because it allows me feel the full surface of my feet at all times.)

在我「之前」蹲著的照片中，如上所述，我的雙腳向外滾動，或旋後，這是一種常見的表型。另一種常見的足部策略是「內旋」或將腳向內折疊——如果您曾經購買過跑鞋，您可能會熟悉這個術語。貝絲將內旋比喻為駕駛一輛輪胎空氣太少的汽車，這意味著你的動作有點晃動，無法有效地將力量傳遞到地面。另一方面，旋後就像輪胎充氣過度，所以你會打滑並四處彈跳。你的腳無法吸收震動，所有的彈跳和震動都會直接轉移到腳踝、臀部、膝蓋和下背部。旋前和旋後這兩種症候群也會使我們面臨足底筋膜炎和膝關節損傷等問題的風險。我們必須能夠進出旋後和旋前，才能有效地移動。現在，當我蹲下或做任何站立舉重時，我的第一步就是雙腳著地，注意所有四個“角”，並

平均分配重量。（同樣重要的是：我更喜歡赤腳或穿著極簡的鞋子舉起，鞋底幾乎沒有緩衝，因為它可以讓我始終感覺到腳的整個表面。）

Feet are also crucial to balance, another important element of stability. One key test in our movement assessment is to have our patients stand with one foot in front of the other and try to balance. Now close your eyes and see how long you can hold the position. Ten seconds is a respectable time; in fact, the ability to balance on one leg at ages fifty and older has been correlated with future longevity, just like grip strength. (Pro tip: balancing becomes a lot easier if you first focus on grounding your feet, as described above.)

腳對於平衡也至關重要，平衡是穩定性的另一個重要因素。我們運動評估的一項關鍵測試是讓患者將一隻腳放在另一隻腳前面站立並嘗試保持平衡。現在閉上眼睛，看看你能保持這個姿勢多久。十秒是一個值得尊敬的時間；事實上，五十歲及以上的人單腳平衡的能力與未來的壽命有關，就像握力一樣。（專業提示：如果您首先專注於雙腳接地，平衡就會變得容易得多，如上所述。）

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The structure we most want to protect—and a major focus of stability training in general—is the spine. We spend so much of our time in car seats, in desk chairs, at computers, and peering at our various devices that modern life sometimes seems like an all-out assault on the integrity of our spine.

我們最想保護的結構——也是穩定性訓練的主要焦點——是脊椎。我們把太多的時間花在汽車座椅、桌椅、電腦前，盯著各種設備，現代生活有時似乎是對我們脊椎完整性的全面攻擊。

The spine has three parts: lumbar (lower back), thoracic (midback), and cervical (neck) spine. Radiologists see so much degeneration in the cervical spine, brought on by years of hunching forward to look at phones, that they have a name for it: “tech neck.”

脊椎由三個部分組成：腰椎（下背部）、胸椎（中背部）和頸椎（頸椎）。放射科醫師發現，由於長年彎腰看手機，頸椎出現了嚴重的退化，因此他們給它起了個名字：「科技頸」。

This is why it's important to (a) put down the phone, and (b) try to develop some proprioceptive awareness around your spine, so that you really understand what extension (bending back) and flexion (bending forward) feel like, at the level of each single vertebra. The easiest way to start this process is to get on your hands and knees and go through an extremely slowed-down, controlled Cat/Cow sequence, similar to the basic yoga poses of the same names.^[*4]

這就是為什麼（a）放下手機，（b）嘗試在脊椎周圍培養一些本體感覺意識，這樣你才能真正理解伸展（向後彎曲）和彎曲（向前彎曲）的感覺。每個椎骨的水平。開始這個過程的最簡單方法是用手和膝蓋著地，進行極其緩慢、受控的貓/牛序列，類似於同名的基本瑜伽姿勢。^[*4]

The difference is that you have to *really, really slow down*, moving so slowly and deliberately from one end of your spine to the other that you can feel each individual vertebra changing position, all the way from your tailbone up to your neck, until your spine is bent like a sway-backed cow. Then reverse the movement, tilting your pelvis forward and bending your spine one vertebra at a time until your back is arched again, like a really scared cat. (Note: Inhale on Cow, exhale on Cat.)

不同之處在於，你必須非常非常慢地慢下來，從脊椎的一端緩慢而刻意地移動到另一端，這樣你就能感覺到每一塊椎骨都在改變位置，從尾骨一直到頸部，直到你的脊椎彎曲，像一頭搖晃著背部的牛。然後反轉動作，向前傾斜骨盆，一次一根椎骨地彎曲脊柱，直到背部再次弓起，就像一隻非常害怕的貓一樣。（註：牛吸氣，貓咪呼氣。）

The point of this exercise is not how much extension or flexion you can reach in extreme Cat or Cow but rather how much segmental control you can achieve, going from one extreme to the other. You should learn to feel the position of each vertebra, which in turn helps you better distribute load and

force throughout the spine. Now when I deadlift, this segmental control allows me to maintain a more neutral arc from my thoracic to lumbar spine, spreading the load evenly; before, my spine would have a sharp lordotic bend, meaning I was taking too much force on its hinge points. That's what stability is about: safe and powerful transmission of force through muscles and bones, and not joints or spinal hinge points.

這項練習的重點不在於你在貓式或牛式極限運動中能達到多少伸展或彎曲，而是你能實現多少分段控制，從一個極端到另一個極端。您應該學會感受每個椎骨的位置，這反過來又可以幫助您更好地在整個脊椎上分配負荷和力量。現在，當我硬舉時，這種分段控制使我能夠從胸椎到腰椎保持更中立的弧線，從而均勻地分散負荷；以前，我的脊椎會出現嚴重的前凸彎曲，這意味著我在其鉸接點上承受了太多的力量。這就是穩定性的意義所在：透過肌肉和骨骼，而不是關節或脊椎鉸點，安全且強大地傳遞力量。

Next we come to the shoulders, which are both complex and evolutionarily interesting. The scapulae (shoulder blades) sit on top of the ribs and have a great ability to move around. The shoulder joint is controlled by a complex set of muscles that attach in various positions to the scapula and the upper portion of the humerus, the long bone in the upper arm (which is why we medical types call it the *glenohumeral* joint). If you compare this ball-and-socket joint to the far more stable and solid one in your hip, it becomes clear that evolution made a huge trade-off when our ancestors began to stand up: we gave up a lot of stability in that shoulder joint in exchange for a much greater range of motion and, in practical terms, the all-important ability to throw a spear. But because there are so many different muscular attachments in the shoulder (no fewer than seventeen), it is much more vulnerable than the hip as I learned in my boxing and swimming careers.

接下來我們來看看肩膀，它既複雜又在進化上很有趣。肩胛骨（肩胛骨）位於肋骨頂部，具有強大的活動能力。肩關節由一組複雜的肌肉控制，這些肌肉以不同的位置附著在肩胛骨和肱骨上部（上臂的長骨）上（這就是為什麼我們醫學上稱之為盂肱關節）。如果你將這種球窩關節與臀部中更穩定、更堅固的關節進行比較，你會發現，當我

們的祖先開始站立時，演化做出了巨大的權衡：我們放棄了很多穩定性。肩關節換取更大的運動範圍，實際上，這是最重要的投擲長矛的能力。但由於肩部有許多不同的肌肉附著點（不少於十七個），因此正如我在拳擊和游泳生涯中了解到的那樣，它比臀部更容易受到傷害。

Beth taught me a simple exercise to help understand the importance of scapular positioning and control, a movement known as Scapular CARs, for *controlled articular rotations*: Stand with your feet shoulder-width apart and place a medium to light resistance band under your feet, one handle in each hand (a very light dumbbell also works). Keeping your arms at your sides, raise your shoulder blades, and then squeeze them back and together; this is *retraction*, which is where we want them to be when under load. Then drop them down your back. Finally, bring them forward to the starting point. We start out moving in squares like this, but the goal is to learn enough control that we can move our scapulae in smooth circles. A large part of what we're working on in stability training is this kind of neuromuscular control, reestablishing the connection between our brain and key muscle groups and joints.

Beth 教了我一個簡單的練習，幫助我理解肩胛骨定位和控制的重要性，這種運動被稱為肩胛骨CAR，用於控制關節旋轉：雙腳分開站立，與肩同寬，在腳下放置一個中度至輕度阻力帶，一根每隻手握住手柄（也可以使用非常輕的啞鈴）。將手臂放在身體兩側，抬起肩胛骨，然後將它們向後併攏；這就是收縮，這就是我們希望它們在負載下時所處的位置。然後把它們放在你的背上。最後，將他們帶到起點。我們開始像這樣以正方形移動，但目標是學習足夠的控制力，以便我們可以以平滑的圓圈移動肩胛骨。我們在穩定性訓練中所做的很大一部分工作就是這種神經肌肉控制，重建我們的大腦與關鍵肌肉群和關節之間的連結。

Almost everything we do in fitness, and in our daily lives, goes through our hands. If our feet are our contact with the ground, absorbing force, our hands are how we transmit force. They are our interface with the rest of our world. Grip strength—how hard you can squeeze—is only part of the equation. Our

hands are quite amazing, actually, in that they are powerful enough to crush the juice out of a lemon yet dexterous enough to play a Beethoven sonata on the piano. Our grip can be firm yet feathery, transmitting force with finesse.

我們在健身和日常生活中所做的幾乎所有事情都經過我們的雙手。如果我們的腳是我們與地面的接觸點，吸收力，那麼我們的手就是我們傳遞力的方式。它們是我們與世界其他地方的介面。握力——你能用多大的力量擠壓——只是等式的一部分。事實上，我們的雙手非常神奇，因為它們的力量足以壓碎檸檬汁，但又足夠靈巧，可以在鋼琴上彈奏貝多芬奏鳴曲。我們的握力既牢固又輕柔，巧妙地傳遞力量。

It's all about how you distribute force. If you can transmit and modulate force through your hands, then you can push and pull efficiently. This force originates in the powerful muscles of the trunk and is transmitted down the chain, from rotator cuff to elbow to forearm to wrist. There is a strong correlation between having a weak rotator cuff (shoulder) and weak grip strength.

這完全取決於你如何分配力量。如果你可以透過雙手傳遞和調節力，那麼你就可以有效地推和拉。這種力量源自於軀幹的強大肌肉，並沿著鏈條傳遞，從肩袖到肘部，再到前臂，再到手腕。肩袖（肩部）較弱與握力較弱之間有強烈的相關性。

But it starts with finger strength—which, unfortunately, is another thing that we have sacrificed to comfort and convenience. Back when we carried things, we had to have strong hands to survive. No longer. Many of us don't really even use our hands for much besides typing and swiping. This weakness means pushing and pulling movements bring a higher risk for elbow and shoulder injury.

但這始於手指的力量——不幸的是，這是我們為了舒適和便利而犧牲的另一件事。以前搬東西的時候，我們必須有一隻有力的手才能生存。不再。除了打字和滑動之外，我們中的許多人實際上並不用雙手做太多事情。這種弱點意味著推拉動作會增加手肘和肩部受傷的風險。

Because we are not “training” grip in our daily lives, we must be deliberate in our workouts, focusing on initiating movement with the hands and utilizing all the fingers with our upper body movements. Adding carries to your training is a great way to train grip, but it is important always to be mindful of what your fingers are doing and how force is being transmitted through them.

因為我們不是在日常生活中「訓練」握力，所以我們在運動時必須深思熟慮，專注於用手發起運動，並利用所有手指進行上身運動。在訓練中增加動作是訓練握力的好方法，但重要的是要始終注意手指的動作以及力量如何透過手指傳遞。

One way that Beth likes to illustrate the importance of this is via a basic bicep curl with a (light) dumbbell. First, try the curl with your wrist bent slightly backward, just a bit out of line with your forearm. Now try the same bicep curl with your wrist straight. Which one felt stronger and more powerful? Which one felt like the fingers were more involved? It's about building awareness of the importance of your fingers, as the last link in the chain.

貝絲喜歡用（輕）啞鈴進行基本的二頭肌彎舉來說明這一點的重要性。首先，嘗試彎舉時手腕稍微向後彎曲，與前臂稍微偏離一條直線。現在試試同樣的二頭肌彎舉，手腕伸直。哪一個感覺更強大、更有力量？哪一個感覺手指參與得比較多？這是為了讓人們認識到手指作為鏈條中最後一個環節的重要性。

One last way in which grip is important is in situations requiring reactivity—being able to grab (or let go of) a dog's leash when needed, or gripping a railing to prevent a fall. Our grip and our feet are what connect us to the world, so that our muscles can do what they need to do. Even in a deadlift: one of the key things Beth taught me is that a deadlift is as much about feet and hands as hamstrings and glutes. We're pushing the floor away as we lift with our fingers.

握力很重要的最後一種方式是在需要反應的情況下——在需要時能夠抓住（或放開）狗的皮帶，或抓住欄桿以防止跌倒。我們的握力和雙腳將我們與世界聯繫起來，以便我們的肌肉可以做它們需要做的事

情。即使在硬舉中：貝絲教我的關鍵事情之一是，硬舉與腿筋和臀肌一樣，也涉及腳和手。當我們用手指抬起時，我們正在將地板推開。

These moves and drills that I've described thus far represent only the very basic elements of stability work. They may seem simple, but they require a great deal of focus; in my practice, we don't even allow our patients to work out with heavy loads until they work on these basic principles for at least six months.

到目前為止，我所描述的這些動作和練習僅代表了穩定性工作的最基本要素。它們看似簡單，但需要高度關注；在我的實踐中，我們甚至不允許患者進行大負荷鍛煉，直到他們遵循這些基本原則至少六個月。

One more note: Trainers can be useful for some purposes, such as basic instruction, accountability, and motivation, but we discourage patients from becoming overly reliant on trainers to tell them exactly what to do every single time they work out. I liken this to learning to swim in a wetsuit. Initially, a wetsuit can help give someone confidence because of the additional flotation it provides. But over the longer term, a wetsuit robs you of the need to figure out your balance in the water. Balance is the real challenge with swimming, because our center of mass is way off from our center of volume, causing our hips to sink. Good swimmers learn to overcome this imbalance with training. But if you never take off the wetsuit, you will never learn how to fix this problem.

還有一點要注意的是：訓練師對於某些目的可能很有用，例如基本指導、責任和激勵，但我們不鼓勵患者過度依賴訓練師告訴他們每次運動時該做什麼。我把這比喻成穿著潛水衣學習游泳。最初，潛水衣可以幫助人們增強信心，因為它提供了額外的漂浮能力。但從長遠來看，潛水服會讓你不再需要在水中保持平衡。平衡是游泳的真正挑戰，因為我們的質心遠離體積中心，導致我們的臀部下沉。優秀的游泳選手透過訓練學會克服這種不平衡。但如果你從不脫掉潛水服，你就永遠不會學會如何解決這個問題。

Similarly, trainers can be helpful in teaching you the basics of different exercises, and to motivate you to get in the habit of working out. But if you never learn to do the exercises on your own, or never try different ways of doing them, you will never develop the proprioception needed to master your ideal movement patterns. You will rob yourself of the learning progression that is such an important part of stability training—the process of narrowing the gap between what you think you are doing and what you are actually doing.

同樣，培訓師可以幫助您教授不同練習的基礎知識，並激勵您養成運動的習慣。但是，如果您從未學會自己進行練習，或者從未嘗試過不同的練習方法，那麼您將永遠無法發展掌握理想運動模式所需的本體感覺。你會剝奪自己的學習進程，而學習進程是穩定訓練的重要組成部分——縮小你認為自己在做什麼和實際在做什麼之間差距的過程。

Everything that we've covered in this last section serves two purposes: as a drill, and as an assessment. I would urge you to film yourself working out from time to time, to compare what you think you are doing to what you are actually doing with your body. I do this daily—my phone on the tripod is one of my most valuable pieces of equipment in the gym. I film my ten most important sets each day and watch the video between sets, to compare what I see to what I think I was doing. Over time, that gap has been narrowing.

我們在最後一節中介紹的所有內容都有兩個目的：作為練習和評估。我建議你不時拍攝自己的運動過程，將你認為自己正在做的事情與你實際對身體所做的事情進行比較。我每天都會這樣做——三腳架上的手機是我在健身房裡最有價值的設備之一。我每天都會拍攝十個最重要的場景，並在場景之間觀看視頻，以將我所看到的與我認為我正在做的事情進行比較。隨著時間的推移，這種差距正在縮小。

—

It was really difficult, at first, to accept that I wasn't going to be lifting heavy weights anymore, but Beth and Michael Stromsness were persuasive. I

couldn't even squat properly or perform a simple pull-up correctly, so doing anything more than that would put me at risk of (further) injury.

起初，我真的很難接受我不再舉重的事實，但貝絲和麥可·斯特羅姆斯內斯很有說服力。我甚至無法正確蹲下或正確執行簡單的引體向上，因此做更多的事情會讓我面臨（進一步）受傷的風險。

I fumed over this for a while. How could I live without weight training? It took several months of work, but eventually I had learned enough that I could deadlift again. Where in the past I'd done four hundred pounds or more, now Beth had me begin at just ninety-five pounds, which seemed like hardly any weight at all.

我為此生氣了一段時間。沒有重量訓練怎么生活？這花了幾個月的時間，但最終我學到了足夠的知識，可以再次硬舉了。過去我的體重是四百磅甚至更多，而現在貝絲讓我從九十五磅開始，這看起來幾乎沒有什麼重量。

It helped to recall something that my driving coach, Thomas Merrill, often tells me. He is an incredible driver who in 2022 placed second in the one of the most prestigious motor races in the world, the 24 Hours of Le Mans; he knows what he's talking about. One of his mantras is that in order to go faster, you need to go slower.

這有助於回憶起我的駕駛教練托馬斯·梅里爾經常告訴我的事情。他是一位令人難以置信的車手，2022 年，他在世界上最負盛名的賽車比賽之一——勒芒 24 小時耐力賽中獲得了第二名；他知道他在說什麼。他的口頭禪之一是，為了走得更快，你需要走得更慢。

Here's what he means: when you "overdrive" a car, as when you're trying too hard to drive as fast as possible, you make mistakes. In driving, mistakes compound. When you spin in turn 5, it's because you probably missed the apex in turn 2 and didn't correct in turn 3. You need to slow down and get the car in the right spot, and it'll take care of the rest.

他的意思是這樣的：當你「超速駕駛」一輛汽車時，就像當你太努力地試圖開得盡可能快時，你就會犯錯。在駕駛過程中，錯誤會加劇。當你在第5 個彎道打滑時，那是因為你可能錯過了第2 個彎道的頂點，

並且在第3 個彎道沒有糾正。你需要減速並讓車停在正確的位置，剩下的事情它會處理的。

Slow down, go fast. It's the same, I think, with learning stability.

慢點，快點。我認為學習穩定性也是如此。

Hip-Hinging 101: How to Do a Step-Up

髖部鉸接 101：如何進行上台階

Rather than try to describe multiple exercises, I think it's more instructive to provide a deeper explanation of one exercise. I've chosen a step-up, simply stepping up onto a box or a chair, for three reasons. First, it's a hip-hinging movement, one of our core elements of strength training. Second, it's a single-leg exercise that does not require much axial (spine) loading, even with weights in your hands, which means it's very safe, even for beginners (you'll start with just your body weight). Third, it's one of the best exercises to target the eccentric phase of the movement as well as the concentric phase. I also like it because it demonstrates some of the key stability concepts we have been learning in this chapter.

我認為對一項練習提供更深入的解釋更有啟發性，而不是試圖描述多項練習。我選擇了台階，簡單地走到一個盒子或椅子上，有三個原因。首先，它是髖部鉸鏈運動，也是我們肌力訓練的核心要素之一。其次，這是一種單腿練習，即使手中有重物，也不需要太多的軸向（脊柱）負荷，這意味著它非常安全，即使對於初學者也是如此（您只需從體重開始）。第三，它是針對運動的偏心階段和向心階段的最佳練習之一。我喜歡它也因為它演示了我們在本章中學習的一些關鍵穩定性概念。

First, find a box or a sturdy chair such that when your foot is on the step your thigh will be parallel to the floor. For most people this is about sixteen to twenty inches, but if that is too difficult start with twelve inches. Place one foot on the box, making sure that the big toe and pinky toe mounds and the entire heel are connected firmly to its surface (I like to do these barefoot). The back foot remains on the floor, roughly twelve inches behind the box, with roughly 40 percent of your weight on the back leg and 60 percent on the front leg. Keep your front hip flexed, spine tall, chest heavy (ribs down), arms relaxed by your sides, and eyes forward.

首先，找到一個盒子或一把堅固的椅子，這樣當你的腳踩在台階上時，你的大腿將與地板平行。對於大多數人來說，這大約是十六到二十英寸，但如果這太困難，請從十二英寸開始。將一隻腳放在盒子上，確保大腳趾和小腳趾丘以及整個腳跟牢固地連接到其表面（我喜歡赤腳做這些）。後腳保持在地板上，距離箱子大約 12 英寸，大約 40% 的體重在後腿上，60% 在前腿上。保持前髖部彎曲，脊椎挺直，胸部沉重（肋骨向下），手臂放鬆放在身體兩側，眼睛向前看。

Now, slightly shift your head, ribs, and pelvis forward at the same time as you quietly but fully inhale through your nose, allowing the diaphragm to descend and creating intra-abdominal pressure. You should feel pressure in the center of the front foot, toward the heel, but keep your toes connected to the box. Glide your front femur back slightly, so that you feel a stretch in both the hamstring and the glute max; they should be very slightly loaded. This sensation is the essence of the hip-hinge. You want to lead with your glutes and hamstrings, not pelvis or ribs. All of your power will come from these muscles working together, and not your back. Keep your knee behind your toes, and your pelvis and ribs in alignment, and load your front foot evenly, not favoring either the toes/forefoot or heel.

現在，稍微向前移動你的頭部、肋骨和骨盆，同時透過鼻子安靜但充分地吸氣，讓橫膈膜下降並產生腹內壓力。您應該感覺到前腳中心朝向腳跟的壓力，但保持腳趾與盒子相連。將股骨前部稍微向後滑動，這樣你就會感覺到腿筋和臀大肌都有伸展感；它們的負載應該很小。這種感覺就是髖鉸鏈的本質。你想用臀肌和腿筋來引導，而不是骨盆或肋骨。你所有的力量都將來自這些肌肉的協同工作，而不是你的背部。將膝蓋保持在腳趾後面，使骨盆和肋骨保持對齊，使前腳均勻受力，不要偏向腳趾/前腳或腳跟。

With your front foot, push down on the box with intent and with *minimal push-off assistance from the back foot*. Lift yourself off the floor, exhaling as you initiate the movement, extend the hip, and stand up straight on top of the box. Your head and ribs should finish directly over the pelvis. Bring your rear leg through to finish beside and a little in front of the working leg. Everything should arrive at the same time, as you complete the exhale (feeling the compression in the ribs). Hold this position for a second or two.

用前腳用力向下推箱子，並用後腳的最小推力輔助。將自己從地板上抬起，開始運動時呼氣，伸展臀部，然後在盒子頂部站直。您的頭部和肋骨應直接位於骨盆上方。將後腿穿過，完成時位於工作腿旁且稍靠前的位置。當你完成呼氣時（感覺肋骨受壓），所有的事情都應該同時到達。保持這個姿勢一兩秒鐘。

On the way down, step the nonworking (now front) foot off the back of the box as your head, ribs, and shoulders shift slightly forward and the hip flexes to (once again) prepare the hamstring and glute to lower your weight. Load the front of the stationary

foot, the toes actively flexed into the box. As you lower your body down and back through space, feel the weight shifting from the forefoot into the midfoot, and finally to the heel, in a smooth, coordinated fashion that is controlled by the hamstring (think: slowly rocking backward).

在下降的過程中，將不工作的腳（現在是前面的）從箱子的後面移開，同時你的頭部、肋骨和肩膀稍微向前移動，並且臀部彎曲（再次）準備腿筋和臀部以降低你的體重。給固定腳的前部施加負載，腳趾主動彎曲到盒子裡。當你在空間中向下和向後降低身體時，感覺重量從前腳轉移到中腳，最後轉移到腳後跟，由腿筋控制，以一種平滑、協調的方式轉移（想想：慢慢向後搖晃）。

Keep the tempo as slow and even as possible; aim for three seconds from step-off to landing (difficult; two seconds is good). As the back foot lowers, your weight continues to shift back until you “land.” Avoid shifting more than 40 percent of your weight to the back foot, to reduce the temptation to use forward momentum to start the next rep. Repeat.

盡可能保持節奏緩慢、均勻；從邁步到著陸的目標是三秒（很難；兩秒就很好）。隨著後腳降低，您的體重繼續向後轉移，直到「落地」。避免將超過 40% 的體重轉移到後腳，以減少使用向前動力開始下一次動作的誘惑。重複。

Do five to six reps on each side. Start with body weight only, but once you have the movement and sensation down, you can add weights, ideally a dumbbell or kettlebell in each hand. (Bonus points: Now you are training grip strength as well as hip-hinging.)

每側重複五到六次。從體重開始，但一旦你的運動和感覺下降，你就可以增加重量，最好是每隻手一個啞鈴或壺鈴。（加分點：現在您正在訓練握力以及髖部鉸鏈。）

The loaded exercise is essentially the same in terms of sequence and position, with a few caveats:

負荷練習在順序和位置方面基本上相同，但有一些注意事項：

1. Load is now a function of two things: weight and box height. Box height can be an issue if mobility (flexibility and loading tolerance) is a factor.

負載現在是兩個因素的函數：重量和盒子高度。如果移動性（靈活性和負載容差）是一個因素，那麼箱子高度可能是一個問題。

2. The weights must hang straight down from the shoulders. The brain will find any way to conserve energy and “cheat,” so avoid the subconscious urge to swing the weights forward or lift the shoulders to initiate the step-up (highly likely if the load is too heavy). The glute and hamstring should be doing *all* the work.

重物必須從肩膀垂直垂下。大腦會找到任何方法來保存能量和“作弊”，因此請避免潛意識中向前擺動重物或抬起肩膀以啟動台階的衝動（如果負載太重，則很有可能）。臀肌和腿筋應該承擔所有的工作。

3. If the eccentric phase (step-down) cannot be controlled, the weight is too heavy. You never want to feel as if you are falling back. Try using less weight, or a shorter (two-second) step-down at first.

如果偏心階段（降壓）無法控制，則表示重量過重。你永遠不想感覺自己正在倒退。首先嘗試使用較小的重量或較短（兩秒）的下降幅度。

4. It is crucial to keep the ribs and head above or slightly ahead of the pelvis as you initiate the step-up. If you lead with the pelvis, you will be bending your back and also putting too much pressure on the knee.

當你開始上台階時，保持肋骨和頭部位於骨盆上方或稍微前方是至關重要的。如果你用骨盆引導，你會彎曲你的背部，也會對膝蓋造成太大的壓力。

You will find more video demonstrations on my website, at www.peterattiamd.com/outlive/videos.

您可以在我的網站 www.peterattiamd.com/outlive/videos 上找到更多影片示範。

The Power of Exercise: Barry

運動的力量：巴里

As a former athlete and lifelong exerciser, I already had a substantial fitness base built up, even if I wasn't necessarily moving or lifting correctly. Many of my problems stemmed from lifting *too much*, cycling *too much*, or swimming *too much*. The vast majority of people have the opposite problem: They're not doing enough. Or they haven't done enough. Or they can't do very much at all. For most people, this is the real challenge. They need a jump start. The good news is that these are the very people who can benefit the most. They have the most to gain.

作為一名前運動員和終身鍛鍊者，我已經建立了堅實的健身基礎，即使我不一定能正確移動或舉重。我的許多問題都源自於舉重過多、騎自行車過多或游泳過多。絕大多數人都有相反的問題：他們做得不夠。或者他們做得還不夠。或者他們根本不能做很多事。對大多數人來說，這是真正的挑戰。他們需要一個快速啟動。好消息是，這些人正是受益最多的人。他們的收穫最大。

This is also where we see the true power of exercise—its ability to transform people, to make them functionally younger. It's quite incredible. I mentioned earlier how taking up weight training in her sixties changed my mom's life. But there's no better exemplar, I think, than the amazing, inspiring Barry.

這也是我們看到鍛鍊真正力量的地方——它能夠改變人，讓他們在功能上更年輕。這太不可思議了。我之前提到過，我媽媽在六十多歲時開始舉重訓練如何改變了她的生活。但我認為，沒有比令人驚嘆、鼓舞人心的巴里更好的榜樣了。

Barry was another client of Beth's (but not a patient of mine), an entrepreneur and executive who had spent his career building a successful business, putting in long hours at work and spending virtually no time on anything else, including his fitness. He took cycling trips occasionally, but that was about it.

巴里是貝絲的另一位客戶（但不是我的病人），他是一位企業家和高管，他的職業生涯建立了一個成功的企業，長時間工作，幾乎沒有時間花在其他事情上，包括健身。他偶爾騎自行車旅行，但僅此而已。

I see that a lot among my own patients: they trade health for wealth. Then they reach a certain age and realize they are on a bad path. This was Barry: After spending basically fifty years sitting in a chair, he retired and it dawned on him that he was in terrible shape. Not only was his physical capacity very limited, but he was in almost constant pain. He was then closing in on eighty years old and looking at some painful years ahead—a bad Marginal Decade.

我在自己的病人身上看到了很多這樣的情況：他們用健康換取財富。然後他們到了某個年齡，意識到自己走在一條糟糕的道路上。這就是

巴里：在椅子上坐了大約五十年之後，他退休了，他意識到自己的狀況很糟。他不僅體力非常有限，而且幾乎一直處於疼痛之中。當時他已年近八十，展望未來的痛苦歲月——糟糕的邊緣十年。

He began to wonder: Why had he worked so hard? In the state he was in, retirement no longer seemed very appealing.

他開始思考：自己為什麼要這麼努力？以他現在的狀態，退休似乎不再有吸引力。

At some point, he had a revelation: instead of retiring, he would give himself a new job. This “job,” as he saw it, was to rebuild his neglected body so he could get more enjoyment out of life. He began working with Beth and kept on going even as the pandemic made it impossible to train in person for a while. He was highly motivated. Beth has to remind many of her clients to stick with their workout schedule, but with Barry she had the opposite problem: he wanted to spend *too* much time in the gym. She had to make him take breaks and rest.

在某個時候，他得到了一個啟示：他不會退休，而是會給自己一份新工作。在他看來，這份「工作」就是重建他被忽視的身體，這樣他就能從生活中獲得更多樂趣。他開始與貝絲一起工作，並繼續工作，儘管疫情使他暫時無法親自訓練。他的積極性很高。貝絲必須提醒她的許多客戶堅持運動計劃，但巴里卻遇到了相反的問題：他想在健身房花太多時間。她必須讓他休息一下。

Barry's goals are different from mine, obviously, but they went well beyond vaguely wanting to “get healthier.” He wanted to be able to do a pull-up—that was his stated fitness goal. What he really wanted was to feel strong, and to be able to move in the world with confidence again, without fear of falling, just as he had done as a younger man. But he was nowhere near that; if Beth had put him on a pull-up bar, he likely would have hurt himself. He could barely walk without pain. So he had to begin at a much more basic level, learning how to do simple movement patterns safely.

顯然，巴里的目標與我的目標不同，但他們遠遠超出了模糊地想要「變得更健康」的範圍。他希望能夠做引體向上——這是他既定的健

身目標。他真正想要的是感覺堅強，能夠再次充滿信心地在世界上行走，而不用擔心跌倒，就像他年輕時所做的那樣。但他遠遠沒有達到這個目標。如果貝絲把他放在引體向上桿上，他很可能會受傷。他幾乎無法在不疼痛的情況下行走。因此，他必須從更基礎的層次開始，學習如何安全地進行簡單的運動模式。

Beth started him off with some of the same introductory exercises I'd done: abdominal breathing, progressing into the slowed-down, segmental Cat/Cow. To lessen his risk of falling she had him focus on balance-related movements, beginning with his feet—learning to move and feel his toes again, after decades of having been shoved into shoes. He then progressed into one-leg walking and standing drills. Beth even had him dance, to help him relearn how to move his feet and how to react to visual cues to keep his balance.

貝絲用我做過的一些入門練習開始了他：腹式呼吸，逐漸進入緩慢的、分段的貓/牛式。為了減少他跌倒的風險，她讓他專注於與平衡相關的運動，從他的腳開始——在幾十年的穿鞋經歷之後，重新學習移動和感覺腳趾。然後他進行了單腳行走和站立訓練。貝絲甚至讓他跳舞，幫助他重新學習如何移動雙腳以及如何對視覺提示做出反應以保持平衡。

They then progressed into building basic strength, beginning with walking lunges to fortify his lower body. His abdominals were still weak from surgery twenty years earlier—it's not uncommon, I've observed, for these things to affect people decades after the fact. So they worked on his abdominal strength, beginning (as I did) with building intra-abdominal pressure. And gradually, they worked toward building his upper and midbody strength—and the scapular stability—he would need. Before long he could do better push-ups than most twenty-something gym bros.

然後，他們開始增強基本力量，從弓箭步開始，以加強他的下半身。由於二十年前的手術，他的腹部仍然很虛弱——據我觀察，這些事情在事發幾十年後仍然影響著人們，這並不罕見。因此，他們鍛鍊了他的腹部力量，從增強腹內壓力開始（就像我所做的那樣）。逐漸地，他們致力於增強他所需的上半身力量以及肩胛骨的穩定性。不久之後，他就能比大多數二十多歲的健身兄弟做更好的伏地挺身了。

Beth put him through drills designed to improve his ability to react and stay balanced. She had him use an agility ladder, similar to what NFL players and other field-sport athletes use to develop balance, quickness, and footwork. If you're training to be an athlete of life, then you're training to be an athlete, period.

貝絲讓他進行了旨在提高他反應和保持平衡能力的訓練。她讓他使用敏捷梯，類似於 NFL 球員和其他田徑運動員用來培養平衡、速度和步法的梯子。如果你正在訓練成為生活運動員，那麼你就是在訓練成為運動員，就這樣。

Last, she had Barry work on jumping drills, which is definitely out of the comfort zone of most octogenarians. He was nervous, but eventually he got to the point where he could hop off a pair of yoga blocks and land in a squat—and stick it. The idea was to prepare him for the unexpected, so that if he did find himself stepping off an unexpected stair or curb, he could catch himself and not fall. Most people instinctively brace themselves, out of fear; they don't trust their “brakes,” their eccentric strength, and that almost always makes their landing less safe. With stability, you have to be fluid and prepared to react, almost like a dancer.

最後，她讓巴里進行跳躍訓練，這絕對超出了大多數八旬老人的舒適區。他很緊張，但最終他能夠從一對瑜珈磚上跳下來，深蹲著地——然後堅持下去。這個想法是讓他為意外情況做好準備，這樣，如果他發現自己走下意想不到的樓梯或路緣石，他可以抓住自己而不會摔倒。大多數人出於恐懼，本能地做好準備；他們不相信自己的“煞車”，不相信自己的古怪力量，這幾乎總是讓他們著陸變得不那麼安全。為了保持穩定性，你必須保持流暢並準備好做出反應，就像舞者一樣。

Another important move that they worked on was simply to get Barry to be able to get up off the ground, using only one arm (or ideally, no arms). This is one of those things that we who are younger take for granted. Of course, we can get up off the ground—until, suddenly, we can't. Children learn to do it without a second thought. But somewhere along the way, adults lose the ability

to execute this basic move. Even if we have the requisite physical strength, we might lack neuromuscular control; the message from our brain just doesn't reach our muscles. For someone who is eighty-one, like Barry (at this writing), this is a big deal; it could make the difference between continuing to live independently and having to think about going into a nursing home. So Beth taught him a choreographed sequence of movements that would allow him to stand up from a seated position, and he worked on them until he had mastered it.

他們研究的另一個重要舉措是讓巴里能夠只使用一隻手臂（或理想情況下，沒有手臂）從地面上站起來。這是我們年輕人認為理所當然的事情之一。當然，我們可以從地面上站起來——直到突然間我們不能了。孩子們不假思索地學會了這樣做。但在這個過程中，成年人失去了執行這項基本動作的能力。即使我們擁有必要的體力，我們也可能缺乏神經肌肉控制；來自我們大腦的訊息無法到達我們的肌肉。對於像巴里（在撰寫本文時）這樣八十一歲的人來說，這是一件大事；它可能會導致繼續獨立生活和不得不考慮進入療養院之間的差異。於是貝絲教他一系列精心設計的動作，讓他能夠從坐姿站起來，他不斷地練習這些動作，直到他掌握為止。

The “Barry Get-Up” has become a key part of the fitness assessment that we do with all our patients, as well as one of the key events in the Centenarian Decathlon (it should be in yours, too). It's an important move, whether you're picking yourself up off the ground after a stumble or playing with grandchildren on the floor. (For a video demonstration of the Barry Get-Up, please visit www.peterattiamd.com/outlive/videos.) Everyone should be able to do it.

「巴里起床」已成為我們對所有患者進行的健康評估的關鍵部分，也是百歲十項全能的關鍵項目之一（也應該是您的項目）。無論您是在跌倒後從地上爬起來，還是在地板上與孫子們玩耍，這都是一個重要的舉動。（有關 Barry Get-Up 的視訊演示，請訪問 www.peterattiamd.com/outlive/videos。）每個人都應該能夠做到。

But I think it's also a metaphor for what's possible with exercise training (and, of course, stability). People like Barry help us to rewrite that narrative of

decline that trapped my friend's mom, Sophie, and so many other people. Exercise has the power to change us profoundly, even if we're starting from zero, as Barry was. It gives us the ability to pick ourselves up off the ground—literally and figuratively—and become stronger and more capable. It's not about slowing the decline, it's about getting better, and better, and better.

但我認為這也是運動訓練（當然還有穩定性）的可能性的隱喻。像巴里這樣的人幫助我們改寫了困擾我朋友的媽媽蘇菲和其他許多人的衰落故事。運動有能力深刻地改變我們，即使我們像巴里一樣從零開始。它讓我們有能力從字面上和比喻上重新站起來，變得更強大、更有能力。這不是為了減緩衰退，而是為了變得更好、更好、更好。

As Barry puts it, "If you're not pushing ahead, you're going backwards."
正如巴里所說，“如果你不前進，你就會倒退。”

SKIP NOTES

跳過註釋

*1 A torn labrum is a pretty common injury, but many people never require surgery to fix it. Though endless swimming is what made it worse, the injury was caused by the frequent subluxations or mild dislocations that I had experienced growing up. Each time the shoulder joint is subluxed it gnaws away at the labrum and increases the odds for further shoulder instability and pain.

*1 孟唇撕裂是一種相當常見的損傷，但許多人不需要手術來修復它。雖然無止盡的游泳讓情況變得更糟，但傷害是由我成長過程中經常經歷的半脫位或輕度脫位造成的。每次肩關節半脫位時，它都會侵蝕孟唇，並增加肩膀進一步不穩定和疼痛的可能性。

*2 Back when I used to fly every week, I tried a clever trick that Michael Rintala showed me: put two tennis balls in an athletic sock about four to six inches apart, and position them just about at the level of my kidneys, or where my thoracic spine meets my lumbar spine. Then, with every breath I try to make sure I expand fully enough to feel the tennis balls on both sides. The idea is that it cues your breathing. When I did this, I could get off a five-hour flight and feel as if I had not been sitting for longer than about five minutes. (It also kept my seatmates from talking to me when I was trying to work.) It's worth trying on a long flight or drive.

*2 當我每週飛行時，我嘗試了邁克爾·林塔拉（Michael Rintala）向我展示的一個聰明技巧：將兩個網球放入運動襪中，間隔約四到六英寸，並將它們放置在我的腎臟的水平位置，或我的胸椎與腰椎相交的地方。然後，每次呼吸時，我都會盡力確保自己充分伸展，以感覺到兩側的網球。這個想法是它會提示你的呼吸。當我這樣做時，我可以在五個小時的飛行後感覺好像我沒有坐超過五分鐘。（當我試圖工作時，這也阻止了我的座位上的人跟我說話。）在長途飛行或開車時值得嘗試。

[*3](#) If you really want to go all in on toe yoga, get a set of “toe spacers,” which help restore the toes to a more natural, spread position, particularly in people with bunions or other shoe-related issues. I wear these things around the house a lot. I’m typing right now while wearing them. My kids mock me relentlessly.

*3 如果您真的想全身心投入腳趾瑜伽，請購買一套“腳趾墊片”，它有助於將腳趾恢復到更自然、展開的位置，特別是對於患有拇囊炎或其他與鞋子相關問題的人。我在家裡常穿這些東西。我現在戴著它們打字。我的孩子無情地嘲笑我。

[*4](#) Some of these basic DNS stability moves that I am describing have analogues in classic yoga poses, and a top-notch yoga instructor can help you develop the neuromuscular control and awareness that are essential to proper stability, but most yoga classes are too vague and loose for my taste.

*4 我所描述的一些基本DNS 穩定性動作與經典瑜伽姿勢有類似之處，一流的瑜伽教練可以幫助您培養對適當穩定性至關重要的神經肌肉控制和意識，但大多數瑜伽課程都過於模糊而且很適合我的口味。

CHAPTER 14

第14章

Nutrition 3.0

營養3.0

You Say Potato, I Say “Nutritional Biochemistry”

你說馬鈴薯，我說“營養生物化學”

Religion is a culture of faith; science is a culture of
doubt.

宗教是一種信仰文化；科學是一種懷疑文化。

—RICHARD FEYNMAN

——理查·費曼

I dread going to parties, because when people find out what I really do
for a living (not buying my usual lies about being a shepherd or a race car

driver), they always want to talk about the topics I dread most: “diet” and “nutrition.”

我害怕參加聚會，因為當人們發現我真正以什麼為生時（而不是相信我通常關於成為牧羊人或賽車手的謊言），他們總是想談論我最害怕的話題：「飲食」和「營養」。

I will do whatever it takes to get out of that conversation—go and get a drink, even if I’m already holding one, or pretend to answer my phone, or, if all else fails, feign a grand mal seizure. Like politics or religion, it’s just not a fit topic of conversation, in my view. (And if I seemed like kind of a jerk to you at a party once, my apologies.)

我會盡一切努力擺脫這場談話——去喝一杯，即使我已經拿著一杯酒，或者假裝接電話，或者，如果其他方法都失敗了，假裝癲癇發作。在我看來，就像政治或宗教一樣，這不是一個合適的話題。（如果有一次在聚會上我看起來像個混蛋，我很抱歉。）

Diet and nutrition are so poorly understood by science, so emotionally loaded, and so muddled by lousy information and lazy thinking that it is impossible to speak about them in nuanced terms at a party or, say, on social media. Yet most people these days are conditioned to want bullet-point “listicles,” bumper-sticker slogans, and other forms of superficial analysis. It reminds me of a story about the great physicist (and one of my heroes) Richard Feynman being asked at a party to explain, briefly and simply, why he was awarded his Nobel Prize. He responded that if he could explain his work briefly and simply, it probably would not have merited a Nobel Prize.

科學界對飲食和營養的理解是如此之少，人們的情緒如此沉重，並且被糟糕的信息和懶惰的思維所混淆，以至於不可能在聚會上或社交媒體上以細緻入微的方式談論它們。然而，現在大多數人都習慣想要要點式的「清單」、保險桿貼紙標語和其他形式的膚淺分析。這讓我想起了一個關於偉大的物理學家（也是我的英雄之一）理查德·費曼

（Richard Feynman）在一次聚會上被要求簡短而簡單地解釋為什麼他被授予諾貝爾獎的故事。他回答說，如果他能簡單明了地解釋他的工作，它可能不會獲得諾貝爾獎。

Feynman's rule also applies to nutrition, with one caveat: we actually know far *less* about this subject than we do about subatomic particles. On the one hand, we have made-for-clickbait epidemiological “studies” that make absurd claims, such as that eating an ounce of tree nuts each day will lower your cancer risk by exactly 18 percent (not making this up). On the other, we have clinical trials that tend almost without exception to be flawed. Thanks to the poor quality of the science, we actually don't know that much about how what we eat affects our health. That creates a tremendous opportunity for a multitude of would-be nutrition gurus and self-proclaimed experts to insist, loudly, that only *they* know the true and righteous diet. There are forty thousand diet books on Amazon; they can't all be right.

費曼的規則也適用於營養，但有一個警告：我們對這個主題的了解實際上遠少於對亞原子粒子的了解。一方面，我們進行了一些旨在吸引標題的流行病學“研究”，其中提出了荒謬的主張，例如每天吃一盎司堅果就能將患癌症的風險降低整整 18%（這不是編造的）。另一方面，我們的臨床試驗幾乎無一例外都存在缺陷。由於科學品質較差，我們實際上不太了解我們的飲食如何影響我們的健康。這為眾多未來的營養專家和自稱為專家的人創造了巨大的機會，讓他們大聲堅持只有他們知道真正正確的飲食。亞馬遜上有四萬本飲食書；他們不可能都是對的。

Which brings us to my final quibble about the world of nutrition and diets, which is the extreme tribalism that seems to prevail there. Low-fat, vegan, carnivore, Paleo, low-carb, or Atkins—every diet has its zealous warriors who will proclaim the superiority of their way of eating over all others until their dying breath, despite a total lack of conclusive evidence.

這讓我們想到了我對營養和飲食世界的最後一個爭論，那就是那裡似乎盛行的極端部落主義。低脂、純素、肉食、原始人飲食、低碳水化合物或阿特金斯飲食——每種飲食都有其熱心的鬥士，他們會宣稱自己的飲食方式優於其他飲食方式，直到臨死為止，儘管完全缺乏確切的證據。

Once upon a time, I too was one of those passionate advocates. I spent three years on a ketogenic diet and have written and blogged and spoken

extensively about that journey. For better and for worse, I'm indelibly associated with low-carb and ketogenic diets. Giving up added sugar—literally, putting down the Coke that I held in my hand, on September 8, 2009, moments after my lovely wife suggested I “work on being a little less not thin”—was the first step on a long, life-changing, but also frustrating journey through the world of diet and nutrition science. The good news is that it reversed my incipient metabolic syndrome and may have saved my life. It also led to me writing this book. The bad news is that it exhausted my patience for the “diet debate.”

曾幾何時，我也是那些熱情的倡導者之一。我花了三年的時間進行生酮飲食，並撰寫、撰寫部落格並廣泛談論了這段旅程。無論好壞，我都與低碳水化合物和生酮飲食有著不可磨滅的關聯。放棄添加糖——確切地說，是在 2009 年 9 月 8 日，就在我可愛的妻子建議我“努力變得不那麼瘦”之後，放下了我手裡的可樂——這是長期、飲食和營養科學世界的旅程改變了生活，但也令人沮喪。好消息是它逆轉了我早期的代謝綜合症，並可能挽救了我的生命。這也促使我寫了這本書。壞消息是，它耗盡了我對「飲食辯論」的耐心。

Consider this chapter my penance.

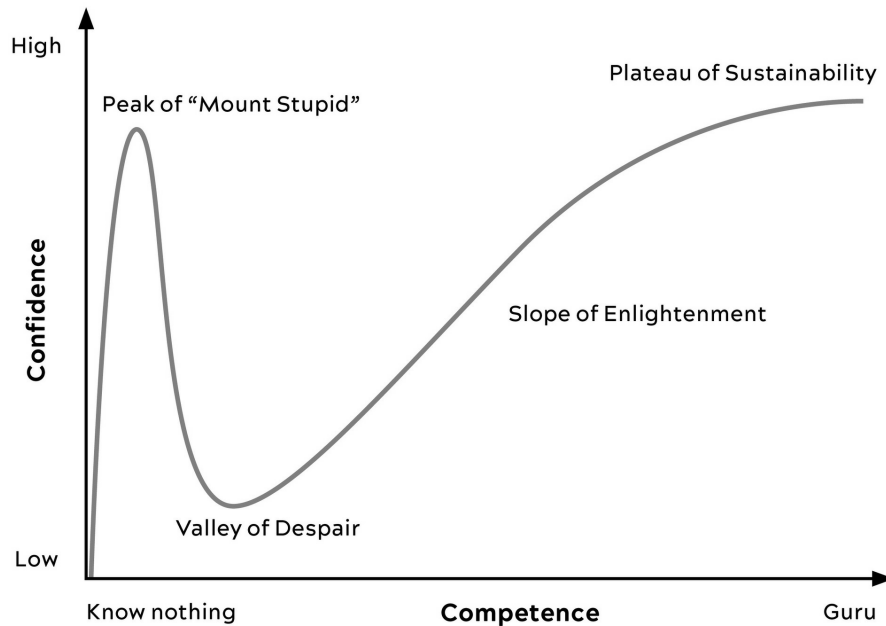
將此章視為我的懺悔。

Overall, I think most people spend either too little or too much time thinking about this topic. Probably more on the “too little” side, as evidenced by the epidemic of obesity and metabolic syndrome. But those on the “too much” side are loud and insistent (check out nutrition Twitter). I was completely guilty of this myself, in the past. Looking back, I now realize that I was too far on the left on the Dunning-Kruger curve, caricatured below in figure 14—my maximal confidence and relatively minimal knowledge having propelled me quite close to the summit of “Mount Stupid.”

總的來說，我認為大多數人花在思考這個主題的時間要么太少要么太多。可能更多的是「太少」的一面，肥胖和代謝症候群的流行就證明了這一點。但那些「太多」的人卻大聲而堅持（查看營養推特）。過去，我自己也為此感到完全內疚。回想起來，我現在意識到，我在鄧

寧-克魯格曲線上離左邊太遠了，如下圖14 所示——我最大的信心和相對最少的知識使我非常接近「愚蠢山」的頂峰。

Figure 14. Dunning-Kruger Effect



Source: Wikimedia Commons, (2020).

資料來源：維基共享資源，（2020）。

Now I might be halfway up the Slope of Enlightenment on a good day, but one key change I have made is that I am no longer a dogmatic advocate of any particular way of eating, such as a ketogenic diet or any form of fasting. It took me a long time to figure this out, but the fundamental assumption underlying the diet wars, and most nutrition research—that there is one perfect diet that works best for every single person—is absolutely incorrect. More than anything I owe this lesson to my patients, whose struggles have taught me a humility about nutrition that I never could have learned from reading scientific papers alone.

現在，在美好的一天裡，我可能正處於啟蒙斜坡的半路上，但我所做的一個關鍵改變是，我不再是任何特定飲食方式的教條倡導者，例如

生酮飲食或任何形式的禁食。我花了很長時間才弄清楚這一點，但飲食大戰和大多數營養研究背後的基本假設——即有一種最適合每個人的完美飲食——是絕對錯誤的。最重要的是，我把這個教訓歸功於我的病人，他們的掙扎教會了我對營養的謙遜，這是我僅靠閱讀科學論文永遠無法學到的。

I encourage my patients to avoid using the term *diet* at all, and if I were a dictator, I might ban it entirely. When you eat a slice of prosciutto or a Rice Krispies square, you are ingesting a multitude of different chemical compounds. Just as their chemical makeup differentiates them in terms of taste, the molecules in the foods that we consume affect multiple enzymes and pathways and mechanisms in our bodies, many of which we have discussed in previous chapters. These food molecules—which are basically nothing more than different arrangements of carbon, nitrogen, oxygen, phosphorus, and hydrogen atoms—also interact with our genes, our metabolism, our microbiome, and our physiologic state. Moreover, each of us will react to these food molecules in different ways.

我鼓勵我的患者完全避免使用「飲食」這個詞，如果我是獨裁者，我可能會完全禁止它。當您吃一片火腿或一塊脆米花時，您會攝取多種不同的化學物質。正如它們的化學組成在味道上有所不同一樣，我們所吃的食物中的分子會影響我們體內的多種酵素、途徑和機制，其中許多我們在前面的章節中已經討論過。這些食物分子基本上只不過是碳、氮、氧、磷和氫原子的不同排列，它們也與我們的基因、新陳代謝、微生物組和生理狀態相互作用。此外，我們每個人都會以不同的方式對這些食物分子做出反應。

Instead of diet, we should be talking about *nutritional biochemistry*. That takes it out of the realm of ideology and religion—and above all, emotion—and places it firmly back into the realm of science. We can think of this new approach as Nutrition 3.0: scientifically rigorous, highly personalized, and (as we'll see) driven by feedback and data rather than ideology and labels. It's not about telling you what to eat; it's about figuring out what works for your body and your goals—and, just as important, what you can stick to.

我們該談的不是飲食，而是營養生物化學。這將它帶出了意識形態和

宗教的領域——尤其是情感的領域——並將其牢牢地放回科學領域。我們可以將這種新方法視為營養 3.0：科學嚴謹、高度個人化，並且（正如我們將看到的）由回饋和數據驅動，而不是意識形態和標籤。這不是告訴你該吃什麼；而是告訴你該吃什麼。這是關於弄清楚什麼對你的身體和你的目標有效，而且同樣重要的是，你可以堅持什麼。

What problem are we trying to solve here? What is our goal with Nutrition 3.0?

我們在這裡試圖解決什麼問題？我們營養3.0的目標是什麼？

I think it boils down to the simple questions that we posited in chapter 10: 我認為這可以歸結為我們在第 10 章中提出的簡單問題：

1. Are you *undernourished*, or *overnourished*?

你是營養不良還是營養過剩？

2. Are you *undermuscled*, or *adequately muscled*?

你是肌肉不足還是肌肉充足？

3. Are you *metabolically healthy* or not?

您的新陳代謝健康嗎？

The correlation between poor metabolic health and being overnourished and undermuscled is very high. Hence, for a majority of patients the goal is to reduce energy intake while adding lean mass. This means we need to find ways to get them to consume fewer calories while also increasing their protein intake, and to pair this with proper exercise. This is the most common problem we are trying to solve around nutrition.

代謝健康狀況不佳與營養過剩和肌肉不足之間的相關性非常高。因此，對於大多數患者來說，目標是減少能量攝入，同時增加瘦體重。這意味著我們需要找到方法讓他們消耗更少的熱量，同時增加蛋白質

的攝取量，並將其與適當的運動結合。這是我們試圖解決的營養方面最常見的問題。

When my patients are undernourished, it's typically because they are not taking in enough protein to sustain muscle mass, which as we saw in the previous chapters is a crucial determinant of both lifespan and healthspan. So any dietary intervention that compromises muscle, or lean body mass, is a nonstarter—for both the under- and overnourished groups.

當我的患者營養不良時，通常是因為他們沒有攝取足夠的蛋白質來維持肌肉質量，正如我們在前面的章節中看到的那樣，肌肉質量是壽命和健康壽命的關鍵決定因素。因此，任何損害肌肉或去脂體重的飲食幹預措施對於營養不良和營養過剩的群體來說都是不可能的。

I used to think that diet and nutrition were the one path to perfect health. Years of experience, with myself and my patients, have led me to temper my expectations a bit. Nutritional interventions can be powerful tools with which to restore someone's metabolic equilibrium and reduce risk of chronic disease. But can they extend and improve lifespan and healthspan, almost magically, the way exercise does? I'm no longer convinced that they can.

我曾經認為飲食和營養是實現完美健康的唯一途徑。多年與我自己和我的病人打交道的經驗讓我稍微降低了自己的期望。營養幹預措施可以成為恢復人體代謝平衡和降低慢性病風險的強大工具。但它們能像運動一樣神奇地延長和改善壽命和健康嗎？我不再相信他們可以。

I still believe that most people need to address their eating pattern in order to get control of their metabolic health, or at least not make things worse. But I also believe that we need to differentiate between behavior that *maintains* good health versus tactics that *correct* poor health and disease. Wearing a cast on a broken bone will allow it to heal. Wearing a cast on a perfectly normal arm will cause it to atrophy. While this example is obvious, it's amazing how many people fail to translate it to nutrition. It seems quite clear that a nutritional intervention aimed at correcting a serious problem (e.g., highly restricted diets, even fasting, to treat obesity, NAFLD, and type 2 diabetes)

might be different from a nutritional plan calibrated to maintain good health (e.g., balanced diets in metabolically healthy people).

我仍然相信大多數人需要解決他們的飲食模式，以控制他們的代謝健康，或至少不會讓事情變得更糟。但我也認為，我們需要區分維持健康的行為和糾正不良健康和疾病的策略。在斷骨上打上石膏可以使其癒合。在完全正常的手臂上佩戴石膏會導致其萎縮。雖然這個例子很明顯，但令人驚訝的是有多少人未能將其轉化為營養。似乎很明顯，旨在糾正嚴重問題的營養幹預（例如，嚴格限制飲食，甚至禁食，以治療肥胖、NAFLD 和 2 型糖尿病）可能不同於旨在保持良好健康的營養計劃（例如，代謝健康人群的均衡飲食）。

Nutrition is relatively simple, actually. It boils down to a few basic rules: don't eat too many calories, or too few; consume sufficient protein and essential fats; obtain the vitamins and minerals you need; and avoid pathogens like *E. coli* and toxins like mercury or lead. Beyond that, we know relatively little with complete certainty. Read that sentence again, please.

其實營養相對簡單。它歸結為一些基本規則：不要吃太多或太少的卡路里；攝取足夠的蛋白質和必需脂肪；獲得您所需的維生素和礦物質；避免大腸桿菌等病原體以及汞或鉛等毒素。除此之外，我們完全確定的了解相對較少。請再讀一遍這句話。

Directionally, a lot of the old cliché expressions are probably right: If your great-grandmother would not recognize it, you're probably better off not eating it. If you bought it on the perimeter of the grocery store, it's probably better than if you bought it in the middle of the store. Plants are very good to eat. Animal protein is "safe" to eat. We evolved as omnivores; ergo, most of us can probably find excellent health as omnivores.

從方向上來說，許多古老的陳詞濫調可能是正確的：如果你的曾祖母不認識它，你最好不要吃它。如果您在雜貨店外圍購買，可能比在商店中間購買更好。植物非常適合食用。動物性蛋白質可以「安全」食用。我們進化為雜食動物；因此，作為雜食動物，我們大多數人可能擁有良好的健康狀況。

Don't get me wrong, I still have a lot to say—that's why these chapters on nutrition are not short. There is so much ideological bickering and utter bullshit out there that I hope to inject at least a little bit of clarity into the discussion. But most of this chapter and the next will be aimed at changing the way you *think* about diet and nutrition, rather than telling you to *eat this, not that*. My goal here is to give you the tools to help you find the right eating pattern for yourself, one that will make your life better by protecting and preserving your health.

不要誤會我的意思，我還有很多話要說——這就是為什麼這些關於營養的章節不短的原因。那裡有太多意識形態的爭吵和胡言亂語，我希望至少能在討論中注入一點清晰度。但本章和下一章的大部分内容旨在改變你對飲食和營養的看法，而不是告訴你要吃這個，而不是那個。我的目標是為您提供工具，幫助您找到適合自己的飲食模式，透過保護和維護您的健康來改善您的生活。

What We Sort of Know About Nutritional Biochemistry (and How We Sort of Know It)

我們對營養生物化學的了解（以及我們如何了解它）

One of my biggest frustrations in the area of nutrition—sorry, *nutritional biochemistry*—has to do with how little we actually know about it for certain. The problem is rooted in the poor quality of much nutrition research, which leads to bad reporting in the media, lots of arguing on social media, and rampant confusion among the public. What are we supposed to eat (and not eat)? What is the right diet for *you*?

我在營養領域（抱歉，營養生物化學）最大的挫折感之一是我們對它的了解實在太少了。這個問題的根源在於許多營養研究的品質低下，

導致媒體報導不佳、社交媒體上存在大量爭論以及公眾普遍的困惑。我們應該吃什麼（而不是吃什麼）？什麼是適合您的飲食？

If all we have to go on is media reporting about the latest big study from Harvard, or the wisdom of some self-appointed diet guru, then we will never escape this state of hopeless confusion. So before we delve into the specifics, it's worth taking a step back to try to understand what we do and don't know about nutrition—what kinds of studies might be worth heeding and which ones we can safely ignore. Understanding how to discern signal from noise is an important first step in coming up with our own plan.

如果我們要做的只是媒體報導哈佛大學最新的大型研究，或是一些自封的飲食大師的智慧，那麼我們將永遠無法擺脫這種無望的困惑狀態。因此，在我們深入研究具體細節之前，值得退一步嘗試了解我們對營養做了什麼和不了解什麼——哪些類型的研究可能值得關注，哪些我們可以安全地忽略。了解如何從噪音中辨別訊號是製定我們自己的計劃的重要的第一步。

Our knowledge of nutrition comes primarily from two types of studies: epidemiology and clinical trials. In epidemiology, researchers gather data on the habits of large groups of people, looking for meaningful associations or correlations with outcomes such as a cancer diagnosis, cardiovascular disease, or mortality. These epidemiological studies generate much of the diet “news” that pops up in our daily internet feed, about whether coffee is good for you and bacon is bad, or vice versa.

我們的營養知識主要來自兩種類型的研究：流行病學和臨床試驗。在流行病學中，研究人員收集大量人口的習慣數據，尋找與癌症診斷、心血管疾病或死亡率等結果的有意義的關聯或相關性。這些流行病學研究產生了我們日常網路上出現的大部分飲食“新聞”，關於咖啡是否對你有益而培根是否有害，反之亦然。

Epidemiology has been a useful tool for sleuthing out the causes of epidemics, including (famously) stopping a cholera outbreak in nineteenth-century London, and (less famously) saving boy chimney sweeps from an epidemic of scrotal cancer that turned out to be linked to their employment.

[*1] It has propelled some real public health triumphs, such as the advent of smoking bans and widespread treatment of drinking water. But in nutrition it has proved less insightful. Even at face value, the “associations” that nutritional epidemiologists come up with are often absurd: Will eating twelve hazelnuts every day *really* add two years to my lifespan, as one study suggested?[*2] I wish.

流行病學一直是找出流行病原因的有用工具，包括（著名的）阻止了十九世紀倫敦的霍亂爆發，以及（不太出名的）拯救掃煙囪的男孩免受陰囊癌流行的影響，而陰囊癌的流行與他們的就業。 [*1] 它推動了一些真正的公共衛生勝利，例如禁煙令的出現和飲用水的廣泛處理。但事實證明，在營養學方面，它的洞察力不夠。即使從表面上看，營養流行病學家提出的「關聯」也常常是荒謬的：每天吃十二個榛果真的會像一項研究表明的那樣讓我的壽命延長兩年嗎？ [*2] 我希望。

The problem is that epidemiology is incapable of distinguishing between correlation and causation. This, aided and abetted by bad journalism, creates confusion. For example, multiple studies have found a strong association between drinking diet sodas and abdominal fat, hyperinsulinemia, and cardiovascular risk. Sounds like diet soda is bad stuff that causes obesity, right? But that is not what those studies actually demonstrate, because they fail to ask an important question: Who drinks diet soda?

問題在於流行病學無法區分相關性和因果關係。在糟糕的新聞報導的幫助和慫恿下，這種情況造成了混亂。例如，多項研究發現飲用無糖汽水與腹部脂肪、高胰島素血症和心血管風險之間有密切關聯。聽起來無糖汽水是導致肥胖的壞東西，對吧？但這並不是這些研究實際證明的內容，因為它們沒有提出一個重要的問題：誰喝無糖汽水？

People who are concerned about their weight or their diabetes risk, that's who. They may drink diet soda *because* they are heavy, or worried about becoming heavy. The problem is that epidemiology is not equipped to determine the direction of causality between a given behavior (e.g., drinking diet soda) and a particular outcome (e.g., obesity) any more than one of my chickens is able to scramble the egg she has just laid for me.

那些關心自己體重或糖尿病風險的人就是這樣的人。他們可能因為體重過重而喝無糖汽水，或擔心自己會變重。問題在於，流行病學無法確定特定行為（例如喝無糖汽水）與特定結果（例如肥胖）之間的因果關係方向，就像我的一隻雞無法炒她剛剛吃的雞蛋一樣為我準備的。

To understand why, we must consult (again) Sir Austin Bradford Hill, a British scientist whom we met in chapter 11. Hill had helped sleuth out the link between smoking and lung cancer in the early 1950s, and he came up with nine criteria for evaluating the strength of epidemiological findings and determining the likely direction of causality, which we also referenced in regard to exercise.^[*3] The most important of these, and the one that can best separate correlation from causation, is the trickiest to implement in nutrition: experiment. Try proposing a study where you would test the effects of a lifetime of eating fast food by randomizing young boys and girls either to Big Macs or a non-fast-food diet. Even if you did somehow receive institutional review board approval for this terrible idea, there are a bunch of different ways in which even a simple experiment can go wrong. Some of the Big Mac kids might secretly go vegetarian, while the controls might decide to frequent the Golden Arches. The point is that humans are terrible study subjects for nutrition (or just about anything else) because we are unruly, disobedient, messy, forgetful, confounding, hungry, and complicated creatures.

為了理解其中的原因，我們必須（再次）諮詢奧斯汀·布拉德福德·希爾爵士（Sir Austin Bradford Hill），他是一位英國科學家，我們在第11章中遇到了他。希爾在20世紀50年代初幫助調查了吸煙與肺癌之間的聯繫，他提出了九個標準：評估流行病學發現的強度並確定因果關係的可能方向，我們在運動方面也提到了這一點。^[*3] 其中最重要的一項，也是最能區分相關性和因果關係的一項，也是營養學中最棘手的一項：實驗。嘗試提出一項研究，透過隨機分配年輕男孩和女孩吃巨無霸或非快餐飲食來測試一生吃快餐的影響。即使你確實以某種方式獲得了機構審查委員會對這個糟糕想法的批准，但即使是一個簡單的實驗也可能透過多種不同的方式出錯。有些巨無霸小孩可能會偷偷地吃素，而控制者可能會決定經常光顧金拱門。關鍵是，人類對於營養

學（或其他任何事物）來說都是一個糟糕的研究對象，因為我們是不守規矩、不聽話、凌亂、健忘、混亂、飢餓和複雜的生物。

This is why we rely on epidemiology, which derives data from observation and often from the subjects themselves. As we saw earlier, the epidemiology around exercise passes the Bradford Hill criteria with flying colors—but using epidemiology to study nutrition often flunks those tests miserably, beginning with the effect size, the power of the association, often expressed as a percentage. While the epidemiology of smoking (like exercise) easily passes the Bradford Hill tests because the effect size is so overwhelming, in nutrition the effect sizes are typically so small that they could easily be the product of other, confounding factors.

這就是我們依賴流行病學的原因，流行病學從觀察中獲取數據，通常來自受試者本身。正如我們之前所看到的，圍繞運動的流行病學出色地通過了布拉德福德希爾標準，但使用流行病學來研究營養通常會慘敗於這些測試，首先是效應大小，即通常以百分比表示的關聯強度。雖然吸煙（如運動）的流行病學很容易通過布拉德福德希爾測試，因為其影響大小是如此巨大，但在營養學中，影響大小通常很小，很容易成為其他混雜因素的產物。

Case in point: The claim that eating red meats and processed meats “causes” colorectal cancer. According to a very well-publicized 2017 study from the Harvard School of Public Health and the World Health Organization, eating those kinds of meats raises one’s risk of colon cancer by 17 percent ($HR = 1.17$). That does sound scary—but does it pass the Bradford Hill tests? I don’t think so, because the association is so weak. For comparison’s sake, someone who smokes cigarettes is at more like 1,000 to 2,500 percent (ten to twenty-five times) increased risk of lung cancer, depending on the population being studied. This suggests that there might actually be some sort of causation at work. Yet very few published epidemiological studies show a risk increase of even 50 percent ($HR = 1.50$) for any given type of food.

例證：食用紅肉和加工肉類「導致」大腸直腸癌的說法。根據哈佛大學公共衛生學院和世界衛生組織 2017 年一項廣為人知的研究，吃這些肉類會使人罹患結腸癌的風險增加 17%（ $HR = 1.17$ ）。這聽起來確實

很可怕，但它能通過布拉德福德山測試嗎？我不這麼認為，因為協會太弱了。為了進行比較，吸菸的人罹患肺癌的風險大約增加 1,000% 到 2,500%（十到二十五倍），具體取決於所研究的人群。這表明實際上可能存在某種因果關係。然而，很少有已發表的流行病學研究顯示，任何特定類型的食物的風險甚至會增加 50% (HR = 1.50)。

Second, and far more damning, is that the raw data on which these conclusions are typically based are shaky at best. Many nutritional epidemiological studies collect information on subjects via something called a “food frequency questionnaire,” a lengthy checklist that asks users to recall everything they ate over the last month, or even the last year, in minute detail. I’ve tried filling these out and it’s almost impossible to recall exactly what I ate two days ago, let alone three weeks.^[*4] So how reliable can studies based on such data possibly be? How much confidence do we have in, say, the red meat study?

其次，也是更嚴重的一點是，這些結論所依據的原始資料充其量也是不穩定的。許多營養流行病學研究透過所謂的「食物頻率問卷」收集受試者信息，這是一份冗長的清單，要求用戶詳細回憶上個月甚至去年吃的東西。我嘗試過填寫這些內容，但幾乎不可能準確地記得兩天前吃了什麼，更不用說三週了。[*4] 那麼基於這些數據的研究有多可靠呢？例如，我們對紅肉研究有多少信心？

So do red and processed meats actually cause cancer or not? We don’t know, and we will probably never get a more definitive answer, because a clinical trial testing this proposition is unlikely ever to be done. Confusion reigns. Nevertheless, I’m going to stick my neck out and assert that a risk ratio of 1.17 is so minimal that it might not matter that much whether you eat red/processed meats versus some other protein source, like chicken. Clearly, this particular study is very far from providing a definitive answer to the question of whether red meat is “safe” to eat. Yet people have been fighting about it for years.

那麼紅肉和加工肉類真的會致癌嗎？我們不知道，而且我們可能永遠不會得到更明確的答案，因為測試這個命題的臨床試驗不太可能進行。混亂盛行。儘管如此，我仍會堅持不懈地斷言，1.17 的風險比非

常小，因此無論您吃紅肉/加工肉還是吃其他蛋白質來源（例如雞肉），可能都沒有那麼重要。顯然，這項特殊的研究還遠遠沒有為紅肉是否「安全」食用的問題提供明確的答案。然而人們多年來一直在爭論這個問題。

This is another problem in the world of nutrition: too many people are majoring in the minor and minoring in the major, focusing too much attention on small questions while all but ignoring the bigger issues. Small variations in what we eat probably matter a lot less than most people assume. But bad epidemiology, aided and abetted by bad journalism, is happy to blow these things way out of proportion.

這是營養學界的另一個問題：太多人主修副修，輔修主修，過度關注小問題，而幾乎忽略了更大的問題。我們吃的東西的微小變化可能比大多數人想像的要小得多。但糟糕的流行病學在糟糕的新聞報導的幫助和慫恿下，很樂意把這些事情誇大到不成比例。

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Bad epidemiology so dominates our public discussion of nutrition that it has inspired a backlash by skeptics such as John Ioannidis of the Stanford Prevention Research Center, a crusader against bad science in all its forms. His basic argument is that food is so complex, made up of thousands of chemical compounds in millions of possible combinations that interact with human physiology in so many ways—in other words, nutritional biochemistry—that epidemiology is simply not up to the task of disentangling the effect of any individual nutrient or food. In an interview with the CBC, the normally soft-spoken Ioannidis was brutally direct: “Nutritional epidemiology is a scandal,” he said. “It should just go into the waste bin.”

糟糕的流行病學如此主導了我們對營養的公開討論，以至於引起了懷疑論者的強烈反對，例如斯坦福預防研究中心的約翰·約安尼迪斯

（John Ioannidis），他是反對一切形式的不良科學的鬥士。他的基本論點是，食物是如此複雜，由數以千計的化合物組成，有數百萬種可能的組合，它們以多種方式與人類生理相互作用（換句話說，營養生

物化學），以至於流行病學根本無法完成解開這一問題的任務。任何單一營養素或食物的作用。在接受加拿大廣播公司 (CBC) 採訪時，一向說話溫和的約安尼迪斯異常直接：「營養流行病學是一個醜聞，」他說。「它應該扔進垃圾桶。」

The true weakness of epidemiology, at least as a tool to extract reliable, causal information about human nutrition, is that such studies are almost always hopelessly confounded. The factors that determine our food choices and eating habits are unfathomably complex. They include genetics, social influences, economic factors, education, metabolic health, marketing, religion, and everything in between—and they are almost impossible to disentangle from the biochemical effects of the foods themselves.

流行病學的真正弱點，至少作為提取有關人類營養的可靠因果資訊的工具，是這樣的研究幾乎總是令人絕望地混淆。決定我們食物選擇和飲食習慣的因素極為複雜。它們包括遺傳、社會影響、經濟因素、教育、代謝健康、行銷、宗教以及介於兩者之間的一切——而且它們幾乎不可能與食物本身的生化效應分開。

A few years ago, a scientist and statistician named David Allison ran an elegant experiment that illustrates how epidemiological methods can lead us astray, even in the most tightly controlled research model possible: laboratory mice, which are genetically identical and housed in identical conditions. Allison created a randomized experiment using these mice, similar to the caloric restriction experiments we discussed in chapter 5. He split them into three groups, differing only in the quantity of food they were given: a low-calorie group, a medium-calorie group, and a high-calorie, *ad libitum* group of animals who were allowed to eat as much as they wanted. The low-calorie mice were found to live the longest, followed by medium-calorie mice, and the high-calorie mice lived the shortest, on average. This was the expected result that had been well established in many previous studies.

幾年前，一位名叫大衛·艾利森（David Allison）的科學家兼統計學家進行了一項巧妙的實驗，該實驗說明了流行病學方法如何使我們誤入歧途，即使是在控制最嚴格的研究模型中：實驗室小鼠，它們基因相同，飼養條件相同。艾利森使用這些小鼠進行了一項隨機實驗，類似

於我們在第5 章中討論的熱量限制實驗。他將它們分為三組，僅在給予食物的數量上有所不同：低熱量組、中熱量組，以及一組高熱量、隨意進食的動物，它們可以想吃多少就吃多少。研究發現，低熱量小鼠的平均壽命最長，其次是中熱量小鼠，高熱量小鼠的平均壽命最短。這是許多先前研究中已經確立的預期結果。

But then Allison did something very clever. He looked more closely at the high-calorie group, the mice with no maximum limit on food intake, and analyzed this group separately, as its own nonrandomized epidemiological cohort. Within this group, Allison found that some mice chose to eat more than others—and that these hungrier mice actually lived *longer* than the high-calorie mice who chose to eat less. This was exactly the opposite of the result found in the larger, more reliable, and more widely repeated randomized trial.

但隨後艾利森做了一件非常聰明的事情。他更仔細地觀察了高熱量組（食物攝取量沒有最大限制的小鼠），並單獨分析了該組，作為自己的非隨機流行病學隊列。在這一組中，艾利森發現有些老鼠選擇比其他老鼠吃得更多，而這些飢餓的老鼠實際上比選擇吃得少的高熱量老鼠活得更長。這與規模更大、更可靠、重複更廣泛的隨機試驗的結果恰恰相反。

There was a simple explanation for this: the mice that were strongest and healthiest had the largest appetites, and thus they ate more. Because they were healthiest to begin with, they also lived the longest. But if all we had to go on was Allison's epidemiological analysis of this particular subgroup, and not the larger and better-designed clinical trial, we might conclude that eating more calories causes *all* mice to live longer, which we are pretty certain is not the case.

對此有一個簡單的解釋：最強壯、最健康的老鼠胃口最大，因此它們吃得更多。因為他們本來就最健康，所以壽命也最長。但如果我們要做的只是艾利森對這個特定亞群的流行病學分析，而不是更大規模、設計更好的臨床試驗，我們可能會得出這樣的結論：吃更多的卡路里會導致所有小鼠壽命更長，我們非常確定這並不是唯一的結論。案例。

This experiment demonstrates how easy it is to be misled by epidemiology. One reason is because general health is a massive confounder in these kinds of studies. This is also known as healthy user bias, meaning that study results sometimes reflect the baseline health of the subjects more than the influence of whatever input is being studied—as was the case with the “hungry” mice in this study.^[*5]

這個實驗證明了流行病學是多麼容易被誤導。原因之一是，整體健康狀況是這類研究中的一個巨大的混雜因素。這也被稱為健康用戶偏見，這意味著研究結果有時更多地反映了受試者的基線健康狀況，而不是所研究的任何輸入的影響，就像本研究中「飢餓」小鼠的情況一樣。^[*5]

One classic example of this, I believe, lies in the vast, well-publicized literature correlating “moderate” drinking with improved health outcomes. This notion has become almost an article of faith in the popular media, but these studies are also almost universally tainted by healthy user bias—that is, the people who are still drinking in older age tend to do so *because* they are healthy, and not the other way around. Similarly, people who drink zero alcohol often have some health-related reason, or addiction-related reason, for avoiding it. And such studies also obviously exclude those who have already died of the consequences of alcoholism.

我認為，這方面的一個典型例子是大量廣為人知的文獻，這些文獻將「適度」飲酒與改善健康結果聯繫起來。這個概念幾乎已經成為大眾媒體的信條，但這些研究也幾乎普遍受到健康使用者偏見的影響——也就是說，老年仍在飲酒的人傾向於這樣做是因為他們很健康，而不是因為他們很健康。另一種方式。同樣，零飲酒的人通常有一些與健康相關的原因或與成癮相關的原因而避免飲酒。而這類研究顯然也排除了那些已經死於酗酒後果的人。

Epidemiology sees only a bunch of seemingly healthy older people who all drink alcohol and concludes that alcohol is the cause of their good health. But a recent study in *JAMA*, using the tool of Mendelian randomization we discussed back in chapter 3, suggests that this might not be true. This study found that once you remove the effects of other factors that may accompany

moderate drinking—such as lower BMI, affluence, and not smoking—any observed benefit of alcohol consumption completely disappears. The authors concluded that there is *no* dose of alcohol that is “healthy.”

流行病學只看到一群看似健康的老年人都喝酒，並得出結論認為酒精是他們健康的原因。但《美國醫學會雜誌》最近的一項研究使用了我們在第三章中討論過的孟德爾隨機化工具，表明這可能不是真的。這項研究發現，一旦消除了適度飲酒可能帶來的其他因素（例如較低的體重指數、富裕程度和不吸煙）的影響，任何觀察到的飲酒益處就會完全消失。作者的結論是，沒有任何劑量的酒精是「健康的」。

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Clinical trials would seem like a much better way to evaluate one diet against another: One group of subjects eats diet X, the other group is on diet Y, and you compare the results. (Or, to continue the alcohol example, one group drinks moderately, one group drinks heavily, and the control group abstains altogether.)

臨床試驗似乎是評估一種飲食與另一種飲食的更好方法：一組受試者吃 X 飲食，另一組吃 Y 飲食，然後比較結果。（或者，繼續酒精的例子，一組適度飲酒，一組大量飲酒，而對照組完全戒酒。）

These are more rigorous than epidemiology, and they offer some ability to infer causality thanks to the process of randomization, but they too are often flawed. There's a trade-off between sample size, study duration, and control. To do a long study in a large group of subjects, you essentially have to trust that they are following the prescribed diet, whether the Big Mac diet in our hypothetical example from above, or a simple low-fat diet. If you want to ensure that your subjects are actually eating the diet, you need to feed each subject, observe them eating, and keep them locked in the metabolic ward of a hospital (to be sure they are not eating anything else). All of this is doable, but only for a handful of subjects for a few weeks at a time, which is not nearly a large enough sample or long enough duration to infer anything beyond mechanistic insights about nutrients and health.

這些比流行病學更加嚴格，並且由於隨機化過程，它們提供了一些推斷因果關係的能力，但它們也經常存在缺陷。樣本量、研究持續時間和控制之間需要權衡。要對一大群受試者進行長期研究，你基本上必須相信他們遵循規定的飲食，無論是上面假設的例子中的巨無霸飲食，還是簡單的低脂飲食。如果你想確保你的受試者實際上正在吃飲食，你需要餵養每個受試者，觀察他們的飲食，並將他們鎖在醫院的代謝病房中（以確保他們不吃其他任何東西）。所有這些都是可行的，但僅限於一次持續幾週的少數受試者，這還不夠大的樣本或足夠長的持續時間，無法推斷出有關營養和健康的機械見解之外的任何內容。

These studies make pharmaceutical studies seem simple. Determining whether pill X lowers blood pressure enough to prevent heart attacks requires only that study subjects remember to take their pill every day for however many months or years, and even that simple compliance poses a challenge. Now imagine trying to ensure that study subjects lower their dietary fat content to no more than 20 percent of total calories and consume at least five servings of fruits and vegetables daily for a year. In fact, I'm convinced that compliance is the *key* issue in nutrition research, and with diets in general: Can you stick to it? The answer is different for almost everyone. This is why it's so difficult for experiments to answer the central questions about the relationship between diet and disease, no matter how big and ambitious they are.

這些研究讓藥物研究看起來很簡單。確定 X 藥是否能降低血壓足以預防心臟病發作，只需要研究對象記住每天服藥，持續數月或數年，即使是簡單的依從性也會構成挑戰。現在想像一下，試著確保研究對象將飲食脂肪含量降低至不超過總熱量的 20%，並且一年內每天至少食用五份水果和蔬菜。事實上，我堅信依從性是營養研究和一般飲食的關鍵問題：你能堅持嗎？幾乎每個人的答案都不同。這就是為什麼實驗很難回答有關飲食與疾病之間關係的核心問題，無論實驗規模有多大、雄心勃勃。

One classic example of a well-intended nutrition study that created more confusion than clarity is the Women's Health Initiative (WHI), an enormous

randomized controlled trial that was meant to test a low-fat, high-fiber diet in nearly fifty thousand women. Begun in 1993, it lasted eight years and cost nearly \$750 million (and if it sounds familiar, that is because of the study's highly publicized other arm, discussed earlier, which looked at the effects of hormone replacement therapy on older women). In the end, despite all this effort, the WHI found no statistically significant difference between the low-fat and control diet groups in terms of incidence of breast cancer, colorectal cancer, cardiovascular disease, or overall mortality.^[*6]

婦女健康倡議(WHI) 是一項善意的營養研究的一個典型例子，它造成的困惑多於清晰度，這是一項大型隨機對照試驗，旨在測試近5 萬名女性的低脂肪、高纖維飲食。這項研究從1993 年開始，歷時八年，耗資近7.5 億美元（如果聽起來很熟悉，那是因為該研究的另一部分廣為人知，如前所述，該部分研究激素替代療法對老年女性的影響）。最終，儘管付出了所有這些努力，WHI 發現低脂飲食組和對照飲食組在乳癌、大腸癌、心血管疾病或整體死亡率方面沒有統計上的顯著差異。^[*6]

Many people, myself included, argued that the results of this study demonstrated the lack of efficacy of low-fat diets. But in reality, it probably told us nothing about a low-fat diet because the “low-fat” intervention group consumed around 28 percent of their calories from fat, while the control group got about 37 percent of their calories from fat. (And that's even assuming the investigators were able to be remotely accurate in their assessment of what the subjects actually ate over the years, a big assumption.) So this study compared two diets that were pretty similar, and found that they had pretty similar outcomes. Big surprise. Nevertheless, flawed as it was, the WHI study has been fought over for years by partisans of different ways of eating.

許多人，包括我自己，都認為這項研究的結果顯示低脂飲食缺乏功效。但實際上，它可能沒有告訴我們任何有關低脂飲食的信息，因為「低脂」幹預組大約 28% 的卡路里來自脂肪，而對照組大約 37% 的卡路里來自脂肪。（甚至假設研究人員能夠遠端準確地評估受試者多年來的實際飲食，這是一個很大的假設。）因此，這項研究比較了兩

種非常相似的飲食，發現它們的結果非常相似。大驚喜。然而，儘管 WHI 研究有缺陷，但多年來，不同飲食方式的支持者一直在爭論這項研究。

Just as an aside, the WHI study does provide a clear example of why it is so important to evaluate any intervention, nutritional or otherwise, through the lens of *efficacy* versus *effectiveness*. Efficacy tests how well the intervention works under perfect conditions and adherence (i.e., if one does everything exactly as prescribed). Effectiveness tests how well the intervention works under real-world conditions, in real people. Most people confuse these and therefore fail to appreciate this nuance of clinical trials. The WHI was not a test of the efficacy of a low-fat diet for the simple reasons that (a) it failed to test an actual low-fat diet, and (b) study subjects did not adhere to the diet perfectly. So it can't be argued from the WHI that low-fat diets do not improve health, only that the *prescription* of a low-fat diet, in this population of patients, did not improve health. See the difference?

順便說一句，WHI 研究確實提供了一個明確的例子，說明為什麼從功效與效果的角度評估任何干預措施（無論是營養干預還是其他干預措施）如此重要。功效測試介入措施在完美條件和遵守情況下的效果（即，如果一個人完全按照規定做每件事）。有效性測試介入措施在現實條件下對真人的效果。大多數人混淆了這些，因此無法理解臨床試驗的細微差別。WHI 並不是對低脂飲食功效的測試，原因很簡單：(a) 它未能測試實際的低脂飲食，以及 (b) 研究對象沒有完全遵守飲食。因此，從 WHI 來看，不能說低脂飲食不能改善健康，只能說低脂飲食處方在該患者群體中並不能改善健康。看到不同？

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That said, some clinical trials have provided some useful bits of knowledge. One of the best, or least bad, clinical trials ever executed seemed to show a clear advantage for the Mediterranean diet—or at least, for nuts and olive oil. This study also focused on the role of dietary fats.

也就是說，一些臨床試驗提供了一些有用的知識。有史以來最好的（或最不壞的）臨床試驗之一似乎顯示出地中海飲食的明顯優勢，或至少是堅果和橄欖油的優勢。這項研究也關注飲食脂肪的作用。

The large Spanish study known as PREDIMED (PREvención con DIeta MEDiterránea) was elegant in its design: rather than telling the nearly 7,500 subjects exactly what they were supposed to eat, the researchers simply gave one group a weekly “gift” of a liter of olive oil, which was meant to nudge them toward other desired dietary changes (i.e., to eat the sorts of things that one typically prepares with olive oil). A second group was given a quantity of nuts each week and told to eat an ounce per day, while the control group was simply instructed to eat a lower-fat diet, with no nuts, no excess fat on the meat they did eat, no *sofrito* (a garlicky Spanish tomato sauce with onions and peppers that sounds delicious), and weirdly, no fish.

名為PREDIMED（PREvención con DIeta MEDiterránea）的西班牙大型研究的設計很優雅：研究人員並沒有告訴近7,500名受試者到底應該吃什麼，而是只是每週給一組受試者一份一公升橄欖的「禮物」油，這是為了推動他們進行其他所需的飲食改變（即吃人們通常用橄欖油準備的食物）。第二組每週給予一定量的堅果，並被告知每天吃一盎司，而對照組則簡單地被指示吃低脂飲食，不吃堅果，吃的肉上沒有多餘的脂肪，沒有sofrito（一種帶有大蒜味的西班牙番茄醬，配上洋蔥和辣椒，聽起來很美味），奇怪的是，沒有魚。

The study was meant to last six years, but in 2013 the investigators announced that they had halted it prematurely, after just four and a half years, because the results were so dramatic. The group receiving the olive oil had about a one-third lower incidence (31 percent) of stroke, heart attack, and death than the low-fat group, and the mixed-nuts group showed a similar reduced risk (28 percent). It was therefore deemed unethical to continue the low-fat arm of the trial. By the numbers, the nuts-or-olive-oil “Mediterranean” diet appeared to be as powerful as statins, in terms of number needed to treat (NNT), for primary prevention of heart disease—meaning in a population that had not yet experienced an “event” or a clinical diagnosis.^[*7]

這項研究本來要持續六年，但在 2013 年，研究人員宣布他們在短短四年半後就提前停止了這項研究，因為結果是如此引人注目。與低脂組相比，接受橄欖油的組別中風、心臟病和死亡的發生率降低了約三分之一（31%），而混合堅果組的風險也降低了約三分之一（28%）。因此，繼續進行低脂試驗被認為是不道德的。從數字來看，堅果或橄欖油「地中海」飲食似乎與他汀類藥物一樣有效，就需要治療的人數（NNT）而言，對於心臟病的一級預防來說，這意味著在尚未接受過他汀類藥物治療的族群中曾經歷過「事件」或臨床診斷。[*7]

It looked like a slam dunk; it's rare when investigators can report hard outcomes like death or heart attack, as opposed to simple weight loss, in a mere dietary study. It did help that the subjects already had at least three serious risk factors, such as type 2 diabetes, smoking, hypertension, elevated LDL-C, low HDL-C, overweight or obesity, or a family history of premature coronary heart disease. Yet despite their elevated risk, the olive oil (or nuts) diet had clearly helped them delay disease and death. A post hoc analysis of PREDIMED data also found cognitive improvement in those allocated the Mediterranean-style diet(s), versus cognitive decline in those allocated the low-fat diet.

看起來就像是灌籃；研究人員很少能在一項飲食研究中報告死亡或心臟病等嚴重後果，而不是簡單的體重減輕。受試者已經患有至少三種嚴重危險因素，如第2型糖尿病、吸菸、高血壓、低密度脂蛋白膽固醇升高、高密度脂蛋白膽固醇低、超重或肥胖，或早發冠心病家族史，這確實有幫助。然而，儘管風險較高，橄欖油（或堅果）飲食顯然幫助他們延緩了疾病和死亡。對 PREDIMED 數據的事後分析也發現，接受地中海飲食的人的認知能力有所改善，而接受低脂飲食的人的認知能力卻有所下降。

But does that mean a Mediterranean diet is right for everyone, or that extra-virgin olive oil is the healthiest type of fat? Possibly—but not necessarily.

但這是否意味著地中海飲食適合每個人，或者特級初榨橄欖油是最健康的脂肪類型？有可能——但不一定。

To me, perhaps the most vexing issue with diet and nutrition studies is the degree of variation between *individuals* that is found but often obscured. This is especially true in studies looking mostly or entirely at weight loss as an end point. The published studies report average results that are almost always underwhelming, subjects losing a few pounds on average. In reality, some individuals may have lost quite a bit of weight on the diet, while others lost none or even gained weight.

對我來說，也許飲食和營養研究中最令人煩惱的問題是個體之間的差異程度，這種差異被發現但常常被掩蓋。在大部分或完全以減重為終點的研究中尤其如此。已發表的研究報告的平均結果幾乎總是令人印象深刻，受試者平均減掉了幾磅。事實上，有些人可能透過節食減掉了不少體重，而有些人卻沒有減重，甚至體重增加。

There are two issues at play here. The first is compliance: how well can you stick to the diet? That differs for everyone; we all have different behaviors and thought patterns around food. The second issue is how a given diet affects you, with your individual metabolism and other risk factors. Yet these are too often ignored, and we end up with generalizations about how diets “don’t work.” What that really means is that diet X or diet Y doesn’t work for *everyone*.

這裡有兩個問題。第一個是依從性：你能在多大程度上堅持飲食？這對每個人來說都是不同的；我們對於食物都有不同的行為和思考模式。第二個問題是特定的飲食如何影響您，以及您的個人新陳代謝和其他風險因素。然而，這些往往被忽視，我們最終得出關於節食如何「不起作用」的概括。這實際上意味著 X 飲食或 Y 飲食並不適合所有人。

Our goal in the next chapter is to help you figure out the best eating plan for *you*, as an individual. To do that, we must move beyond labels and dive into nutritional biochemistry.

我們下一章的目標是幫助您找出最適合您個人的飲食計劃。為此，我們必須超越標籤，深入研究營養生物化學。

*1 Back in 1775, Percival Pott, an English surgeon, became the first person on record to demonstrate that cancer may be caused by an environmental factor (now known as a carcinogen). Pott noticed an increase in the number of cases of scrotal warts in young chimney boys, who were given the task of climbing inside chimneys to remove the ash and soot. Pott's investigations led him to the conclusion that the cause of this cancer—a squamous cell carcinoma of the skin—was particles of soot becoming lodged in the ridges of the scrotum.

*1 早在 1775 年，英國外科醫生 Percival Pott 就成為第一個證明癌症可能是由環境因素（現在稱為致癌物質）引起的人。波特注意到，年輕的煙囪男孩患有陰囊疣的病例增加，他們的任務是爬進煙囪內部清除煙灰和煙灰。波特的研究使他得出結論，這種癌症（皮膚鱗狀細胞癌）的原因是煙灰顆粒滯留在陰囊的脊部。

*2 According to a 2013 study by Bao et al., people who ate a dozen hazelnuts per day reduced their chances of dying in the next thirty years by 20 percent. (No word on the exact mechanism behind this miraculous outcome.)

*2 根據 Bao 等人 2013 年的研究，每天吃一打榛果的人在未來 30 年內的死亡幾率降低了 20%。（沒有說明這奇蹟般結果背後的确切機制。）

*3 The Bradford Hill criteria are (1) strength of the association (i.e., effect size), (2) consistency (i.e., reproducibility), (3) specificity (i.e., is it an observation of disease in a very specific population at a specific site, with no other likely explanation?), (4) temporality (i.e., does the cause precede the effect?), (5) dose response (i.e., does the effect get stronger with a higher dose?), (6) plausibility (i.e., does it make sense?), (7) coherence (i.e., does it agree with data from controlled experiments in animals?), (8) experiment (i.e. is there experimental evidence to back up the findings?), and (9) analogy (i.e., the effect of similar factors may be considered).

*3 Bradford Hill 標準是 (1) 關聯強度（即效應大小）、(2) 一致性（即再現性）、(3) 特異性（即是否是在特定人群中觀察到的疾病）一個特定的位點，沒有其他可能的解釋？），（4）暫時性（即原因是否先於效果？），（5）劑量反應（即劑量越高，效果是否會更強？），（6）合理性（即它有意義嗎？），（7）一致性（即它與動物對照實驗的數據一致嗎？），（8）實驗（即是否有實驗證據支持研究結果？），（9）類比（即可以考慮類似因素的影響）。

*4 If you'd like to try, Google "Food Frequency Questionnaire," and good luck to you.

*4 如果您想嘗試，請搜尋“食物頻率問卷”，祝您好運。

*5 I think healthy user bias is also the single biggest confounder in the exercise epidemiology literature. Healthy people tend to do more exercise in part because they are healthy.

*5 我認為健康的使用者偏見也是運動流行病學文獻中最大的混雜因素。健康的人往往會做更多的運動，部分原因是他們身體健康。

*6 While this study did not find a statistically significant difference in death from breast cancer at either the 8.5 or 16.1 year follow-up, it did find a statistically significant reduction in deaths from any cause

in those women diagnosed with breast cancer, but the difference in absolute risk was insignificant. At 8.5 years the reduction in deaths was 0.013% and at 16.5 years it was a mere 0.025%.

*6 雖然這項研究在8.5年或16.1年的隨訪中沒有發現乳腺癌死亡人數存在統計學上的顯著差異，但它確實發現被診斷患有乳腺癌的女性的任何原因導致的死亡人數在統計上顯著減少，但絕對風險差異不顯著。8.5年時死亡人數減少了0.013%，16.5年時僅0.025%。

[*7](#) In secondary prevention, statins tend to show a somewhat lower NNT. The PREDIMED study was later retracted and reanalyzed to correct for errors in randomization (that is, the subjects were not assigned a particular intervention on a truly random basis); the new analysis did not materially change the study's conclusions, however. In my opinion, the biggest problem with PREDIMED is something called *performance bias*, meaning subjects in the two treatment arms may have changed their behavior due to having more interaction with the investigators than the controls.

*7 在二級預防中，他汀類藥物往往表現出較低的NNT。PREDIMED研究後來被撤回並重新分析，以糾正隨機化中的錯誤（即，受試者沒有在真正隨機的基礎上被分配特定的干預措施）；然而，新的分析並沒有實質改變研究的結論。在我看來，PREDIMED的最大問題是所謂的表現偏差，這意味著兩個治療組的受試者可能因為與研究人員的互動比對照組更多而改變了他們的行為。

CHAPTER 15

第15章

Putting Nutritional Biochemistry into Practice

將營養生物化學付諸實踐

How to Find the Right Eating Pattern for You

如何找到適合您的飲食模式

My doctor told me to stop having intimate dinners for
four. Unless there are three other people.

我的醫生告訴我不要再吃四人份的親密晚餐。除
非還有另外三個人。

—ORSON WELLES

——奧森威爾斯

Most of my patients are already on some sort of “diet” when they come to me. One thing that almost all of them have in common is that they are dissatisfied with the results.

我的大多數患者來找我時已經在進行某種「節食」。他們幾乎所有人的一個共同點就是對結果不滿意。

I can empathize. During residency, when I was actually even fatter than Not-Thin Peter, I tried a vegan diet for a while. Theoretically, going vegan should have made it easy to lose weight, simply because you have to chew your way through an awful lot of salad to match the caloric content of a ribeye. But in reality, I was taking most of my meals in the hospital, so that meant a lot of chips and other snacks, and a veggie sub every day for lunch. I didn't lose a single freaking pound in six months. Looking back, the problem should have been obvious. While I was technically following a virtuous “vegan” diet, I was basically eating a bunch of junk food that just didn't happen to contain animal products. In other words, I was on a vegan version of the SAD, the Standard American Diet.

我能感同身受。在實習期間，當我實際上比不瘦的彼得還胖時，我嘗試了一段時間的純素飲食。從理論上講，成為素食主義者應該很容易減肥，因為你必須咀嚼大量的沙拉才能與肋眼牛排的熱量含量相匹配。但實際上，我的大部分餐點都是在醫院吃的，所以這意味著每天午餐要吃很多薯條和其他零食，以及素食替代品。六個月內我一磅都沒減。回想起來，問題應該是顯而易見的。雖然從技術上講我遵循的是良性的「素食」飲食，但我基本上吃的是一堆垃圾食品，而這些垃圾食品恰好不含動物產品。換句話說，我吃的是純素版的 SAD（美國標準飲食）。

Even going vegan is not enough to free you from the clutches of the SAD. It is our default food environment, occupying the middle of the grocery store: the boxed and frozen and bagged bounty of an agricultural system that produces subsidized corn, flour, sugar, and soybeans by the megaton. On one level, it's brilliant, a solution to four problems that have plagued humanity since the beginning: (1) how to produce *enough* food to feed almost everyone;

(2) how to do so *inexpensively*; (3) how to *preserve* that food so it can be stored and transported safely; and (4) how to make it highly *palatable*. If you optimize for all four of these characteristics, you're pretty much guaranteed to end up with the SAD, which is not so much a diet as a business model for how to feed the world efficiently. Two cheers for modern industrial food systems.

即使成為素食主義者也不足以讓你擺脫季節性情緒失調的魔掌。這是我們預設的食品環境，佔據了雜貨店的中間：農業系統的盒裝、冷凍和袋裝豐富品，生產百萬噸級的補貼玉米、麵粉、糖和大豆。從某種程度上來說，它非常出色，它解決了自誕生以來一直困擾人類的四個問題：（1）如何生產足夠的食物來養活幾乎每個人；（2）如何生產足夠的食物來養活幾乎所有人；（3）如何以低廉的成本做到這一點；（4）如何保存該食品以便安全儲存和運輸；（5）如何使其味道鮮美。如果你針對所有這四個特徵進行最佳化，那麼你幾乎肯定會最終得到 SAD，這與其說是一種飲食，不如說是一種如何有效養活世界的商業模式。為現代工業食品系統歡呼兩聲。

But notice that a fifth criterion is missing: how to *make it harmless*. The SAD was not specifically intended to do harm, of course. The fact that it does harm most of us, if consumed in excess, is a consequence of the four points above colliding with millions of years of evolution that have optimized us to be highly efficient fat-storage vehicles. It is an unfortunate externality of its business model, sort of like with cigarettes. Tobacco manufacturers set out to make a lot of money from a plentiful agricultural commodity, but the solution they devised, the cigarette, had an unfortunate side effect: it slowly killed the customer.

但請注意，缺少第五個標準：如何使其無害。當然，SAD 並不是專門為了造成傷害。事實上，如果攝取過量，它確實會對我們大多數人造成傷害，這是上述四點與數百萬年進化相衝突的結果，這些進化使我們成為高效的脂肪儲存工具。這是其商業模式的一個不幸的外部性，有點像香菸。菸草製造商打算從豐富的農產品中賺很多錢，但他們設計的解決方案——捲菸——產生了不幸的副作用：它慢慢地殺死了顧客。

The elements that constitute the SAD are almost as devastating to most

people as tobacco when consumed in large quantities, as intended: added sugar, highly refined carbohydrates with low fiber content, processed oils, and other very densely caloric foods. I should note that this does not mean *all* “processed” foods are bad. Almost everything we eat, aside from fresh vegetables, is processed to some degree. For example, cheese is a processed food, invented as a way to preserve milk, which would otherwise spoil quickly without refrigeration. What we’re really talking about, when we talk about the SAD, is *junk* food.

構成 SAD 的元素對大多數人來說幾乎與大量食用菸草一樣具有破壞性：添加糖、低纖維含量的高度精製碳水化合物、加工油和其他熱量非常高的食物。我應該指出，這並不意味著所有「加工」食品都是不好的。除了新鮮蔬菜之外，我們吃的幾乎所有東西都經過一定程度的加工。例如，起司是一種加工食品，是為了保存牛奶而發明的，否則牛奶如果不冷藏就會很快變質。當我們談論悲傷時，我們真正談論的是垃圾食物。

The basic problem we face is that, for perhaps the first time in human history, ample calories are available to many if not most people on the planet. But evolution has not prepared us for this situation. Nature is quite happy for us to be fat and frankly doesn’t care if we get diabetes. Thus, the SAD foils our key objectives with regard to nutrition: it induces us to eat more than we need to, becoming overnourished, while its preponderance of low-quality, ultraprocessed ingredients tends to displace other nutrients that we need, such as protein, to maintain optimal health.

我們面臨的基本問題是，這也許是人類歷史上第一次，地球上的許多人（如果不是大多數人）都可以獲得充足的卡路里。但進化並沒有讓我們為這種情況做好準備。大自然很高興我們發胖，坦白說，它並不關心我們是否會患上糖尿病。因此，SAD 挫敗了我們在營養方面的關鍵目標：它導致我們吃得比我們需要的多，導致營養過剩，而其大量的低品質、超加工成分往往會取代我們需要的其他營養素，例如蛋白質、以保持最佳健康狀態。

The SAD disrupts the body’s metabolic equilibrium. It places enormous strain on our ability to control our blood glucose levels, and causes us to store

fat when we should be utilizing it. The leading source of calories that Americans consume is a category called “grain-based desserts,” like pies, cakes, and cookies, according to the US Department of Agriculture. That is our *number one* “food group.” If we consume a bunch of grain-based desserts in a Cheesecake Factory binge, our blood glucose levels will surge. And if we do it over and over and over again, as we saw in previous chapters, we will eventually overwhelm our ability to handle all those calories in a safe way. The SAD essentially wages war on our metabolic health, and, given enough time, most of us will lose the war.

SAD 破壞了身體的代謝平衡。它給我們控制血糖水平的能力帶來了巨大的壓力，並導致我們在應該利用脂肪的時候儲存脂肪。根據美國農業部的數據，美國人消耗的卡路里的主要來源是一種稱為「穀物甜點」的類別，例如派、蛋糕和餅乾。這是我們排名第一的「食物組」。如果我們在起司蛋糕工廠狂吃一堆穀物甜點，我們的血糖水平就會飆升。如果我們一次又一次地這樣做，正如我們在前幾章中看到的那樣，我們最終將壓垮我們以安全方式處理所有這些卡路里的能力。SAD 本質上是對我們的代謝健康發動戰爭，如果有足夠的時間，我們大多數人都會輸掉這場戰爭。

The farther away we get from the SAD, the better off we will be. This is the common goal of most “diets”—to help us break free of the powerful gravitational pull of the SAD so that we can eat less, and hopefully eat better. But eating less is the primary aim. Once you strip away the labels and the ideology, almost all diets rely on at least one of the following three strategies to accomplish this:

我們離 SAD 越遠，我們的生活就越好。這是大多數「節食」的共同目標——幫助我們擺脫 SAD 的強大引力，這樣我們就可以吃得更少，並有望吃得更好。但少吃是首要目標。一旦去掉標籤和意識形態，幾乎所有飲食都至少依賴以下三種策略之一來實現這一目標：

1. CALORIC RESTRICTION, or CR: eating less in total, but without attention to what is being eaten or when it's being eaten

熱量限制（CR）：整體吃得較少，但不注意吃什麼或何時吃

2. DIETARY RESTRICTION, or DR: eating less of some particular element(s) within the diet (e.g., meat, sugar, fats)

飲食限制 (DR)：減少飲食中某些特定元素的攝取（例如肉、糖、脂肪）

3. TIME RESTRICTION, or TR: restricting eating to certain times, up to and including multiday fasting

時間限制 (TR)：將進食限制在特定時間，最多包括多日禁食

In other words, if you are overnourished, and statistically speaking about two-thirds of us are, you will need to apply at least one of these methods of caloric reduction: deliberately tracking (and reducing) what you eat; cutting out certain foods; and/or giving yourself less time in which to eat. That's it. Breaking down our approach to nutrition to these three strategies allows us to speak about dietary interventions more objectively, instead of relying on labels such as “low-fat” or “Mediterranean” that don't tell us very much. If we modify none of these variables—eating whatever we want, whenever we want, in as great a quantity as we want—we end up right back at the SAD.

換句話說，如果您營養過剩（從統計數據來看，大約有三分之二的人營養過剩），您將需要應用至少一種減少熱量的方法：刻意追蹤（並減少）您吃的東西；戒掉某些食物；和/或減少自己吃飯的時間。就是這樣。將我們的營養方法分解為這三種策略，使我們能夠更客觀地談論飲食幹預措施，而不是依賴「低脂」或「地中海」等不能告訴我們太多資訊的標籤。如果我們不改變這些變數中的任何一個——無論什麼時候想吃什麼，想吃多少就吃多少——我們最終就會回到SAD。

Each of these approaches has its pros and cons, as I've observed over a decade of working on nutrition issues with countless patients. These will be covered in more detail below, but here is the tl;dr:

正如我十多年來與無數患者一起解決營養問題所觀察到的那樣，這些方法都有其優點和缺點。以下將更詳細地介紹這些內容，但這裡是

tl;dr:

1. From the standpoint of pure efficacy, CR or caloric restriction is the winner, hands down. This is how bodybuilders shed weight while holding on to muscle mass, and it also allows the most flexibility with food choices. The catch is that you have to do it perfectly—tracking every single thing you eat, and not succumbing to the urge to cheat or snack—or it doesn't work. Many people have a hard time sticking with it.

從純粹功效的角度來看，CR 或熱量限制無疑是贏家。這就是健美運動員在保持肌肉質量的同時減輕體重的方法，而且它還可以在食物選擇上提供最大的靈活性。問題是你必須做得完美——記錄你吃的每一樣東西，而不是屈服於作弊或吃零食的衝動——否則它就不起作用。很多人都很難堅持下去。

2. DR or dietary restriction is probably the most common strategy employed for reducing energy intake. It is conceptually simple: pick a type of food, and then don't eat that food. It only works, obviously, if that food is both plentiful and significant enough that eliminating it will create a caloric deficit. Saying you're going on the "no lettuce" diet is pretty much doomed to fail. And you can still overeat while adhering perfectly to a particular DR, as I found out when I attempted to go vegan.

DR 或飲食限制可能是減少能量攝取最常用的策略。概念上很簡單：選擇一種食物，然後不吃那種食物。顯然，只有當這種食物既充足又足夠重要以至於消除它會造成熱量赤字時，它才有效。說你要進行「不吃生菜」的飲食幾乎注定會失敗。當我完全遵守特定的飲食方案時，你仍然可能吃得太多，正如我在嘗試素食時發現的那樣。

3. TR or time restriction—also known as intermittent fasting—is the latest trend in ways to cut calories. In some ways I think it's the easiest. When I was a cyclist, and I was trying to drop that six final pounds from my already very light (for me) frame, this became my jam. I would allow myself only one meal per day, despite doing about three hours per day of

training. But this can still backfire if you overeat. I have, much to my amusement, watched patients gain weight on a one-meal-a-day approach by turning their meal into a contest to see who could eat the most pizza and ice cream. But the more significant downside of this approach is that most people who try it end up very protein deficient (we'll cover protein needs later in this chapter). One not uncommon scenario that we see with TR is that a person loses weight on the scale, but their body composition alters for the worse: they lose lean mass (muscle) while their body fat stays the same or even increases.

TR 或時間限制（也稱為間歇性斷食）是減少卡路里攝取量的最新趨勢。從某些方面來說，我認為這是最簡單的。當我還是自行車手時，我試圖從我已經很輕的（對我來說）身體中減掉最後六磅，這成了我的果醬。儘管每天訓練大約三個小時，但我每天只吃一餐。但如果你吃得過多，這仍然會適得其反。令我感到非常有趣的是，我看到患者透過每天一餐的方法增加體重，將他們的餐點變成一場比賽，看誰能吃最多的披薩和冰淇淋。但這種方法更顯著的缺點是，大多數嘗試這種方法的人最終都會嚴重缺乏蛋白質（我們將在本章後面介紹蛋白質需求）。我們在TR中看到的一種並不罕見的情況是，一個人在體重計上體重減輕了，但他們的身體組成卻發生了更糟的變化：他們失去了瘦體重（肌肉），而身體脂肪卻維持不變甚至增加。

These three approaches are what we'll spend the rest of the chapter exploring, beginning with the most important: how much we eat.

我們將在本章的其餘部分中探討這三種方法，從最重要的開始：我們吃多少。

CR: Calories Matter

CR: 卡路里很重要

I may be starting to sound like a broken record, but it should be obvious by now that many of the problems we want to address or avoid stem from consuming calories in excess of what we can use or safely store. If we take in more energy than we require, the surplus ends up in our adipose tissue, one way or another. If this imbalance continues, we exceed the capacity of our “safe” subcutaneous fat tissue, and excess fat spills over into our liver, our viscera, and our muscles, as we discussed in chapter 6.

我可能開始聽起來像是破紀錄了，但現在應該很明顯，我們想要解決或避免的許多問題都源於消耗的卡路里超過了我們可以使用或安全儲存的卡路里。如果我們攝取的能量多於我們需要的能量，多餘的能量最終會以某種方式進入我們的脂肪組織。如果這種不平衡持續下去，我們就會超越「安全」皮下脂肪組織的容量，多餘的脂肪就會溢出到我們的肝臟、內臟和肌肉中，正如我們在第 6 章中討論的那樣。

How many calories you consume has a huge impact on everything else we're talking about in this book. If you're ingesting one thousand extra calories a day, of anything, you're going to have problems sooner or later. In prior chapters, we've seen how excess calories contribute to many chronic diseases, not only metabolic disorders but also heart disease, cancer, and Alzheimer's disease. We also know from decades of experimental data (chapter 5) that eating *fewer* calories tends to lengthen lifespan, at least in lab animals such as rats and mice—although there is debate over whether this represents true lifespan extension or an elimination of the known hazards of overfeeding, the default state of the control animals in most of these experiments. (And also, of many modern humans.)

你消耗的卡路里量對我們在本書中討論的其他一切都有巨大的影響。如果你每天攝取一千卡路里的額外熱量，那麼你遲早會遇到問題。在前面的章節中，我們已經了解了過多的熱量如何導致許多慢性疾病，不僅是代謝紊亂，還包括心臟病、癌症和阿茲海默症。我們也從數十年的實驗數據（第 5 章）中得知，攝取較少的卡路里往往會延長壽命，至少在大鼠和小鼠等實驗動物中是如此，儘管這是否代表真正的壽命延長或已知危害的消除存在爭議過度餵養，這是大多數實驗中對照動物的預設狀態。（而且，對於許多現代人來說也是如此。）

In human beings, as opposed to laboratory animals, caloric restriction typically goes by a different name: *calorie counting*. There is plenty of research showing that people who count their calories and limit them can and do lose weight, the primary end point of such studies. This is how Weight Watchers works. The biggest obstacles to doing this successfully are first of all hunger and second the requirement that you track what you eat in meticulous detail. The apps that help you do this today are better than ten years ago, but it's still not easy. For the right person, this approach works incredibly well—it's a favorite of bodybuilders and athletes—but for many, the requirement of constant tracking makes it unfeasible.

與實驗動物不同，在人類中，熱量限制通常有一個不同的名稱：熱量計數。有大量研究表明，計算卡路里並限制卡路里的人可以而且確實減肥，這是此類研究的主要終點。這就是慧儷輕體的運作方式。成功做到這一點的最大障礙首先是飢餓，其次是要求你詳細記錄你吃的東西。如今幫助您做到這一點的應用程式比十年前更好，但這仍然不容易。對於合適的人來說，這種方法效果非常好 - 它是健美運動員和運動員的最愛 - 但對於許多人來說，持續追蹤的要求使其不可行。

One slight advantage is that calorie counting is agnostic to food choices; you can eat whatever you want so long as you stay within your daily allowance. But if you make too many poor decisions, you will be very hungry, so buyer beware. You can lose weight on a restricted-calorie diet consisting only of Snickers bars, but you will feel much better if you opt for steamed broccoli and chicken breasts instead.

一個小小的優點是卡路里計算與食物選擇無關。只要不超出每天的攝取量，您就可以吃任何您想吃的東西。但如果你做出太多錯誤的決定，你就會非常飢餓，所以買家要小心。您可以透過僅包含士力架的限制熱量飲食來減肥，但如果您選擇蒸西蘭花和雞胸肉，您會感覺好多了。

There has been a long-running controversy over whether caloric restriction could or should be applied to humans as a tool to enhance longevity. It did seem to work for Luigi Cornaro, the dieting Italian gentleman from the sixteenth century—he claimed to have lived to one hundred, although he was

probably actually in his eighties when he died. This supposed longevity benefit is, obviously, a difficult proposition to study in human beings over the long term, for some of the reasons I've just outlined. So the hypothesis was tested in monkeys, in two long-running primate studies. The results were so surprising that they are still being debated.

關於熱量限制是否可以或應該應用於人類作為延長壽命的工具一直存在爭議。這對十六世紀節食的意大利紳士路易吉·科納羅（Luigi Cornaro）來說似乎確實有效——他聲稱自己活了一百歲，儘管他去世時實際上可能已經八十多歲了。顯然，出於我剛才概述的一些原因，從長遠來看，這種所謂的長壽益處是一個很難在人類身上進行研究的命題。因此，這個假設在兩項長期靈長類動物研究中在猴子身上得到了檢驗。結果如此令人驚訝，以至於仍在爭論中。

In July of 2009, a study published in *Science* found that rhesus monkeys that had been fed a reduced-calorie diet for more than two decades had lived markedly longer than those who were allowed to eat freely. “Dieting Monkeys Offer Hope for Living Longer,” declared the headline on the front page of *The New York Times*. The accompanying photos told the story: on the left was a monkey named Canto, looking trim and spry at the relatively advanced age of twenty-seven, while on the right sat Owen, just two years older but looking like Canto's flabby, dissipated uncle. Canto had been on a calorically restricted diet for most of his life, while Owen had eaten just about as much food as he wanted.

2009年7月，發表在《科學》雜誌上的一項研究發現，二十多年來一直被餵食低熱量飲食的恒河猴比那些自由進食的恒河猴壽命明顯更長。

《紐約時報》頭版的標題是「節食猴子帶來了長壽的希望」。隨附的照片講述了這個故事：左邊是一隻名叫坎託的猴子，二十七歲了，看上去身材苗條、精神抖擻；右邊坐著歐文，只比坎託大兩歲，但看起來就像坎託鬆弛、放蕩的叔叔。坎託一生中大部分的時間都在限制熱量飲食，而歐文幾乎想吃多少就吃多少。

Owen and Canto were two of seventy-six monkeys in this study, begun two decades earlier at the University of Wisconsin–Madison. Half of the monkeys (the control group) were fed *ad libitum*, meaning they could eat as much food

as they wanted, while the other half were placed on a “diet” allowing them about 25 percent fewer calories than the controls. They then lived out their lives as the researchers observed them growing older.

歐文和坎托是這項研究中的 76 隻猴子中的兩隻，這項研究是二十年前在威斯康辛大學麥迪遜分校開始的。一半的猴子（對照組）隨意餵食，這意味著它們可以想吃多少食物就吃多少，而另一半則進行“節食”，使它們比對照組減少約 25% 的卡路里。然後，當研究人員觀察到他們逐漸變老時，他們就度過了自己的一生。

Aging studies tend to be about as exciting as watching paint dry, but the end results were pretty dramatic. In the end, the calorically restricted monkeys lived significantly longer and proved far less likely to die of age-related diseases than the *ad libitum*-fed control monkeys. They were healthier by many other measures, such as insulin sensitivity. Even their brains were in better shape than those of the controls, retaining more gray matter as they aged. “These data demonstrate that caloric restriction slows aging in a primate species,” the study authors concluded.

老化研究往往與觀察油漆乾燥一樣令人興奮，但最終結果卻相當引人注目。最終，與隨意餵食的對照組猴子相比，熱量限制猴子的壽命明顯更長，並且死於與年齡相關的疾病的可能性要小得多。透過許多其他衡量標準，例如胰島素敏感性，他們更加健康。甚至他們的大腦也比對照組更好，隨著年齡的增長，保留了更多的灰質。研究作者總結道：“這些數據表明，熱量限制可以減緩靈長類動物的衰老。”

Case closed, or so it seemed.

案子結束了，或者看起來是這樣。

Three years later, in August 2012, another monkey study made the front page of the *Times*, but with a markedly different headline: “Severe Diet Doesn’t Prolong Life,” the paper declared grimly, adding, “At Least in Monkeys.” This study, also begun in the 1980s, was conducted under the auspices of the National Institute on Aging, one of the National Institutes of Health, and the study design was nearly identical to the Wisconsin study, with one group of monkeys being fed about 25 to 30 percent less than the other.

Yet the NIH researchers found that their calorically restricted monkeys had *not* lived longer than the controls. There was no statistically significant difference in the lifespans of the two groups. From a headline writer's point of view, caloric restriction had not "worked."

三年後，即2012年8月，另一項猴子研究登上了《泰晤士報》頭版，但標題明顯不同：“嚴格飲食不會延長壽命”，該報冷酷地宣稱，並補充道，“至少在猴子身上是這樣。”這項研究也是在20世紀80年代開始的，是在美國國立衛生研究院之一的國家老化研究所的贊助下進行的，研究設計幾乎與威斯康辛州的研究相同，其中一組猴子被餵食約25%比其他產品低30%。然而，美國國立衛生研究院的研究人員發現，他們的熱量限制猴子並沒有比對照組猴子活得更長。兩組的壽命沒有統計上的顯著差異。從頭條新聞作者的角度來看，熱量限制並沒有「發揮作用」。

Journalists love it when a study contradicts whatever the last well-publicized study said. In the small world of people who study aging, the NIH results caused consternation. Everyone had expected that the NIH monkey study would confirm the results seen in Wisconsin. Now it appeared as if the two research teams had spent tens of millions of dollars in federal grant money to demonstrate that caloric restriction lengthens monkey lifespans in Wisconsin but not in Maryland, where the NIH monkeys were kept.

當一項研究與上一次廣為人知的研究所說的話相矛盾時，記者們就會喜歡它。在研究老化的人們的小世界裡，美國國立衛生研究院的結果引起了震驚。每個人都預計美國國立衛生研究院的猴子研究將證實威斯康辛州的結果。現在看來，這兩個研究小組似乎花費了數千萬美元的聯邦撥款來證明熱量限制可以延長威斯康辛州猴子的壽命，但不能延長美國國立衛生研究院猴子飼養地馬裡蘭州的壽命。

But sometimes science tells us more when an experiment "fails" than when it yields the expected results, and so it was with the monkeys. When examined side by side, the two monkey studies had some seemingly minor differences that turned out to be hugely significant—and very pertinent to our strategy as well. Together, the dueling monkey studies constitute one of the most rigorous experiments ever done about the complex relationship between nutrition and

long-term health. And like many of the best scientific experiments, this one happened at least partly by accident.

但有時科學告訴我們的更多是當實驗「失敗」時，而不是當它產生預期結果時，猴子就是如此。當並排檢查時，這兩項猴子研究有一些看似微小的差異，但結果卻非常重要——而且也與我們的策略非常相關。總之，決鬥猴子的研究構成了迄今為止關於營養與長期健康之間複雜關係的最嚴格的實驗之一。和許多最好的科學實驗一樣，這項實驗的發生至少有部分是偶然的。

The most profound difference between the two studies was also the most fundamental, for a diet study: the food that the monkeys ate. The Wisconsin animals ate an off-the-shelf commercial monkey chow that was “semipurified,” meaning its ingredients were highly processed and rigorously titrated. The NIH monkeys were fed a diet that was similar in its basic macronutrient profile, but their chow was “natural” and less refined, custom formulated from whole ingredients by an in-house primate nutritionist at NIH. The most glaring contrast: while the NIH monkey chow contained about 4 percent sugar, the Wisconsin diet comprised an astonishing 28.5 percent sucrose, by weight. That is a greater proportion of sugar than you’ll find in vanilla Häagen-Dazs ice cream.

對於飲食研究來說，這兩項研究之間最深刻的差異也是最基本的：猴子吃的食物。威斯康辛州的動物吃的是現成的「半純化」商業猴糧，這意味著其成分經過高度加工和嚴格滴定。NIH 的猴子被餵食的飲食在基本大量營養素方面相似，但它們的食物是「天然」的，不太精煉，是由 NIH 內部靈長類營養師用完整成分定製配製的。最明顯的對比是：以重量計算，NIH 猴糧含有約 4% 的糖，而威斯康辛州的飲食中蔗糖含量高達 28.5%。這比哈根達斯香草冰淇淋中的糖含量還要高。

Could that alone have explained the difference in survival outcomes? Possibly: more than 40 percent of the Wisconsin control monkeys, the ones not subject to calorie limitations, developed insulin resistance and prediabetes, while just one in seven of the NIH controls became diabetic.^[*1] And the Wisconsin control monkeys proved far more likely to die from cardiovascular

causes and cancer than monkeys from any other group. This could suggest that caloric restriction was eliminating early deaths because of the bad Wisconsin diet more than it was actually slowing aging—which is still useful information, as avoiding diabetes and related metabolic disorders is important to our strategy.

光是這一點就能解釋生存結果的差異嗎？可能是：超過 40% 的威斯康辛州對照組猴子（不受熱量限制的猴子）出現了胰島素抗性和糖尿病前期，而 NIH 對照組中只有七分之一患有糖尿病。[*1] 事實證明，威斯康辛州對照組猴子比任何其他群體的猴子更有可能死於心血管原因和癌症。這可能表明，熱量限制消除了由於威斯康辛州糟糕的飲食習慣而導致的過早死亡，而不是實際上減緩了衰老——這仍然是有用的信息，因為避免糖尿病和相關的代謝紊亂對我們的策略很重要。

The Wisconsin researchers defended their diet as more similar to what Americans actually eat, which is a fair point. The comparison is not exact by any means, but in human terms the Wisconsin monkeys were more or less living on fast food, while the NIH monkeys were eating at the salad bar. The Wisconsin control monkeys ate the most calories, of the worst food, and their health suffered. Makes sense; if your diet consists mostly of cheeseburgers and milkshakes, then eating fewer cheeseburgers and milkshakes is going to help you.

威斯康辛州的研究人員辯稱，他們的飲食更接近美國人的實際飲食，這是一個公平的觀點。這種比較無論如何都不準確，但從人類的角度來看，威斯康辛州的猴子或多或少都是靠快餐生活的，而國立衛生研究院的猴子則在沙拉吧吃飯。威斯康辛州的對照組猴子吃了最多的卡路里、最糟糕的食物，它們的健康受到了影響。說得通；如果您的飲食主要由起司漢堡和奶昔組成，那麼少吃起司漢堡和奶昔會對您有所幫助。

The NIH diet was much higher in quality. Instead of ultraprocessed ingredients like corn oil and cornstarch (another 30 percent of the Wisconsin diet), the NIH monkey chow contained ground whole wheat and corn, and thus more phytochemicals and other possibly beneficial micronutrients like those typically found in fresh food. While not exactly natural, it was at least

closer to what rhesus monkeys would actually eat in the wild. So giving the NIH monkeys more or less of that feed may have had less of an impact because the diet was not as harmful to begin with. Upshot: the *quality* of your diet may matter as much as the *quantity*.

NIH 的飲食品質要高得多。NIH 猴糧不含玉米油和玉米澱粉（威斯康辛州飲食的另外30%）等超加工成分，而是含有磨碎的全麥和玉米，因此含有更多的植物化學物質和其他可能有益的微量營養素，如新鮮食品中常見的營養素。雖然不完全是天然的，但它至少更接近恒河猴在野外實際吃的東西。因此，給國立衛生研究院的猴子提供或多或少的這種飼料可能產生的影響較小，因為這種飲食一開始就沒有那麼有害。結論：飲食的品質可能與數量一樣重要。

Taken together, then, what do these two monkey studies have to tell us about nutritional biochemistry?

那麼，綜合起來，這兩項猴子研究能夠告訴我們有關營養生物化學的什麼資訊呢？

1. Avoiding diabetes and related metabolic dysfunction—especially by eliminating or reducing junk food—is very important to longevity.

避免糖尿病和相關的代謝功能障礙——尤其是透過消除或減少垃圾食物——對長壽非常重要。

2. There appears to be a strong link between calories and cancer, the leading cause of death in the control monkeys in both studies. The CR monkeys had a 50 percent lower incidence of cancer.

卡路里與癌症之間似乎存在密切聯繫，而癌症是兩項研究中對照猴子死亡的主要原因。CR 猴子的癌症發生率降低了 50%。

3. The *quality* of the food you eat could be as important as the *quantity*. If you're eating the SAD, then you should eat much less of it.

您所吃食物的品質與數量一樣重要。如果你吃的是 SAD，那你應該少吃一點。

4. Conversely, if your diet is high quality to begin with, and you are metabolically healthy, then only a slight degree of caloric restriction—or simply not eating to excess—can still be beneficial.

相反，如果您的飲食一開始就是高品質的，並且您的新陳代謝健康，那麼只需輕微程度的熱量限制 - 或者只是不吃過量 - 仍然是有益的。

I think this last point is key. These two studies suggest that if you are eating a higher-quality diet—and are metabolically healthy to begin with—then severe caloric restriction may not even be necessary. The NIH control monkeys ate as much as they wanted of their better diet and *still* lived nearly as long as the CR monkeys in both studies. Interestingly, the post facto analyses also revealed that the NIH control monkeys naturally consumed about 10 percent fewer calories per day than the Wisconsin controls, likely because their higher-quality diet left them feeling less hungry. The researchers speculated that even this very slight degree of caloric reduction may have been significant—certainly, it supports our thesis that it is better to avoid being overnourished.

我認為最後一點是關鍵。這兩項研究表明，如果您的飲食品質較高，且新陳代謝一開始就健康，那麼嚴格的熱量限制可能就沒有必要。在這兩項研究中，NIH 對照組的猴子想吃多少就吃多少，但它們的壽命仍然與 CR 猴子幾乎一樣長。有趣的是，事後分析還顯示，NIH 對照組的猴子每天消耗的熱量自然比威斯康辛州對照組的猴子少 10% 左右，這可能是因為它們的高品質飲食讓它們感覺不那麼飢餓。研究人員推測，即使是這種非常輕微的熱量減少也可能是顯著的——當然，它支持了我們的論點，即最好避免營養過剩。

Note that these study results do *not* suggest that everyone needs to undertake a drastic, severe reduction in caloric intake. Limiting calories can be helpful for people who are metabolically unhealthy and/or overnourished. But I'm not convinced that whatever longevity boost long-term, deep caloric restriction may confer is worth some of the trade-offs—including potentially weakened immunity and greater susceptibility to cachexia and sarcopenia

(muscle loss), not to mention constant hunger. These unwanted side effects would accelerate some of the negative processes that already go along with aging, suggesting that in older people especially, caloric restriction might do more harm than good.

請注意，這些研究結果並不能表明每個人都需要大幅減少熱量攝取。限制卡路里對於代謝不健康和/或營養過剩的人很有幫助。但我不相信，無論長期、深度熱量限制可能帶來的長壽效果如何，都值得做出一些權衡——包括潛在的免疫力減弱、更容易患惡病質和肌少症（肌肉減少），更不用說持續的飢餓了。這些不必要的副作用會加速一些已經伴隨老化而來的負面過程，這表明特別是對於老年人來說，熱量限制可能弊大於利。

The monkeys teach us that if you are metabolically healthy and not over-nourished, like the NIH animals, then avoiding a crap diet may be all you need. Some of the NIH CR monkeys ended up with some of the longest lifespans ever recorded in rhesus monkeys. It seems quite clear, then, that even for monkeys, limiting caloric intake *and* improving diet quality “works”—it’s how you pull it off that is tricky. As we’ll see in the next section, there are many other strategies we can adopt to limit the calories we consume and to tailor our food consumption to suit our metabolism and way of life.

猴子告訴我們，如果你新陳代謝健康並且沒有營養過剩，就像美國國立衛生研究院的動物一樣，那麼避免垃圾飲食可能就是你所需要的。一些 NIH CR 猴子的壽命達到了恒河猴有史以來最長的壽命。那麼，似乎很清楚，即使對於猴子來說，限制熱量攝取和改善飲食品質也是「有效的」——關鍵是如何實現它，這很棘手。正如我們將在下一節中看到的，我們可以採取許多其他策略來限制我們消耗的卡路里並調整我們的食物消耗以適應我們的新陳代謝和生活方式。

DR: The Nutritional Biochemistry “Diet”

DR: 營養生化“飲食”

Dietary restriction (DR) represents the land of conventional “diets,” where 90 percent of the attention—and research funding, and energy, and anger, and, of course, arguing—over nutritional biochemistry is focused. But it is pretty simple, when you get down to it: identify one or more bogeymen in your nutrition world, such as wheat gluten (for example), and exclude it. The more ubiquitous the bogeyman, the more restrictive the “diet,” and the more likely you are to reduce your overall caloric intake. Even if you decided to eat nothing but potatoes, you would still lose weight, because a human being can only choke down so many potatoes in a day. I’ve seen people do this, and it works. The hard part is figuring out *what* foods to eliminate or restrict.

飲食限制 (DR) 代表了傳統「飲食」領域，其中 90% 的注意力（以及研究經費、精力、憤怒，當然還有關於營養生物化學的爭論）都集中在這一領域。但當你認真對待它時，它非常簡單：識別你的營養世界中的一個或多個怪物，例如小麥麩質（例如），並將其排除。惡魔越普遍，「飲食」就越嚴格，你就越有可能減少整體熱量攝取。即使你決定只吃土豆，你仍然會減肥，因為一個人一天只能吞下這麼多土豆。我看過有人這麼做，而且很有效。困難的部分是弄清楚要消除或限制哪些食物。

This wasn’t an issue for our ancestors. There is ample evidence to suggest that they were opportunistic omnivores, out of necessity. They ate anything and everything they could get their hands on: lots of plants, lots of starch, animal protein whenever they could, honey and berries whenever possible. They also seemed to be, at least on the basis of the study of the few remaining hunter-gatherer societies, very metabolically healthy.

對我們的祖先來說，這不是問題。有充分的證據表明，出於必要，他們是機會主義的雜食動物。他們吃任何他們能得到的東西：大量的植物、大量的澱粉、盡可能的動物蛋白、盡可能的蜂蜜和漿果。至少根據對僅存的少數狩獵採集社會的研究來看，他們的新陳代謝似乎也非常健康。

Should we do the same? Should we be opportunistic omnivores eating anything and everything we can get our hands on? That’s how evolution has formed us, but our modern food environment makes it a little too easy to find

food. Thus, being overnourished and metabolically unhealthy is now commonplace. We have too many choices and too many delicious ways to take calories into our body. Hence the need for dietary restriction. We need to erect walls around what we can and cannot (or should not) eat.

我們也應該這樣做嗎？我們是否應該成為機會主義的雜食動物，吃任何我們能得到的東西？這就是進化形成我們的方式，但我們現代的食物環境讓尋找食物變得有點太容易了。因此，營養過剩和代謝不健康現在已經很常見了。我們有太多的選擇和太多美味的方式來將卡路里攝入體內。因此需要限制飲食。我們需要在我們能吃和不能（或不應該）吃的東西周圍築起圍牆。

The advantage of DR is that it is highly individualized; you can impose varying degrees of restriction, depending on your needs. For example, you could decide to eliminate all sugar-sweetened beverages, and that would be a great first step (and a relatively easy one). You could go a step further and quit drinking sweet fruit juices as well. You could quit eating other foods with added sugar. Or you could go as far as reducing or eliminating carbohydrates in general.

DR的優點是個性化程度高；您可以根據您的需求施加不同程度的限制。例如，您可以決定消除所有含糖飲料，這將是很好的第一步（也是相對容易的一步）。您還可以更進一步，停止喝甜果汁。您可以停止吃其他添加糖的食物。或者你可以盡量減少或消除一般碳水化合物。

One reason carbohydrate restriction is so effective for many people is that it tends to reduce appetite as well as food choices. But some people have a harder time maintaining it than others. (Even I am pretty sure I could never go back to a ketogenic diet for more than a few days.) While fat restriction also limits food choices, it can be less effective at reducing appetite if you pick the wrong low-fat foods to eat (e.g., high-carb junk food). If you consume most of your carbohydrates in the form of Fruit Loops, for example, you will still be very hungry all the time.

碳水化合物限制對許多人如此有效的原因之一是它往往會減少食慾和食物選擇。但有些人比其他人更難維持它。（即使我很確定我不可能再回到生酮飲食超過幾天。）雖然脂肪限制也限制了食物的選擇，但如果你選擇了錯誤的低脂食物，它在降低食慾方面可能會不太有效（例如，高碳水化合物垃圾食物）。例如，如果您以水果圈的形式消耗大部分碳水化合物，您仍然會一直很餓。

A major risk with DR is that you can still easily end up overnourished if you are not deliberate about it. People tend to (erroneously) assume you can't eat too much if you're just restricting *fill-in-the-blank* (e.g., carbohydrates). This is incorrect. Even if done correctly and strictly, DR can still result in overnutrition. If you cut out carbohydrates altogether but overdo it on the Wagyu steaks and bacon, you will fairly easily find yourself in a state of caloric excess. The key is to pick a strategy to which you can adhere but that also helps achieve your goals. This takes patience, some willpower, and a willingness to experiment.

DR 的一個主要風險是，如果您不慎重考慮，您仍然很容易營養過剩。如果你只是限制填空（例如碳水化合物），人們往往（錯誤地）認為你不能吃太多。這是不正確的。即使正確且嚴格地進行，DR 仍然會導致營養過剩。如果你完全不吃碳水化合物，但過量食用和牛牛排和培根，你很容易就會發現自己處於熱量過剩的狀態。關鍵是選擇一個你可以堅持但也有助於實現你的目標的策略。這需要耐心、一定的意志力和嘗試的意願。

We also want to be sure we're not compromising our other goals along the way. Any form of DR that restricts protein, for example, is probably a bad idea for most people, because it likely also impairs the maintenance or growth of muscle. Similarly, replacing carbohydrates with lots of saturated fats can backfire if it sends your apoB concentration (and thus your cardiovascular disease risk) sky-high.

我們還希望確保在此過程中不會損害我們的其他目標。例如，任何形式的限制蛋白質的 DR 對大多數人來說可能都是一個壞主意，因為它也可能損害肌肉的維持或生長。同樣，用大量飽和脂肪代替碳水化合

物可能會適得其反，如果它會使您的 apoB 濃度（從而導致您的心血管疾病風險）極高。

A more significant issue with DR is that everyone's metabolism is different. Some people will lose tremendous amounts of weight and improve their metabolic markers on a low-carbohydrate or ketogenic diet, while others will actually gain weight and see their lipid markers go haywire—on the exact same diet. Conversely, some people might lose weight on a low-fat diet, while others will gain weight. I have seen this happen time and again in my own practice, where similar diets yield very different outcomes, depending on the individual.

DR 的一個更重要的問題是每個人的新陳代謝都不同。有些人在低碳水化合物或生酮飲食中會減掉大量體重，並改善代謝指標，而有些人實際上會在完全相同的飲食中增加體重，並看到他們的脂質指標失控。相反，有些人透過低脂飲食可能會減肥，而有些人則會體重增加。我在自己的實踐中一次又一次地看到這種情況發生，相似的飲食會產生截然不同的結果，這取決於個人。

For example, when my patient Eduardo came to see me a few years ago with what turned out to be a case of full-blown type 2 diabetes, cutting his carbohydrate intake was clearly the way to go. Type 2 diabetes is a condition of impaired carbohydrate metabolism, after all. From the outside, Eduardo seemed like a pretty healthy guy, with a soccer player's build and a physical job in construction. He certainly did not fit the (bogus) stereotype of the lazy, gluttonous diabetic. But tests showed that he had almost no ability to store excess sugar that he consumed. His hemoglobin A1c was 9.7 percent, well into the diabetic red zone. Being Latino meant that Eduardo was at a higher risk of NAFLD and diabetes to begin with, thanks to his genes. He wasn't even forty, but unless we did something drastic, he more than likely was going to die a painful and early death.

例如，幾年前，當我的病人愛德華多 (Eduardo) 來找我時，他發現自己患有嚴重的 2 型糖尿病，減少碳水化合物的攝取量顯然是正確的選擇。畢竟，2 型糖尿病是碳水化合物代謝受損的疾病。從外表上看，愛德華多看起來是一個非常健康的人，有著足球員的體格和建築業的

體力工作。他當然不符合人們對懶惰、貪吃的糖尿病患者的（虛假的）刻板印象。但測試表明，他幾乎沒有能力儲存他消耗的多餘糖分。他的糖化血紅素為 9.7%，完全處於糖尿病紅色區域。由於愛德華多的基因，身為拉丁裔意味著他患 NAFLD 和糖尿病的風險更高。他還不到四十歲，但除非我們採取一些激烈的行動，否則他很可能會痛苦而早逝。

The obvious first step was to wean Eduardo off carbohydrates almost entirely. No more tortillas, rice, or starchy beans—and no Gatorade, either. Because he worked outside in the heat, he was pounding about three or four liters of “sports drinks” each day. I never once described this diet as “ketogenic,” and Eduardo certainly wasn’t telling the guys on the job site about his new trendy keto diet. He just wasn’t drinking Gatorade anymore. (I also put him on the diabetes drug metformin, which is cheap as well as effective.) Within about five months, Eduardo’s markers had all normalized, and his diabetes seemed to have been reversed; his hemoglobin A1c was now a completely normal 5.3 percent, just thanks to dietary changes and metformin. And along the way he lost about twenty-five pounds. I’m not saying this diet was the only possible path to this result, but this relatively simple and achievable form of DR created enough of an energy imbalance that he lost weight, and everything else improved in lockstep.

顯而易見的第一步是讓 Eduardo 幾乎完全戒掉碳水化合物。不再有玉米餅、米飯或澱粉豆，也不再有佳得樂。由於他在炎熱的室外工作，他每天要喝大約三到四公升的「運動飲料」。我從來沒有把這種飲食描述為“生酮”，愛德華多當然也沒有告訴工作現場的人他新流行的生酮飲食。他只是不再喝佳得樂了。（我還讓他服用了糖尿病藥物二甲雙胍，這種藥物既便宜又有效。）大約五個月內，Eduardo 的指標全部恢復正常，他的糖尿病似乎也得到了逆轉；他的病情似乎得到了改善。由於飲食的改變和二甲雙胍的幫助，他的糖化血紅蛋白現在完全正常，為 5.3%。一路上他減掉了大約二十五磅。我並不是說這種飲食是實現這一結果的唯一可能途徑，但這種相對簡單且可實現的 DR 形式造成了足夠的能量不平衡，使他體重減輕了，而其他一切都同步改善。

In the past, I was a huge proponent of ketogenic diets, finding them particularly useful to manage or prevent diabetes in patients like Eduardo. I also like that they have a strict definition, unlike “low carb” or “low fat.” A ketogenic diet means restricting carbohydrates to such an extent that the body begins metabolizing fat into “ketone bodies” that the muscles and brain can utilize as fuel. A ketogenic diet helped fix Not-Thin Peter, and it had likely saved Eduardo’s life. I thought it was the medicine that every metabolically unhealthy person needed.

過去，我是生酮飲食的大力支持者，發現它們對於控制或預防像愛德華多這樣的患者的糖尿病特別有用。我還喜歡它們有嚴格的定義，不像“低碳水化合物”或“低脂肪”。生酮飲食意味著限制碳水化合物的攝取量，使身體開始將脂肪代謝成“酮體”，肌肉和大腦可以將其用作燃料。生酮飲食幫助修復了不瘦的彼得，而且很可能挽救了愛德華多的生命。我認為這是每個代謝不健康的人都需要的藥物。

But my patients brought me back to earth, as they so often do. As a physician, one often receives feedback in a very direct, personal way. If I give someone a medication or a recommendation, I will find out pretty quickly whether it is working. It’s not “data” in the strict sense, but it can be equally powerful. I’ve had more than one patient for whom a ketogenic diet has completely failed. They didn’t lose weight, and their liver enzymes and other biomarkers failed to improve. Or they found it impossible to sustain. I’ve had other patients who were able to stick to the diet, but then their lipid numbers (especially their apoB) went through the roof, probably because of all the saturated fats they were eating.

但我的病人把我帶回了現實，就像他們經常做的那樣。作為一名醫生，人們經常以非常直接、個人化的方式收到回饋。如果我給某人藥物或建議，我很快就會發現它是否有效。它不是嚴格意義上的“數據”，但它同樣強大。我有不只一位生酮飲食完全失敗的患者。他們的體重沒有減輕，肝臟酵素和其他生物標記也沒有改善。或者他們發現無法維持下去。我遇過其他能夠堅持這種飲食的患者，但隨後他們的血脂數值（尤其是 apoB）卻急劇上升，這可能是因為他們吃的都是飽和脂肪。

At the time, this confused me. What was wrong with them? Why couldn't they just follow the diet correctly? I had to remind myself of what Steve Rosenberg used to say when a patient's cancer progressed despite treatment: *The patient has not failed the treatment; the treatment has failed the patient.*

當時，這讓我很困惑。他們出了什麼問題？為什麼他們不能正確遵循飲食呢？我必須提醒自己，史蒂夫·羅森伯格（Steve Rosenberg）在患者的癌症經過治療後仍出現進展時常說的話：患者並沒有失敗，而是治療失敗了。治療使病人失敗了。

These patients needed a different treatment.

這些患者需要不同的治療。

The real art to dietary restriction, Nutrition 3.0–style, is not picking which evil foods we're eliminating. Rather, it's finding the best mix of macronutrients for our patient—coming up with an eating pattern that helps them achieve their goals, in a way that they can sustain. This is a tricky balancing act, and it requires us (once again) to forget about labels and viewpoints and drill down into nutritional biochemistry. The way we do this is by manipulating our four macronutrients: alcohol, carbohydrates, protein, and fat. How well do you tolerate carbohydrates? How much protein do you require? What sorts of fats suit you best? How many calories do you require each day? What is the optimal combination *for you*?

營養 3.0 風格的飲食限制的真正藝術不是選擇我們要消除哪些有害食物。相反，它是為我們的患者找到最佳的常量營養素組合——提出一種飲食模式，幫助他們以一種能夠維持的方式實現他們的目標。這是一個棘手的平衡行為，它要求我們（再次）忘記標籤和觀點，深入研究營養生物化學。我們做到這一點的方法是控制四種常量營養素：酒精、碳水化合物、蛋白質和脂肪。您對碳水化合物的耐受程度如何？你需要多少蛋白質？哪種脂肪最適合您？您每天需要多少卡路里？最適合您的組合是什麼？

Let's now look at each of the four macronutrients in more detail.

現在讓我們更詳細地了解四種常量營養素中的每一種。

Alcohol

酒精

It's easy to overlook, but alcohol should be considered as its own category of macronutrient because it is so widely consumed, it has such potent effects on our metabolism, and it is so calorically dense at 7 kcal/g (closer to the 9 kcal/g of fat than the 4 kcal/g of both protein and carbohydrate).

這很容易被忽視，但酒精應該被視為自己的常量營養素類別，因為它的消費如此廣泛，它對我們的新陳代謝有如此強大的影響，而且它的熱量密度如此之高，為7 kcal/g（接近9 kcal/g）。g 脂肪比4 kcal/g 蛋白質和碳水化合物）。

Alcohol serves no nutritional or health purpose but is a purely hedonic pleasure that needs to be managed. It's especially disruptive for people who are overnourished, for three reasons: it's an "empty" calorie source that offers zero nutrition value; the oxidation of ethanol delays fat oxidation, which is the exact opposite of what we want if we're trying to lose fat mass; and drinking alcohol very often leads to mindless eating.

酒精沒有營養或健康的目的，而是純粹的享樂，需要加以控制。對於營養過剩的人來說，這尤其具有破壞性，原因有三：它是一種「空」的卡路里來源，營養價值為零；乙醇的氧化會延遲脂肪的氧化，這與我們想要減少脂肪量的情況恰恰相反；飲酒常常會導致無意識的飲食。

While I certainly enjoy an occasional glass of my favorite Belgian beer, Spanish red wine, or Mexican tequila (never in the same sitting, obviously), I also believe that drinking alcohol is a net negative for longevity. Ethanol is a potent carcinogen, and chronic drinking has strong associations with Alzheimer's disease, mainly via its negative effect on sleep, but possibly via additional mechanisms. Like fructose, alcohol is preferentially metabolized in the liver, with well-known long-term consequences in those who drink to excess. Last, it loosens inhibitions around other kinds of food consumption;

give me a few drinks, and the next thing you know I'm elbow-deep in the Pringles can as I pace around the pantry looking for my next snack.

雖然我確實喜歡偶爾喝一杯我最喜歡的比利時啤酒、西班牙紅酒或墨西哥龍舌蘭酒（顯然，我從來沒有在同一個地方喝過），但我也相信飲酒對長壽有淨負面影響。乙醇是一種強效致癌物，長期飲酒與阿茲海默症有密切關係，主要是透過其對睡眠的負面影響，但也可能透過其他機制。與果糖一樣，酒精優先在肝臟中代謝，過量飲酒會產生眾所周知的長期後果。最後，它放鬆了其他食物消費的限制。給我喝幾杯，接下來你知道的，當我在食品儲藏室裡踱步尋找下一份零食時，我已經深陷品客薯片罐頭了。

There have been numerous well-publicized studies suggesting that moderate levels of alcohol consumption can be beneficial, for example by improving endothelial function and reducing clotting factors, both of which would reduce cardiovascular disease risk. But heavier drinking tends to reverse those effects. And as shown by the Mendelian randomization study in *JAMA* that we talked about in the previous chapter, “moderate drinking” is so confounded by healthy user bias that it is impossible to put much faith in these studies purporting to show a health benefit for drinking.

有大量廣為人知的研究表明，適量飲酒是有益的，例如可以改善內皮功能和減少凝血因子，這兩者都可以降低心血管疾病的風險。但大量飲酒往往會扭轉這些影響。正如我們在上一章中討論的《美國醫學會雜誌》中的孟德爾隨機化研究所表明的那樣，“適度飲酒”被健康的用戶偏見所混淆，以至於人們不可能對這些聲稱顯示飲酒對健康有益的研究抱持太大的信心。

Nevertheless, for many of my patients, the lifestyle around moderate drinking (e.g., a nice glass of wine with a non-SAD dinner) helps them dissipate stress. My personal bottom line: if you drink, try to be mindful about it. You'll enjoy it more and suffer fewer consequences. Don't just keep drinking because they're serving it on the plane. I strongly urge my patients to limit alcohol to fewer than seven servings per week, and ideally no more than two on any given day, and I manage to do a pretty good job adhering to this rule myself.

然而，對於我的許多患者來說，適度飲酒的生活方式（例如，在非悲傷的晚餐中喝一杯好酒）可以幫助他們緩解壓力。我個人的底線是：如果你有喝酒，請盡量小心。你會更享受它並承受更少的後果。不要因為飛機上提供飲料就繼續喝酒。我強烈敦促我的患者將飲酒量限制在每週七份以下，最好每天不超過兩份，而我自己也很好地遵守了這項規則。

Carbohydrates

碳水化合物

The balance of our nonalcohol diet consists of carbohydrates, protein, and fat, and it's largely a job of finding the right mix for you as an individual. In the days of labeled diets, we would assemble our macronutrients and sort out the different types of foods, using rules and arbitrary boundaries—you can eat this, but not that; these, but not those. We would basically be guessing at the right mix. And then we would wait to see whether it “worked,” typically defined in terms of whether the person lost weight over a period of weeks or months. Now we have more sophisticated ways of looking at macronutrients, beginning with the most abundant: carbohydrates.

我們的無酒精飲食的平衡由碳水化合物、蛋白質和脂肪組成，這在很大程度上是為您個人找到合適的組合的工作。在標籤飲食時代，我們會使用規則和任意界限來組合常量營養素並分類不同類型的食物——你可以吃這個，但不能吃那個；你可以吃這個，但不能吃那個；你可以吃這個，但不能吃那個；你可以吃這個，但不能吃那個；這些，但不是那些。我們基本上會猜測正確的組合。然後我們會等著看它是否“有效”，通常是根據一個人是否在幾週或幾個月內減肥來定義。現在，我們有更複雜的方法來看待常量營養素，從最豐富的碳水化合物開始。

Carbs probably create more confusion than any other macro. They are neither “good” nor “bad”—although some types are better than others. Overall, it's more a question of matching dose to tolerance and demand, which

is much less tricky than it used to be. Thanks to advancements in technology, we no longer need to guess; we now have data.

碳水化合物可能比任何其他宏更容易造成混亂。它們既不是「好」也不是「壞」——儘管有些類型比其他類型更好。總的來說，這更多的是一個將劑量與耐受性和需求相匹配的問題，這比以前要簡單得多。由於技術的進步，我們不再需要猜測；我們現在有數據了。

Carbohydrates are our primary energy source. In digestion, most carbohydrates are broken down to glucose, which is consumed by all cells to create energy in the form of ATP. Excess glucose, beyond what we need immediately, can be stored in the liver or muscles as glycogen for near-term use or socked away in adipose tissue (or other places) as fat. This decision is made with the help of the hormone insulin, which surges in response to the increase in blood glucose.

碳水化合物是我們主要的能量來源。在消化過程中，大多數碳水化合物會分解為葡萄糖，所有細胞都會消耗葡萄糖以產生 ATP 形式的能量。超出我們立即所需的多餘葡萄糖可以作為肝醣儲存在肝臟或肌肉中以供近期使用，或作為脂肪儲存在脂肪組織（或其他地方）中。這個決定是在胰島素激素的幫助下做出的，胰島素會隨著血糖的升高而激增。

We already know that it's not good to consume excessive calories. In the form of carbohydrates, those extra calories can cause a multitude of problems, from NAFLD to insulin resistance to type 2 diabetes, as we saw in chapter 6. We know that elevated blood glucose, over a long enough period of time, amplifies the risk of all the Horsemen. But there is also evidence suggesting that repeated blood glucose spikes, and the accompanying rise(s) in insulin, may have negative consequences in and of themselves.

我們已經知道攝取過多的熱量是不好的。以碳水化合物的形式，這些額外的熱量會導致多種問題，從NAFLD 到胰島素抗性再到2 型糖尿病，正如我們在第6 章中看到的那樣。我們知道，在足夠長的時間內，血糖升高會放大所有騎士的風險。但也有證據表明，反覆的血糖高峰以及隨之而來的胰島素升高本身可能會產生負面後果。

Each person will respond differently to an influx of glucose. Too much glucose (or carbohydrate) for one person might be barely enough for another. An athlete who is training or competing in high-level endurance events might easily take in—and burn up—six hundred or eight hundred grams of carbohydrates per day. If I consumed that much now, day to day, it would probably render me a diabetic within a year. So how much is too much? And what about quality? Obviously that piece of pie is going to affect an endurance athlete differently from a sedentary person—and the pie will also have a different effect than a baked potato or french fries.

每個人對葡萄糖的流入都會有不同的反應。對一個人來說太多的葡萄糖（或碳水化合物）可能對另一個人來說幾乎不夠。正在訓練或參加高水平耐力賽事的運動員每天可能會輕鬆攝取並燃燒六百或八百克碳水化合物。如果我現在每天消耗這麼多，可能會在一年內讓我患上糖尿病。那麼多少才算太多呢？那麼質量呢？顯然，這塊餡餅對耐力運動員的影響與久坐的人不同，而且餡餅的效果也與烤土豆或炸薯條不同。

Now we have a tool to help us understand our own individual carbohydrate tolerance and how we respond to specific foods. This is called continuous glucose monitoring, or CGM, and it has become a very important part of my armamentarium in recent years.^[*2]

現在我們有一個工具可以幫助我們了解我們自己的碳水化合物耐受性以及我們對特定食物的反應。這稱為連續血糖監測（CGM），近年來它已成為我的裝備中非常重要的一部分。^[*2]

The device consists of a microscopic filament sensor that is implanted in the upper arm, attached to a fingertip-sized transmitter that sends data^[*3] to the patient's phone in real time. As its name suggests, CGM gives continuous, real-time information on blood glucose levels, which is extraordinary: the patient can see, moment by moment, how their blood sugar levels are responding to whatever they eat, whether a doughnut, a steak, or a handful of Raisinets. More importantly, it also keeps track of glucose levels over time, capturing historical averages and variance, and registering each and every time that blood glucose spikes upward or crashes downward.

該裝置由植入上臂的微型燈絲感測器組成，連接到指尖大小的發射器，將資料 [*3] 即時發送到患者的手機。顧名思義，CGM 提供有關血糖水平的連續、實時信息，這是非凡的：患者可以時時刻刻看到他們的血糖水平如何響應他們所吃的任何食物，無論是甜甜圈、牛排、或一把葡萄乾。更重要的是，它還可以追蹤一段時間內的血糖水平，捕獲歷史平均值和方差，並記錄每次血糖飆升或下降的情況。

CGM represents a huge improvement over the Medicine 2.0 standard of one fasting glucose test per year, which in my opinion tells you almost nothing of value. Think back to my self-driving cars analogy from Part I: fasting blood glucose, annually, does tell us something, but it's not too far from strapping a brick to the gas pedal. With CGM, you start to approximate the sensors currently found on cars with elaborate driver-assistance tools.

CGM 代表了醫學 2.0 標準（每年一次空腹血糖測試）的巨大進步，在我看來，這幾乎沒有告訴你任何有價值的資訊。回想一下我在第一部分中對自動駕駛汽車的類比：每年的空腹血糖確實告訴我們一些東西，但這與在油門踏板上綁一塊磚相差不遠。透過 CGM，您可以開始使用複雜的駕駛員輔助工具來模擬目前汽車上的感測器。

The power of CGM is that it enables us to view a person's response to carbohydrate consumption in real time and make changes rapidly to flatten the curve and lower the average. Real-time blood glucose serves as a decent proxy for the insulin response, which we also look to minimize. And, last, I find that it is much more accurate, and more actionable, than HbA1c, the traditional blood test used to estimate average blood glucose over time.

CGM 的強大之處在於，它使我們能夠即時查看一個人對碳水化合物消耗的反應，並迅速做出改變以拉平曲線並降低平均值。即時血糖可以作為胰島素反應的良好指標，我們也希望將其最小化。最後，我發現它比 HbA1c（用於估計一段時間內平均血糖的傳統血液檢查）更準確，也更可操作。

At the moment, CGM is available only by prescription and is most commonly worn by patients diagnosed with type 1 or type 2 diabetes, who need to monitor their glucose levels from moment to moment. For these

people, CGM is an essential tool that can protect them from life-threatening swings in blood glucose. But I think nearly every adult could benefit from it, at least for a few weeks, and it will likely be available to consumers without a prescription in the not-too-distant future.^[*4] It's currently fairly easy for a nondiabetic to obtain a CGM from one of several online metabolic health start-ups.

目前，CGM 只能透過處方獲得，最常被診斷為 1 型或 2 型糖尿病的患者佩戴，他們需要隨時監測血糖水平。對於這些人來說，連續血糖監測是一種重要的工具，可以保護他們免受危及生命的血糖波動的影響。但我認為幾乎每個成年人都可以從中受益，至少在幾週內，在不久的將來，消費者很可能無需處方即可使用它。[*4] 目前，對於非糖尿病患者來說，從幾家線上代謝健康新創公司之一獲得 CGM 相當容易。

Yet some experts and evidence-based medicine types have criticized the growing use of CGM in nondiabetic people. They argue, as these sorts of people always do, that the “cost” is excessive. CGM costs about \$120 a month, which is not insignificant—but I would argue that even this is still far cheaper than allowing someone to slide into metabolic dysfunction and eventually type 2 diabetes. Insulin treatment alone can cost hundreds of dollars a month. Also, as CGM becomes more common, and more readily available without a prescription, the cost is sure to come down. Typically, my healthy patients need to use CGM only for a month or two before they begin to understand what foods are spiking their glucose (and insulin) and how to adjust their eating pattern to obtain a more stable glucose curve. Once they have this knowledge, many of them no longer need CGM. It's a worthwhile investment.

然而，一些專家和實證醫學類型批評了在非糖尿病患者中越來越多地使用 CGM。正如這類人一貫所做的那樣，他們認為「成本」過高。CGM 每月的費用約為 120 美元，這並不是微不足道的，但我認為即使這樣，仍然比讓某人陷入代謝功能障礙並最終患上 2 型糖尿病要便宜得多。光是胰島素治療每月就需要花費數百美元。此外，隨著 CGM 變得越來越普遍，並且無需處方即可輕鬆獲得，成本肯定會下降。通常情況下，我的健康患者只需要使用 CGM 一兩個月，然後他們就開

始了解哪些食物會增加他們的血糖（和胰島素）以及如何調整他們的飲食模式以獲得更穩定的血糖曲線。一旦他們掌握了這些知識，他們中的許多人就不再需要 CGM。這是一項值得的投資。

The second argument against using CGM in healthy patients is also pretty typical: There are no randomized clinical trials showing a benefit from the technology. This is true, strictly speaking, but it is also a weak argument. For one thing, use of CGM is growing so fast and the technology is advancing so much that by the time you are reading this there may very well be published RCTs (assuming a study can be designed to test the metrics that matter most over a long enough period of time).

反對在健康患者中使用 CGM 的第二個論點也很典型：沒有隨機臨床試驗顯示該技術有益處。嚴格來說，這是事實，但也是一個站不住腳的論點。一方面，CGM 的使用成長如此之快，而且技術進步如此之大，以至於當您閱讀本文時，很可能已經發布了 RCT（假設可以設計一項研究來測試長期內最重要的指標）足夠長的時間）。

I am confident that such studies will show a benefit, if done correctly, because there are already ample data showing how important it is to keep blood glucose low and stable. A 2011 study looking at twenty thousand people, mostly *without* type 2 diabetes, found that their risk of mortality increased monotonically with their average blood glucose levels (measured via HbA1c). The higher their blood glucose, the greater their risk of death—even in the nondiabetic range of blood glucose. Another study in 2019 looked at the degree of variation in subjects' blood glucose levels and found that the people in the highest quartile of glucose variability had a 2.67 times greater risk of mortality than those in the lowest (most stable) quartile. From these studies, it seems quite clear that we want to lower average blood glucose *and* reduce the amount of variability from day to day and hour to hour. CGM is a tool that can help us achieve that. We use it in healthy people in order to help them stay healthy. That shouldn't be controversial.

我相信，如果做得正確，此類研究將顯示出益處，因為已經有足夠的數據表明保持低血糖和穩定是多麼重要。2011 年的一項研究對 2 萬人進行了調查，其中大部分沒有 2 型糖尿病，發現他們的死亡風險隨著

平均血糖水平（透過 HbA1c 測量）單調增加。他們的血糖越高，死亡的風險就越大——即使在非糖尿病範圍內也是如此。2019 年的另一項研究檢視了受試者血糖值的變化程度，發現血糖變化最高四分位的人的死亡風險是最低（最穩定）四分位的人的 2.67 倍。從這些研究中可以清楚看出，我們希望降低平均血糖並減少每天、每小時的變化量。CGM 是一個可以幫助我們實現這一目標的工具。我們將它用於健康人，以幫助他們保持健康。這應該沒有爭議。

When I've put my patients on CGM, I've observed that there are two distinct phases to the process. The first is the insight phase, where you learn how different foods, exercise, sleep (especially lack thereof), and stress affect your glucose readings in real time. The benefit of this information can't be overstated. Almost always, patients are stunned to see how some of their favorite foods send their glucose soaring, then crashing back to earth. This leads to the second phase, which is what I call the behavior phase. Here you mostly know how your glucose is going to respond to that bag of potato chips, and that knowledge is what prevents you from mindlessly eating it. I've found that CGM powerfully activates the Hawthorne effect, the long-observed phenomenon whereby people modify their behavior when they are being watched. (The Hawthorne effect is also what makes it difficult to study what people actually eat, for the same reason.)

當我讓患者進行連續血糖監測時，我觀察到這個過程有兩個不同的階段。第一個是洞察階段，您可以了解不同的食物、運動、睡眠（尤其是缺乏睡眠）和壓力如何即時影響您的血糖讀數。這些資訊的好處怎麼強調都不為過。幾乎總是，患者會驚訝地發現他們最喜歡的一些食物如何使他們的血糖飆升，然後又急劇下降。這就進入了第二階段，也就是我所說的行為階段。在這裡，你基本上知道你的葡萄糖將如何回應那袋薯片，而這些知識可以防止你盲目地吃它。我發現 CGM 能夠強有力地激活霍桑效應，這是一種長期觀察到的現象，人們在被監視時會改變自己的行為。（同樣的原因，霍桑效應也使得研究人們實際吃什麼變得困難。）

Typically, the first month or so of using CGM is dominated by insights. Thereafter, it's really dominated by behavior modification. But both are quite

powerful, and even after my patients stop using CGM, I find that the Hawthorne effect persists, because they know what that bag of potato chips will do to their glucose levels. (Those who need more “training” to break their snacking habit will typically need to use CGM for longer.) CGM has proved especially useful in patients with *APOE e4*, where we often see big glucose spikes, even in relatively young people. In these patients, the behavior modification that CGM prompts is an important part of their Alzheimer’s disease prevention strategy.

通常，使用 CGM 的第一個月左右主要是洞察力。此後，它實際上以行為矯正為主。但兩者都非常強大，即使在我的患者停止使用 CGM 後，我發現霍桑效應仍然存在，因為他們知道那袋薯片會對他們的血糖水平產生什麼影響。（那些需要更多「訓練」來改掉吃零食習慣的人通常需要更長時間地使用CGM。）CGM 已被證明對APOE e4 患者特別有用，我們經常會看到血糖大幅上升，即使在相對年輕的人中。對於這些患者來說，CGM 促進的行為改變是其阿茲海默症預防策略的重要組成部分。

The real beauty of CGM is that it allows me to titrate a patient’s diet while remaining flexible. No longer do we need to try to hit some arbitrary target for carbohydrate or fat intake and hope for the best. Instead, we can observe in real time how their body handles the food they are eating. Is their average blood glucose a little bit high? Are they “spiking” above 160 mg/dL more often than I would like? Or could they perhaps tolerate a little bit *more* carbohydrate in their diet? Not everyone needs to restrict carbohydrates; some people can handle more than others, and some have a hard time sticking to severe carbohydrate restriction. Overall, I like to keep average glucose at or below 100 mg/dL, with a standard deviation of less than 15 mg/dL.^[*5] These are aggressive goals: 100 mg/dL corresponds to an HbA1c of 5.1 percent, which is quite low. But I believe that the reward, in terms of lower risk of mortality and disease, is well worth it given the ample evidence in nondiabetics and diabetics alike.

CGM 的真正美妙之處在於它使我能夠在保持靈活性的同時調整患者的飲食。我們不再需要嘗試達到碳水化合物或脂肪攝取量的任意目標並

希望得到最好的結果。相反，我們可以即時觀察他們的身體如何處理他們所吃的食物。他們的平均血糖有點高嗎？它們「峰值」超過 160 mg/dL 的頻率是否比我希望的要高？或者他們可以忍受飲食中多一點碳水化合物嗎？並非每個人都需要限制碳水化合物；有些人可以比其他他人處理更多的食物，而有些人則很難堅持嚴格的碳水化合物限制。總體而言，我喜歡將平均血糖保持在 100 mg/dL 或以下，標準差小於 15 mg/dL。[*5] 這些都是激進的目標：100 mg/dL 對應的 HbA1c 為 5.1%，相當低。但我相信，鑑於非糖尿病患者和糖尿病患者的充分證據，就降低死亡率和疾病風險而言，這是非常值得的。

All of this takes experimentation and iteration; dietary restriction has to be adaptive, changing with the patient's lifestyle, age, exercise habits, and so on. It's always interesting to see which specific foods cause elevated CGM readings in some patients but not in others. The SAD sends most people's CGM readings through the roof, as all the sugar and processed carbohydrates dump into the bloodstream at once, provoking a strong insulin response, which is what we don't want. But seemingly "healthy" meals, for example certain kinds of vegetarian tacos, can also send glucose levels soaring in some people but not others. It also depends on when those carbs are eaten. If you eat 150 grams of carbohydrates as a serving of rice and beans in one sitting, that has a different effect than eating the same amount of rice and beans spread out over the day (and, obviously, much different from ingesting 150 grams of carbs in the form of Frosted MiniWheats). Also, everyone tends to be more insulin sensitive in the morning than in the evening, so it makes sense to front-load our carb consumption earlier in the day.

所有這一切都需要實驗和迭代；飲食限制必須是適應性的，隨著患者的生活方式、年齡、運動習慣等而改變。看看哪些特定食物會導致某些患者的 CGM 讀數升高，而有些患者則不會，這總是很有趣的。SAD 讓大多數人的 CGM 讀數飆升，因為所有糖和加工過的碳水化合物都會立即進入血液，引發強烈的胰島素反應，這是我們不想要的。但看似「健康」的膳食，例如某些素食炸玉米餅，也會導致某些人的血糖水平飆升，但其他人卻不會。這也取決於這些碳水化合物的食用時間。如果您一次吃下150 克碳水化合物作為一份米飯和豆類，這與

一天中分散吃等量的米飯和豆類有著不同的效果（而且，顯然，這與攝取150 克碳水化合物有很大不同）以磨砂迷你小麥的形式）。此外，每個人在早上往往比晚上對胰島素更敏感，因此在一天中早些時候提前攝取碳水化合物是有意義的。

One thing CGM pretty quickly teaches you is that your carbohydrate tolerance is heavily influenced by other factors, especially your activity level and sleep. An ultraendurance athlete, someone who is training for long rides or swims or runs, can eat many more grams of carbs per day because they are blowing through those carbs every time they train—and they are also vastly increasing their ability to dispose of glucose via the muscles and their more-efficient mitochondria.^[*6] Also, sleep disruption or reduction dramatically impairs glucose homeostasis over time. From years of experience with my own CGM and that of my patients, it still amazes me how much even one night of horrible sleep cripples our ability to dispose of glucose the next day.

CGM 很快告訴您的一件事是，您的碳水化合物耐受性很大程度上受到其他因素的影響，尤其是您的活動量和睡眠。超耐力運動員，即進行長途騎行、游泳或跑步訓練的人，每天可以吃更多克的碳水化合物，因為他們每次訓練時都會消耗掉這些碳水化合物，而且他們還通過以下方式大大提高了處理葡萄糖的能力：肌肉及其更有效率的粒線體。

[*6] 此外，隨著時間的推移，睡眠中斷或減少會嚴重損害葡萄糖穩態。根據我自己和我的患者多年來的 CGM 經驗，我仍然感到驚訝的是，即使是一晚糟糕的睡眠也會嚴重削弱我們第二天處理葡萄糖的能力。

Another surprising thing I've learned thanks to CGM is about what happens to a patient's glucose levels during the night. If she goes to bed at, say, 80 mg/dL, but then her glucose ramps up to 110 for most of the night, that tells me that she is likely dealing with psychological stress. Stress prompts an elevation in cortisol, which in turn stimulates the liver to drip more glucose into circulation. This tells me that we need to address her stress levels and probably also her sleep quality.

感謝 CGM，我了解到的另一件令人驚訝的事情是患者夜間血糖水平的變化。如果她上床睡覺時的血糖濃度為 80 毫克/分升，但隨後她的血

糖在整個晚上的大部分時間都上升至 110，這表明她可能正在應對心理壓力。壓力會導致皮質醇升高，從而刺激肝臟將更多的葡萄糖滴入循環中。這告訴我，我們需要解決她的壓力水平，或許還有她的睡眠品質。

This doesn't need to be an exercise in deprivation: one patient of mine gleefully confessed that his CGM, which he had only reluctantly agreed to wear, had given him a “superpower” to cheat. By eating certain “forbidden” types of carbohydrates only at certain times, either mixed with other foods or after exercising, he had figured out how he could hit his average glucose goals while still enjoying all the foods he loved. He was gaming his CGM, but he had also unwittingly discovered another rule of nutrition, which is that timing is important: If you scarf a large baked potato before working out, it will leave much less of a footprint on your daily glucose profile than if you eat it right before bedtime.

這並不一定是一種剝奪的練習：我的一位病人興高采烈地承認，他只是不情願地同意佩戴的 CGM 賦予了他作弊的「超能力」。透過僅在特定時間吃某些「禁止」類型的碳水化合物，無論是與其他食物混合還是在運動後，他已經弄清楚如何在達到平均血糖目標的同時仍然享受所有他喜歡的食物。他在玩他的CGM，但他也無意中發現了另一條營養規則，那就是時機很重要：如果你在鍛煉前吃一個大烤土豆，它對你每日血糖曲線的影響會比如果你在運動前吃一個大烤馬鈴薯要少得多。你在睡覺前吃它。

It is important to remember the limitations of CGM—chiefly, that it measures *one* variable. This variable happens to be very important, but it is not the only one. Thus, CGM data alone are not going to help you find the ideal diet. Eating bacon for breakfast, lunch, and dinner might give you a great CGM tracing, even though it's obviously not an optimal diet. Similarly, a bathroom scale will suggest that smoking is good for you because you lost weight. This is why I monitor my patients' other biomarkers closely as well, to ensure that their CGM-driven choices are not increasing their risk of something else, such as cardiovascular disease. We also monitor other variables that are relevant to diet, beginning with weight (obviously) but

continuing with body composition, the ratios of lean mass and fat mass, and how they change. We can also look at biomarkers such as lipids, uric acid, insulin, and liver enzymes. All of these taken together start to give us a better way to evaluate our progress than any one in isolation.

重要的是要記住 CGM 的局限性——主要是它測量一個變數。這個變數恰好非常重要，但它不是唯一的。因此，僅 CGM 數據並不能幫助您找到理想的飲食。早餐、午餐和晚餐吃培根可能會給你帶來很好的 CGM 追蹤效果，儘管這顯然不是最佳飲食。同樣，浴室秤會表明吸煙對你有好處，因為你可以減肥。這就是為什麼我也密切監測患者的其他生物標記，以確保他們的 CGM 驅動的選擇不會增加他們患其他疾病（例如心血管疾病）的風險。我們還監測與飲食相關的其他變量，從體重（顯然）開始，然後繼續關注身體組成、瘦體重和脂肪質量的比率以及它們如何變化。我們也可以查看脂質、尿酸、胰島素和肝臟酵素等生物標記。所有這些加在一起開始為我們提供一種比任何孤立的方法更好的方法來評估我們的進展。

Lessons from Continuous Glucose Monitoring

連續血糖監測的經驗教訓

In the years that I have used CGM, I have gleaned the following insights—some of which may seem obvious, but the power of confirmation cannot be ignored:

在我使用 CGM 的這些年裡，我收集了以下見解——其中一些看似顯而易見，但確認的力量不容忽視：

1. Not all carbs are created equal. The more refined the carb (think dinner roll, potato chips), the faster and higher the glucose spike. Less processed carbohydrates and those with more fiber, on the other hand, blunt the glucose impact. I try to eat more than fifty grams of fiber per day.

並非所有碳水化合物都是一樣的。碳水化合物越精製（如餐卷、洋芋片），葡萄糖高峰就越快、越高。另一方面，加工較少的碳水化合物和纖維較多的碳水化合物會減弱對葡萄糖的影響。我嘗試每天吃超過五十克的纖維。

2. Rice and oatmeal are surprisingly glycemic (meaning they cause a sharp rise in glucose levels), despite not being particularly refined; more surprising is that brown rice is only slightly less glycemic than long-grain white rice.

米和燕麥片儘管沒有經過特別精製，但其升糖指數卻令人驚訝（這意味著它們會導致血糖水平急劇上升）；更令人驚訝的是，糙米的升糖指數只略低於長粒白米。

3. Fructose does *not* get measured by CGM, but because fructose is almost always consumed in combination with glucose, fructose-heavy foods will still likely cause blood-glucose spikes.

連續血糖監測無法測量果糖，但由於果糖幾乎總是與葡萄糖一起食用，因此富含果糖的食物仍然可能導致血糖升高。

4. Timing, duration, and intensity of exercise matter a lot. In general, aerobic exercise seems most efficacious at removing glucose from circulation, while high-intensity exercise and strength training tend to *increase* glucose transiently, because the liver is sending more glucose into the circulation to fuel the muscles. Don't be alarmed by glucose spikes when you are exercising.

運動的時間、持續時間和強度非常重要。一般來說，有氧運動似乎最有效地從循環中去除葡萄糖，而高強度運動和肌力訓練往往會暫時增加葡萄糖，因為肝臟將更多的葡萄糖輸送到循環中為肌肉提供能量。運動時，不要因血糖峰值而驚慌。

5. A good versus bad night of sleep makes a world of difference in terms of glucose control. All things equal, it appears that sleeping just five to six hours (versus eight hours) accounts for about a 10 to 20 mg/dL (that's a lot!) jump in peak glucose response, and about 5 to 10 mg/dL in overall levels.

良好的睡眠與糟糕的睡眠對於血糖控制來說有著天壤之別。在所有條件相同的情況下，睡眠 5 至 6 小時（而不是 8 小時）似乎可使峰值血糖反應躍升約 10 至 20 mg/dL（這很多！），總體躍升約 5 至 10 mg/dL 水平。

6. Stress, presumably, via cortisol and other stress hormones, has a surprising impact on blood glucose, even while one is fasting or restricting carbohydrates. It's difficult to quantify, but the effect is most visible during sleep or periods long after meals.

據推測，壓力會透過皮質醇和其他壓力荷爾蒙對血糖產生令人驚訝的影響，即使在禁食或限制碳水化合物攝取的情況下也是如此。這很難量化，但效果在睡眠或飯後很長一段時間最為明顯。

7. Nonstarchy veggies such as spinach or broccoli have virtually no impact on blood sugar. Have at them.

菠菜或綠花椰菜等非澱粉類蔬菜其實對血糖沒有影響。對付他們。

8. Foods high in protein *and fat* (e.g., eggs, beef short ribs) have virtually no effect on blood sugar (assuming the short ribs are not coated in sweet sauce), but large amounts of lean protein (e.g., chicken breast) will elevate glucose slightly. Protein shakes, especially if low in fat, have a more pronounced effect (particularly if they contain sugar, obviously).

高蛋白質和脂肪的食物（例如雞蛋、牛小排）對血糖幾乎沒有影響（假設小排沒有塗上甜醬），但大量的瘦肉蛋白（例如雞胸肉）會升高血糖輕微地。蛋白質奶昔，尤其是低脂的蛋白質奶昔，具有更明顯的效果（尤其是如果它們含有糖，顯然）。

9. Stacking the above insights—in both directions, positive or negative—is very powerful. So if you're stressed out, sleeping poorly, *and* unable to make time to exercise, be as careful as possible with what you eat.

將上述見解（無論是正面的還是負面的）疊加起來是非常強大的。因此，如果您壓力很大、睡眠品質不佳且無法騰出時間鍛鍊身體，請盡可能小心飲食。

10. Perhaps the most important insight of them all? Simply tracking my glucose has a positive impact on my eating behavior. I've come to appreciate the fact that CGM creates its own Hawthorne effect, a phenomenon where study subjects change their behavior *because* they are being observed. It makes me think twice when I see the bag of chocolate-covered raisins in the pantry, or anything else that might raise my blood glucose levels.

也許其中最重要的見解是什麼？簡單地追蹤我的血糖對我的飲食行為有正面的影響。我開始意識到 CGM 創造了自己的霍桑效應，這是研究對象因為被觀察而改變行為的現象。當我看到食品儲藏室裡的一袋巧克力葡萄乾或任何其他可能會提高我的血糖水平的東西時，我會三思而後行。

Protein

蛋白質

Why is protein so important? One clue lies in the name, which is derived from the Greek word *proteios*, meaning “primary.” Protein and amino acids are the

essential building blocks of life. Without them, we simply cannot build or maintain the lean muscle mass that we need. As we saw in chapter 11, this is absolutely critical to our strategy, because the older we get, the more easily we lose muscle, and the more difficult it becomes to rebuild it.

為什麼蛋白質如此重要？一個線索就在於這個名字，它源自於希臘語“*proteios*”，意思是“主要的”。蛋白質和胺基酸是生命的重要組成部分。沒有它們，我們根本無法建立或維持我們所需的瘦肌肉質量。正如我們在第 11 章中所看到的，這對我們的策略絕對至關重要，因為我們年齡越大，我們就越容易失去肌肉，而重建肌肉就越困難。

Remember the study we discussed in chapter 11 that looked at the effect of strength training in sixty-two frail seniors? The subjects who did only strength training for six months gained no muscle mass. What I didn't mention there was that another group of subjects was given protein supplementation (via a protein shake); those subjects added an average of about three pounds of lean mass. The extra protein likely made the difference.[\[*7\]](#)

還記得我們在第 11 章中討論的一項研究，該研究檢視了 62 名體弱老年人的肌力訓練效果嗎？只進行六個月肌力訓練的受試者並沒有增加肌肉量。我沒有提到的是，另一組受試者補充了蛋白質（透過蛋白質奶昔）；這些受試者平均增加了約三磅的瘦體重。額外的蛋白質可能會產生影響。[\[*7\]](#)

Unlike carbs and fat, protein is not a primary source of energy. We do not rely on it in order to make ATP,[\[*8\]](#) nor do we store it the way we store fat (in fat cells) or glucose (as glycogen). If you consume more protein than you can synthesize into lean mass, you will simply excrete the excess in your urine as urea. Protein is all about structure. The twenty amino acids that make up proteins are the building blocks for our muscles, our enzymes, and many of the most important hormones in our body. They go into everything from growing and maintaining our hair, skin, and nails to helping form the antibodies in our immune system. On top of this, we *must* obtain nine of the twenty amino acids that we require from our diet, because we can't synthesize them.

與碳水化合物和脂肪不同，蛋白質不是主要的能量來源。我們不依賴它來製造 ATP，[*8]，也不以儲存脂肪（在脂肪細胞中）或葡萄糖（作為肝糖）的方式儲存它。如果你消耗的蛋白質多於你能合成的瘦體重，你就會以尿素的形式從尿液中排出多餘的蛋白質。蛋白質與結構有關。構成蛋白質的二十種胺基酸是我們的肌肉、酵素和體內許多最重要的荷爾蒙的組成部分。它們涉及從生長和維護頭髮、皮膚和指甲到幫助形成免疫系統中的抗體等各個方面。除此之外，我們必須從飲食中獲取所需的二十種氨基酸中的九種，因為我們無法合成它們。

The first thing you need to know about protein is that the standard recommendations for daily consumption are a joke. Right now the US recommended dietary allowance (RDA) for protein is 0.8 g/kg of body weight. This may reflect how much protein we need to stay alive, but it is a far cry from what we need to thrive. There is ample evidence showing that we require more than this—and that consuming less leads to worse outcomes. More than one study has found that elderly people consuming that RDA of protein (0.8 g/kg/day) end up *losing* muscle mass, even in as short a period as two weeks. It's simply not enough.

關於蛋白質，您需要了解的第一件事是，每日攝取量的標準建議只是一個笑話。目前美國建議的蛋白質飲食攝取量（RDA）為0.8克/公斤體重。這可能反映了我們維持生命需要多少蛋白質，但這與我們茁壯成長所需的蛋白質相去甚遠。有充分的證據表明，我們的需求遠不止於此，而且攝取較少會導致更糟糕的結果。不只一項研究發現，攝取 RDA 蛋白質（0.8 克/公斤/天）的老年人最終會失去肌肉質量，即使在短短兩週內也是如此。這根本不夠。

On a related note, some of you may have the impression that low-protein diets are helpful for longevity purposes. Certainly, a number of mouse studies have suggested that restricting protein can improve mouse lifespan. I am not convinced that these results are applicable to humans, however. Mice and human beings respond very differently to low protein, and numerous studies suggest that low protein in the elderly leads to low muscle mass, yielding greater mortality and worse quality of life. I am more persuaded by this human data than I am by studies in mice, who are simply not the same as us.

與此相關的是，你們中的一些人可能會有這樣的印象：低蛋白飲食有助於長壽。當然，許多小鼠研究表明限制蛋白質可以延長小鼠的壽命。然而，我不相信這些結果適用於人類。小鼠和人類對低蛋白質的反應非常不同，大量研究表明老年人的低蛋白質會導致肌肉質量低，從而導致更高的死亡率和更差的生活品質。與小鼠研究相比，我更相信這些人類數據，因為小鼠與我們根本不一樣。

How much protein do we actually need? It varies from person to person. In my patients I typically set 1.6 g/kg/day as the minimum, which is twice the RDA. The ideal amount can vary from person to person, but the data suggest that for active people with normal kidney function, one gram per *pound* of body weight per day (or 2.2 g/kg/day) is a good place to start—nearly triple the minimal recommendation.

我們實際上需要多少蛋白質？這因人而異。對於我的患者，我通常將最低攝取量設定為 1.6 克/公斤/天，這是 RDA 的兩倍。理想的攝取量因人而異，但數據表明，對於腎功能正常、活躍的人來說，每天每磅體重 1 克（或 2.2 克/公斤/天）是一個不錯的起點，幾乎是三倍最低限度的建議。

So if someone weighs 180 pounds, they need to consume a minimum of 130 grams of protein per day, and ideally closer to 180 grams, especially if they are trying to add muscle mass. This is a lot of protein to eat, and the added challenge is that it should not be taken in one sitting but rather spread out over the day to avoid losing amino acids to oxidation (i.e., using them to produce energy when we want them to be available for muscle protein synthesis). The literature suggests that the ideal way to achieve this is by consuming four servings of protein per day, each at ~0.25 g/lb of body weight. A six-ounce serving of chicken, fish, or meat will provide about 40 to 45 grams (at about 7 grams of actual protein per ounce of meat), so our hypothetical 180-pound person should eat four such servings a day.

因此，如果某人體重 180 磅，他們每天至少需要攝取 130 克蛋白質，最好接近 180 克，特別是如果他們想增加肌肉質量。需要吃的蛋白質很多，額外的挑戰是，不應一次性攝入，而應分散在一天中，以避免

因氧化而損失氨基酸（即，當我們希望它們產生能量時，使用它們來產生能量）可用於肌肉蛋白質合成）。文獻表明，實現這一目標的理想方法是每天攝取四份蛋白質，每份蛋白質含量約為 0.25 克/磅體重。一份 6 盎司的雞肉、魚或肉可提供約 40 至 45 克（每盎司肉約含 7 克實際蛋白質），因此我們假設的 180 磅重的人每天應該吃四份這樣的食物。

Most people don't need to worry about consuming too much protein. It would require an overwhelming effort to eat more than 3.7 g/kg/day (or ~1.7 g/lb of body weight), defined as the safe upper limit of protein consumption (too much stress on the kidneys, for one). For someone my size, that maximum amount would be nearly 300 grams per day, or the equivalent of seven or eight chicken breasts.

大多數人不需要擔心攝取過多的蛋白質。每天攝取超過 3.7 克/公斤（或約 1.7 克/磅體重）需要巨大的努力，這被定義為蛋白質消耗的安全上限（例如，對腎臟造成太大壓力）。對我這個體型的人來說，每天的最大攝取量接近 300 克，相當於七、八塊雞胸肉。

How much protein you need depends on your sex, body weight and lean body mass, activity level, and other factors, including age. There is some evidence that older people might require more protein because of the anabolic resistance that develops with age—that is, their greater difficulty in gaining muscle. Unfortunately, there's no CGM for protein, so it becomes a bit of a process of trial and error. I try to consume enough to maintain muscle mass as I train. If I find that I'm losing muscle mass, then I endeavor to eat more. Older people in particular should try to keep track of their lean mass, such as via a body-composition-measuring scale (or better yet, DEXA scan), and adjust their protein intake upwards if lean mass declines. For me and my patients, this works out to four servings, as described, with at least one of them being a whey protein shake. (It's very difficult for me to consume four actual meals. Typically, I will consume a protein shake, a high-protein snack, and two protein meals.)

您需要多少蛋白質取決於您的性別、體重和去脂體重、活動量以及其他因素，包括年齡。有一些證據表明，老年人可能需要更多的蛋白

質，因為隨著年齡的增長，合成代謝阻力會增加，也就是說，他們獲得肌肉的難度更高。不幸的是，蛋白質沒有 CGM，所以它變成了一個反覆試驗的過程。我在訓練時嘗試攝取足夠的熱量來維持肌肉質量。如果我發現我正在失去肌肉質量，那麼我會努力吃得更多。老年人尤其應該嘗試追蹤他們的瘦體重，例如透過身體組成測量量表（或更好的是，DEXA 掃描），並在瘦體重下降時向上調整蛋白質攝取量。對我和我的患者來說，如上所述，這相當於四份，其中至少一份是乳清蛋白奶昔。（對我來說，吃四餐真正的餐點是非常困難的。通常，我會吃一杯蛋白質奶昔、一份高蛋白零食和兩餐蛋白質餐。）

Now, a word on plant protein. Do you need to eat meat, fish, and dairy to get sufficient protein? No. But if you choose to get all your protein from plants, you need to understand two things. First, the protein found in plants is there for the benefit of the plant, which means it is largely tied up in indigestible fiber, and therefore less bioavailable to the person eating it. Because much of the plant's protein is tied to its roots, leaves, and other structures, only about 60 to 70 percent of what you consume is contributing to your needs, according to Don Layman, professor emeritus of food science and human nutrition at the University of Illinois Urbana-Champaign, and an expert on protein.

現在，談談植物性蛋白質。您需要吃肉、魚和乳製品才能獲得足夠的蛋白質嗎？不。但如果您選擇從植物中獲取所有蛋白質，您需要了解兩件事。首先，在植物中發現的蛋白質是為了植物的利益而存在的，這意味著它很大程度上與不可消化的纖維結合在一起，因此食用它的人的生物利用度較低。該大學食品科學和人類營養學榮譽教授唐·雷曼 (Don Layman) 表示，由於植物的大部分蛋白質與其根、葉和其他結構有關，因此您消耗的蛋白質中只有約60% 至70% 能滿足您的需求伊利諾伊州厄巴納-香檳分校的博士，蛋白質專家。

Some of this can be overcome by cooking the plants, but that still leaves us with the second issue. The distribution of amino acids is not the same as in animal protein. In particular, plant protein has less of the essential amino acids methionine, lysine, and tryptophan, potentially leading to reduced protein synthesis. Taken together, these two factors tell us that the overall quality of

protein derived from plants is significantly lower than that from animal products.

其中一些問題可以透過烹飪植物來解決，但這仍然給我們留下了第二個問題。胺基酸的分佈與動物性蛋白質不同。特別是，植物蛋白含有較少的必需胺基酸蛋氨酸、賴氨酸和色氨酸，可能導致蛋白質合成減少。綜合起來，這兩個因素告訴我們，植物來源的蛋白質的整體品質明顯低於動物產品。

The same is true of protein supplements. Whey protein isolate (from dairy) is richer in available amino acids than soy protein isolate. So if you forgo protein from animal sources, you need to do the math on your protein quality score. In truth, this can get pretty complicated pretty quick, because you get wrapped around the axle of something called the Digestible Indispensable Amino Acid Score (DIAAS) and the Protein Digestibility-Corrected Amino Acid Score (PDCAAS). These are great if you have the time to comb through databases all day, but for those of us with day jobs, Layman suggests focusing on a handful of important amino acids, such as leucine, lysine, and methionine. Focus on the absolute amount of these amino acids found in each meal, and be sure to get about three to four grams per day of leucine and lysine and at least one gram per day of methionine for maintenance of lean mass. If you are trying to increase lean mass, you'll need even more leucine, closer to two to three grams per serving, four times per day.

蛋白質補充劑也是如此。乳清分離蛋白（來自乳製品）比大豆分離蛋白含有更豐富的可用胺基酸。因此，如果您放棄動物來源的蛋白質，您需要計算您的蛋白質品質分數。事實上，這很快就會變得非常複雜，因為你會陷入可消化必需胺基酸評分 (DIAAS) 和蛋白質消化率校正胺基酸評分 (PDCAAS) 的軸心。如果您有時間整天梳理資料庫，那麼這些就很棒，但對於我們這些從事日常工作的人來說，萊曼建議專注於少數重要的氨基酸，例如亮氨酸、賴氨酸和蛋氨酸。注意每餐中這些氨基酸的絕對含量，並確保每天攝取約三到四克的亮氨酸和賴氨酸，以及每天至少一克的蛋氨酸，以維持瘦體重。如果您想增加瘦體重，則需要更多的亮氨酸，每份接近兩到三克，每天四次。

Multiple studies suggest that the more protein we consume, in general, the better. A large prospective study called the Healthy Aging and Body Composition Study, with more than two thousand elderly subjects, found that those who ate the most protein (about 18 percent of caloric intake) kept more of their lean body mass over three years than those in the lowest quintile of protein consumption (10 percent of calories). The difference was significant: the low-protein group lost 40 percent more muscle than the high-protein group.

多項研究表明，一般來說，我們攝取的蛋白質越多越好。一項名為「健康老化和身體組成研究」的大型前瞻性研究對2000多名老年受試者進行了研究，結果發現，那些吃蛋白質最多（約佔熱量攝取量18%）的人在三年內比那些吃蛋白質的人維持了更多的去脂體重。蛋白質消耗量最低的五分之一（卡路里的10%）。差異非常顯著：低蛋白組比高蛋白組流失的肌肉多40%。

You could make the case that protein is a performance-enhancing macronutrient. Other studies have found that boosting protein intake even moderately above the RDA can slow the progressive loss of muscle mass in older people, including patients with heart failure and cachexia (wasting). Adding thirty grams of milk protein to the diet of frail elderly people, in another study, significantly improved their physical performance.

您可以證明蛋白質是一種增強性能的常量營養素。其他研究發現，增加蛋白質攝取量，即使略高於每日建議攝取量，也可以減緩老年人肌肉質量的逐漸喪失，包括心臟衰竭和惡病質（體重減輕）的患者。另一項研究顯示，在體弱老年人的飲食中添加三十克牛奶蛋白可以顯著改善他們的身體機能。

Beyond its role in building muscle, protein may have beneficial effects on our metabolism. One study found that giving elderly people supplements containing essential amino acids (that is, mimicking some effects of increasing dietary protein) lowered their levels of liver fat and circulating triglycerides. Another study in men with type 2 diabetes found that doubling their protein intake from 15 to 30 percent of total calories, while cutting carbohydrates by half, improved their insulin sensitivity and glucose control.

Eating protein also helps us feel satiated, inhibiting the release of the hunger-inducing hormone ghrelin, so we eat fewer calories overall.

除了在增強肌肉方面的作用之外，蛋白質還可能對我們的新陳代謝產生有益的影響。一項研究發現，為老年人提供含有必需氨基酸的補充劑（即模仿增加膳食蛋白質的一些效果）可以降低他們的肝臟脂肪和循環三酸甘油酯水平。另一項針對 2 型糖尿病男性的研究發現，將總熱量的 15% 至 30% 的蛋白質攝取量增加一倍，同時將碳水化合物減少一半，可以改善他們的胰島素敏感性和血糖控制。吃蛋白質還可以幫助我們感到飽足，抑制飢餓激素胃飢餓素的釋放，因此我們整體攝取的熱量較少。

In case my point here isn't clear enough, let me restate it: don't ignore protein. It's the one macronutrient that is absolutely essential to our goals. There's no minimum requirement for carbohydrates or fats (in practical terms), but if you shortchange protein, you will most certainly pay a price, particularly as you age.

如果我的觀點不夠清楚，讓我重申一下：不要忽視蛋白質。它是對我們的目標絕對重要的常量營養素。對碳水化合物或脂肪沒有最低要求（實際上），但如果你少吃蛋白質，你肯定會付出代價，尤其是隨著年齡的增長。

Fat

胖的

The balance of our diet is composed of fat—or rather fats, plural. Fat is essential, but too much can be problematic both in terms of total energy intake and also metabolically. It should be relatively straightforward, but dietary fat has a sordid past that also creates a lot of confusion.

我們飲食的平衡是由脂肪組成的——或者更確切地說是脂肪，複數。脂肪是必不可少的，但過多可能會在總能量攝取和代謝方面產生問題。這應該是相對簡單的，但膳食脂肪有一個骯髒的過去，也造成了很多混亂。

Fats have long had a bad rap, on two counts: their high caloric content (9 kcal/g) and their role in raising LDL cholesterol and thus heart disease risk. Like carbohydrates, fats are often labeled “good” or “bad” on the basis of one’s tribal or political stripes; in actuality, of course, it’s not that black and white. Fats have an important place in any diet, and therefore it’s important to understand them.

長期以來，脂肪在兩個方面一直受到詬病：它們的熱量含量高（9 kcal/g），以及它們在提高低密度脂蛋白膽固醇（LDL-C）和心臟病風險方面的作用。與碳水化合物一樣，脂肪通常根據一個人的部落或政治立場被貼上「好」或「壞」的標籤。當然，實際上，事情並不是那麼黑白分明。脂肪在任何飲食中都佔有重要地位，因此了解它們很重要。

While carbohydrates are primarily a source of fuel and amino acids are primarily building blocks, fats are both. They are very efficient fuel for oxidation (think: slow-burning logs) and also the building blocks for many of our hormones (in the form of cholesterol) and cell membranes. Eating the right mix of fats can help maintain metabolic balance, but it is also important for the health of our brain, much of which is composed of fatty acids. On a practical level, dietary fat also tends to leave one feeling more satiated than many types of carbohydrates, especially when combined with protein.

雖然碳水化合物主要是燃料來源，氨基酸主要是組成部分，但脂肪兩者都是。它們是非常有效的氧化燃料（想想：緩慢燃燒的原木），也是我們許多荷爾蒙（以膽固醇的形式）和細胞膜的組成部分。吃正確的脂肪組合可以幫助維持代謝平衡，但它對我們大腦的健康也很重要，因為大腦大部分是由脂肪酸組成。在實踐層面上，膳食脂肪也往往比許多類型的碳水化合物更讓人有飽足感，尤其是與蛋白質結合時。

There are (broadly) three types of fats: saturated fatty acids (SFA), monounsaturated fatty acids (MUFA), and polyunsaturated fatty acids (PUFA).^[*9] The differences between these have to do with differences in their chemical structure; a “saturated” fat simply has more hydrogen atoms

attached to its carbon chain.^[*10] Within PUFA, we make one more important distinction, which is to separate the omega-6 from the omega-3 variants (also a chemical distinction having to do with the position of the first double bond). We can further subdivide omega-3 PUFA into marine (EPA, DHA) and nonmarine sources (ALA). Salmon and other oil-rich seafood provide the former, nuts and flaxseed the latter.

脂肪（大致）分為三種：飽和脂肪酸（SFA）、單元不飽和脂肪酸（MUFA）和多元不飽和脂肪酸（PUFA）。[*9] 它們之間的差異與其化學結構的差異有關；「飽和」脂肪只是在其碳鏈上附著了更多的氫原子。[*10] 在 PUFA 中，我們做了一個更重要的區別，即將 omega-6 與 omega-3 變體分開（也是與第一個雙鍵的位置有關的化學區別）。我們可以將 omega-3 PUFA 進一步細分為海洋來源（EPA、DHA）和非海洋來源（ALA）。鮭魚和其他富含油脂的海鮮提供前者，堅果和亞麻籽提供後者。

The key thing to remember—and somehow this is almost always overlooked—is that virtually no food belongs to just one group of fats. Olive oil and safflower oil might be as close as you can get to a pure monounsaturated fat, while palm and coconut oil might be as close as you can get to a pure saturated fat, but all foods that contain fats typically contain *all three* categories of fat: PUFA, MUFA, and SFA. Even a ribeye steak contains a lot of monounsaturated fats.

要記住的關鍵一點是，幾乎沒有食物只屬於一組脂肪，但不知何故，這幾乎總是被忽略。橄欖油和紅花油可能最接近純單元不飽和脂肪，而棕櫚油和椰子油可能最接近純飽和脂肪，但所有含有脂肪的食物通常都含有三類脂肪：PUFA、MUFA 和 SFA。即使是肋眼牛排也含有大量單元不飽和脂肪。

So it's not really possible or feasible to try to eliminate certain categories of fatty acids from the diet entirely; instead, we try to tweak the ratios. The default fat state of most of my patients (i.e., their baseline fat consumption when they come to me) works out to about 30–40 percent each of MUFA and SFA, and 20–30 percent PUFA—and within that PUFA group, they are

generally consuming about six to ten times more omega-6 than omega-3s and usually scant amounts of EPA and DHA.

因此，嘗試從飲食中完全消除某些類別的脂肪酸實際上是不可能或不可行的。相反，我們嘗試調整比率。我的大多數患者的預設脂肪狀態（即他們來找我時的基線脂肪消耗量）計算得出，MUFA 和SFA 各約為30-40%，PUFA 為20-30%，在該PUFA 組中，他們一般來說，Omega-6 的消耗量是 omega-3 的六到十倍，而且 EPA 和 DHA 的含量通常很少。

From our empirical observations and what I consider the most relevant literature, which is less than perfect, we try to boost MUFA closer to 50–55 percent, while cutting SFA down to 15–20 percent and adjusting total PUFA to fill the gap. We also boost EPA and DHA, those fatty acids that are likely important to brain and cardiovascular health, with marine fat sources and/or supplementation. We titrate the level of EPA and DHA in our patients' diets by measuring the amount of each found in the membranes of their red blood cells (RBC), using a specialized but readily available blood test.^[*11] Our target depends on a person's *APOE* genotype and other risk factors for neurodegenerative and cardiovascular disease, but for most patients the range we look for is between 8 and 12 percent of RBC membrane composed of EPA and DHA.

根據我們的經驗觀察和我認為最相關的文獻（但並不完美），我們嘗試將 MUFA 提高到接近 50-55%，同時將 SFA 降低至 15-20%，並調整 PUFA 總量以填補空白。我們也透過海洋脂肪來源和/或補充劑來增強 EPA 和 DHA，這些脂肪酸可能對大腦和心血管健康很重要。我們透過使用專門但現成的血液檢查來測量患者紅血球（RBC）膜中 EPA 和 DHA 的含量，從而滴定患者飲食中 EPA 和 DHA 的水平。[*11] 我們的目標取決於一個人的APOE 基因型以及神經退化性疾病和心血管疾病的其他危險因素，但對於大多數患者來說，我們尋找的範圍是由 EPA 和DHA 組成的紅血球膜的8% 到12%。

Putting all these changes into practice typically means eating more olive oil and avocados and nuts, cutting back on (but not necessarily eliminating) things like butter and lard, and reducing the omega-6-rich corn, soybean, and

sunflower oils—while also looking for ways to increase high-omega-3 marine PUFAs from sources such as salmon and anchovies.^[*12]

將所有這些改變付諸實踐通常意味著吃更多的橄欖油、酪梨和堅果，減少（但不一定消除）黃油和豬油等食物，並減少富含omega-6 的玉米油、大豆油和葵花籽油，同時也尋找方法從鮭魚和鯷魚等來源中增加高 omega-3 海洋多元不飽和脂肪酸。^[*12]

But once again, this is where the SAD, our modern food environment, comes in to complicate things. A hundred years ago, our ancestors would have gotten all their fat from animals, in the form of butter, lard, and tallow, and/or fruits, such as olives, coconuts, and avocados. They would have done so mostly by consuming these foods in their relatively natural state, and achieving a reasonable balance of fatty acids would have come fairly easily. Over the course of the twentieth century, advances in food-processing technology enabled us to chemically and mechanically extract oil from vegetables and seeds that otherwise would have been impossible to get. These new technologies suddenly allowed vast quantities of oils high in polyunsaturated fats, such as corn and cottonseed oil (aka linoleic acid, a PUFA), to flood into the food supply. Our per capita consumption of soybean oil, for example, has increased over a thousand-fold since 1909; meanwhile, studies have found that levels of linoleic acid found in human fat tissue have also increased, by 136 percent over the last half century.

但這又是我們現代食品環境 SAD 的用武之地，讓事情變得複雜。一百年前，我們的祖先從動物身上獲取所有脂肪，以奶油、豬油和牛脂的形式，和/或水果，如橄欖、椰子和酪梨。他們主要透過食用這些相對自然狀態的食物來做到這一點，並且相當容易實現合理的脂肪酸平衡。在二十世紀的過程中，食品加工技術的進步使我們能夠透過化學和機械方法從蔬菜和種子中提取油，否則這是不可能獲得的。這些新技術突然使大量富含多元不飽和脂肪的油，如玉米油和棉籽油（又稱亞麻油酸，一種多元不飽和脂肪酸）湧入食品供應。例如，自1909年以來，我們的人均豆油消費量增加了一千多倍；同時，研究發現人體脂肪組織中的亞麻油酸含量也有所增加，在過去半個世紀中增加了136%。

This industrial fat revolution also helped create trans fats, listed on ingredient labels as “partially hydrogenated vegetable oils” (think: margarine), which in turn helped enable the proliferation of the SAD, in part because they allowed foods to remain shelf stable for longer periods. But trans fats also contributed to atherosclerosis (by raising apoB) and have been banned by the FDA.

這場工業脂肪革命也幫助創造了反式脂肪，在成分標籤上列為「部分氫化植物油」（想想：人造奶油），這反過來又促進了SAD 的擴散，部分原因是它們使食品能夠在更長的時間內保持貨架穩定期間。但反式脂肪也會導致動脈粥狀硬化（透過提高 apoB），因此已被 FDA 禁止使用。

It is tempting to indict this massive proliferation of soybean and other seed oils as the dietary bad guy responsible for our obesity and metabolic syndrome epidemic. Anything that goes up by a thousand-fold in the same few decades in which our health goes to hell in a handbasket can't be good, right? Even just a few years ago, I used to think this was the case. But the closer and closer I look at the data, the less and less sure I am that we can say much in this regard.

人們很容易將大豆和其他種子油的大量擴散歸因於導致肥胖和代謝症候群流行的飲食壞人。在這幾十年裡，我們的健康狀況每況愈下，任何事情增加千倍都不會是什麼好事，對吧？就在幾年前，我也曾這樣認為。但我越仔細研究數據，我就越不確定我們在這方面可以說些什麼。

In fact, the most comprehensive review of this topic, *Polyunsaturated Fatty Acids for the Primary and Secondary Prevention of Cardiovascular Disease*, published by the Cochrane Collaboration in 2018—a 422-page summation of all relevant literature from forty-nine studies, randomizing over twenty-four thousand patients—drew the following conclusion: “Increasing PUFA probably makes little or no difference (*neither benefit nor harm*) to our risk of death, and may make little or no difference to our risk of dying from cardiovascular disease. However, increasing PUFA probably slightly reduces

our risk of heart disease events and of combined heart and stroke events (moderate-quality evidence).”

事實上，該主題最全面的綜述是《多元不飽和脂肪酸用於心血管疾病的一級和二級預防》，由Cochrane Collaboration 於2018 年出版，該書長達422 頁，總結了49 項研究的所有相關文獻，隨機分組了20 多項四千名患者得出以下結論：「增加多元不飽和脂肪酸可能對我們的死亡風險影響很小或沒有影響（既沒有好處也沒有壞處），並且可能對我們死於心血管疾病的風險影響很小或沒有影響。然而，增加多元不飽和脂肪酸可能會略微降低心臟病事件以及心臟病和中風合併事件的風險（中等品質的證據）。」

Slight advantage to increasing PUFA, noted. A more recent publication by the Cochrane Collaboration, published in 2020 as a 287-page treatise titled *Reduction in Saturated Fat Intake for Cardiovascular Disease*, looked at fifteen RCTs in over fifty-six thousand patients and found, among other things, that “reducing dietary saturated fat reduced the risk of combined cardiovascular events by 17%.” Interesting. But the same review also found “little or no effect of reducing saturated fat on all-cause mortality or cardiovascular mortality.” Furthermore, “There was little or no effect on cancer mortality, cancer diagnoses, diabetes diagnosis, HDL cholesterol, serum triglycerides or blood pressure, and small reductions in weight, serum total cholesterol, LDL cholesterol and BMI.”

注意到增加 PUFA 略有優勢。Cochrane Collaboration 於 2020 年出版了一篇 287 頁的論文，題為“減少心血管疾病的飽和脂肪攝入量”，該出版物對超過 56000 名患者進行了 15 項隨機對照試驗，發現“減少飲食飽和脂肪可將合併心血管事件的風險降低17%。”有趣的。但同一篇評論也發現“減少飽和脂肪對全因死亡率或心血管死亡率影響很小或沒有影響。”此外，「對癌症死亡率、癌症診斷、糖尿病診斷、高密度脂蛋白膽固醇、血清三酸甘油酯或血壓影響很小或沒有影響，且體重、血清總膽固醇、低密度脂蛋白膽固醇和體重指數略有下降。」

Slight disadvantage to saturated fats, but no observed effect on mortality. Last, yet another recent review, published in late 2020, titled *Total Dietary Fat Intake, Fat Quality, and Health Outcomes: A Scoping Review of Systematic*

Reviews of Prospective Studies, examined fifty-nine systematic reviews of RCTs or prospective cohort studies and found “mainly no association of total fat, monounsaturated fatty acid (MUFA), polyunsaturated fatty acid (PUFA), and saturated fatty acid (SFA) with risk of chronic diseases.”

比飽和脂肪略有劣勢，但沒有觀察到對死亡率的影響。最後，另一篇最近發表於2020 年底的評論，題為膳食脂肪攝入總量、脂肪質量和健康結果：前瞻性研究系統評價的範圍界定審查，審查了59 項隨機對照試驗或前瞻性隊列研究的系統性評價，發現“總脂肪、單元不飽和脂肪酸（MUFA）、多元不飽和脂肪酸（PUFA）和飽和脂肪酸（SFA）與慢性病風險之間主要沒有關聯。”

I could go on, but I think you get the point. The data are very unclear on this question, at least at the population level. As we discussed in the introduction to Medicine 3.0 and earlier in this chapter, any hope of using broad insights from evidence-based medicine is bound to fail when it comes to nutrition, because such population-level data cannot provide much value at the individual level when the effect sizes are so small, as they clearly are here. All Medicine 2.0 has to offer is broad contours: MUFA seems to be the “best” fat of the bunch (based on PREDIMED and the Lyon Heart study), and after that the meta-analyses suggest PUFA has a slight advantage over SFA. But beyond that, we are on our own.

我可以繼續說下去，但我想你明白了。關於這個問題的數據非常不清楚，至少在人口層面是如此。正如我們在醫學 3.0 簡介和本章前面所討論的那樣，在營養方面，任何利用循證醫學的廣泛見解的希望都注定會失敗，因為此類人口層面的數據無法在個人層面提供太多價值當效應如此之小時，正如它們顯然在這裡一樣。醫學 2.0 必須提供的只是廣泛的輪廓：MUFA 似乎是這組脂肪中「最好」的（基於 PREDIMED 和里昂心臟研究），之後的薈萃分析表明 PUFA 比 SFA 稍有優勢。但除此之外，我們只能靠自己了。

Medicine 3.0 asks, what is the “best” mix of fats for our patient? I use an expanded lipid panel to keep track of how changes in fatty acid consumption may affect my patients’ cholesterol synthesis and reabsorption, and their overall lipid and inflammatory response. Subtle changes in fat intake,

particularly of saturated fats, can make a significant difference in lipid levels in some people, as I have learned over and over again—but not in others. Some people (like me)^[*13] can consume saturated fats with near impunity, while others can hardly even look at a slice of bacon without their apoB number jumping to the 90th percentile.

醫學 3.0 提出的問題是，對於我們的患者來說，「最佳」的脂肪組合是什麼？我使用擴展的脂質面板來追蹤脂肪酸消耗的變化如何影響患者的膽固醇合成和重吸收，以及他們的整體脂質和發炎反應。正如我一遍又一遍地了解到的那樣，脂肪攝入量（尤其是飽和脂肪攝入量）的細微變化可能會對某些人的血脂水平產生顯著影響，但對其他人則不然。有些人（像我）^[*13] 幾乎可以不受懲罰地攝取飽和脂肪，而其他人甚至連看一片培根的時候，他們的 apoB 值都會躍升至第 90 個百分位。

Medicine 2.0 says this proves that nobody should eat saturated fats, period. Medicine 3.0 takes these data and says, “While it is obviously not good that our patient’s apoB has gone up this much, it now presents us with a choice: Should we consider medication to lower their apoB, or reduce their intake of saturated fats? Or both?” There is no obvious or uniform answer here, and addressing this not-too-uncommon situation comes down to a judgment call.

醫學 2.0 說這證明沒有人應該吃飽和脂肪，就這樣。Medicine 3.0 在取得這些數據後說：「雖然我們患者的apoB 上升這麼多顯然不好，但它現在給我們提供了一個選擇：我們應該考慮透過藥物來降低他們的 apoB，還是減少飽和脂肪的攝取量？或兩者？」這裡沒有明顯或統一的答案，解決這種不太罕見的情況可以歸結為判斷。

In the final analysis, I tell my patients that on the basis of the least bad, least ambiguous data available, MUFAs are probably the fat that should make up most of our dietary fat mix, which means extra virgin olive oil and high-MUFA vegetable oils. After that, it’s kind of a toss-up, and the actual ratio of SFA and PUFA probably comes down to individual factors such as lipid response and measured inflammation. Finally, unless they are eating a lot of fatty fish, filling their coffers with marine omega-3 PUFA, they almost always need to take EPA and DHA supplements in capsule or oil form.

在最後的分析中，我告訴我的患者，根據現有的最不壞、最明確的數據，MUFA 可能是我們飲食脂肪組合中的大部分脂肪，這意味著特級初榨橄欖油和高 MUFA 蔬菜油。之後，這是一個難以抉擇的問題，SFA 和 PUFA 的實際比例可能取決於個體因素，例如脂質反應和測量的發炎。最後，除非他們吃大量富含脂肪的魚，並用海洋 omega-3 PUFA 填滿他們的庫房，否則他們幾乎總是需要服用膠囊或油形式的 EPA 和 DHA 補充劑。

TR: The Case for (and Against) Fasting

TR: 支持（和反對）禁食的理由

Fasting, or time-restricted (TR) eating (regulating *when* you eat), presents us with a tactical conundrum. On the one hand, it is a powerful tool for accomplishing some of our goals, large and small. On the other, fasting has some potentially serious downsides that limit its usefulness. While intermittent fasting and eating “windows” have become popular and even trendy in recent years, I’ve grown skeptical of their effectiveness. And frequent longer-term fasting has enough negatives attached to it that I am reluctant to use it in all but the most metabolically sick patients. The jury is still out on the utility of infrequent (e.g., yearly) prolonged fasts. Overall, I’ve come to believe that fasting-based interventions must be utilized carefully and with precision.

禁食或限時 (TR) 飲食（控制進食時間）為我們帶來了一個戰術難題。一方面，它是實現我們一些大大小小的目標的強大工具。另一方面，禁食有一些潛在的嚴重缺點，限制了它的用途。雖然間歇性斷食和「窗口飲食」近年來變得流行甚至流行，但我對它們的有效性越來越懷疑。頻繁的長期禁食有足夠的負面影響，除了代謝最嚴重的患者外，我不願意將其用於所有患者。對於不頻繁（例如每年）長時間禁食的效用尚無定論。總的來說，我開始相信基於禁食的干預措施必須謹慎、精確地使用。

There is no denying that some good things happen when we are not eating. Insulin drops dramatically because there are no incoming calories to trigger an insulin response. The liver is emptied of fat in fairly short order. Over time, within three days or so, the body enters a state called “starvation ketosis,” where fat stores are mobilized to fulfill the need for energy—yet at the same time, as I often noticed when I was undergoing regular lengthy fasts, hunger virtually disappears. This paradoxical phenomenon is likely due to the ultrahigh levels of ketones that this state produces, which tamp down feelings of hunger.

不可否認，當我們不吃飯時，就會發生一些好事。胰島素急劇下降，因為沒有攝取熱量來引發胰島素反應。肝臟中的脂肪會在相當短的時間內被清空。隨著時間的推移，在三天左右的時間裡，身體進入一種稱為「飢餓酮症」的狀態，脂肪儲存被動員起來以滿足能量需求——但與此同時，正如我在定期進行長時間禁食時經常注意到的那樣，飢餓幾乎消失了。這種矛盾的現象很可能是由於這種狀態產生了超高水平的酮，從而抑制了飢餓感。

Fasting over long periods also turns down mTOR, the pro-growth and pro-aging pathway we discussed in chapter 5. This would also be desirable, one might think, at least for some tissues. At the same time, lack of nutrients accelerates autophagy, the cellular “recycling” process that helps our cells become more resilient, and it activates *FOXO*, the cellular repair genes that may help centenarians live so long. In short, fasting triggers many of the physiological and cellular mechanisms that we want to see. So why don't I recommend it to all my patients?

長時間禁食也會降低 mTOR，這是我們在第 5 章中討論的促生長和促進衰老途徑。人們可能認為，這也是可取的，至少對於某些組織而言。同時，營養的缺乏會加速自噬，這是一種細胞「回收」過程，可以幫助我們的細胞變得更有彈性，並且它會激活FOXO，一種細胞修復基因，可以幫助百歲老人活更長久。簡而言之，禁食會觸發許多我們希望看到的生理和細胞機制。那我為什麼不向所有患者推薦它呢？

It's a tricky question, because the scientific literature on fasting is still relatively weak, notwithstanding the many popular books that have been

written about fasting in its various forms. I have recommended (and practiced) different forms of fasting myself, from time-restricted feeding (eating in a defined time period each day) to water-only fasting for up to ten days. Because my thinking about fasting has evolved considerably, I feel that I need to address the topic here. I still think it can be useful sometimes, in some patients—typically the ones with the most severe metabolic dysfunction—but I am less persuaded that it is the panacea that some believe it to be.

這是一個棘手的問題，因為儘管有許多關於各種形式的禁食的流行書籍，但有關禁食的科學文獻仍然相對薄弱。我自己推薦（並實踐）了不同形式的禁食，從限時進食（每天在規定的時間內進食）到長達十天的僅喝水禁食。因為我對禁食的看法已經發生了很大的變化，所以我覺得我需要在這裡討論這個主題。我仍然認為它有時對某些患者（通常是代謝功能障礙最嚴重的患者）有用，但我不太相信它是某些人認為的萬靈藥。

There are really three distinct categories of time-restricted feeding, and we'll look at each of them in order. First, we have the short-term eating windows that we've mentioned previously, where someone will limit their consumption of food to a specific time frame, such as six or eight hours out of the day. In practice, that could mean skipping breakfast, eating a first meal at 11 a.m. and finishing dinner by 7 p.m. every evening; or someone could eat breakfast at 8 a.m., another meal at 2 p.m., and nothing thereafter.

限時餵食實際上分為三種不同的類別，我們將按順序查看每種。首先，我們有前面提到的短期飲食窗口，人們會將食物消耗量限制在特定的時間範圍內，例如一天中的六到八小時。實際上，這可能意味著不吃早餐，上午 11 點吃第一頓飯，晚上 7 點吃完晚餐。每個夜晚；或者有人可以早上 8 點吃早餐，下午 2 點再吃一頓飯，此後什麼都不吃。

There are an almost infinite number of variations on this, but the trick is that it works only provided you make the feeding window small enough. The standard 16/8 (sixteen hours of fasting, eight hours to eat) is barely enough for most people, but it can work. Usually a narrower window, such as 18/6 or 20/4, is needed to eke out enough of a caloric deficit. For a time, I was

experimenting with a two-hour eating window, which basically meant that I would eat one huge meal per day. I always enjoyed the look on a waiter's face when I would order multiple entrees.

這方面的變化幾乎是無限的，但訣竅是，只有當您將餵食窗口設定得足夠小時，它才有效。標準的 16/8（十六小時禁食，八小時進食）對大多數人來說勉強夠用，但它可以發揮作用。通常需要更窄的窗口，例如 18/6 或 20/4，以彌補足夠的熱量不足。有一段時間，我正在嘗試兩個小時的飲食窗口，這基本上意味著我每天會吃一頓大餐。當我點多道主菜時，我總是很喜歡服務生臉上的表情。

In my experience, most people find this to be the easiest way to reduce their caloric intake, by focusing on *when* they are eating rather than *how much* and/or *what* they are eating. But I am not convinced that short-term time-restricted feeding has much of a benefit beyond this.

根據我的經驗，大多數人發現這是減少熱量攝取的最簡單方法，透過專注於何時進食而不是吃多少和/或吃什麼。但我不相信短期限時餵食還有其他好處。

The original 16/8 model came from a study conducted in mice. This study found that mice fed in only eight hours out of the day, and fasted for the other sixteen, were healthier than mice fed continuously. The time-restricted mice gained less weight than the mice that ate whenever they wanted, even though the two groups consumed the same number of calories. This study gave birth to the eight-hour diet fad, but somehow people lost sight of the fact that this is a big extrapolation from research *in mice*. Because a mouse lives for only about two to three years—and will die after just forty-eight hours without food—a sixteen-hour fast for a mouse is akin to a multiday fast for a human. It's just not a valid comparison.

最初的 16/8 模型來自於對小鼠進行的一項研究。這項研究發現，每天只餵食八小時，其餘十六小時禁食的小鼠比連續餵食的小鼠更健康。儘管兩組消耗的卡路里數量相同，但受時間限制的小鼠的體重增長卻比隨心所欲進食的小鼠要少。這項研究催生了八小時節食熱潮，但不知何故，人們忽略了一個事實：這是對老鼠研究的重大推論。因為老

鼠的壽命只有大約兩到三年，並且在不進食的四十八小時後就會死亡，所以對老鼠來說，十六小時的禁食類似於人類的多日禁食。這不是一個有效的比較。

Human trials of this eating pattern have failed to find much of a benefit. A 2020 clinical trial by Ethan Weiss and colleagues found no weight loss or cardiometabolic benefits in a group of 116 volunteers on a 16/8 eating pattern. Two similar studies also found minimal benefit. One other study did find that shifting the eating window to early in the day, from 8 a.m. to 2 p.m., actually did result in lower twenty-four-hour glucose levels, reduced glucose excursions, and lower insulin levels compared to controls. So perhaps an early-day feeding window could be effective, but in my view sixteen hours without food simply isn't long enough to activate autophagy or inhibit chronic mTOR elevation, or engage any of the other longer-term benefits of fasting that we would want to obtain.

這種飲食模式的人體試驗未能發現太多好處。Ethan Weiss 及其同事在 2020 年進行的一項臨床試驗發現，116 名志願者採用 16/8 的飲食模式，並沒有減輕體重或改善心臟代謝。兩項類似的研究也發現了微乎其微的好處。另一項研究確實發現，與對照組相比，將進食窗口移至早上 8 點至下午 2 點實際上確實會降低 24 小時血糖水平、減少血糖波動和降低胰島素水平。因此，也許早期的進食窗口可能是有效的，但在我看來，16 小時不進食根本不足以激活自噬或抑制慢性 mTOR 升高，或發揮禁食的任何其他長期益處，我們認為想要獲得。

Another drawback is that you are virtually guaranteed to miss your protein target with this approach (see “Protein,” above). This means that a person who needs to gain lean body mass (i.e., undernourished or undermuscle), should either abandon this approach completely or consume a pure protein source outside their feeding window (which more or less defeats the purpose of time-restricted feeding). Also, it's very easy to fall into the trap of overindulgence during your feeding window and mindlessly consume, say, a half gallon of ice cream in one sitting. Taken together, this combo of too little protein and too many calories can have the exact opposite effect we want: gaining fat and losing lean body mass. In my clinical experience, this result is quite common.

另一個缺點是，使用這種方法幾乎肯定會錯過蛋白質目標（請參閱上面的「蛋白質」）。這意味著需要增加瘦體重（即營養不良或肌肉不足）的人應該完全放棄這種方法，或者在進食窗口之外攝入純蛋白質來源（這或多或少違背了限時進食的目的）。此外，在餵食窗口期間很容易陷入過度放縱的陷阱，不經意就吃了半加侖的冰淇淋。總而言之，蛋白質過少和熱量過多的組合可能會產生與我們想要的完全相反的效果：增加脂肪並減少去脂體重。根據我的臨床經驗，這種結果是很常見的。

As I said, I will sometimes put certain patients on a time-restricted eating pattern because I've found it helps them reduce their overall caloric intake with minimal hunger. But it's more of a disciplinary measure than a diet. Setting time limits around food consumption helps foil a key feature of the SAD, which is that it's difficult to *stop* eating it. Time-restricted feeding is a way of putting the brakes on snacking and late-night meals—the type of mindless eating-just-to-eat that the Japanese call *kuchisabishii*, for “lonely mouth.” But beyond that, I don't think it's particularly useful.

正如我所說，我有時會讓某些患者實行限時飲食模式，因為我發現這有助於他們減少整體熱量攝入，同時盡量減少飢餓感。但這更像是一種紀律措施，而不是飲食。圍繞食物消耗設定時間限制有助於掩蓋 SAD 的關鍵特徵，即很難停止進食。限時餵食是一種抑制零食和深夜進餐的方法——這種無意識的飲食方式——只是為了吃，日本人稱之為“kuchisabishii”，意為“孤獨的嘴”。但除此之外，我認為它並不是特別有用。

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Next, we have alternate-day fasting (ADF), which has also become popular. This is where you eat normally or even a bit more than normal one day, and then very little (or nothing) the next. There is more extensive research into this eating pattern in humans—and, of course, there have been books written about it too—but the results are not particularly appealing. Some studies have found that subjects can indeed lose weight on alternate-day fasting diets, but more

nuanced research suggests there are some significant downsides. One small but revealing study found that subjects on an alternate-day fasting diet did lose weight—but they also lost more lean mass (i.e., muscle) than subjects who simply ate 25 percent fewer calories every day.

接下來，我們還有隔日斷食（ADF），它也變得很流行。這是指您一天吃得正常，甚至比平常多一點，然後第二天吃得很少（或不吃）。對人類的這種飲食模式進行了更廣泛的研究——當然，也有關於它的書籍——但結果並不是特別吸引人。一些研究發現，隔日斷食確實可以減肥，但更細緻的研究表明，隔日斷食有一些顯著的缺點。一項小型但具有啟發意義的研究發現，隔日斷食的受試者確實減輕了體重，但與每天攝取熱量減少25% 的受試者相比，他們也失去了更多的瘦體重（即肌肉）。

This study was limited because of its small size and short duration, but it suggests that fasting might cause some people, especially lean people, to lose too much muscle.^[*14] On top of this, the ADF group had much lower activity levels during the study, which suggests that they were not feeling very good on the days they were not eating. With longer-term fasting, these effects only become more pronounced, particularly the loss of muscle mass. Therefore, I am inclined to agree with lead investigator James Betts: “If you are following a fasting diet, it is worth thinking about whether prolonged fasting periods [are] actually making it harder to maintain muscle mass and physical activity levels, which are known to be very important factors for long-term health.”

這項研究由於規模小且持續時間短而受到限制，但它表明禁食可能會導致某些人，尤其是瘦人，失去過多的肌肉。 [*14] 除此之外，ADF組在研究期間的活動量要低得多，這表明他們在不進食的日子裡感覺不太好。隨著禁食時間的延長，這些影響只會變得更加明顯，尤其是肌肉質量的損失。因此，我傾向於同意首席研究員詹姆斯貝茨(James Betts) 的觀點：「如果您遵循禁食飲食，那麼值得考慮的是，長時間禁食是否實際上會導致更難維持肌肉質量和體力活動水平，而眾所周知對於長期健康來說是非常重要的因素。」

As a result of this and other research, I have become convinced that frequent, prolonged fasting may be neither necessary nor wise for most

patients. The cost, in terms of lost lean mass (muscle) and reduced activity levels, simply does not justify whatever benefits it may bring. My rule of thumb for any eating pattern, in fact, is that you *must* eat enough to maintain lean mass (muscle) and long-term activity patterns. That is part of what makes any diet sustainable. If we are going to use a powerful tool like fasting, we must do so carefully and deliberately.

根據這項研究和其他研究的結果，我確信對於大多數患者來說，頻繁、長時間的禁食可能既不必要也不明智。就失去瘦體重（肌肉）和降低活動量而言，其成本根本無法證明它可能帶來的任何好處。事實上，我對任何飲食模式的經驗法則是，您必須吃得足夠多，以維持瘦體重（肌肉）和長期活動模式。這是任何飲食可持續的部分原因。如果我們使用像禁食這樣強大的工具，我們必須小心謹慎地這樣做。

But fasting can still prove useful sometimes, in some patients—generally, patients for whom no other dietary intervention has worked. Case in point: my friend Tom Dayspring, the lipidologist whom we met in chapter 7. Tom became a patient of mine a few years ago because I was so concerned about his metabolic health. Then in his midsixties, he was carrying 240 pounds on his five-eight frame, giving him a BMI of 36.5, well into the obese range. Blood tests revealed that he was also working on a serious case of NAFLD, if not outright NASH. Over the years, I had nagged him constantly until he finally agreed to try to do something about it. Given his issues, a ketogenic diet was the obvious place to start. If we limited his carb intake, I figured, he'd lose weight and hopefully his NAFLD would have a chance to dissipate, and his biomarkers and weight would also come under control.

但禁食有時對某些患者仍然有用——通常是其他飲食幹預措施都無效的患者。典型的例子是：我的朋友湯姆·戴斯普林（Tom Dayspring），我們在第七章遇到的脂質學家。湯姆幾年前成為我的病人，因為我非常關心他的代謝健康。當時，他 60 多歲，身高 58 英寸，體重 240 磅，體重指數為 36.5，完全屬於肥胖範圍。血液檢查顯示，他也正在治療嚴重的 NAFLD 病例，甚至是徹底的 NASH 病例。多年來，我不斷地嘮叨他，直到他最終同意嘗試做點什麼。考慮到他的問題，生酮飲食顯然是開始的地方。我想，如果我們限制他的碳水化合物攝取

量，他的體重就會減輕，希望他的 NAFLD 有機會消散，他的生物標記和體重也會得到控制。

But they didn't. After Tom struggled for six months to stay on the diet, his liver enzymes, and his weight, had failed to budge. A year later, same story. Two years, three years, nothing had changed. In the meantime, his health continued to deteriorate, to the point where he had difficulty walking a single city block. He eventually required both a hip replacement and spinal fusion. The problem was that Tom was simply unable to stay on the strict ketogenic diet for very long. He would be fine for two weeks or so, but then he would break down and eat a sandwich or a plate of pasta. It simply wasn't sustainable for him.

但他們沒有。湯姆努力堅持節食六個月後，他的肝臟酵素和體重卻沒有改變。一年後，同樣的故事。兩年，三年，一切都沒有改變。同時，他的健康狀況持續惡化，甚至連步行一個街區都變得困難。他最終需要髖關節置換術和脊椎融合術。問題是湯姆根本無法長期堅持嚴格的生酮飲食。他會在兩週左右的時間裡表現良好，但隨後他就會崩潰並吃一個三明治或一盤義大利麵。這對他來說根本不可持續。

Tom clearly required some sort of stronger medicine, and I concluded that he needed to try fasting. Unfortunately, like many SAD-trained North Americans, Tom hated the very thought of hunger. This was why he had difficulty adhering to the strict ketogenic diet for very long—he felt hungry, and he craved his old familiar carb-heavy foods. Thus, he was never able to switch his metabolism into ketosis and drive down his hunger. Because of his persistently high insulin, his fat cells were refusing to give up the energy they had stored. So he felt hungry all the time, and he could not lose any fat. Clearly, he needed to break out of this vicious cycle.

湯姆顯然需要某種更強效的藥物，我得出的結論是他需要嘗試禁食。不幸的是，像許多受過 SAD 訓練的北美一樣，湯姆討厭飢餓的想法。這就是為什麼他很難長期堅持嚴格的生酮飲食——他感到飢餓，並且渴望吃以前熟悉的高碳水化合物食物。因此，他永遠無法將新陳代謝轉變為酮症並降低飢餓感。由於胰島素持續偏高，他的脂肪細胞

拒絕放棄其儲存的能量。所以他一直覺得很餓，而且減不掉任何脂肪。顯然，他需要打破這個惡性循環。

At first, Tom was horrified by the very notion of fasting. But he is also a scientist, and after delving into some of the research on nutrient deprivation and putting that together with what he already knew about lipids and metabolism and disease risk, he agreed to give it a try. His scientific mind was persuaded, but I think at some point he also realized that he was staring down the barrel of what might be the last five years of his life unless he made some drastic changes. We came up with an aggressive plan, at the limit of what he thought he could tolerate: one week per month, Monday through Friday, Tom would subsist on a drastically reduced diet of about seven hundred calories per day, comprising mostly fat, with a little protein and almost no carbohydrates.

起初，湯姆對禁食的概念感到震驚。但他也是一名科學家，在深入研究了一些有關營養剝奪的研究並將其與他已經了解的有關脂質、新陳代謝和疾病風險的知識結合起來後，他同意嘗試一下。他的科學頭腦被說服了，但我認為在某些時候他也意識到，除非他做出一些重大改變，否則他可能會面臨生命的最後五年。我們提出了一個激進的計劃，在他認為自己可以忍受的限度內：每月一周，從週一到週五，湯姆將每天大幅減少約700卡路里的飲食，其中大部分是脂肪，還有少量的脂肪。蛋白質很少，幾乎不含碳水化合物。

This kind of fasting is called “hypocaloric” because you are not truly fasting in the sense of eating no food at all. You are eating just enough to quell the worst hunger pangs, but not so much that your body thinks you are fully fed. For twenty-five days out of each month, Tom ate a “normal” diet (though in his case, very starch- and sugar-restricted), and only between noon and 8 p.m.; during his fasting week, a typical day’s menu might consist of a salad with light dressing, an avocado, and some macadamia nuts or olives. He was surprised at how good he felt. “It wasn’t as horrific as I thought it was going to be,” he told me later. “After day three, the hunger disappears.”

這種禁食被稱為“低熱量”，因為你並不是真正意義上的完全不吃食物的禁食。你吃的食物剛好足以平息最嚴重的飢餓感，但又不會讓你的身體認為你已經吃飽了。每個月有 25 天，湯姆吃的是「正常」飲食

（儘管對他來說，澱粉和糖的攝取量非常有限），而且只在中午到晚上 8 點之間；在禁食週期間，典型的一天菜單可能包括淡醬沙拉、酪梨和一些澳洲堅果或橄欖。他對自己的感覺如此良好感到驚訝。「事情並不像我想像的那麼可怕，」他後來告訴我。「第三天之後，飢餓感就消失了。」

It did not take long for his blood biomarkers to improve dramatically: where his complete blood chemistry report used to be largely yellow and red—meaning, most of his values were borderline to “bad”—it is now almost entirely green. His lipids are under control, and his liver enzymes have plummeted back to safe, normal ranges. After several cycles of this, he was able to do things like climb a flight of steps or walk several city blocks again without feeling out of breath. His blood pressure is lower, and he has been able to stop taking many of the countless medications he was on. Last, he now weighs sixty-seven pounds less than he used to, a sign that his metabolic health really is back on track, and a powerful incentive for him to keep at it. “The weight just poured off,” he told me.

沒多久，他的血液生物標記就得到了顯著改善：他的完整血液化學報告過去主要是黃色和紅色的——這意味著他的大部分數值都處於「壞」的邊緣——現在幾乎完全是綠色的。他的血脂得到了控制，肝酵素也已降至安全、正常範圍。經過幾次這樣的循環後，他能夠做一些事情，例如爬一段台階或再次行走幾個街區而不會感到氣喘吁籲。他的血壓降低了，而且他已經能夠停止服用他所服用的無數藥物中的許多藥物。最後，他現在的體重比以前減輕了六十七磅，這表明他的新陳代謝健康確實回到了正軌，也是他堅持下去的強大動力。「體重只是減輕，」他告訴我。

Fasting had effectively reset or rebooted his crashed metabolism in a way that no other dietary intervention was able to achieve. Because it has such deleterious effects on muscle mass, I only use it in hard-to-fix patients like Tom. Tom was so overweight to begin with that he could tolerate the loss of muscle because he was losing so much fat at the same time. But most people can't safely lose muscle mass, so fasting is a tool that we can only really use in extremis, when there are no other viable options.

禁食有效地重置或重新啟動了他崩潰的新陳代謝，這是其他飲食幹預措施無法實現的。因為它對肌肉質量有如此有害的影響，所以我只將它用於像湯姆這樣難以治癒的患者。湯姆一開始就超重，他可以忍受肌肉的損失，因為他同時失去了很多脂肪。但大多數人無法安全地失去肌肉質量，因此禁食是一種只有在沒有其他可行選擇的情況下才能真正使用的工具。

Conclusion

結論

In the last two chapters, we have explored the impact of what we eat—and sometimes what we do not eat—on our health, and the importance of moving our thinking toward a Nutrition 3.0 mindset, based on feedback and data rather than labels and trends and ideology.

在最後兩章中，我們探討了我們吃的東西（有時是我們不吃的東西）對健康的影響，以及基於反饋和數據而不是標籤和資訊將我們的思維轉向營養 3.0 思維方式的重要性。趨勢和意識形態。

I once believed that diet and nutrition could cure almost all ills, but I no longer feel that strongly about it. Nutritional biochemistry is an important component of our tactics, but it is not the only path to longevity, or even the most powerful one. I see it more as a rescue tactic, particularly for patients like Eduardo and Tom, with really severe metabolic problems such as NAFLD and type 2 diabetes. It is also essential for older people who need to build or maintain muscle mass. But its power to leverage increased lifespan and healthspan is more limited. Bad nutrition can hurt us more than good nutrition can help us. If you're already metabolically healthy, nutritional interventions can only do so much.

我曾經相信飲食和營養可以治癒幾乎所有疾病，但我不再那麼強烈地相信它。營養生物化學是我們策略的重要組成部分，但它不是長壽的唯一途徑，甚至不是最強大的途徑。我更將其視為一種救援策略，特

別是對於像 Eduardo 和 Tom 這樣患有嚴重代謝問題（例如 NAFLD 和 2 型糖尿病）的患者。對於需要增強或維持肌肉質量的老年人來說，它也很重要。但它延長壽命和健康壽命的能力更為有限。不良營養對我們的傷害大於良好營養對我們的幫助。如果您的新陳代謝已經很健康，那麼營養幹預的作用就有限了。

I know this seems hard to believe, after all we've been conditioned to think and given all the grandstanding that goes into promoting this diet versus that one. But in reality, the first-, second-, and third-order terms in this problem come down to energy balance. CR, DR, and TR are just tools to reduce energy intake, to correct the state of being overnourished and/or metabolically unhealthy.

我知道這似乎很難相信，畢竟我們已經習慣於思考，並考慮到推廣這種飲食與那種飲食的所有譁眾取寵。但實際上，這個問題中的一階、二階和三階項都歸結於能量平衡。CR、DR 和 TR 只是減少能量攝取、矯正營養過剩和/或代謝不健康狀態的工具。

The bad news is that most Americans are *not* metabolically healthy, so they need to pay attention to nutrition. In most cases, addressing the problem means reducing overall energy intake—cutting calories—but in a way that is sustainable for the individual person. We also have to focus on eliminating those types of foods that raise blood glucose too much, but in a way that also does not compromise protein intake and lean body mass.

壞消息是，大多數美國人的新陳代謝並不健康，因此需要注意營養。在大多數情況下，解決這個問題意味著減少整體能量攝取——減少卡路里——但以個人可持續的方式進行。我們也必須集中精力消除那些導致血糖過高的食物，但同時又不能影響蛋白質攝取和去脂體重。

This is where it can get tricky. Protein is actually the most important macronutrient, the one macro that should not be compromised. Remember, most people will be overnourished—but also undermuscle. It is counterproductive for them to limit calories at the expense of protein and hence muscle mass.

這就是事情變得棘手的地方。蛋白質其實是最重要的常量營養素，是一種不應受到損害的常量營養素。請記住，大多數人都會營養過剩，但肌肉也會不足。對他們來說，以犧牲蛋白質和肌肉質量為代價來限制卡路里會適得其反。

This is also where other tactics can play a role. As we saw in chapter 12, zone 2 aerobic training can have a huge impact on our ability to dispose of glucose safely, and also on our ability to access energy we have stored as fat. And the more muscle mass we have, the more capacity we have to use and store excess glucose, and utilize stored fat. In the next chapter, we will see how important good sleep can be to maintaining metabolic balance.

這也是其他策略可以發揮作用的地方。正如我們在第 12 章中所看到的，2 區有氧訓練可以對我們安全處理葡萄糖的能力以及我們獲取以脂肪形式儲存的能量的能力產生巨大影響。我們擁有的肌肉質量越多，我們使用和儲存多餘葡萄糖以及利用儲存脂肪的能力就越大。在下一章中，我們將了解良好的睡眠對於維持代謝平衡有多重要。

If your issues fall more in the domain of lipoproteins and cardiovascular risk, then it makes sense to focus on the fats side of the equation as well, meaning mostly saturated fats, which raise apoB in some people, although this is relatively easy to control pharmacologically. Excessive carbohydrate intake can also have spillover effects on apoB, in the form of elevated triglycerides. (If there is one type of food that I would eliminate from everyone's diet if I could, it would be fructose-sweetened drinks, including both sodas *and* fruit juices, which deliver too much fructose, too quickly, to a gut and liver that much prefer to process fructose slowly. Just eat fruit and let nature provide the right amount of fiber and water.)

如果您的問題更屬於脂蛋白和心血管風險領域，那麼專注於脂肪方面也是有意義的，這意味著主要是飽和脂肪，它會提高某些人的apoB，儘管這在藥理學上相對容易控制。碳水化合物攝取過多也會對 apoB 產生溢出效應，表現為三酸甘油酯升高。（如果可以的話，我會從每個人的飲食中消除一種食物，那就是含果糖的飲料，包括蘇打水和果

汁，它們會過快地向腸道和肝臟輸送過多的果糖喜歡慢慢地處理果糖。只吃水果，讓大自然提供適量的纖維和水。）

In the end, the best nutrition plan is the one that we can sustain. How you manipulate the three levers of diet—calorie restriction, dietary restriction, and time restriction—is up to you. Ideally, your plan improves or maintains all the parameters we care about—not only blood glucose and insulin but also muscle mass and lipid levels, and possibly even weight—while reducing your risk of your most proximate Horseman or Horsemen. Your nutrition goals depend on your individual risk profile: Are you more at risk of metabolic dysfunction, or cardiovascular disease? There is no one right answer for everyone; each patient finds their own balance, their own best approach. Hopefully, in this chapter I've given you some tools with which to come up with a plan that works for you.

最後，最好的營養計劃是我們能夠維持的計劃。如何控制飲食的三個槓桿——熱量限制、飲食限制和時間限制——取決於你自己。理想情況下，您的計劃可以改善或維持我們關心的所有參數——不僅是血糖和胰島素，還有肌肉質量和脂質水平，甚至可能是體重——同時降低您最接近的騎士的風險。您的營養目標取決於您的個人風險狀況：您是否更容易罹患代謝功能障礙或心血管疾病？沒有一個適合所有人的正確答案；每個患者都會找到自己的平衡點，找到自己的最佳方法。希望在本章中我為您提供了一些工具來制定適合您的計劃。

And, one last thing. If, after reading this chapter, you're upset because you don't quite agree with some detail I've covered—be it the ratio of MUFA to PUFA to SFA, or the exact bioavailability of soy protein, the role of seed oils and lectins, or the ideal target for average blood glucose levels—or if I have offended your sensibilities because I didn't say *your* diet is the *best* diet, I have one final piece of advice. Stop overthinking nutrition so much. Put the book down. Go outside and exercise.

最後一件事。如果在讀完本章後，您因為不太同意我所介紹的一些細節而感到不安，無論是 MUFA 與 PUFA 與 SFA 的比例，還是大豆蛋白的確切生物利用度、種子油的作用和凝集素，或者平均血糖水平的理想目標——或者如果我因為我沒有說你的飲食是最好的飲食而冒犯

了你的感受，我有最後一條建議。別再過度考慮營養了。把書放下。出去鍛鍊身體。

[SKIP NOTES](#)

[跳過註釋](#)

[*1](#) The Wisconsin researchers recorded markers of diabetes such as insulin resistance, while the NIH researchers only noted the diagnosis of type 2 diabetes.

*1 威斯康辛州研究人員記錄了胰島素抗性糖尿病標記物，而 NIH 研究人員僅記錄了第 2 型糖尿病的診斷。

[*2](#) Disclosure: I have used CGM periodically since 2015, and in 2021 I was a paid adviser to a company (Dexcom) that manufactures and sells CGM devices, though my work with them focused on the measurement of other (nonglucose) analytes.

*2 揭露：自 2015 年以來，我定期使用 CGM，並在 2021 年擔任一家製造和銷售 CGM 設備的公司 (Dexcom) 的付費顧問，儘管我與他們的合作重點是其他（非葡萄糖）分析物的測量。

[*3](#) The filament does not actually touch the patient's blood but measures glucose levels in the interstitial fluid and extrapolates blood glucose levels from that.

*3 細絲實際上並沒有接觸患者的血液，而是測量組織液中的葡萄糖水平，並據此推斷血糖水平。

[*4](#) In the meantime, you can approximate your own CGM with a simple drugstore glucose monitor, simply by taking a reading every hour on the hour and plotting out the results (noting mealtimes and snacks, as well). It's also enlightening to take glucose measurements before and after a meal, at thirty-minute intervals up to two hours postprandial, and to observe how different foods and combinations of foods affect your glucose "curve."

*4 同時，您可以使用簡單的藥局血糖監測儀來估算您自己的 CGM，只需每小時按時讀取讀數並繪製結果（同時注意用餐時間和零食時間）。在餐前和餐後（餐後兩小時內每隔 30 分鐘測量一次血糖）並觀察不同食物和食物組合如何影響血糖「曲線」也很有啟發性。

[*5](#) Standard deviation, a statistical calculation that indicates the extent of variation within a group (or within an individual), gives us an idea how much the patient's glucose levels are fluctuating *around* that average and also serves as a poor man's proxy for how much insulin they are likely secreting to accomplish the job of glucose disposal. A higher standard deviation means there are greater fluctuations, and probably much more insulin is required to bring their glucose under control. This, to me, is a key early warning sign of hyperinsulinemia.

*5 標準差是一種統計計算，顯示群體內（或個體內）的變異程度，讓我們了解患者的血糖水平在平均值附近波動了多少，也可以作為窮人的代表。它們可能會分泌胰島素來完成葡萄糖處理的工作。標準差越高意味著波動越大，並且可能需要更多的胰島素來控制血糖。對我來說，這是高胰島素血症的關鍵早期預警信號。

*6 As we saw in the previous chapter, this glucose disposal takes place both with and without insulin.

*6 正如我們在上一章中所看到的，無論有或沒有胰島素，這種葡萄糖處理都會發生。

*7 Similar results have been found in multiple other studies, although it remains unclear whether protein supplementation helps to improve muscle *strength* as well as muscle mass.

*7 在多項其他研究中也發現了類似的結果，儘管目前尚不清楚補充蛋白質是否有助於提高肌肉力量和肌肉質量。

*8 Although it can. The liver can turn amino acids into glucose via a process known as gluconeogenesis. This is not a primary source of glucose, nor is it a preferred use for protein.

*8 雖然可以。肝臟可以透過稱為糖質新生作用的過程將胺基酸轉化為葡萄糖。這不是葡萄糖的主要來源，也不是蛋白質的優選用途。

*9 There are also the dreaded trans fats, but they have largely been removed from our diet, so I'll omit them from this discussion.

*9 還有可怕的反式脂肪，但它們基本上已從我們的飲食中去除，因此我將在本次討論中省略它們。

*10 The differences between types of fats all come down to organic chemistry. Fatty acids are essentially chains of carbon atoms of various lengths. That's why we refer to some fats as medium-chain fatty acids versus long-chain fatty acids, for example. A saturated fat gets its name from the fact that it is fully "saturated" with hydrogen atoms attached to that carbon chain. A "monounsaturated" fat refers to the fact that the chain is not fully saturated with hydrogens, and in this case, the reason is that there is one (i.e., mono) double bond in the chain of carbons rather than a single bond. With polyunsaturated fats, there is more than one double bond (confused yet?). Double bonds cause bends in the carbon chain and make the fatty acid more prone to oxidation. Saturated fats are more stable and do not easily react with other molecules. Since saturated fats are linear and can be densely packed together, they can be more solid at room temperature. Because unsaturated fats have kinks in their structure, they are more likely to be liquid at room temperature.

*10 脂肪類型之間的差異都歸結於有機化學。脂肪酸本質上是不同長度的碳原子鏈。這就是為什麼我們將某些脂肪稱為中鏈脂肪酸而不是長鏈脂肪酸。飽和脂肪因其碳鏈上附著的氫原子完全「飽和」而得名。「單元不飽和」脂肪是指碳鏈未完全被氫飽和，在這種情況下，原因是碳鏈中有一個（即單）雙鍵而不是單鍵。對於多元不飽和脂肪，有多個雙鍵（還困惑嗎？）。雙鍵導致碳鏈彎曲，使脂肪酸更容易氧化。飽和脂肪較穩定，不易與其他分子反應。由於飽和脂肪是線性的並且可以緊密地堆積在一起，因此它們在室溫下可以更加固態。由於不飽和脂肪的結構存在扭結，因此它們在室溫下更有可能呈現液態。

*11 The fancy version of this test can also determine a person's omega-6/omega-3 ratio as well as the levels of all fatty acids in their blood.

*11 此測試的奇特版本還可以確定一個人的 omega-6/omega-3 比率以及血液中所有脂肪酸的含量。

*12 Interestingly, the baseline composition of human fat tissue, made up of roughly 55 percent MUFA, 30 percent SFA, and 15 percent PUFA (Seidelin 1995), falls right in line with the *dietary* fat

distribution that works well in most of my patients.

*12 有趣的是，人體脂肪組織的基線組成由大約 55% MUFA、30% SFA 和 15% PUFA 組成（Seidelin 1995），與對我的大多數患者有效的飲食脂肪分佈完全一致。

*13 In my keto days I was consuming about 250 to 350 grams of fat per day, easily 40 to 50 percent of which was SFA, yet I had perfectly normal lipids and unmeasurable inflammatory markers. I have zero idea why, other than perhaps I was also exercising about three to four hours per day.

*13 在我吃生酮的日子裡，我每天消耗大約 250 到 350 克脂肪，其中 40% 到 50% 是 SFA，但我的血脂完全正常，發炎標記物無法測量。我不知道為什麼，除了也許我每天也運動大約三到四個小時。

*14 I experienced something like this in my cycling phase. At my peak I was doing very strict time-restricted feeding to the tune of about 20/4 every day. Lunch was a basically a chicken salad at 2 p.m. and dinner was normal size at 6 p.m., and I was twenty pounds lighter than I am today—mostly because I had less muscle. It was great for cycling, where light weight is an advantage, but bad for upper-body muscle mass.

*14 我在騎乘階段也經歷過類似的事情。在我的巔峰時期，我每天的餵食時間非常嚴格，大約是 20/4。下午 2 點，午餐基本上就是一份雞肉沙拉。下午 6 點的晚餐是正常量，我比今天輕了 20 磅——主要是因為我的肌肉較少。這對於騎自行車來說非常有用，因為重量輕是一個優勢，但對上身肌肉質量不利。

CHAPTER 16

第16章

The Awakening

覺醒

How to Learn to Love Sleep, the Best Medicine for
Your Brain

如何學會愛睡眠，它是大腦的最佳良藥

Each night, when I go to sleep, I die. And the next
morning, when I wake up, I am reborn.

每天晚上，當我入睡時，我就死了。第二天早
上，當我醒來時，我就重生了。

—MAHATMA GANDHI

-聖雄甘地

There's a reason why medical residency is called “residency”: You're basically living at the hospital, day and night, for the duration. At one point, I was averaging nearly 120 hours per week at work, often for more than thirty hours at a stretch. That left a grand total of about 48 hours a week for eating, sleeping, working out, going on dates (mostly first-and-last), and everything else in life. A friend who had been a year ahead of me in medical school offered what seemed like sage advice: “Even if you spend every single one of those free hours sleeping, you will still be tired—and if you only work and sleep, you will be miserable. So live a little. Sleep can be sacrificed.”

住院醫師實習被稱為「住院醫師實習」是有原因的：在住院期間，你基本上日日夜夜都住在醫院裡。有一段時間，我平均每週工作近 120 小時，經常連續工作 30 多個小時。這樣一來，每週總共大約有 48 個小時用於吃飯、睡覺、運動、約會（主要是第一次和最後一次約會）以及生活中的其他事情。一位在醫學院比我早一年的朋友提出了看似明智的建議：「即使你把所有的空閒時間都花在睡覺上，你仍然會感到疲倦——如果你只工作和睡覺，你就會感到疲倦。」很痛。所以，活一點吧。睡眠可能會被犧牲。”

One summer evening during my internship, after an unusually long stint at work, I got a taste of what acute sleep deprivation could do. One of my co-residents was sick and I volunteered to take his call shift, which was the night before my own scheduled call. That meant I was at work from 5:30 a.m. Monday until 6 p.m. on Wednesday. When I left the hospital, I got into my car and headed for the freeway to drive home. As I sat at a traffic light, my head suddenly snapped upright. *Holy shit*, I said to myself. *I just fell asleep behind the wheel*. At the next light, it happened again, and this time my left foot slipped off the clutch and the engine stalled.

在實習期間的一個夏天的晚上，在經歷了一段異常長時間的工作之後，我嚐到了嚴重睡眠不足的後果。我的一位同事生病了，我自願接他的電話輪班，那是我自己預定的電話的前一天晚上。這意味著我從週一早上 5:30 一直工作到下午 6 點。週三。當我離開醫院時，我上了車，沿著高速公路開車回家。當我坐在紅綠燈前時，我的頭突然直了

起來。天哪，我對自己說。我剛剛在方向盤後面睡著了。到了下一個紅綠燈時，這種情況又發生了，這次我的左腳滑離了離合器，引擎熄火了。

To this day I thank the stars that, despite having gone more than sixty hours without sleep, I was at least able to muster the vestigial good judgment required to save my own life. I pulled over to the curb along Eastern Avenue and got out of the car for some fresh air. There was a nice warm breeze, and the low-hanging sun felt good on my face. There happened to be a park right there, and I decided to set the alarm on my pager (yes, my pager) for thirty minutes later and lie down on the grass to “rest my eyes.”

直到今天，我仍然感謝星星，儘管我已經有六十多個小時沒有睡覺，但我至少能夠恢復挽救自己生命所需的殘餘良好判斷力。我把車停在東大道的路邊，下車呼吸新鮮空氣。一陣溫暖的微風吹過，低垂的陽光照在我的臉上，感覺很好。那裡剛好有一個公園，我決定將我的尋呼機（是的，我的尋呼機）的鬧鐘設定為三十分鐘後，然後躺在草地上「休息一下我的眼睛」。

Six hours later, I woke up in the middle of Baltimore's Patterson Park, then an open-air heroin market and thriving hub for prostitution. Our ER had patched up quite a few of the locals. It was now the middle of the night, and I was sprawled out on my back in my bright green scrubs, with a puddle of drool at my neck. I had mysterious bite marks on my forearms, and there were a few syringes scattered around. Otherwise, I was fine. Apparently, nobody had dared mess with the crazy guy sleeping on the ground in his hospital scrubs.

六個小時後，我在巴爾的摩帕特森公園的中央醒來，當時是一個露天海洛因市場和繁榮的賣淫中心。我們的急診室已經治癒了許多當地人。現在已經是半夜了，我穿著亮綠色的手術服，仰躺著，脖子上有一灘口水。我的前臂上有神秘的咬痕，周圍散落著一些注射器。否則，我很好。顯然，沒有人敢惹這個穿著醫院手術衣睡在地上的瘋子。

I would like to be able to say that I learned my lesson from this scary incident and that I immediately recognized the importance of sleep. I didn't. In truth, it took almost another decade for the message of that episode to sink in, in part because such extreme examples of acute sleep debt were easy to dismiss as artifacts of residency. It was just part of the deal. This was not the only time this kind of thing had happened to me: on another occasion, I fell asleep in my car in the parking lot of the gym with the radio on, and Jill had to come give me a jump start at 2 a.m., after only a few months of dating. (I'm a lucky man.)

我想說的是，我從這次可怕的事件中吸取了教訓，並且立即認識到了睡眠的重要性。我沒有。事實上，這事件的訊息又花了近十年的時間才被人們所接受，部分原因是這種嚴重睡眠債的極端例子很容易被視為居住的假象而被忽視。這只是交易的一部分。這並不是我唯一一次遇到這樣的事情：還有一次，我在健身房停車場的車裡睡著了，收音機還開著，吉爾不得不在凌晨 2 點來給我提個醒。，僅約會幾個月後。（我是一個幸運的人。）

At the time of my unplanned nap in the park, there was a huge debate over residents' working hours, and I am embarrassed to admit that I was ardently opposed to reducing them. The proposal was to limit the maximum number of hours we could work to just 80, down from more than 110. I thought it would make us all soft, and many of my senior colleagues agreed.

當我在公園裡無意中小睡時，關於居民的工作時間存在著巨大的爭論，我很尷尬地承認我強烈反對減少工作時間。該提議是將我們的最長工作時間從 110 多小時限制為 80 小時。我認為這會讓我們都變得軟弱，我的許多高級同事也同意。

Looking back, it is shocking that such a cavalier disregard for sleep was tolerated, even cultivated, in a medical setting. It's almost as if they had encouraged us to smoke and drink heavily while on the job. This is not an idle analogy: We now know that even one sleepless night can create a state that is the functional equivalent of being legally drunk. Studies have found that sleep-deprived medical personnel, in particular, commit many more errors and cause many more deaths than those who are well rested. Count me among

them: one of my worst moments as a sleep-starved resident came during yet another absurdly long shift (more than forty-eight hours), when I face-planted into the drapery of a patient on whom I was about to perform a “lap chole,” a laparoscopic gallbladder removal. Luckily nothing bad happened to the patient, but the memory still makes me cringe.

回想起來，令人震驚的是，在醫療環境中，這種對睡眠的漫不經心的漠視竟然被容忍，甚至被培養。就好像他們鼓勵我們在工作時大量吸煙和飲酒。這並不是一個無聊的類比：我們現在知道，即使是一個不眠之夜也可以創造出一種相當於合法醉酒的狀態。研究發現，與休息良好的醫護人員相比，睡眠不足的醫護人員尤其會犯更多錯誤，造成更多死亡。把我算作其中之一：作為一名睡眠不足的住院醫師，我最糟糕的時刻之一是在另一個荒謬的長時間輪班（超過四十八小時）期間，當時我臉埋在我即將為其做手術的病人的帷幔上。“lap chole”，即腹腔鏡膽囊切除術。幸運的是，病人沒有發生什麼不好的事情，但記憶仍然讓我感到畏縮。

Even then, less than twenty years ago, we knew relatively little about why we sleep, what happens *while* we are asleep, and the importance of sleep to both short-term performance and long-term health. We now know that chronic sleep debt is a far more insidious killer than the acute sleep deprivation that results in falling asleep at stop signs. Many studies have found powerful associations between insufficient sleep (less than seven hours a night, on average) and adverse health outcomes ranging from increased susceptibility to the common cold to dying of a heart attack. Poor sleep dramatically increases one's propensity for metabolic dysfunction, up to and including type 2 diabetes, and it can wreak havoc with the body's hormonal balance. Looking back, I now suspect that at least some of my own health issues, in my thirties, had their roots in my cavalier disregard of sleep.

即便如此，不到二十年前，我們對為什麼睡覺、睡覺時會發生什麼以及睡眠對短期表現和長期健康的重要性知之甚少。我們現在知道，與導致在停車標誌處睡著的嚴重睡眠不足相比，慢性睡眠債是更陰險的殺手。許多研究發現，睡眠不足（平均每晚少於七小時）與不良健康結果（從增加對普通感冒的易感性到死於心臟病）之間存在密切關

聯。睡眠不佳會顯著增加代謝功能障礙的可能性，甚至包括第 2 型糖尿病，並且會嚴重破壞身體的荷爾蒙平衡。回想起來，我現在懷疑，至少我自己在三十多歲時的一些健康問題的根源在於我對睡眠的漫不經心的忽視。

As important as sleep is for the body, it may even be more so for the brain. Good sleep, in terms of not only quantity but quality, is critical to our cognitive function, our memory, and even our emotional equilibrium. We feel better, in every way, after a night of good sleep. Even while we are unconscious, our brain is still working, processing thoughts and memories and emotions (hence, dreams). It even cleans itself, in a manner similar to a city sweeping the streets. Relatedly, there is a growing body of evidence that sleeping well is essential to preserving our cognition as we age and staving off Alzheimer's disease.

睡眠對身體來說很重要，對大腦來說更是如此。良好的睡眠，不僅在數量上，而且在品質上，對於我們的認知功能、記憶力，甚至情緒平衡都至關重要。經過一晚的良好睡眠後，我們在各方面都感覺好多了。即使我們處於無意識狀態，我們的大腦仍在工作，處理思想、記憶和情緒（因此，夢）。它甚至可以自我清潔，就像城市清掃街道一樣。與此相關的是，越來越多的證據表明，隨著年齡的增長，良好的睡眠對於保持我們的認知能力和預防阿茲海默症至關重要。

These conclusions are mainly based on observational studies, which I questioned in chapter 14 as they pertain to nutrition, and they share some of the same flaws—notably, that subjects' recollections of how much they sleep might not be terribly accurate. (Do you know exactly how long, and how well, you slept last night? Likely not.) But these studies differ from nutritional epidemiology because there is only one input, sleep; several of their key findings have been confirmed in more rigorous clinical studies; and the data are more uniform, consistently pointing in the same direction.

這些結論主要基於觀察性研究，我在第 14 章中對這些研究提出了質疑，因為它們與營養有關，並且它們具有一些相同的缺陷，尤其是受試者對睡眠時間的回憶可能不是非常準確。（你確切知道你昨晚睡了多久、睡得怎麼樣？很可能不知道。）但這些研究與營養流行病學不

同，因為只有一種輸入：睡眠；睡眠；睡眠。他們的一些關鍵發現已在更嚴格的臨床研究中得到證實；而且數據更加統一，始終指向同一方向。

The long and the short of it is that poor sleep can take a wrecking ball to both your long-term health and your ability to function day-to-day. When you look at the ripple effects of this, across a society that places as little value on sleep as I once did, a devastating picture emerges.

總而言之，睡眠品質不佳會嚴重損害您的長期健康和日常工作能力。當你看到這所帶來的連鎖反應時，在一個像我以前一樣不重視睡眠的社會中，一幅毀滅性的畫面就會出現。

“[The] decimation of sleep throughout industrialized nations is having a catastrophic impact on our health, our life expectancy, our safety, our productivity, and the education of our children,” declares Matthew Walker, director of the Center for Human Sleep Science at the University of California at Berkeley, in his book *Why We Sleep*. I’ve found that my own patients’ health problems can often be traced to poor sleep—and that fixing their sleep issues makes our other tactics more effective.

「整個工業化國家的睡眠品質大幅下降，對我們的健康、預期壽命、安全、生產力以及孩子的教育產生了災難性的影響，」美國人類睡眠科學中心主任馬修·沃克 (Matthew Walker) 表示。加州大學柏克萊分校在他的著作《我們為什麼睡覺》中寫道。我發現我自己的患者的健康問題通常可以追溯到睡眠不佳，而解決他們的睡眠問題可以使我們的其他策略更有效。

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Luckily, it did not take another near disaster to awaken me to the importance of sleep. Rather, it was a pointed question from my friend Kirk Parsley, a former Navy SEAL who later tended SEALs as a naval physician. Over dinner one night in 2012, I had been arguing to Kirk that five to six hours a night was more than enough sleep, and if I didn’t feel tired, then I didn’t need more sleep. In fact, I went so far as to declare that it was a pity that we needed to

waste time in bed at all. Imagine how much more we could accomplish if we just cut out sleep entirely!

幸運的是，沒有發生另一場近乎災難的事情讓我意識到睡眠的重要性。相反，這是我的朋友柯克·帕斯利（Kirk Parsley）提出的一個尖銳的問題，他是一名前海豹突擊隊員，後來作為一名海軍醫生照顧海豹突擊隊。2012年的一個晚上，我在晚餐時一直跟柯克爭論，每晚五到六個小時的睡眠已經足夠了，如果我不感到疲倦，那麼我就不需要更多的睡眠。事實上，我甚至宣稱，我們根本需要在床上浪費時間，這真是太遺憾了。想像一下，如果我們完全不睡覺，我們可以取得多少成就！

There I was again, bravely ascending the flanks of Mount Stupid. But Kirk stopped me short with a simple, Socratic question. If sleep is so unimportant, he asked, then why hasn't evolution gotten rid of it?

我再次勇敢地登上愚蠢山的側翼。但柯克用一個簡單的蘇格拉底式問題打斷了我。他問道，如果睡眠如此不重要，那麼為什麼進化沒有擺脫它？

His logic was inarguable. When we are asleep, we are accomplishing nothing useful: we are not reproducing, gathering food, or protecting our family. Even worse, in that slumbering state we are extremely vulnerable to predators and enemies, as I had been in Patterson Park. This, he argued, demonstrates precisely why sleep is so important. Why would evolution allow us to spend up to a third of our lives in a state of unconsciousness, where we could easily be killed or eaten? He pressed the issue: Don't you think natural selection would have eliminated the need to sleep hundreds of millions of years ago—unless, somehow, it was absolutely essential?

他的邏輯是無可爭議的。當我們睡著時，我們沒有完成任何有用的事情：我們沒有繁殖、收集食物或保護我們的家人。更糟的是，在這種沉睡狀態下，我們非常容易受到掠食者和敵人的攻擊，就像我在帕特森公園一樣。他認為，這恰恰說明了為什麼睡眠如此重要。為什麼演化會讓我們生命中三分之一的時間處於無意識狀態，這樣我們很容易

被殺死或吃掉？他強調了這個問題：你不認為自然選擇在數億年前就已經消除了睡眠的需要嗎——除非，不知何故，睡眠是絕對必要的？

He was so right that it was as if he had struck a gong inside my brain. Every animal engages in some form of sleep; scientists have found no exceptions, so far. Horses can do it standing up; dolphins sleep one half of their brain at a time; and even great white sharks, who never stop moving, spend time in a sleep-like, restful state. Elephants sleep only four hours per day, while the brown bat snoozes for nineteen hours per twenty-four, which strikes me as perhaps a bit too much, but the point is that every animal that has been carefully studied to date sleeps in some way. Kirk was correct: evolutionarily, sleep is non-negotiable.

他說得太對了，就像在我的腦袋裡敲響了鑼一樣。每隻動物都會進行某種形式的睡眠。到目前為止，科學家們還沒有發現任何例外。馬可以站著做；海豚每次只睡一半腦；甚至連不停移動的大白鯊也會在睡眠般的寧靜狀態中度過一段時間。大象每天只睡四個小時，而棕色蝙蝠每二十四小時打瞌睡十九個小時，這在我看來可能有點太多了，但重點是迄今為止經過仔細研究的每一種動物都以某種方式睡覺。柯克是對的：從演化的角度來看，睡眠是不容妥協的。

I was not alone in ignoring or dismissing the importance of sleep; it had long been shortchanged by science and in Western, industrialized society. Decades ago, sleep was considered merely a blank state, a period of unconsciousness during which nothing of any importance happened. Nowadays, our high-achieving culture still seems to regard sleeping as wasted time, something that only babies, dogs, and lazy people need. But the science of sleep has taken off in the last three decades, and newer findings suggest that this attitude is exactly wrong. We now know that sleep is as fundamental to our health as stability is fundamental to strength.

我並不是唯一一個忽視或忽視睡眠重要性的人。它長期以來一直被科學和西方工業化社會所忽視。幾十年前，睡眠被認為只是一種空白狀態，一段無意識的時期，在此期間沒有發生任何重要的事情。如今，我們的高成就文化似乎仍然認為睡眠是浪費時間，只有嬰兒、狗和懶人才需要的東西。但睡眠科學在過去三十年中已經蓬勃發展，最新的

研究結果顯示這種態度是完全錯誤的。我們現在知道，睡眠對我們的健康至關重要，就像穩定性對力量而言一樣重要。

Now that I've made sleep a priority in my own life, I reap the benefits every day. There's no feeling more powerful than waking up after I've slept really, really well. My brain is brimming with new ideas, I feel like crushing my workout, and I am a genuinely better person to those around me. But when was the last time you woke up feeling that way? This morning? Last week? Last month? You can't remember?

現在我已經把睡眠當作自己生活的重中之重，我每天都受益匪淺。沒有什麼比睡得非常非常好的醒來更強烈的感覺了。我的大腦充滿了新的想法，我想要粉碎我的鍛煉，而且對於周圍的人來說，我確實是一個更好的人。但你上一次醒來時有這種感覺是什麼時候？今天早上？上個星期？上個月？你不記得了？

If this is you, then you need to be taking stock of your sleep patterns and sleep quality, and working to fix them—just as much as you should address your lipoproteins, your metabolic health, or your markers of physical fitness. It's that important.

如果你是這樣，那麼你需要評估你的睡眠模式和睡眠質量，並努力解決它們——就像你應該解決你的脂蛋白、你的代謝健康或你的身體健康指標一樣。這很重要。

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How long do we need to sleep? This question is tricky, because our sleep cycles are powerfully influenced by external cues such as sunlight, noise, and artificial lighting, not to mention our own emotions and stresses. Also, we are quite good at adapting to inadequate sleep, at least for a while. But many, many studies have confirmed what your mother told you: We need to sleep about seven and a half to eight and a half hours a night. There is even some evidence, from studies conducted in dark caves, that our eight-ish-hour sleep cycle may be hard-wired to some extent, suggesting that this requirement is

non-negotiable. Getting significantly less sleep than this, or significantly more, will almost inevitably cause problems in the long run.

我們需要睡多久？這個問題很棘手，因為我們的睡眠週期受到陽光、噪音和人工照明等外部暗示的強烈影響，更不用說我們自己的情緒和壓力了。此外，我們非常善於適應睡眠不足，至少在一段時間內是如此。但很多很多研究都證實了你母親告訴你的話：我們每晚需要睡大約七個半到八個半小時。在黑暗洞穴中進行的研究甚至有一些證據表明，我們八小時左右的睡眠週期在某種程度上可能是與生俱來的，這表明這項要求是不容協商的。從長遠來看，睡眠時間明顯少於或較多，幾乎不可避免地會導致問題。

Even a single night of bad sleep has been found to have deleterious effects on our physical and cognitive performance. Athletes who sleep poorly the night before a race or a match perform markedly worse than when they are well rested. Endurance drops, VO_2 max drops, and one-rep-max strength drops. Even our ability to perspire is impaired. And we are more likely to be injured: A 2014 observational study found that young athletes who slept less than six hours per night were more than two and a half times more likely to experience an injury than their peers who slept eight hours or more.

研究發現，即使是一晚睡眠不好也會對我們的身體和認知表現產生有害影響。比賽前一晚睡眠不好的運動員的表現明顯比休息良好時的表現差。耐力下降、最大攝氧量 VO_2 下降、最大一次力量下降。甚至我們流汗的能力也受到損害。而且我們更有可能受傷：2014 年的一項觀察性研究發現，每晚睡眠時間少於 6 小時的年輕運動員受傷的可能性是睡 8 小時或以上的同齡人的兩倍半以上。

Good sleep is like a performance-enhancing drug. In one study, Stanford basketball players were encouraged to strive for ten hours of sleep per day, with or without naps, and to abstain from alcohol or caffeine. After five weeks, their shooting accuracy had improved by 9 percent, and their sprint times had also gotten faster.^[*1] LeBron James makes sleep a key part of his recovery routine, always trying for nine and sometimes ten hours of sleep per night, plus a daily nap. “When you get in that good sleep, you just wake up,

and you feel fresh,” he has said. “You don’t need an alarm clock. You just feel like, okay, I can tackle this day at the highest level that you can get to.”

良好的睡眠就像一劑提升表現的藥物。在一項研究中，史丹佛大學的籃球運動員被鼓勵每天爭取十個小時的睡眠（無論是否小睡），並戒除酒精或咖啡因。五週後，他們的射擊準確度提高了 9%，衝刺時間也變得更快。[*1] 詹姆斯將睡眠作為他恢復日常工作的關鍵部分，他總是嘗試每晚睡九個小時，有時甚至十個小時，再加上每日小睡。「當你睡得很好時，你就會醒來，感覺神清氣爽，」他說。「你不需要鬧鐘。你只是覺得，好吧，我可以以你能達到的最高水平來應對這一天。」

For those of us who are not professional athletes, sleep is still essential to performance in more mundane—and dangerous—tasks, such as driving. One study found that after a night of sleep deprivation, a group of professional drivers displayed far worse reaction time in situations such as braking to avoid a crash. Unfortunately, there’s no breathalyzer for sleep-impaired driving, so it’s harder to capture precise statistics. But a survey conducted by AAA found that nearly one in three drivers (32 percent) reported that in the past thirty days they had driven when they were so tired they had a hard time keeping their eyes open.

對於我們這些不是職業運動員的人來說，睡眠對於執行更平凡且危險的任務（例如駕駛）仍然至關重要。一項研究發現，經過一晚的睡眠不足後，一群職業司機在煞車以避免撞車等情況下的反應時間要差得多。不幸的是，沒有針對睡眠障礙駕駛的呼氣分析儀，因此很難獲得精確的統計數據。但美國汽車協會 (AAA) 進行的一項調查發現，近三分之一的駕駛 (32%) 表示，在過去 30 天裡，他們在開車時感到非常疲倦，難以睜開眼睛。

Yet we are often unaware of the devastating effect that poor sleep is having on our energy levels and our performance. Research has found that people who are sleep deprived almost always underestimate its effects on them, because they adapt to it. As anyone who has had infant children knows, we come to accept the resulting state of mild exhaustion and mental fog as a new normal, a process called “baseline resetting.” I know I did. I assumed I

was sleeping sufficiently, as a resident and then as a consultant, because I didn't have anything to compare it to. Now that I sleep better, I'm amazed that I survived for as long as I did in that state. It's like, a regular TV looks fine if that's all you've ever seen. But once you see a 4K screen, you realize that your old cathode-ray tube TV was not very clear after all. The difference is that dramatic.

然而，我們常常沒有意識到睡眠不足對我們的能量水平和表現的破壞性影響。研究發現，睡眠不足的人幾乎總是低估睡眠對他們的影響，因為他們已經適應了。任何養過嬰兒的人都知道，我們逐漸接受由此產生的輕度疲憊和精神迷霧狀態作為一種新常態，這一過程稱為「基線重置」。我知道我做到了。我以為我作為住院醫師和顧問的睡眠充足，因為我沒有任何東西可以比較。現在我睡得更好了，我很驚訝我在那種狀態下還能活這麼久。就像，如果你只見過普通電視，那麼它看起來就不錯。但當你看到4K螢幕時，你會發現你的舊陰極射線管電視畢竟不是很清晰。差別就是這麼戲劇性。

Old-Man Blood

老人血

Scary as it can be in some situations, the short-term harm done by a night or three of poor sleep pales in comparison to the damage that we do to ourselves if this situation continues. Kirk Parsley observed this when he was a physician to the SEALs. Outwardly, these men appeared to be prime physical specimens, finely honed by their rigorous training. But when Parsley analyzed their blood tests, he was shocked: many of these young guys had the hormone levels and inflammatory markers of men several decades older than them —“old-man blood,” Parsley called it. Because their training exercises and missions often began at odd hours of the night and required them to stay awake for twenty-four hours or more at a stretch, they were chronically sleep deprived, their natural sleep-wake cycles utterly disrupted.

儘管在某些情況下可能很可怕，但與這種情況持續下去對我們自己造成的傷害相比，一到三個晚上睡眠品質不佳所造成的短期傷害就顯得微不足道了。柯克·帕斯利（Kirk Parsley）在擔任海豹突擊隊隊醫時觀察到了這一點。從表面上看，這些人似乎都是經過嚴格訓練磨練出來的優秀體格標本。但當歐芹分析他們的血液測試時，他感到震驚：這些年輕人中的許多人都擁有比他們年長數十歲的男性的激素水平和炎症標誌物——歐芹稱之為「老人血」。由於他們的訓練演習和任務經常在夜間的零星時間開始，並要求他們連續二十四小時或更長時間保持清醒，因此他們長期睡眠不足，自然的睡眠-覺醒週期完全被打亂。

When Kirk told me that story, I experienced a jolt of recognition: I, too, had had “old-man blood,” during my Not-Thin Peter phase, with elevated insulin, high triglycerides, and a testosterone level in the bottom 5 percent of men in the United States. I had always attributed my poor health and hormone imbalance at that point to my lousy diet, and diet alone, but I had also spent at least a decade in a state of severe sleep deprivation, in residency and afterward. Belatedly, I realized that not sleeping had actually caught up to me as well. It was probably even evident in my face: studies have found that people who sleep less chronically tend to have older-looking, flabbier skin than people their same age who sleep more.

當柯克告訴我這個故事時，我猛然意識到：在我的「不瘦彼得」階段，我也有「老人血統」，胰島素水平升高，甘油三酯水平升高，睾酮水平排在倒數第五位。美國男性的百分比。我一直將當時的健康狀況不佳和荷爾蒙失衡歸因於我糟糕的飲食，而且只是飲食，但我在住院期間和之後也至少有十年處於嚴重睡眠不足的狀態。後來，我意識到失眠其實也困擾著我。這一點在我的臉上也很有明顯：研究發現，與同齡睡眠較多的人相比，長期睡眠較少的人往往會顯得更老、皮膚更鬆弛。

Now I recognize that sleep, diet, and risk of long-term diseases are all intimately connected to each other. Knowing what I do now, I would bet that a few months of perfect sleep could have fixed 80 percent of my problems back then, even on a crappy diet.

現在我意識到，睡眠、飲食和長期疾病的風險都相互密切相關。知道我現在所做的事情，我敢打賭，幾個月的完美睡眠可以解決我當時 80% 的問題，即使飲食很糟糕。

This may come as a surprise to you, as it did to me, but poor sleep wreaks havoc on our metabolism. Even in the short term, sleep deprivation can cause profound insulin resistance. Sleep researcher Eve van Cauter of the University of Chicago subjected healthy young people to severely restricted sleep, just 4.5 hours a night, and found that after four days they had the elevated insulin levels of obese middle-aged diabetics and, worse yet, approximately a 50 percent reduction in their capacity for glucose disposal. This turns out to be one of the most consistent findings in all of sleep research. No fewer than nine different studies have found that sleep deprivation increases insulin resistance by up to a third. Very rarely in medicine do we see such consistent findings, with experimental evidence confirming the epidemiology so powerfully, so it's worth paying attention. It seems quite clear that poor or inadequate sleep can help tilt us into metabolic dysfunction.

這可能會讓你感到驚訝，就像我一樣，但睡眠不足會對我們的新陳代謝造成嚴重破壞。即使在短期內，睡眠不足也會導致嚴重的胰島素抗性。芝加哥大學的睡眠研究員Eve van Cauter 對健康的年輕人進行了嚴格的睡眠限制，每晚僅4.5 小時，結果發現，四天后，他們的胰島素水平與肥胖的中年糖尿病患者一樣升高，更糟糕的是，大約葡萄糖處理能力降低 50%。事實證明，這是所有睡眠研究中最一致的發現之一。不少於九項不同的研究發現，睡眠不足會使胰島素阻抗增加多達三分之一。在醫學領域，我們很少看到如此一致的發現，實驗證據如此有力地證實了流行病學，因此值得關注。很明顯，睡眠不足或不足會導致我們出現代謝功能障礙。

Unfortunately, similar longer-term trials haven't been done, but observational studies suggest a clear link between short sleep and long-term metabolic disturbances. Multiple large meta-analyses of sleep studies have revealed a close relationship between sleep duration and risk of type 2 diabetes and the metabolic syndrome. But it cuts both ways: *long* sleep is also a sign of problems. People who sleep eleven hours or more nightly have a

nearly 50 percent higher risk of all-cause mortality, likely because long sleep = poor quality sleep, but it may also reflect an underlying illness. Similar risk associations have been found between poor or short sleep and hypertension (17 percent), cardiovascular diseases (16 percent), coronary heart diseases (26 percent), and obesity (38 percent). Taken together, these findings all suggest that the long-term effects of inadequate sleep parallel what we would expect from the short-term studies: increased insulin resistance and more of the diseases that accompany it, from NASH and type 2 diabetes to heart disease. If your sleep is chronically compromised, then your metabolism might be too.

不幸的是，類似的長期試驗尚未進行，但觀察性研究顯示睡眠不足與長期代謝紊亂之間有明顯關聯。多項睡眠研究的大型統合分析揭示了睡眠時間與第 2 型糖尿病和代謝症候群風險之間的密切關係。但這是雙向的：長時間睡眠也是問題的徵兆。每晚睡眠 11 小時或以上的人全因死亡的風險高出近 50%，可能是因為睡眠時間長 = 睡眠品質差，但也可能反映出潛在的疾病。睡眠不足或睡眠不足與高血壓（17%）、心血管疾病（16%）、冠狀動脈心臟病（26%）和肥胖（38%）之間也存在類似的風險關聯。總而言之，這些發現都表明，睡眠不足的長期影響與我們從短期研究中預期的結果相似：胰島素阻抗增加以及隨之而來的更多疾病，從 NASH 和 2 型糖尿病到心臟病。如果您的睡眠長期受到損害，那麼您的新陳代謝也可能會受到影響。

This association between sleep and metabolic health seems puzzling at first, but I think the missing link here is stress. Higher stress levels can make us sleep poorly, as we all know, but poor sleep also makes us more stressed. It's a feedback loop. Both poor sleep and high stress activate the sympathetic nervous system, which—despite its name—is the opposite of calming. It is part of our fight-or-flight response, prompting the release of hormones called glucocorticoids, including the stress hormone cortisol. Cortisol raises blood pressure; it also causes glucose to be released from the liver, while inhibiting the uptake and utilization of glucose in the muscle and fat tissues, perhaps in order to prioritize glucose delivery to the brain. In the body, this manifests as elevated glucose due to stress-induced insulin resistance. I see this often, in myself and some of my patients: high overnight glucose on CGM is almost

always a sign of excessive cortisol, sometimes exacerbated by late-night eating and drinking. If it persists, this elevated blood glucose can lead to type 2 diabetes.

睡眠和代謝健康之間的這種連結一開始似乎令人費解，但我認為這裡缺少的環節是壓力。眾所周知，較高的壓力水平會讓我們睡不好，但睡眠不好也會讓我們更有壓力。這是一個回饋循環。睡眠不足和壓力大都會激活交感神經系統，儘管它的名字如此，但它與平靜相反。它是我們戰鬥或逃跑反應的一部分，促使糖皮質激素的釋放，包括壓力荷爾蒙皮質醇。皮質醇會升高血壓；它還會導致肝臟釋放葡萄糖，同時抑制肌肉和脂肪組織對葡萄糖的吸收和利用，也許是為了優先將葡萄糖輸送到大腦。在體內，這表現為由於壓力引起的胰島素抗性而導致的血糖升高。我經常在我自己和我的一些患者身上看到這樣的情況：連續血糖監測（CGM）時夜間血糖過高幾乎總是皮質醇過多的徵兆，有時深夜飲食會加劇這種情況。如果這種情況持續存在，血糖升高可能會導致第 2 型糖尿病。

Compounding the problem, poor sleep also changes the way we behave around food. Studies by Eve van Cauter's group have found that limiting subjects' sleep to four or five hours a night suppresses their levels of leptin, the hormone that signals to us that we are fed, while increasing levels of ghrelin, the "hunger" hormone. When we sleep poorly, we can be desperately, irrationally hungry the next day, and more likely to reach for high-calorie and sugary foods than their healthy alternatives. Studies show that people who are more sleep deprived tend to have a higher likelihood of indulging in a fourth meal late in the evening. Follow-up studies by van Cauter's group have found that short-sleeping subjects ate about three hundred extra calories' worth of food the following day, compared with when they were well rested. Taken together, this all adds up to a perfect recipe for the beginnings of NAFLD and insulin resistance.

讓問題更加複雜的是，睡眠不足還會改變我們對食物的行為。Eve van Cauter 小組的研究發現，將受試者每晚的睡眠時間限制在四到五個小時會抑制他們的瘦素水平，瘦素是一種向我們發出吃飽信號的激素，同時會增加胃飢餓素（“飢餓”激素）的水平。當我們睡眠品質不佳

時，第二天我們可能會感到極度、非理性的飢餓，並且更有可能選擇高熱量和高糖食物，而不是健康的替代品。研究表明，睡眠不足的人更有可能在深夜吃第四餐。van Cauter 小組的後續研究發現，與休息良好時相比，睡眠時間短的受試者第二天會多吃約 300 卡路里的食物。總而言之，這一切構成了 NAFLD 和胰島素阻抗的完美根源。

Sleep and Cardiovascular Disease

睡眠與心血管疾病

The sympathetic nervous system may also help explain why poor sleep is so strongly associated with cardiovascular disease and heart attacks. When we perceive a threat, it takes over, mobilizing stress hormones such as cortisol and adrenaline, which raise our heart rate and blood pressure. Unfortunately, poor sleep has much the same effect, putting the sympathetic nervous system on permanent alert; we get stuck in fight-or-flight mode, and our blood pressure and heart rate remain elevated. This, in turn, multiplies the stress placed on our vasculature. I've noticed this myself, via some of the self-tracking devices that I like to play with: During a night of poor sleep, my resting heart rate will be higher (bad), and my heart rate variability will be lower (also bad).

交感神經系統也可能有助於解釋為什麼睡眠不佳與心血管疾病和心臟病發作密切相關。當我們感知到威脅時，它就會接管，調動皮質醇和腎上腺素等壓力激素，從而提高我們的心率和血壓。不幸的是，睡眠不足也會產生同樣的影響，使交感神經系統永遠處於警覺狀態。我們陷入戰鬥或逃跑模式，血壓和心率仍然升高。這反過來又增加了我們脈管系統的壓力。我自己透過一些我喜歡玩的自我追蹤設備注意到了這一點：在睡眠不佳的夜晚，我的靜止心率會更高（不好），而我的心率變異性會更低（也壞的）。

This may explain why inadequate sleep over long periods is associated with an increased risk of cardiac events. This is something that is difficult to

study definitively, as in a randomized controlled trial. Two large meta-analyses have found that short sleep (defined as less than six hours a night) is associated with about a 6 to 26 percent increase in cardiovascular disease. This does not tell us about causality. Surely, some of the reasons why people are sleeping poorly may also be contributing to their risk of heart disease: longer work hours, less income, more stress, et cetera. But one particularly interesting study compared observational and Mendelian randomization data in people with previously identified genetic variants that either increase or decrease their lifelong exposure to longer or shorter sleep duration. The MR data confirmed the observational findings, that sleeping less than six hours a night was associated with about a 20 percent higher risk of a heart attack. Even more noteworthy, the researchers found that sleeping six to nine hours a night (i.e., adequately, by the researchers' definition) was associated with a reduction in heart attack risk—even among individuals with a high genetic predisposition for coronary artery disease.

這也許可以解釋為什麼長期睡眠不足會增加心臟事件的風險。這是很難明確研究的事情，就像在隨機對照試驗中一樣。兩個大型統合分析發現，睡眠不足（定義為每晚少於 6 小時）與心血管疾病增加約 6% 至 26% 有關。這並沒有告訴我們因果關係。當然，人們睡眠品質不佳的一些原因也可能增加心臟病的風險：工作時間更長、收入更少、壓力更大等等。但一項特別有趣的研究比較了先前發現的基因變異群體的觀察數據和孟德爾隨機數據，這些基因變異會增加或減少他們終生睡眠時間更長或更短的時間。MR 數據證實了觀察結果，每晚睡眠少於 6 小時與心臟病發作的風險增加約 20% 相關。更值得注意的是，研究人員發現，每晚睡眠六到九小時（即根據研究人員的定義，睡眠充足）與心臟病發作風險降低有關，即使對於具有冠狀動脈疾病高遺傳易感性的個體也是如此。

Translation: good sleep may help mitigate some of the genetic risk of heart disease faced by people like me. All of the above has convinced me to make sleep a top priority in my own life, and to pay attention to my patients' sleep habits.

換句話說：良好的睡眠可能有助於減輕像我這樣的人所面臨的心臟病遺傳風險。所有這些都促使我將睡眠作為自己生活中的首要任務，並專注於患者的睡眠習慣。

Sleep and the Brain

睡眠與大腦

What is really striking about most of what we've discussed so far in this chapter—the crucial role that sleep plays in metabolic health and cardiovascular health—is how much of this effect is mediated through the brain. Sleep plays a major role in brain health, especially as we get older, not only in terms of daily cognitive function but also in terms of our long-term cognitive health, a crucial pillar of healthspan.

本章到目前為止我們所討論的大部分內容（睡眠在代謝健康和心血管健康中發揮的關鍵作用）真正引人注目的是這種影響有多少是透過大腦介導的。睡眠在大腦健康中發揮著重要作用，尤其是隨著年齡的增長，不僅在日常認知功能方面，而且在我們的長期認知健康方面也發揮著重要作用，而長期認知健康是健康壽命的重要支柱。

We have all felt groggy and slow after a restless night; our brain simply is not as sharp as it should be. A good night's sleep or even a solid nap usually restores us. But sleep researchers are revealing myriad ways in which good sleep is essential to long-term brain health—and how bad sleep inflicts major damage. Poor sleep was long considered to be one of the first symptoms of incipient Alzheimer's disease. Subsequent research, however, has pointed to chronic bad sleep as a powerful potential *cause* of Alzheimer's disease and dementia. Sleep, it turns out, is as crucial to maintaining brain health as it is to brain function.

經過一個不安寧的夜晚後，我們都感到昏昏沉沉、行動緩慢；我們的大腦根本就沒有應有的敏銳。睡個好覺甚至小睡通常都能讓我們恢復元氣。但睡眠研究人員正在揭示良好的睡眠對長期大腦健康至關重要

的多種方式，以及不良睡眠如何造成重大損害。長期以來，睡眠不佳一直被認為是阿茲海默症初期的首要症狀之一。然而，隨後的研究指出，長期睡眠不足是阿茲海默症和失智症的重要潛在原因。事實證明，睡眠對於維持大腦健康和大腦功能同樣重要。

When we get into bed and close our eyes, a series of physiological changes begins to take place as we descend into sleep. Our heart rate slows, our core temperature drops, and our breathing becomes regular as we wait for sleep to overtake us. Meanwhile, our brain is embarking on its own journey.

當我們上床閉上眼睛時，隨著我們進入睡眠狀態，一連串的生理變化開始發生。當我們等待睡眠到來時，我們的心率減慢，核心體溫下降，呼吸變得規律。與此同時，我們的大腦正踏上自己的旅程。

Researchers now know that we sleep in a series of well-defined stages, each of which has a specific function and a specific electrical brain wave “signature,” which is how researchers initially identified the different sleep stages. To visualize these stages, imagine that when you go to bed and close your eyes, you are embarking on a deep-ocean dive in a submarine. As your body relaxes, you fall asleep, hopefully within a few minutes, and your metaphorical vessel slips beneath the waves and begins its descent.

研究人員現在知道，我們的睡眠處於一系列明確的階段，每個階段都有特定的功能和特定的腦電波“特徵”，這就是研究人員最初識別不同睡眠階段的方式。為了形象化這些階段，想像一下當你上床睡覺並閉上眼睛時，你正在一艘潛艇中開始深海潛水。當你的身體放鬆時，你會睡著，希望在幾分鐘之內，你的隱喻船在波浪下滑動並開始下降。

Normally, our descent is quite rapid: we plunge into the depths, passing through a period of light sleep before dropping into deep sleep. This sleep stage is called non-REM, or NREM, sleep, and it comes in two strengths, light NREM and deep NREM. The latter is the more important of the two, especially for neurological health. In our submersible analogy, this is when we descend into the lightless depths of the sea, where our brain is immune from external stimuli. But that does not mean that there is nothing going on. As we descend into deep sleep, our brain waves slow until they reach an extremely

low frequency, a chanting rhythm of about one to four cycles per second. This deep sleep dominates the first half of the night, although we typically cycle back and forth between deep and lighter NREM.

通常情況下，我們的下降速度相當快：我們陷入深處，經過一段淺睡眠期，然後進入深度睡眠。這個睡眠階段稱為非快速動眼睡眠，或 NREM 睡眠，它有兩種強度：輕度 NREM 和深度 NREM。後者是兩者中更重要的一個，尤其是對於神經健康而言。在我們的潛水器比喻中，這是當我們潛入無光的海洋深處時，我們的大腦不受外部刺激的影響。但這並不意味著什麼都沒有發生。當我們進入深度睡眠時，我們的腦電波會減慢，直到達到極低的頻率，即每秒大約一到四個週期的吟唱節奏。這種深度睡眠佔據了前半夜的主導地位，儘管我們通常會在深度睡眠和淺度非快速動眼睡眠之間來回循環。

Later in the night, typically, our “submersible” rises back up toward the surface, into a zone called rapid eye movement (REM) sleep. In this state, our eyeballs really will dart around behind our eyelids. We are “seeing” things, but only in our mind. This is where most of our dreaming occurs, as our mind processes images and events that seem familiar but are also strange or dislocated from their typical context. Interestingly, the electrical signature of REM sleep is very similar to that when we are awake; the main difference is that our body is paralyzed, which is probably not accidental, since it prevents us from acting on our bizarre dream thoughts. It wouldn’t be good if we could just get up and run around while we were in REM sleep. (This probably also explains those dreams where we are trying to run away from something and our body just won’t seem to cooperate.)

通常在晚上晚些時候，我們的「潛水器」會升回水面，進入一個稱為快速動眼睡眠 (REM) 的區域。在這種狀態下，我們的眼球真的會在眼瞼後面轉來轉去。我們正在「看到」事物，但只是在我們的腦海中。這是我們大多數夢境發生的地方，因為我們的大腦處理看似熟悉但也很奇怪或脫離其典型背景的圖像和事件。有趣的是，快速動眼睡眠的電訊號與我們清醒時的電訊號非常相似。主要的區別是我們的身體癱瘓了，這可能不是偶然的，因為它阻止我們按照奇怪的夢境想法行事。如果我們在快速動眼睡眠時能夠起身跑來跑去，那可就不好了。

（這也可能解釋了那些我們試圖逃離某些東西而我們的身體似乎不配合的夢。）

During a typical night, we will cycle between these sleep stages. These sleep cycles last about ninety minutes, and we may even wake up momentarily in between them—which is likely evolution’s way of protecting us from getting eaten by a lion or attacked by enemies during the night, notes Dr. Vikas Jain, a Stanford-trained sleep physician who works with me on my patients’ sleep issues.

在一個典型的夜晚，我們會在這些睡眠階段之間循環。這些睡眠週期持續大約九十分鐘，我們甚至可能在它們之間短暫醒來——這可能是進化的一種方式，可以保護我們在夜間不被獅子吃掉或被敵人攻擊，史丹佛大學維卡斯·傑恩博士指出。訓練有素的睡眠醫生與我一起解決患者的睡眠問題。

Both REM and deep NREM sleep (which we’ll call “deep sleep” for convenience) are crucial to learning and memory, but in different ways. Deep sleep is when the brain clears out its cache of short-term memories in the hippocampus and selects the important ones for long-term storage in the cortex, helping us to store and reinforce our most important memories of the day. Researchers have observed a direct, linear relationship between how much deep sleep we get in a given night and how well we will perform on a memory test the next day.

快速動眼睡眠和深度非快速動眼睡眠（為方便起見，我們稱之為「深度睡眠」）對於學習和記憶都至關重要，但方式不同。深度睡眠是指大腦清除海馬體中的短期記憶緩存，並選擇重要的記憶在皮質中進行長期存儲，幫助我們儲存和強化當天最重要的記憶。研究人員觀察到，我們在某一晚的深度睡眠時間與我們第二天的記憶測試表現之間存在直接的線性關係。

When we are young, REM sleep is important in helping our brains grow and develop. Even while we are asleep, our brain is forming new connections, expanding our neural network; this is why younger people spend more time in REM. In adulthood, our REM sleep time tends to plateau, but it remains

important, especially for creativity and problem solving. By generating seemingly random associations between facts and memories, and by sorting out the promising connections from the meaningless ones, the brain can often come up with solutions to problems that stumped us the previous day. Research has also found that REM sleep is especially helpful with what is called procedural memory, learning new ways of moving the body, for athletes and for musicians.

當我們年輕時，快速動眼睡眠對於幫助我們的大腦成長和發育很重要。即使我們在睡覺時，我們的大腦也在形成新的連接，擴展我們的神經網路；這就是為什麼年輕人在快速動眼睡眠中花費更多時間的原因。成年後，我們的快速動眼睡眠時間趨於穩定，但它仍然很重要，尤其是對於創造力和解決問題。透過在事實和記憶之間產生看似隨機的關聯，並從無意義的聯繫中篩選出有希望的聯繫，大腦通常可以為前一天困擾我們的問題找到解決方案。研究也發現，快速動眼睡眠對於運動員和音樂家的程序性記憶、學習移動身體的新方法特別有幫助。

Another very important function of REM sleep is to help us process our emotional memories, helping separate our emotions from the memory of the negative (or positive) experience that triggered those emotions. This is why, if we go to bed upset about something, it almost always seems better in the morning. We remember the event but (eventually) forget the pain that accompanied it. Without this break for emotional healing, we would live in a state of constant anxiety, every memory triggering a renewed surge of the emotions around that event. If this sounds like PTSD, you are correct: studies of combat veterans found that they are less able to separate memories from emotions, precisely due to their lack of REM sleep. It turned out that the veterans put out high levels of noradrenaline, the fight-or-flight hormone that effectively prevented their brains from relaxing enough to enter REM.^[*2]

快速動眼睡眠的另一個非常重要的功能是幫助我們處理情緒記憶，幫助我們將情緒與引發這些情緒的負面（或正面）經驗的記憶分開。這就是為什麼，如果我們入睡時因為某件事而心煩意亂，那麼第二天早上看起來似乎就會好一些。我們記得這件事，但（最終）忘了伴隨它

的痛苦。如果沒有這種情緒療癒的休息，我們就會生活在持續焦慮的狀態中，每一個記憶都會引發圍繞該事件的新的情緒激增。如果這聽起來像是創傷後壓力症候群（PTSD），那麼你是對的：對退伍軍人的研究發現，他們不太能夠將記憶與情緒分開，這正是由於他們缺乏快速動眼睡眠。事實證明，退伍軍人體內的去甲腎上腺素水平很高，這種「戰鬥或逃跑」激素可以有效阻止他們的大腦充分放鬆以進入快速動眼睡眠。[*2]

Perhaps most intriguing, REM sleep helps us maintain our emotional awareness. When we are deprived of REM, studies have found, we have a more difficult time reading others' facial expressions. REM-deprived study subjects interpreted even friendly or neutral expressions as menacing. This is not trivial: our ability to function as social animals[*3] depends on our ability to understand and navigate the feelings of others. In short, REM sleep seems to protect our emotional equilibrium, while helping us process memories and information.

也許最有趣的是，快速動眼睡眠可以幫助我們保持情緒意識。研究發現，當我們的快速動眼期睡眠時間被剝奪時，我們就很難讀懂別人的臉部表情。快速動眼睡眠被剝奪的研究對象甚至將友善或中性的表達視為威脅。這並非微不足道：我們作為社會性動物的能力[*3]取決於我們理解和駕馭他人感受的能力。簡而言之，快速動眼睡眠似乎可以保護我們的情緒平衡，同時幫助我們處理記憶和資訊。

Deep sleep, on the other hand, seems to be essential to the very health of our brain as an organ. A few years ago, researchers in Rochester discovered that while we are in deep sleep, the brain activates a kind of internal waste disposal system that allows cerebrospinal fluid to flood in between the neurons and sweep away intercellular junk; while this happens, the neurons themselves pull back to allow this to happen, the way city residents are sometimes required to move their cars to allow street sweepers to pass through. This cleansing process flushes out detritus, including both amyloid-beta and tau, the two proteins linked to neurodegeneration. But if we do not spend enough time in deep sleep, the system cannot work as effectively, and amyloid and tau build up among the neurons. Broader studies have found that people who have

generally slept less than seven hours per night, over decades, tend to have much more amyloid-beta and tau built up in their brains than people who sleep for seven hours or more per night. Tau, the protein that collects in “tangles” inside unhealthy neurons, is itself correlated to sleep disturbances in cognitively normal people and in those with MCI, or mild cognitive impairment, an early stage of dementia.

另一方面，深度睡眠似乎對我們大腦作為一個器官的健康至關重要。幾年前，羅徹斯特的研究人員發現，當我們處於深度睡眠時，大腦會啟動一種內部廢物處理系統，讓腦脊髓液湧入神經元之間，清除細胞間的垃圾；當這種情況發生時，神經元本身會向後拉以允許這種情況發生，就像城市居民有時需要移動他們的汽車以允許街道清潔工通過一樣。這種清潔過程會清除碎屑，包括β澱粉樣蛋白和tau蛋白，這兩種蛋白質與神經退化性變有關。但如果我們沒有花足夠的時間進行深度睡眠，系統就無法有效運作，澱粉樣蛋白和 tau 蛋白就會在神經元中累積。更廣泛的研究發現，幾十年來每晚睡眠時間少於七小時的人，其大腦中往往比每晚睡眠七小時或更長的人積累更多的β-澱粉樣蛋白和tau蛋白。Tau 蛋白是一種在不健康神經元內以「纏結」形式聚集的蛋白質，它本身與認知正常人群和輕度認知障礙（癡呆早期）患者的睡眠障礙有關。

This can become a vicious cycle. If someone has Alzheimer's disease, they are likely to experience sleep disturbances. People with Alzheimer's disease spend progressively less time in deep sleep and REM sleep, and they may also experience dramatic changes in their circadian rhythm (i.e., sleep-wake cycle). Also, up to half of people with Alzheimer's disease develop sleep apnea.

這可能會形成惡性循環。如果有人患有阿茲海默症，他們可能會出現睡眠障礙。患有阿茲海默症的人在深度睡眠和快速動眼睡眠中花費的時間逐漸減少，他們的晝夜節律（即睡眠-覺醒週期）也可能會經歷巨大的變化。此外，多達一半的阿茲海默症患者會出現睡眠呼吸中止症。

But sleep disturbances, in turn, may help create conditions that allow Alzheimer's to progress. Insomnia affects 30 to 50 percent of older adults, and there is ample research showing that sleep disturbances often precede the

diagnosis of dementia by several years; they may even appear before cognitive decline. One study linked poor sleep quality in cognitively normal people with the onset of cognitive impairment—just one year later.

但反過來，睡眠障礙可能為阿茲海默症的進展創造條件。失眠影響 30% 至 50% 的老年人，有大量研究表明，睡眠障礙通常比失智症的診斷早幾年；它們甚至可能出現在認知能力下降之前。一項研究將認知正常的人睡眠品質差與認知障礙的發生聯繫起來——僅僅一年後。

Meanwhile, superior sleep quality in older adults is associated with a lower risk of developing MCI and Alzheimer's disease, and with maintaining a higher level of cognitive function. Successfully treating sleep disturbance may delay the age of onset into MCI—by about eleven years, according to one study—and may improve cognitive function in patients already diagnosed with Alzheimer's disease.

同時，老年人的優質睡眠品質與降低 MCI 和阿茲海默症的風險以及維持較高水平的認知功能有關。一項研究表明，成功治療睡眠障礙可能會延遲 MCI 的發病年齡（約 11 年），並且可能會改善已診斷為阿茲海默症的患者的認知功能。

Clearly, sleep and cognitive health are deeply intertwined; this is why one of the pillars of Alzheimer's disease prevention, particularly for our high-risk patients, is improving their sleep. It is not enough merely to spend time in bed; *good-quality* sleep is essential to long-term brain health. This is the crucial distinction. Sleep that is irregular, or fragmented, or not deep enough will not allow the brain to enjoy any of these benefits.

顯然，睡眠和認知健康密切相關。這就是為什麼預防阿茲海默症的支柱之一，特別是對於我們的高風險患者來說，是改善他們的睡眠。僅僅在床上度過時間是不夠的；優質的睡眠對於長期的大腦健康至關重要。這是關鍵的區別。不規則、零碎或不夠深度的睡眠將無法讓大腦享受任何這些好處。

Unfortunately, our ability to obtain deep sleep declines with age, beginning as soon as our late twenties or early thirties, but worsening as we enter middle age. It's not entirely clear how much this decline in sleep quality

is due to growing older itself, versus the increased likelihood of health conditions that result in poor sleep as we age. One analysis suggests that the bulk of the changes in adult sleep patterns occur between the ages of nineteen and sixty and only minimally decline after that, if one remains in good health (a big if).

不幸的是，我們獲得深度睡眠的能力隨著年齡的增長而下降，從二十歲末或三十歲出頭開始，但隨著我們進入中年而惡化。目前尚不完全清楚睡眠品質的下降在多大程度上是由於年齡增長本身造成的，以及隨著年齡的增長，健康狀況導致睡眠品質下降的可能性增加。一項分析表明，成人睡眠模式的大部分變化發生在 19 歲至 60 歲之間，如果一個人保持良好的健康狀況（這是一個很大的假設），此後只會略有下降。

One possible contributor to this age-related reduction in deep sleep is changes in growth hormone secretion. Growth hormone is typically released in a pulse about one hour after we begin to sleep at night, or around the time at which we're likely to enter deep sleep. On the other hand, inhibiting growth hormone reduces deep sleep, so it's not clear which is cause or effect here. Growth hormone reaches its peak during adolescence, rapidly declines between young adulthood to middle age, and then declines more slowly after that. This pattern parallels the changes in the amount of deep sleep we get as we age.

與年齡相關的深度睡眠減少的一個可能原因是生長激素分泌的變化。生長激素通常在我們晚上開始睡覺後一小時左右或在我們可能進入深度睡眠的時間左右以脈衝形式釋放。另一方面，抑制生長激素會減少深度睡眠，因此尚不清楚其中的因果關係。生長激素在青春期達到高峰，在青年期到中年之間迅速下降，之後下降得更慢。這種模式與我們隨著年齡的增長而深度睡眠時間的變化是一致的。

More research points to the forties and sixties as the decades of life when deep sleep is especially important for the prevention of Alzheimer's disease. People who have slept less during those decades seem to be at higher risk of developing dementia later on. Thus, good sleep in middle age appears to be especially important for maintaining cognitive health.

更多的研究指出，四、六十歲是人生的幾十年，深度睡眠對於預防阿茲海默症尤其重要。在這幾十年裡睡眠較少的人似乎以後患癡呆症的風險更高。因此，中年時期良好的睡眠對於維持認知健康似乎特別重要。

What I realize now is that for all those years when I was sleeping five or six hours a night and thinking I was on top of my game, I was in fact likely performing far below my potential, thanks to my lack of sleep. And at the same time, I was probably putting myself at risk of long-term illness—metabolic, cardiac, and cognitive. I always bragged, “I’ll sleep when I’m dead.”

我現在意識到，多年來，當我每晚睡五到六個小時並認為自己處於最佳狀態時，實際上由於睡眠不足，我的表現可能遠低於我的潛力。同時，我可能會讓自己面臨長期患病的風險——代謝、心臟和認知方面的疾病。我總是吹牛說：“我死了就會睡覺。”

Little did I know that my not sleeping was doing much to hasten that day. 我幾乎不知道我的不睡覺對加速這一天的到來起到了很大的作用。

Assessing Your Sleep

評估您的睡眠

It would be nice if science could locate some sort of “sleep switch,” some brain pathway that could be triggered, or inhibited, to make us fall asleep instantly and cycle smoothly in and out of deep sleep and REM sleep all night, until we wake up feeling refreshed. But that hasn’t happened yet.

如果科學能夠找到某種“睡眠開關”，即某種可以被觸發或抑制的大腦通路，讓我們立即入睡，並整晚順利地進出深度睡眠和快速眼動睡眠，那就太好了。醒來感覺神清氣爽。但這還沒有發生。

It’s not for lack of effort on the part of big pharma. Sleep is such a problem for so many people that there are about a dozen FDA-approved sleep medications on the market. The first real blockbuster sleeping medication,

Ambien (zolpidem), generated \$4 billion in revenues within the first two years after it was approved in the 1990s. The demand was huge, but the phenomenon goes back much further than that. The drug morphine, first isolated from the opium poppy in 1806, was named for Morpheus, the god of dreams, because it put people to sleep quite effectively. This was fitting, in that sleeping and dreaming can be a refuge from both physical and emotional pain. But morphine, being addictive, is obviously not ideal as a sleep drug.

這並不是因為大型製藥公司缺乏努力。睡眠對很多人來說都是一個大問題，市場上有大約十幾種經 FDA 批准的睡眠藥物。第一個真正的重磅安眠藥 Ambien（唑吡坦）在 20 世紀 90 年代獲得批准後的頭兩年內創造了 40 億美元的收入。需求龐大，但這種現象的歷史遠不止於此。嗎啡於 1806 年首次從罌粟分離出來，以夢之神 Morpheus 的名字命名，因為它可以非常有效地使人入睡。這是恰當的，因為睡眠和做夢可以成為逃避身體和情緒痛苦的避難所。但嗎啡具有成癮性，身為安眠藥顯然並不理想。

Currently, the US sleep medication market is estimated to be worth about \$28 billion a year. But the number of prescriptions has actually been declining recently, perhaps because consumers are catching on to the fact that, by and large, these medicines do not actually work very well. They can be good at inducing unconsciousness, but then again, so was Muhammad Ali's right cross. Sleep medications such as Ambien and Lunesta do not promote healthy, long-lasting sleep so much as they tend to promote a sleep-like state of unconsciousness that does not really accomplish much if any of the brain-healing work of either REM or deep sleep. One study found that Ambien actually decreased slow-wave sleep (deep sleep) without increasing REM, meaning people who take it are basically trading high-quality sleep for low-quality sleep. Meanwhile, Ambien has the well-publicized side effect that some users have been known to walk around and do things while "sleeping," leading to all sorts of problems.

目前，美國睡眠藥物市場估計每年價值約280億美元。但最近處方數量實際上一直在下降，也許是因為消費者逐漸意識到，總的來說，這些藥物實際上效果不佳。他們很擅長讓人失去意識，但話又說回來，穆

罕默德·阿里的右傳也是如此。安必恩（Ambien）和魯內斯塔

（Lunesta）等安眠藥物並不能促進健康、持久的睡眠，因為它們往往會促進類似睡眠的無意識狀態，而這種狀態對於快速動眼睡眠或深度睡眠的大腦治癒作用並沒有真正起到多大作用。一項研究發現，安必恩實際上減少了慢波睡眠（深度睡眠），但沒有增加快速動眼睡眠，這意味著服用它的人基本上是在用高品質的睡眠換取低品質的睡眠。同時，安必恩有一個廣為人知的副作用，即一些用戶在「睡覺」時四處走動和做事，從而導致各種問題。

The pharmaceutical industry then came up with a new class of sleep drugs that purportedly solved the sleepwalking problem by blocking a wake-promoting brain chemical called orexin. Interestingly, orexin was initially thought to be more relevant to appetite, which it also regulates (by increasing hunger). But so-called orexin antagonist inhibitors such as Dayvigo (lemborexant) and Quviviq (daridorexant) have been approved for treating insomnia, and they appear to be promising—not least because users have better ability to respond to auditory stimuli at night (e.g., a parent who wants to sleep but still be able to respond if a child is crying). They are, however, quite expensive.

隨後，製藥業開發了一種新型睡眠藥物，據稱透過阻斷一種名為食慾素的促進清醒的大腦化學物質來解決夢遊問題。有趣的是，食慾素最初被認為與食慾更相關，它也可以調節食慾（透過增加飢餓感）。但所謂的食慾素拮抗劑抑制劑，如Dayvigo（lemborexant）和Quviviq（daridorexant）已被批准用於治療失眠，而且它們似乎很有前途，尤其是因為使用者在夜間對聽覺刺激有更好的反應能力（例如，想要睡覺但仍能在孩子哭泣時做出反應的父母）。然而，它們相當昂貴。

Then there are the older benzodiazepine drugs, such as Valium (diazepam) and Xanax (alprazolam), which remain very popular—almost ubiquitous in our society—and are also sometimes used to treat insomnia. These typically induce unconsciousness without improving sleep quality. Somewhat worryingly, their use has also been associated with cognitive decline, and they are generally not recommended for older adults beyond very short-term time horizons (nor is Ambien, by the way).

還有一些較老的苯二氮平類藥物，例如安定（安定）和阿普唑侖（阿普唑侖），它們仍然非常受歡迎，在我們的社會中幾乎無處不在，有時也用於治療失眠。這些通常會導致意識不清，而不會改善睡眠品質。有點令人擔憂的是，它們的使用也與認知能力下降有關，通常不建議老年人在非常短期的時間範圍內使用它們（順便說一下，安必恩也不建議）。

When new patients come into our practice, it is not uncommon for them to be relying on one of these sleep aids. If they are using Ambien or Xanax once a month, or only with travel, or to help them sleep during a time of emotional distress, it's not alarming. But if they are using such drugs regularly, it becomes our highest priority to get them off these sleep aids and have them begin to learn to sleep correctly without them.

當新患者進入我們的診所時，他們依賴其中一種睡眠輔助工具的情況並不少見。如果他們每月使用一次 Ambien 或 Xanax，或僅在旅行時使用，或在情緒困擾時幫助他們入睡，那麼這並不令人擔憂。但如果他們經常使用這類藥物，我們的首要任務就是讓他們擺脫這些助眠劑，並讓他們開始學會在沒有它們的情況下正確睡眠。

One drug that we do find helpful for assisting with sleep is trazodone, a fairly old anti-depressant (approved in 1981) that never really took off. At the doses used to treat depression, two hundred to three hundred milligrams per day, it had the unwanted side effect of causing users to fall asleep. But one man's trash is another man's treasure. That side effect is what we want in a sleep medication, especially if it also improves sleep architecture, which is exactly what trazodone does—and most other sleep meds do not.^[*4] We typically use it at much lower doses, from one hundred milligrams down to fifty milligrams or even less; the optimal dosing depends on the individual, but the goal is to find the amount that improves their sleep quality without next-day grogginess. (We have also had good results with the supplement ashwagandha.)

我們確實發現一種有助於睡眠的藥物是曲唑酮，這是一種相當古老的抗憂鬱藥物（1981 年批准），但從未真正流行起來。在用於治療憂鬱症的劑量（每天 200 至 300 毫克）下，它會產生導致使用者入睡的不

良副作用。但一個人的垃圾卻是另一個人的寶藏。這種副作用正是我們所希望的安眠藥所具有的效果，特別是如果它還能改善睡眠結構，而這正是曲唑酮的作用，而大多數其他安眠藥卻沒有。[*4] 我們通常以低得多的劑量使用它，從一百毫克到五十毫克甚至更少；最佳劑量取決於個人，但目標是找到能夠改善睡眠品質且第二天不會感到昏昏沉沉的劑量。（我們使用南非醉茄補充劑也取得了良好的效果。）

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There is still no pharmacological magic bullet for sleep, but there are some fairly effective things you can do to improve your ability to fall asleep and stay asleep—and, hopefully, sleep well enough to avoid all the scary stuff that we've been talking about in this chapter. Keep in mind, however, that these tips and strategies are not going to be effective if you have a true sleep disorder, such as insomnia or sleep apnea (see below for questionnaire assessments that you can take to your doctor for discussion).

目前還沒有促進睡眠的藥理學靈丹妙藥，但您可以採取一些相當有效的措施來提高入睡和保持睡眠的能力，並且希望睡得足夠好，以避免我們一直在談論的所有可怕的事情關於本章。但請記住，如果您患有真正的睡眠障礙，例如失眠或睡眠呼吸中止症，這些提示和策略將不會有效（請參閱下面的問卷評估，您可以將其提交給您的醫生進行討論）。

The first step in this process echoes the first step in a recovery program: we must renounce our “addiction” to chronic sleep deprivation and admit that we need more sleep, in sufficient quality and quantity. We are giving ourselves permission to sleep. This was actually rather difficult for me at first, as I had spent decades practicing just the opposite. I hope by now I've convinced you of the importance of sleep, across multiple dimensions of health.

這個過程的第一步與恢復計劃的第一步相呼應：我們必須放棄對長期睡眠不足的“上癮”，並承認我們需要更多的睡眠，並且睡眠質量和數量充足。我們允許自己睡。起初這對我來說實際上相當困難，因為我

花了幾十年的時間練習相反的方法。我希望到目前為止我已經讓您相信睡眠在健康的多個方面的重要性。

The next step is to assess your own sleep habits. There are numerous sleep trackers out there that can give you a pretty good idea about how well you are actually sleeping. They work by measuring variables such as heart rate, heart rate variability (HRV), movement, breathing rate, and more. These inputs are used to estimate sleep duration and stage and do so with reasonable (but not perfect) accuracy. While I've found these to be quite helpful in optimizing my own sleep, some people get worked up over poor sleep scores—which can further impair their sleep. In these situations I insist that my patients take a tracker holiday for a few months. It's also worth reiterating that *long* sleep is also often a sign not only of poor sleep quality, but other potential health problems.

下一步是評估您自己的睡眠習慣。有許多睡眠追蹤器可以讓您很好地了解自己的實際睡眠品質。它們的工作原理是測量心率、心率變異性(HRV)、運動、呼吸頻率等變數。這些輸入用於估計睡眠時間和階段，並具有合理（但不完美）的準確性。雖然我發現這些對於優化自己的睡眠非常有幫助，但有些人會因為睡眠分數不佳而感到惱火，這可能會進一步損害他們的睡眠。在這種情況下，我堅持讓我的患者享受幾個月的追蹤假期。另外值得重申的是，長時間睡眠通常不僅是睡眠品質不佳的跡象，也是其他潛在健康問題的跡象。

In parallel, you should make a longer-term assessment of your sleep quality over the last month. Probably the best-validated sleep questionnaire is the Pittsburgh Sleep Quality Index, a four-page document that asks questions about your sleep patterns over the last month: for example, how often you have had trouble falling asleep within thirty minutes, have woken up during the night, have had difficulty breathing (i.e., snoring), have had trouble staying awake during the day (such as while driving), or have “felt a lack of enthusiasm for getting things done.”

同時，您應該對上個月的睡眠品質進行長期評估。也許最有效的睡眠問卷是匹茲堡睡眠品質指數，這是一份四頁的文件，詢問有關您過去一個月的睡眠模式的問題：例如，您在三十分鐘內入睡困難的頻率、

在三十分鐘內醒來的頻率晚上呼吸困難（即打鼾），白天難以保持清醒（例如開車時），或「感覺缺乏完成任務的熱情」。

It's easy to find the questionnaire and scoring key online,^[*5] and I often find that it helps persuade my patients that it's time to take sleep seriously and make it a priority in their lives. There's another, even simpler quiz called the Epworth Sleepiness Scale, which asks users to rate how likely they are to fall asleep in certain situations, on a scale of 0 (not likely) to 3 (very likely):

在網路上很容易找到問捲和評分要點，[*5]，我經常發現這有助於說服我的患者，是時候認真對待睡眠並將其作為生活中的優先事項了。還有另一個更簡單的測驗，稱為 Epworth 嗜睡量表，它要求使用者評估他們在某些情況下入睡的可能性，評分範圍為 0（不太可能）到 3（很可能）：

- Sitting and reading
坐著看書
- Watching TV
看電視
- Sitting in a meeting or other public place
坐在會議或其他公共場所
- As a passenger in a car for an hour
作為乘客在車裡待了一個小時
- Lying down to rest in the afternoon
下午躺著休息
- Sitting and talking to someone
坐著和某人說話
- Sitting after lunch (without alcohol)
午飯後坐著（不含酒精）
- In a car, stopped for a few minutes in traffic

在車裡，在交通堵塞中停了幾分鐘

A total score of 10 or more indicates excessive sleepiness and likely points to an issue with sleep quality.^[*6]

總分為 10 分或以上表示過度困倦，並可能表示睡眠品質有問題。^[*6]

Yet another helpful screening tool is the Insomnia Severity Index, which provides an opportunity to reflect on and report your experience of sleep problems and their impact on your functioning and well-being.^[*7]

另一個有用的篩檢工具是失眠嚴重程度指數，它提供了一個機會來反思和報告您的睡眠問題經驗及其對您的功能和健康的影響。^[*7]

One important but often-ignored factor in sleep assessment is that different people may have widely differing “chronotypes,” which is a fancy way of saying that someone is a “morning person” or “not a morning person.” We all have different relationships to the circadian cycle, and much of that relationship is genetic: a morning person and a night owl will have different circadian genes.^[*8] Studies have found that some individuals are genetically predisposed to leap out of bed first thing in the morning, while others naturally tend to wake up later (and go to sleep later), not really hitting their stride until sometime in the afternoon. The latter are not “lazy,” as was long assumed; they may simply have a different chronotype.

睡眠評估中一個重要但經常被忽視的因素是，不同的人可能有截然不同的“時間型”，這是一種說法某人是“早起的人”或“不是早起的人”的奇特方式。我們每個人都與晝夜節律週期有不同的關係，其中大部分是遺傳的：早起的人和夜貓子有不同的晝夜節律基因。^[*8] 研究發現，有些人在遺傳上傾向於早上第一件事就從床上跳起來，而另一些人自然傾向於較晚醒來（並較晚入睡），直到下午某個時候才真正邁出步伐。後者並不像人們長期以來認為的那樣「懶惰」。他們可能只是有不同的生理時鐘類型。

Like so much else in biology, this has a possible basis in evolution: if all members of a clan or a tribe adhered to the exact same sleep schedule, the

entire group would be vulnerable to predators and enemies for several hours every night. Obviously not ideal. But if their sleep schedules were staggered, with some individuals going to bed early while others were more inclined to stay up late and tend the fire, the group as a whole would be much less vulnerable. This may also explain why teenagers want to go to bed late and then sleep in: Our chronotype appears to undergo a temporary shift in adolescence toward late sleeping and later rising. School start times, unfortunately for both teens and for those of us who are parents, remain stubbornly fixed at very early hours—but there is a growing nationwide movement to push school times later, to better suit adolescent sleep schedules.

就像生物學中的其他許多事情一樣，這可能有進化基礎：如果一個氏族或部落的所有成員都遵守完全相同的睡眠時間表，那麼整個群體每天晚上在幾個小時內都將容易受到掠食者和敵人的攻擊。顯然並不理想。但如果他們的睡眠時間錯開，有些人早睡，而有些人則更傾向於熬夜和照顧生火，那麼整個群體的脆弱性就會大大降低。這也可以解釋為什麼青少年想要晚睡然後睡懶覺：我們的睡眠類型似乎在青春期的經歷了暫時的轉變，轉向晚睡晚起。不幸的是，對於青少年和我們這些為人父母的人來說，上學時間仍然頑固地固定在很早的時間，但全國範圍內越來越多的運動推遲上學時間，以更好地適應青少年的睡眠時間表。

Last, it is important to rule out—or rule in—the possibility of obstructive sleep apnea, which is surprisingly prevalent yet underdiagnosed. It is possible to get a formal test for this, in a sleep lab or at home, but there is yet another questionnaire, called STOP-BANG, that correlates pretty strongly with the formal apnea test.^[*9] If you snore, have high blood pressure, feel tired most days, or if your partner has observed that you stop breathing occasionally during the night, even for a moment, you are a candidate for further sleep apnea testing by a medical professional. (Other risk factors include having a BMI greater than thirty and being male.) Sleep apnea is a serious medical problem that can have implications for cardiovascular health and dementia risk.

最後，重要的是要排除或排除阻塞性睡眠呼吸中止症的可能性，這種情況令人驚訝地普遍但診斷不足。可以在睡眠實驗室或家中進行正式測試，但還有另一份問卷，稱為 **STOP-BANG**，它與正式的呼吸中止測試密切相關。[*9] 如果您打鼾、患有高血壓、大部分時間都感到疲倦，或者如果您的伴侶觀察到您在夜間偶爾停止呼吸，即使只是一小會兒，那麼您就適合由醫療人員進行進一步的睡眠呼吸中止症測試。專業的。（其他風險因素包括體重指數超過 30 和男性。）睡眠呼吸中止症是一個嚴重的醫療問題，可能會影響心血管健康和失智症風險。

Sleeping Better

睡得更好

Once you have ruled out (or addressed) serious problems like sleep apnea, there are concrete steps that you can take to improve your sleep, or at least improve your chances of getting good sleep.

一旦排除（或解決）睡眠呼吸中止症等嚴重問題，您就可以採取具體措施來改善睡眠，或至少提高獲得良好睡眠的機會。

Most important, you must create an environment for yourself that is conducive to sleeping well. The first requirement for good sleep is darkness. Light is the enemy of sleep, full stop. Thus, you want to make your bedroom itself as dark as possible—installing room-darkening curtains if you live somewhere with a lot of outdoor evening light, and removing all light sources in the bedroom, even down to electronic equipment like TVs and cable boxes and such. Their little pinpoint LEDs are more than bright enough to keep you from sleeping well. Digital clocks are especially deadly, not only because of their bright numerals but also because if you wake up and see that it's 3:31 a.m., you might start worrying about your 7 a.m. flight and never fall back asleep.

最重要的是，你必須為自己創造一個有利於良好睡眠的環境。良好睡眠的首要條件是黑暗。光是睡眠的敵人，句點。因此，你想讓你的臥室本身盡可能黑暗——如果你住在室外夜間光線充足的地方，請安裝房間變暗的窗簾，並移除臥室中的所有光源，甚至包括電視和有線電視盒等電子設備等等。它們的小 LED 燈亮度足以讓您睡不好。數位時鐘尤其致命，不僅因為它們明亮的數字，還因為如果你醒來發現現在是凌晨 3:31，你可能會開始擔心早上 7 點的航班，並且再也無法入睡。

This is easier said than done, because it essentially amounts to evicting the twenty-first century from your bedroom. Modern life almost systematically destroys our ability to sleep properly, beginning with the ubiquity of electric light. Not only does non-natural lighting interfere with our natural circadian rhythm, but it also blocks the release of melatonin, the darkness-activated hormone that tells our brain that it is time to fall asleep. It's similar to the way that the SAD interferes with satiety hormones that normally tell us that we are full and we can stop eating.

這說起來容易做起來難，因為這本質上相當於把二十一世紀從你的臥室裡驅逐出去。從無所不在的電燈開始，現代生活幾乎系統性地破壞了我們正常睡眠的能力。非自然光不僅會干擾我們的自然晝夜節律，還會阻止褪黑激素的釋放，褪黑激素是一種黑暗激活的激素，可以告訴我們的大腦是時候入睡了。這類似於 SAD 干擾飽足感荷爾蒙的方式，這種荷爾蒙通常會告訴我們已經吃飽了，可以停止進食了。

Even worse is the relatively recent advent of LED household lighting, which is predominantly on the blue end of the spectrum, meaning it more resembles daylight. When our brain detects that blue light, it thinks it is daytime and that we should be awake, so it tries to block us from falling asleep. Therefore, you should also reduce the amount of bright, LED light that you're exposed to in the evening. A couple of hours before you go to bed, begin turning off unnecessary lights in your house, gradually reducing your light exposure from there. Also, try to swap out blue-intensive LED bulbs for those on the warmer end of the spectrum.

更糟的是最近出現的 LED 家用照明，它主要位於光譜的藍色端，這意味著它更像日光。當我們的大腦偵測到藍光時，它認為現在是白天，我們應該醒著，因此它會試圖阻止我們入睡。因此，您還應該減少晚上接觸的明亮 LED 燈的數量。睡前幾個小時，開始關閉家裡不必要的燈，從那裡逐漸減少光照。另外，嘗試將藍光密集 LED 燈泡換成光譜較暖的 LED 燈泡。

The devices we stare at before bed—phones, laptops, video games—are even worse for our sleep. Not only do they bombard us with more blue light, but they also activate our minds in ways that impede our ability to sleep. One large-scale survey found that the more interactive devices subjects used during the hour before bedtime, the more difficulties they had falling asleep and staying asleep—whereas passive devices such as TV, electronic music players, and, best of all, books were less likely to be associated with poor sleep. This may partially explain why watching TV before bed does not seem to affect sleep quite as negatively as playing video games or scrolling social media does, according to research by Michael Gradisar, a sleep researcher and professor of psychology at Flinders University in Australia.

我們睡前盯著的设备——手機、筆記型電腦、電玩遊戲——對我們的睡眠更不利。它們不僅會用更多的藍光轟炸我們，還會以妨礙我們睡眠的方式啟動我們的思維。一項大規模調查發現，受試者在睡前一小時內使用的互動設備越多，他們入睡和保持睡眠的困難就越大，而電視、電子音樂播放器以及最重要的是書籍等被動設備則較少使用。可能與睡眠不好有關。澳洲弗林德斯大學睡眠研究員兼心理學教授 Michael Gradisar 的研究表明，這可能部分解釋了為什麼睡前看電視似乎不像玩電子遊戲或滾動社交媒體那樣對睡眠產生負面影響。

I am increasingly persuaded that our 24-7 addiction to screens and social media is perhaps our most destructive habit, not only to our ability to sleep but to our mental health in general. So I banish those from my evenings (or at least, I try to). Turn off the computer and put away your phone at least an hour before bedtime. Do NOT bring your laptop or phone into bed with you.

我越來越相信，我們每天 24 小時、每週 7 小時對螢幕和社群媒體的沉迷可能是我們最具破壞性的習慣，不僅影響我們的睡眠能力，而且影響我們的整體心理健康。所以我把這些從我的晚上排除掉（或至少，我嘗試這樣做）。睡前至少一小時關機並收起手機。請勿將筆記型電腦或手機帶入床上。

Another very important environmental factor is temperature. Many people associate sleep with warmth, but in fact the opposite is true: One of the signal events as we are falling asleep is that our body temperature drops by about one degree Celsius. To help that happen, try to keep your bedroom cool—around sixty-five degrees Fahrenheit seems to be optimal. A warm bath before bed may actually help with this process, not only because the bath itself is relaxing but also because when we get out of the bath and climb into our cool bed, our core temperature drops, which signals to our brain that it is time to fall asleep. (There are also a variety of cooling mattresses and mattress toppers out there that could help people who like to sleep cool.)

另一個非常重要的環境因素是溫度。許多人將睡眠與溫暖聯繫在一起，但事實恰恰相反：我們入睡時的信號事件之一是我們的體溫下降約一攝氏度。為了幫助實現這一目標，請盡量保持臥室涼爽——六十五華氏度左右似乎是最佳溫度。睡前洗個熱水澡實際上可能有助於這個過程，不僅因為洗澡本身令人放鬆，還因為當我們走出浴缸並爬上涼爽的床時，我們的核心溫度會下降，這會向我們的大腦發出訊號：是時候睡覺了。（還有各種涼爽的床墊和床墊罩可以幫助那些喜歡涼爽睡眠的人。）

Our internal “environment” is just as important to good sleep. The first thing I tell my patients who are having difficulty sleeping is to cut back on alcohol—or better yet, give it up entirely. It’s counterintuitive, because alcohol initially acts as a sedative, so it can help us fall asleep more quickly. But as the night wears on, alcohol turns from friend of sleep to foe, as it is metabolized into chemicals that impair our ability to sleep. Depending on how much we’ve had to drink, during the second half of the night we may have a harder time entering REM sleep and be more prone to waking up and lingering in unproductive light sleep.

我們的內在「環境」對於良好的睡眠同樣重要。我告訴睡眠困難的患者的第一件事就是減少飲酒——或者更好的是完全戒酒。這是違反直覺的，因為酒精最初起到鎮靜劑的作用，因此它可以幫助我們更快入睡。但隨著夜幕降臨，酒精從睡眠之友變成了敵人，因為它會代謝成損害我們睡眠能力的化學物質。根據我們喝了多少酒，在後半夜，我們可能會更難進入快速動眼睡眠，並且更容易醒來並在低效的淺度睡眠中徘徊。

The effects of alcohol on memory and cognition are apparent even in moderate drinkers. Studies have found that young people who drink heavily are more likely to forget even basic tasks like locking the door or mailing a letter. Students who averaged nine drinks per week (not much, by collegiate standards) performed worse on a word-based memory test. And, in a finding that will surprise no one, students who drank more slept later and felt sleepier in the daytime, as well as performing worse on tests. More alarming is the finding that students who drank heavily two days *after* a bout of learning or study forgot or failed to retain most of what they had learned.

即使對於適度飲酒者來說，酒精對記憶和認知的影響也是顯而易見的。研究發現，酗酒的年輕人更有可能忘記鎖門或寄信等基本任務。平均每週喝九杯酒的學生（按照大學標準，喝得不多）在基於單字的記憶測驗中表現較差。而且，一項不會讓任何人感到驚訝的發現是，喝得更多的學生睡得更晚，白天感覺更困，考試成績也更差。更令人震驚的是，我們發現，在一次學習或學習後兩天大量飲酒的學生會忘記或無法記住他們所學的大部分內容。

Note that these are all findings in young people, students who are presumably at their cognitive peak. If you extrapolate to those of us in middle and older age, who may have a lower tolerance for alcohol and a greater propensity to forget things, the implications are worrisome. I find that my own threshold is two drinks in an evening: any more than that, my sleep goes sideways, and my work performance suffers the next day, no matter how much coffee I drink.

請注意，這些都是針對年輕人和學生的研究結果，他們可能處於認知高峰。如果你推斷我們這些中老年人，他們對酒精的耐受性可能較低，並且更容易忘記事情，那麼其影響是令人擔憂的。我發現我自己的閾值是晚上喝兩杯：超過這個量，我的睡眠就會紊亂，第二天我的工作表現也會受到影響，無論我喝多少咖啡。

Coffee is not a solution to the problem of poor sleep, especially if consumed to excess or (especially) at the wrong time. Most people think of caffeine as a stimulant that somehow gives us energy, but actually it functions more as a sleep blocker. It works by inhibiting the receptor for a chemical called adenosine, which normally helps us go to sleep every night. Over the course of the day, adenosine builds up in our brain, creating what scientists call “sleep pressure,” or the drive to sleep. We may be tired and needing sleep, but if we ingest caffeine it effectively takes the phone off the hook, so our brain never gets the message.

咖啡並不能解決睡眠不佳的問題，尤其是在過量或（特別是）在錯誤的時間飲用的情況下。大多數人認為咖啡因是一種興奮劑，可以在某種程度上給我們能量，但實際上它的作用更多的是作為睡眠阻斷劑。它的作用是抑制一種叫做腺苷的化學物質的受體，這種化學物質通常可以幫助我們每晚入睡。在一天中，腺苷在我們的大腦中積聚，產生科學家所說的「睡眠壓力」或睡眠動力。我們可能很累，需要睡眠，但如果我們攝取咖啡因，它就會有效地讓手機擺脫困境，因此我們的大腦永遠不會收到訊息。

This is obviously helpful in the morning, particularly if our “chronotype” is telling us we should still be asleep at 6 a.m. But the half-life of caffeine in the body is up to six hours, so if we drink a cup of coffee at noon, we will still have half a cup’s worth of caffeine in our system at 6 p.m. Now multiply this by the number of cups of coffee you drink in a day and work forward from the time of your last cup. If you down one last double espresso at 3 p.m., you will still have a full shot’s worth of caffeine in your system at 9. What you won’t have, most likely, is much of an urge to fall asleep anytime soon.

這在早上顯然很有幫助，特別是如果我們的「睡眠類型」告訴我們早上 6 點仍然應該睡覺。但是咖啡因在體內的半衰期長達 6 小時，所以如果我們在早上喝一杯咖啡中午，下午 6 點我們的系統中仍含有半杯咖啡因。現在將其乘以您一天喝咖啡的杯數，並從最後一杯咖啡的時間開始計算。如果你在下午 3 點喝下最後一杯雙份濃縮咖啡，那麼到 9 點時你的體內仍然含有足量的咖啡因。你很可能不會有很快入睡的衝動。

Everyone differs in their caffeine tolerance, based on genes and other factors (23andMe tests for one common caffeine-related gene). I'm a very fast metabolizer, so I can handle that afternoon espresso without it affecting my sleep too much; I can even drink coffee after dinner, and it seems to have no impact (unlike alcohol). Someone who metabolizes caffeine slowly should probably stop at one or two cups, before noon.

根據基因和其他因素，每個人的咖啡因耐受性都不同（23andMe 測試了一個常見的咖啡因相關基因）。我的新陳代謝非常快，所以我可以喝下午的濃縮咖啡，而不會對我的睡眠造成太大影響；我甚至可以在飯後喝咖啡，而且似乎沒有什麼影響（不像酒精）。咖啡因代謝緩慢的人可能應該在中午之前停止喝一兩杯。

This concept of *sleep pressure*, our need or desire for sleep, is key to many of our sleep tactics. We want to cultivate sleep pressure, but in the right amounts, at the right times—not too much, not too little, and not too soon. This is why one of the primary techniques that doctors use to treat patients with insomnia is actually sleep restriction, limiting the hours when they are “allowed” to sleep to six, or less. This basically makes them tired enough that they fall asleep more easily at the end of the day, and (hopefully) their normal sleep cycle is restored. Their sleep pressure builds up to the point where it overwhelms whatever is causing their insomnia. But this also helps explain why napping can be counterproductive. Taking a nap during the day, while sometimes tempting, can also relieve too much of that sleep pressure, making it harder to fall back asleep at night.

睡眠壓力的概念，也就是我們對睡眠的需求或渴望，是我們許多睡眠策略的關鍵。我們想要培養睡眠壓力，但要在適當的時間、適當的量——不要太多，不要太少，也不要太早。這就是為什麼醫生用來治療失眠患者的主要技術之一實際上是睡眠限制，將「允許」睡眠的時間限制為六小時或更少。這基本上使他們足夠疲倦，以至於在一天結束時更容易入睡，並且（希望）他們的正常睡眠週期得到恢復。他們的睡眠壓力逐漸增大，超過了失眠的原因。但這也有助於解釋為什麼小睡會適得其反。白天小睡雖然有時很誘人，但也可以緩解過多的睡眠壓力，使晚上更難重新入睡。

Another way to help cultivate sleep pressure is via exercise, particularly sustained endurance exercise (e.g., zone 2), ideally not within two or three hours of bedtime. My patients often find that a thirty-minute zone 2 session can do wonders for their ability to fall asleep. Even better is exercise that entails some exposure to sunlight (i.e., outdoors). While blue light late in the evening can interfere with sleep, a half-hour dose of strong daylight, during the day, helps keep our circadian cycle on track, setting us up for a good night of sleep.

幫助培養睡眠壓力的另一種方法是透過運動，特別是持續的耐力運動（例如，2 區），最好不要在睡前兩三個小時內進行。我的病人經常發現，三十分鐘的第 2 區療程可以為他們的入睡能力帶來奇蹟。更好的是需要暴露在陽光下的運動（即戶外）。雖然深夜的藍光會干擾睡眠，但白天半小時的強烈日光有助於保持我們的晝夜節律正常，為我們提供良好的睡眠。

It is also important to mentally prepare ourselves for sleeping. For me, this means avoiding anything that might create stress or anxiety, such as reading work emails or especially checking the news. This activates the sympathetic nervous system (the fight-or-flight one) at a time when we want to be destressing and generally winding down. I have to force myself to step away from the computer in the evening; that queue of emails will still be there in the morning. If there's a burning issue that I can't get off my mind, I'll write a few lines about it, creating a plan of action for the next morning. Another way to turn down the sympathetic nervous system and prepare the brain for sleep is

through meditation. There are several very good apps that can help with guided meditations, including some that are focused entirely on sleep.

為睡眠做好心理準備也很重要。對我來說，這意味著避免任何可能造成壓力或焦慮的事情，例如閱讀工作電子郵件或特別查看新聞。當我們想要減壓和放鬆時，這會啟動交感神經系統（戰鬥或逃跑神經系統）。晚上我必須強迫自己離開電腦；早上那堆電子郵件仍然存在。如果有一個我無法擺脫的緊迫問題，我會寫幾行內容，制定第二天早上的行動計畫。另一種降低交感神經系統並使大腦為睡眠做好準備的方法是冥想。有幾個非常好的應用程式可以幫助引導冥想，其中一些完全專注於睡眠。

The overarching point here is that a good night of sleep may depend in part on a good day of wakefulness: one that includes exercise, some outdoor time, sensible eating (no late-night snacking), minimal to no alcohol, proper management of stress, and knowing where to set boundaries around work and other life stressors.

這裡最重要的一點是，一夜的良好睡眠可能部分取決於一整天的清醒：包括運動、一些戶外時間、合理飲食（不吃宵夜）、盡量少喝酒或不喝酒、適當的壓力管理，並知道在哪裡設定工作和其他生活壓力的界線。

How to Improve Your Sleep

如何改善睡眠

The following are some rules or suggestions that I try to follow to help me sleep better. These are not magic bullets but are mostly about creating better conditions for sleeping and letting your brain and body do the rest. The closer you can come to these operating conditions, the better your sleep will be. Of course, I'm not suggesting that it's necessary to do all these things—in general, it's best not to obsess over sleep. But the more of these you can check off, the better your odds of a good night of sleep.

以下是我嘗試遵循的一些規則或建議，以幫助我睡得更好。這些並不是靈丹妙藥，但主要是為睡眠創造更好的條件，讓你的大腦和身體完成剩下的工作。您越接近這些操作條件，您的睡眠就會越好。當然，我並不是說有必要做所有這些事情——一般來說，最好不要沉迷於睡眠。但您檢查的這些內容越多，您睡個好覺的機會就越大。

1. Don't drink any alcohol, period—and if you absolutely, positively must, limit yourself to one drink before about 6 p.m. Alcohol probably impairs sleep quality more than any other factor we can control. Don't confuse the drowsiness it produces with quality sleep.

不要喝酒，就這樣——如果你絕對必須的話，請在下午 6 點左右之前限制自己喝一杯。酒精對睡眠品質的影響可能比我們可以控制的任何其他因素都大。不要將它產生的困倦與優質睡眠混為一談。

2. Don't eat anything less than three hours before bedtime—and ideally longer. It's best to go to bed with just a little bit of hunger (although being ravenous can be distracting.)

睡前三小時內不要吃任何東西，最好是更長的時間。最好在有一點飢餓的情況下上床睡覺（儘管飢餓可能會分散注意力。）

3. Abstain from stimulating electronics, beginning two hours before bed. Try to avoid anything involving a screen if you're having trouble falling asleep. If you must, use a setting that reduces the blue light from your screen.

從睡前兩小時開始，避免使用刺激性電子產品。如果您難以入睡，請盡量避免任何涉及螢幕的事情。如果必須，請使用減少螢幕藍光的設定。

4. For at least one hour before bed, if not more, avoid doing anything that is anxiety-producing or stimulating, such as reading work email or, God help you, checking social media. These get the ruminative, worry-prone areas of our brain humming, which is not what you want.

睡前至少一小時（如果不是更長）避免做任何會產生焦慮或刺激的事情，例如閱讀工作電子郵件或查看社交媒體（上帝保佑你）。這些會讓我們大腦中那些容易沉思、容易擔心的區域嗡嗡作響，這不是你想要的。

5. For folks who have access, spend time in a sauna or hot tub prior to bed. Once you get into the cool bed, your lowering body temperature will signal to your brain that it's time to sleep. (A hot bath or shower works too.)

對於有條件的人，可以在睡前泡個桑拿或熱水浴缸。一旦您進入涼爽的床上，降低的體溫就會向您的大腦發出信號，表示該睡覺了。（洗熱水澡或淋浴也有效。）

6. The room should be cool, ideally in the midsixties. The bed should be cool too. Use a “cool” mattress or one of the many bed-cooling devices out there. These are also great tools for couples who prefer different temperatures at night, since both sides of the mattress can be controlled individually.

房間應該涼爽，最好是六十年代中期。床也應該涼爽。使用“涼爽”床墊或市面上眾多的床冷卻設備之一。對於喜歡夜間不同溫度的夫妻來說，這些也是很好的工具，因為床墊的兩側都可以單獨控制。

7. Darken the room completely. Make it dark enough that you can't see your hand in front of your face with your eyes open, if possible. If that is not achievable, use an eye shade. I use a silky one called Alaska Bear that costs about \$8 and works better than the fancier versions I've tried.

讓房間完全變暗。如果可能的話，讓光線夠暗，讓你睜著眼睛看不到自己的手。如果這無法實現，請使用眼罩。我使用的是一種名為「阿拉斯加熊」的絲質產品，價格約為 8 美元，而且比我嘗試過的更高級的版本效果更好。

8. Give yourself enough time to sleep—what sleep scientists call a sleep opportunity. This means going to bed at least eight hours before you need to wake up, preferably nine. If you don't even give yourself a chance to get adequate sleep, then the rest of this chapter is moot.

給自己足夠的睡眠時間—睡眠科學家稱之為睡眠機會。這意味著您至少在需要起床前八小時上床睡覺，最好是九小時。如果你甚至不給自己一個充足睡眠的機會，那麼本章的其餘部分就沒有意義了。

9. Fix your wake-up time—and don't deviate from it, even on weekends. If you need flexibility, you can vary your bedtime, but make it a priority to budget for at least eight hours in bed each night.

固定你的起床時間，並且不要偏離它，即使在週末。如果您需要靈活性，可以改變就寢時間，但優先考慮每晚至少在床上睡八個小時。

10. Don't obsess over your sleep, especially if you're having problems. If you need an alarm clock, make sure it's turned away from you so you can't see the numbers. Clock-watching makes it harder to fall asleep. And if you find yourself worrying about poor sleep scores, give yourself a break from your sleep tracker.

不要過度關注睡眠，尤其是當您遇到問題時。如果您需要鬧鐘，請確保鬧鐘遠離您，這樣您就看不到數字。看鐘會讓人更難入睡。如果您發現自己擔心睡眠成績不佳，請暫時停止使用睡眠追蹤器。

But what if we *still* can't sleep? This brings us to the last and most vexing sleep problem, true insomnia. We have probably all experienced the inability to fall asleep at some point, but for many people it is a chronic problem. So the first question to ask is: Is it really insomnia? Or are you simply not prepared to sleep properly?

但如果我們還是睡不著怎麼辦？這給我們帶來了最後一個也是最令人煩惱的睡眠問題，也就是真正的失眠。我們可能都經歷過無法入睡的情況，但對許多人來說這是一個長期問題。那麼首先要問的問題是：真的是失眠嗎？還是你根本就沒有準備好好睡覺？

If you find yourself lying awake in bed, unable to get back to sleep, my advice is to stop fighting it. Get up, go into another room and do something relaxing. Fix a cup of tea (noncaffeinated, obviously), and read a (preferably boring) book until you feel sleepy again. The key, says Vikas Jain, is to find something that is relaxing and enjoyable but that serves no function; you never want to give your insomnia a purpose, such as doing work or paying bills, because if you do, your brain will make sure to wake you up for it on a regular basis. Keep in mind, too, that you might not actually have insomnia; you might simply be a night-owl chronotype, thinking you “should” go to bed much earlier than your brain or your body is ready for. So adjust your bedtime and waking time, if possible.

如果你發現自己躺在床上無法入睡，我的建議是停止對抗。站起來，走進另一個房間，做一些放鬆的事情。喝一杯茶（顯然不含咖啡因），然後讀一本（最好是無聊的）書，直到你再次感到困倦。維卡斯·傑恩 (Vikas Jain) 表示，關鍵是要找到一些令人放鬆、令人愉悅但沒有任何功能的東西；你永遠不想給你的失眠一個目的，例如工作或支付帳單，因為如果你這樣做，你的大腦一定會定期叫醒你。還要記住，您可能實際上並沒有失眠；您可能會失眠。您可能只是一個夜貓子睡眠型，認為你「應該」比你的大腦或你的身體準備好更早上床睡覺。因此，如果可能的話，調整你的就寢時間和起床時間。

If the sleeplessness persists, even after following the advice outlined above, the most effective treatment is a form of psychotherapy called Cognitive Behavioral Therapy for Insomnia, or CBT-I. The goal of CBT-I is

to help restore confidence in one's ability to sleep, by helping the patient break bad sleep habits and eliminate any anxieties that may be preventing them from getting to sleep. Therapists will also use sleep restriction, again, as a way of increasing sleep pressure. That, in turn, helps restore confidence in their ability to sleep. Studies of CBT-I techniques have found that they are more effective than sleeping medications.

如果即使遵循了上述建議，失眠現象仍然存在，最有效的治療方法是一種稱為失眠認知行為療法（CBT-I）的心理療法。CBT-I 的目標是透過幫助患者改掉不良的睡眠習慣並消除任何可能妨礙他們入睡的焦慮，幫助患者恢復對睡眠能力的信心。治療師也將再次使用睡眠限製作為增加睡眠壓力的一種方法。這反過來又有助於恢復他們對睡眠能力的信心。CBT-I 技術的研究發現它們比安眠藥更有效。

After ignoring sleep for decades, I'm now a fan. I consider it a kind of performance-enhancing substance, not only physically but cognitively. Long term, this thing called sleep also has the power to improve our healthspan in remarkable ways. Just like exercise, sleep is its own kind of wonder drug, with both global and localized benefits to the brain, to the heart, and especially to our metabolism.

在忽視睡眠數十年後，我現在成了它的粉絲。我認為它是一種增強表現的物質，不僅在身體上而且在認知上。從長遠來看，睡眠這種東西也有能力以顯著的方式延長我們的健康壽命。就像運動一樣，睡眠本身就是一種靈丹妙藥，對大腦、心臟，尤其是新陳代謝都有整體和局部的好處。

So if evolution has made sleep non-negotiable, I'm no longer going to argue the point. Rather, I've embraced it.

因此，如果進化使睡眠變得不可商量，我將不再爭論這一點。相反，我已經接受了它。

[SKIP NOTES](#)

[跳過註釋](#)

*1 It's not just a matter of getting enough sleep; the timing also matters. Studies have looked at winning percentages of teams in the NBA/NFL/NHL, and there is a clear circadian disadvantage for teams who have to travel westward (Roy and Forest, 2018).

*1 這不僅是睡眠充足的問題；時機也很重要。研究檢視了 NBA/NFL/NHL 球隊的勝率，發現必須西行的球隊在晝夜節律上有明顯的劣勢（Roy 和 Forest，2018）。

*2 Noradrenaline can be lowered by the blood pressure drug prazosin.

*2 降血壓藥哌唑嗪可降低去甲腎上腺素。

*3 What's interesting is that REM sleep appeared relatively late in the game of evolution; all animals display NREM sleep, but only birds and nonaquatic mammals experience REM, although recent studies suggest that a REM sleep-like state may exist in nonavian reptiles. (Aquatic mammals need to surface periodically to breathe, so they do not enter deep sleep.)

*3 有趣的是，快速動眼睡眠在演化過程中出現得相對較晚；所有動物都表現出非快速動眼睡眠，但只有鳥類和非水生哺乳動物經歷快速動眼睡眠，儘管最近的研究表明非鳥類爬行動物可能存在類似快速動眼睡眠的狀態。（水生哺乳動物需要定期浮出水面呼吸，因此它們不會進入深度睡眠。）

*4 The use of trazodone for sleep is becoming more common but is still considered an “off-label” use by the FDA. It appears especially helpful for enabling patients to stay asleep and not wake up during the night.

*4 使用曲唑酮促進睡眠變得越來越普遍，但 FDA 仍將其視為「標籤外」用途。它對於讓患者保持睡眠狀態並且在夜間不醒來特別有幫助。

*5 The Pittsburgh Sleep Quality Index questionnaire is available at www.sleep.pitt.edu/instruments/#psqi; for a detailed guide to scoring, see Buysse et al. (1989).

*5 匹茲堡睡眠品質指數問卷可在 www.sleep.pitt.edu/instruments/#psqi 上取得；有關評分的詳細指南，請參閱 Buysse 等人。（1989）。

*6 The Epworth Sleepiness Scale and its scoring can be viewed at www.cdc.gov/niosh/emres/longhourstraining/scale.html.

*6 Epworth 嗜睡量表及其評分可在 www.cdc.gov/niosh/emres/longhourstraining/scale.html 上查看。

*7 The Insomnia Severity Index and information on its scoring and interpretation are available at www.ons.org/sites/default/files/InsomniaSeverityIndex_ISI.pdf.

*7 失眠嚴重程度指數及其評分和解釋資訊可在 www.ons.org/sites/default/files/InsomniaSeverityIndex_ISI.pdf 上取得。

*8 To figure out your sleep chronotype, take the Morningness/Eveningness Questionnaire (MEQ) at <https://reference.medscape.com/calculator/829/morningness-eveningness-questionnaire-meq>.

*8 若要了解您的睡眠時間類型，請填寫早晨/夜間問卷 (MEQ)，網址為 <https://reference.medscape.com/calculator/829/morningness-eveningness-questionnaire-meq>。

*9 The STOP-BANG Questionnaire is available at www.stopbang.ca/osa/screening.php.

*9 STOP-BANG 問卷可在 www.stopbang.ca/osa/screening.php 上取得。

CHAPTER 17

第十七章

Work in Progress

工作正在進行中

The High Price of Ignoring Emotional Health

忽視情緒健康的高昂代價

Every man is a bridge, spanning the legacy he inherited
and the legacy he passes on.

每個人都是一座橋樑，跨越他所繼承的遺產和他
所傳承的遺產。

—TERRENCE REAL

——特倫斯·雷亞爾

New patients arrive every Monday, and I was the first to show up. It was a few weeks before Christmas, and I had flown from San Diego to Nashville and then gotten into a beat-up minivan taxi that reeked of nicotine for a two-hour ride to a place that I'd never heard of called Bowling Green, Kentucky. It was a cold morning, and the driver would not stop looking at his phone as he drove. Strangely, I was not upset by this. I *wanted* us to crash. At least then I would be spared what was to come.

每週一都會有新病人來，我是第一個到達的。那是聖誕節前幾週，我從聖地亞哥飛往納什維爾，然後乘坐一輛破舊的小型貨車出租車，散發著尼古丁的臭味，經過兩個小時的車程，到達了一個我從未聽說過的地方，名叫鮑靈格林，肯塔基州。這是一個寒冷的早晨，司機一邊開車一邊不停地看手機。奇怪的是，我並沒有為此感到不安。我想讓我們崩潰。至少這樣我就可以免於即將發生的事情的影響。

By late morning I was sitting in the common area of a facility called The Bridge to Recovery, an isolated place set deep in the woods. It smelled musty. Waiting for the others to arrive, I wandered through the kitchen and saw a sign that read, "Religion is for people who are afraid of Hell. Spirituality is for people who have been there."

上午晚些時候，我坐在一個名為「康復之橋」的設施的公共區域，這是一個位於樹林深處的偏僻地方。聞起來有霉味。等待其他人到來時，我在廚房裡閒逛，看到一個牌子，上面寫著：「宗教是為那些害怕地獄的人準備的。靈性是為那些去過那裡的人準備的。」

Where the hell am I? I wondered.

我到底在哪裡？我想知道。

The first of the other newcomers was a woman who looked to be about fifty. We stared at each other without saying anything. She looked so sad, as if she had been crying for a year straight. I wondered if I looked the same way to her. By that evening, all the "newbies" were there. They were exhausted, pale, totally depleted. Several were addicts—to drugs, alcohol, sex, or some combination thereof. I looked at them in dismay, thinking I wasn't like them.

為首的是一名五十歲左右的女性。我們面面相覷，什麼也沒說。她看起來很悲傷，好像已經哭了一年了。我想知道我在她眼中是否也是這樣。到了晚上，所有「新手」都到齊了。他們精疲力盡，臉色蒼白，完全精疲力竭。其中有幾個人是癮君子——吸毒、酗酒、性或其中的某種組合。我沮喪地看著他們，心想我和他們不一樣。

After some introductory remarks, we did something called a check-in, where we all took turns describing our emotional state. How we felt at that exact moment. I had no words for how I felt. I was angry beyond words. A simmering rage. I just couldn't do it; I lacked the emotional awareness to even understand my own feelings, let alone articulate them. I was furious that I had needed to come to this place. I was furious that I had failed. I believed that I did not belong here, with these broken people. Every cell in my body wanted to call the Texting Death Cab Company and get out of there.

在一些介紹性的發言之後，我們做了一個叫做「簽到」的事情，我們輪流描述我們的情緒狀態。我們在那一刻的感受。我無法用言語來表達我的感受。我憤怒得無以言表。一股熊熊的怒火。我就是做不到；我缺乏情感意識，甚至無法理解自己的感受，更別說表達出來了。我很憤怒，因為我必須來到這個地方。我對自己的失敗感到憤怒。我相信我不屬於這裡，不屬於這些破碎的人。我體內的每個細胞都想打電話給簡訊死亡計程車公司並離開那裡。

Then one of the veterans, a woman my age named Sarah who was in her third week there (and who always had a way of saying the right thing, I would learn), must have seen the look on my face. Without even knowing my name, she turned to me and said, "Hey, it's okay—nobody shows up here on a winning streak."

然後，其中一位退伍軍人，一位與我年齡相仿，名叫莎拉的女士，已經在那裡工作了第三週（我了解到，她總是有辦法說正確的話），她一定看到了我臉上的表情。她甚至不知道我的名字，就轉向我說：“嘿，沒關係——沒有人在連勝的情況下出現在這裡。”

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I may not have felt like I was at rock bottom, but I was headed in that direction fast. A few weeks earlier, I had nearly gotten into a fistfight with a random guy in a parking lot. I was standing right in his face, begging him to throw the first punch so I could rip his larynx out, a procedure I described in surgical detail, with a few choice epithets to boot. I'm pretty certain that I would have won that fight, but I also could have lost everything: my house, my medical license, my freedom, probably what was left of my marriage. Outwardly, I was a successful-seeming guy with a thriving medical practice, a beautiful wife and kids, wonderful friends, robust health, and a contract to write this book. But in reality, I was out of control.

我可能沒有感覺到自己正處於谷底，但我正在快速地朝那個方向前進。幾週前，我在停車場差點和一個隨機的人打架。我就站在他面前，懇求他先打出第一拳，這樣我就可以撕掉他的喉頭，我以外科手術的細節描述了這個過程，還加上了一些自選的綽號。我很確定我會贏得這場戰鬥，但我也可能會失去一切：我的房子、我的行醫執照、我的自由，可能還有我的婚姻所剩下的一切。從表面上看，我是一個看似成功的人，擁有蓬勃發展的醫療事業、美麗的妻子和孩子、很棒的朋友、健康的身體，以及寫這本書的合約。但事實上，我已經失控了。

I wasn't just some garden-variety road-raging maniac either. It was much worse than that. A few months earlier—on Tuesday, July 11, 2017, at 5:45 p.m., to be exact—I had received a call from Jill, my wife. She was in an ambulance with our infant son, Ayrton, on the way to the hospital. For some reason, he had suddenly stopped breathing and fallen unconscious. His eyes were completely rolled back in their sockets and he was lifeless and blue, with no heartbeat. Only the quick reaction of our nanny had saved him. She rushed him to Jill, who is a nurse. Her instincts took over and she immediately put him on the floor and began performing CPR, rhythmically but carefully pressing her fingers on his tiny sternum as the nanny frantically dialed 911. He was barely a month old.

我也不僅僅是一個普通的公路狂人。情況比那更糟。幾個月前，確切地說，是 2017 年 7 月 11 日星期二下午 5:45，我接到了我妻子吉爾的

電話。她和我們還在襁褓中的兒子艾爾頓一起搭乘救護車前往醫院。不知為何，他突然停止了呼吸，陷入了昏迷。他的眼睛完全翻到了眼窩裡，毫無生氣，臉色青紫，沒有心跳。正是我們保母的快速反應救了他。她趕緊把他送到護士吉爾那裡。她的直覺佔了上風，立即把他放在地板上，開始進行心肺復甦，有節奏但小心地用手指按在他小小的胸骨上，保母瘋狂地撥打了911。他還不到一個月大。

By the time the firefighters stormed into the house, about five minutes later, Ayrton was breathing again, and his skin was turning from blue back to pink as oxygen returned to his body. The firemen were stunned. We never see these kids come back, they told Jill. To this day, we still don't know how or why it happened, but this is likely what occurs when babies die suddenly in their sleep: they choke for a moment on their own saliva, or some other vasovagal insult occurs, and their very immature nervous system fails to restart their breathing.

大約五分鐘後，當消防隊員衝進房子時，艾爾頓再次開始呼吸，隨著氧氣回到他的身體，他的皮膚從藍色變回粉紅色。消防員們驚呆了。他們告訴吉爾，我們再也沒有看到這些孩子回來。直到今天，我們仍然不知道它是如何或為何發生的，但這很可能是嬰兒在睡夢中突然死亡時發生的情況：他們被自己的唾液窒息了一會兒，或者發生了其他一些血管迷走神經損傷，他們的不成熟的神經系統無法重新開始呼吸。

When Jill called me from the ambulance, I was in New York, in a taxi on Fifty-Fourth Street, on my way to dinner. After she finished telling me the story, I just said, without a shred of emotion, "Okay, call me when you get to the hospital, so I can talk to the doctors in the ICU."

當吉爾從救護車上打電話給我時，我正在紐約，在第五十四街的一輛計程車上，正在去吃晚餐的路上。她給我講完這個故事後，我面無表情地說：“好吧，你到了醫院給我打電話，我可以和ICU裡的醫生談談。”

She got off the phone pretty quickly, and, of course, it's obvious why she was upset: our son had nearly died, and the right thing for me to say, the *only*

thing to say, was that I was getting the next flight home.

她很快就掛斷了電話，當然，她難過的原因很明顯：我們的兒子差點就死了，而我該說的、唯一該說的是，我要搭下一班飛機回家。

Jill stayed in the hospital with Ayrton, alone, for four days. She pleaded with me to come home. I called in daily to talk to the doctors and discuss each day's test results, but I stayed in New York, busy with my "important" work. Ayrton's cardiac arrest happened on a Tuesday, but I did not come home to San Diego until Friday of the following week. *Ten days later.*

吉爾獨自和艾爾頓一起在醫院住了四天。她懇求我回家。我每天打電話與醫生交談並討論每天的檢查結果，但我留在紐約，忙於我的「重要」工作。艾爾頓的心臟驟停發生在周二，但我直到下週五才回到聖地牙哥的家。十天後。

Even today, just thinking about what happened, I feel nauseous about my behavior. I can't believe I did that to my family. I can't believe what a blind, selfish, checked-out husband and father I was. And I know I may never fully forgive myself for it, for as long as I live.

即使在今天，只要想到發生的事情，我就對自己的行為感到噁心。我不敢相信我對我的家人做了這樣的事。我簡直不敢相信自己是一個多麼盲目、自私、過度的丈夫和父親。我知道，只要我活著，我可能永遠不會完全原諒自己。

I must have been giving off a very troubled vibe during this period, because around then my close friend Paul Conti, a medical school classmate who is now a brilliant and very intuitive psychiatrist, began urging me to go to this place in Kentucky. I looked it up, and it seemed to be a place for addicts. "This doesn't make sense," I told him. "I'm not an addict."

在這段時間裡，我一定散發出一種非常困擾的氛圍，因為就在那時，我的密友保羅·康蒂（Paul Conti）開始敦促我去肯塔基州的這個地方，他是一位醫學院同學，現在是一位才華洋溢且非常直覺的精神科醫師。我查了一下，這似乎是個癮君子的地方。「這沒有道理，」我告訴他。「我不是癮君子。」

He explained to me, over several months of gentle discussion, that addiction can take many forms, not merely to drugs or alcohol. Often, he continued, it is an outgrowth of some trauma that has happened in a person's past. Paul is an expert in trauma, and he saw that I displayed all the behavioral signs: anger, detachment, obsessiveness, a need to achieve that was fueled by insecurity. "I don't know what it was [that happened], but you just have to trust me on this," he said. He was relentless.

經過幾個月的溫和討論，他向我解釋說，成癮可以有多種形式，而不僅僅是毒品或酒精。他繼續說道，通常情況下，這是一個人過去發生的一些創傷的產物。保羅是創傷的專家，他看到我表現出了所有的行為跡象：憤怒、冷漠、強迫症、不安全感助長了實現目標的需要。

「我不知道發生了什麼，但你必須相信我，」他說。他是無情的。

I agreed to go to Kentucky, but I was still looking for any excuse to get out of it. In early November, a woman from the Bridge called to do my intake interview. It was a long, tedious conversation, and my patience finally expired when she asked, "Have you ever been subject to any kind of abuse?"

我同意去肯塔基州，但我仍在尋找藉口離開。十一月初，一位來自 Bridge 的女士打電話來接受我的入學面試。這是一次漫長而乏味的談話，當她問我「你有沒有受到任何形式的虐待嗎？」時，我的耐心終於耗盡了。

I got so angry I yelled, "Fuck you!" and hung up the phone. After this call I decided to cancel my planned stay. What was wrong with these people, asking such idiotic questions?

我很生氣，大喊：“操你媽的！”然後掛了電話。打完這個電話後，我決定取消我的住宿計畫。這些人到底是怎麼了，問這麼白痴的問題？

That Thanksgiving weekend is still a blur. It was the only Thanksgiving in our life together when we didn't go to a dinner with friends or family, or host one ourselves. We just stayed home alone. On Sunday night, Jill begged me again to go to Kentucky. I can't just go off the grid for that long, I said. My patients need me, and you need help with the kids. This was total bullshit, and

we both knew it. She replied point blank, “You’re of no help to me; in fact, you’re hurting me, and your kids, very badly.”

那個感恩節週末仍然是模糊的。這是我們人生中唯一一次沒有與朋友或家人共進晚餐，也沒有親自舉辦感恩節。我們就一個人待在家裡。週日晚上，吉爾再次懇求我去肯塔基州。我不能脫離電網那麼久，我說。我的病人需要我，你需要幫忙照顧孩子。這完全是胡說八道，我們都知道。她直截了當地回答：「你對我沒有任何幫助；事實上，你深深地傷害了我和你的孩子。」

Confronted with the brutal truth, I knew I had to go.

面對殘酷的現實，我知道我必須離開。

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As should be obvious by now, this chapter will be different from the rest of this book, because in it I am not the physician; I am the patient. And I am a patient who considers himself lucky to be alive. Up until this point, I have focused almost entirely on the physical aspects of healthspan and longevity, but here I will explore their emotional and mental sides, which in some ways are more important than everything else that I’ve laid out thus far.

現在應該很明顯，這一章將與本書的其餘部分有所不同，因為在這一章中我不是醫生；我是一名醫生。我是病人。我是一個認為自己能活著就很幸運的病人。到目前為止，我幾乎完全專注於健康壽命和長壽的身體方面，但在這裡我將探討它們的情感和精神方面，這在某些方面比我迄今為止所闡述的其他所有內容都更重要。

My journey transformed not only my own life, and the life of my family, but also the way that I think about longevity. The process is ongoing, requiring daily work on my part—nearly as much time and effort as I devote to exercise (which is a lot, as you know by now). This is as it should be, I’ve come to realize. Emotional health and physical health are closely intertwined, in ways that mainstream medicine, Medicine 2.0, is still only beginning to grasp. On the most obvious level, an angry episode like my confrontation in that parking

lot could have easily triggered a cardiac event, particularly given my own presumed genetic propensity for heart disease. I could have dropped dead that very afternoon.

我的旅程不僅改變了我自己的生活和家人的生活，也改變了我對長壽的看法。這個過程是持續進行的，需要我每天的工作——幾乎與我投入運動的時間和精力一樣多（正如你現在所知，這是很多）。這是應該的，我已經意識到了。情緒健康和身體健康緊密相連，主流醫學

（醫學 2.0）仍然剛開始掌握。在最明顯的層面上，像我在停車場發生衝突這樣的憤怒事件很容易引發心臟病，特別是考慮到我自己推測的心臟病遺傳傾向。那天下午我可能就死了。

Another very direct way in which mental health affects lifespan is via suicide, which ranks among the top ten causes of death across all age groups, from our teens into our eighties. When I think of suicide, I often think of a man named Ken Baldwin, who leaped off the Golden Gate Bridge in 1985, when he was twenty-eight. Unlike 99 percent of jumpers from that bridge, he survived. As he fell, he later told the author Tad Friend, “I instantly realized that everything in my life that I’d thought was unfixable, was totally fixable—except for having just jumped.”

心理健康影響壽命的另一種非常直接的方式是自殺，自殺是所有年齡層（從十幾歲到八十多歲）的十大死因之一。當我想到自殺時，我經常想起一個名叫肯·鮑德溫的人，他於 1985 年從金門大橋跳下，當時他 28 歲。與那座橋上 99% 的跳傘者不同，他活了下來。當他跌倒時，他後來告訴作家泰德·弗蘭德，“我立刻意識到，我生命中所有我認為無法修復的事情都是完全可以修復的——除了剛剛跳下去。”

Not all suicides jump from bridges. Many more people sort of slow-roll into misery and early death via various roundabout routes, letting stress and anger erode their health, or falling into self-medicating addictions to alcohol and drugs, or engaging in other reckless, life-endangering behaviors that mental health professionals call parasuicide. It’s not a surprise that deaths related to alcohol and drug abuse have surged over the last two decades, especially among people ages thirty to sixty-five; the CDC estimates that more

than one hundred thousand Americans died from drug overdoses between April 2020 and April 2021, about as many as died from diabetes.

並非所有自殺者都是跳橋自殺。更多的人透過各種迂迴途徑慢慢陷入痛苦和早逝，讓壓力和憤怒侵蝕他們的健康，或者陷入酒精和毒品的自我治療成癮，或者從事其他魯莽的、危及生命的行為，這些行為會導致精神崩潰。衛生專業人員稱之為自殺。過去二十年裡，與酗酒和吸毒有關的死亡人數激增，尤其是在三十至六十五歲的人群中，這並不奇怪。疾病預防控制中心估計，2020 年 4 月至 2021 年 4 月期間，超過十萬美國人死於藥物過量，大約與死於糖尿病的人數相同。

These “accidental” overdoses account for almost 40 percent of all accidental deaths, a category that also includes automobile accidents and deaths from falls. Some of these overdoses were no doubt truly accidental, but I’d wager that the vast majority were ultimately attributable to the victims’ mental health issues, on some level. They were slow-motion suicides, deaths of despair—an agonizing but often invisible form of the “slow death” we talked about earlier.

這些「意外」過量服藥幾乎佔所有意外死亡的 40%，這一類別還包括車禍和跌倒死亡。其中一些過量無疑確實是意外的，但我敢打賭，絕大多數最終在某種程度上歸因於受害者的心理健康問題。他們是緩慢的自殺，絕望的死亡——我們之前談到的「緩慢死亡」的一種痛苦但往往是無形的形式。

This category of death has grown so much over the last two decades or so, fueled by the prevalence of addictive opioids in our society, that it has actually helped to diminish life expectancy for some segments of the American population—the first time that this has happened in more than a century. Middle-aged white men and women, in particular, are succumbing to drug and alcohol overdoses, liver disease, and suicide at unprecedented rates, as Anne Case and Angus Deaton first observed in 2015. The substance-abuse crisis has created a longevity crisis, because it is really *a mental health crisis in disguise*.

在過去二十年左右的時間裡，由於我們社會中成癮性鴉片類藥物的盛行，這類死亡人數增長如此之快，以至於它實際上有助於縮短某些美

國人口的預期壽命——這是第一次發生在一個多世紀的時間。正如安妮·凱斯(Anne Case) 和安格斯·迪頓(Angus Deaton) 在2015 年首次觀察到的那樣，中年白人男性和女性正以前所未有的速度死於吸毒和酗酒過量、肝病和自殺。藥物濫用危機造成了長壽危機，因為這確實是一場變相的心理健康危機。

This type of suffering is far more prevalent than suicide rates would suggest. It simply robs you of the joy that enables you to focus on your health, life, and relationships with others, so that instead of living, you are merely waiting to die. This is why I've come to believe that emotional health may represent the most important component of healthspan. Nothing else about longevity is really worth much without some degree of happiness, fulfillment, and connection to others. And misery and unhappiness can also destroy your physical health, just as surely as cancer, heart disease, neurodegenerative disease, and orthopedic injury.

這種類型的痛苦比自殺率所顯示的更為普遍。它只會剝奪你的快樂，讓你無法專注於自己的健康、生活和與他人的關係，這樣你就不是在活著，而是在等待死亡。這就是為什麼我開始相信情緒健康可能是健康壽命最重要的部分。如果沒有某種程度的幸福、滿足感和與他人的聯繫，那麼長壽的其他一切都沒有什麼真正的價值。痛苦和不快樂也會破壞你的身體健康，就像癌症、心臟病、神經退化性疾病和骨科損傷一樣。

Even just living alone, or feeling lonely, is linked to a much higher risk of mortality. While most issues around emotional health are not age dependent, this is the one emotional health “risk factor” that does seem to grow worse with increasing age. Surveys show that older Americans report spending more time alone every day—an average of about seven hours daily, for those age seventy-five—and are far more likely to live alone than people in middle age and younger. And the way things were going for me, I was looking at a sad, lonely, miserable old age.

即使只是獨自生活或感到孤獨，也會導致更高的死亡風險。雖然大多數情緒健康問題與年齡無關，但這是一個情緒健康“危險因素”，似乎隨著年齡的增長而變得更糟。調查顯示，美國老年人每天獨處的時間

更長（75 歲的人平均每天獨處時間約為 7 小時），而且比中年人和年輕人更有可能獨居。就我而言，我的晚年是悲傷、孤獨、悲慘的。

It took me a while to recognize this, but feeling connected and having healthy relationships with others, *and with oneself*, is as imperative as maintaining efficient glucose metabolism or an optimal lipoprotein profile. It is just as important to get your emotional house in order as it is to have a colonoscopy or an Lp(a) test, if not more so. It's just a lot more complicated.

我花了一段時間才認識到這一點，但與他人和自己建立聯繫並保持健康的關係與維持有效的葡萄糖代謝或最佳的脂蛋白狀況一樣重要。整理好你的情緒宮與進行大腸鏡檢查或 Lp(a) 測試同樣重要，甚至更重要。只是情況要複雜得多。

It's a two-way street between emotional and physical health. In my own practice, I witness firsthand how many of my patients' physical and longevity issues are rooted in, or exacerbated by, their emotional health. I see it on a daily basis. It is harder to motivate a patient who is feeling depressed to go and start an exercise program; someone who is overstressed at work and miserable in their personal life may not see the point of early cancer screening or monitoring their blood glucose levels. So they drift along, as their emotional misery drags their physical health down along with it.

這是情緒健康和身體健康之間的雙向路。在我自己的實踐中，我親眼目睹了我的患者有多少身體和長壽問題源於他們的情緒健康，或因他們的情緒健康而加劇。我每天都會看到它。激勵感到憂鬱的患者開始運動計畫是比較困難的；工作壓力過大、個人生活痛苦的人可能看不到早期癌症篩檢或監測血糖值的意義。因此，他們隨波逐流，而他們的情緒痛苦也拖累了他們的身體健康。

My own situation was almost the opposite: I was doing *everything* to live longer, despite being completely miserable emotionally. I was as physically healthy as I'd ever been, circa 2017, but to what end? I was on a horrible path, both emotionally and in terms of my interpersonal relationships. The words of my therapist, Esther Perel, rang in my head practically every day: "Why would you want to live longer if you're so unhappy?"

我自己的情況幾乎相反：儘管我在情感上完全痛苦，但我正在盡一切努力活得更長久。2017 年左右，我的身體狀況一如既往地健康，但結果是什麼？無論是在情感上或人際關係上，我都走在一條可怕的道路。我的治療師埃絲特·佩雷爾的話幾乎每天都在我腦海中響起：“如果你如此不快樂，為什麼還想活得更久呢？”

The one thing that I had in common with some of my patients was that we all found it easier to just avoid dealing with problems that seemed so complex and overwhelming. I didn't even know where to begin—scratch that, I didn't even recognize that I needed help, until long after it was obvious to everyone around me. I had to reach pretty much the end of my rope before I could make myself face up to the truth and go to the Bridge, that godforsaken, difficult, ultimately wonderful place in the woods of Kentucky, and begin to do the work that needed to be done: to begin to acquire the tools that I needed to function better, emotionally.

我和我的一些病人的一個共同點是，我們都發現避免處理看起來如此複雜和難以承受的問題更容易。我甚至不知道從哪裡開始——從頭開始，我甚至沒有意識到我需要幫助，直到很久以後我周圍的每個人都意識到了這一點。在我能夠讓自己面對現實並前往橋，肯塔基州樹林中那個被上帝遺棄的、困難的、最終美妙的地方之前，我必須到達幾乎我的繩索盡頭，並開始做需要的工作。完成：開始獲得我需要的工具，以便在情感上更好地發揮作用。

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My first few days at the Bridge felt like weeks, possibly months. The time just crept by. I had no phone, and they had even taken away my books. This was part of the plan, to force us to sit in our own misery. There was literally nothing else to do. I moved like a zombie through the daily activities, from our one cup of morning coffee to inner-child work to equine therapy. My only solace was my 4:30 a.m. morning workout, which also represented the one addiction in which I was still permitted to indulge. Otherwise, there was no relief, and no solitude.

我在大橋的頭幾天感覺就像幾週，甚至可能是幾個月。時間就這樣悄然而過。我沒有電話，他們甚至拿走了我的書。這是計劃的一部分，目的是迫使我們陷入自己的痛苦之中。實際上沒有其他事可做。我像殭屍一樣經歷日常活動，從早晨的一杯咖啡到內心小孩的工作，再到馬術治療。我唯一的安慰是凌晨 4:30 的早晨鍛煉，這也代表了我仍然可以沉迷的一種癮。否則，就沒有任何解脫，也沒有孤獨。

Before I arrived, I had my assistant call to request a private room. The person on the phone had basically laughed at her. “Tell your Very Important Person that we don’t do that. Everybody has a roommate.” So I had a roommate, who seemed like a nice enough guy, and he had some pretty cool tattoos, but in my rush to judge him (and everyone else) all I could see were the differences. He hadn’t gone to college. He worked in a machine shop. He liked strippers and cocaine. His wife hated him, which is actually something that we might have had in common at that point in time.

在我到達之前，我讓我的助理打電話要求一間私人房間。電話那頭的人基本上是在嘲笑她。「告訴你非常重要的人，我們不會這樣做。每個人都有一個室友。」所以我有一個室友，他看起來是一個足夠好的人，他有一些很酷的紋身，但在我急於評判他（和其他人）時，我所能看到的只是差異。他沒有上過大學。他在一家機械車間工作。他喜歡脫衣舞孃和古柯鹼。他的妻子討厭他，這其實是我們當時可能有的共同點。

At first, I clammed up. The part of the day that I dreaded most was the twice-daily emotional check-ins, where we were supposed to describe exactly what we were feeling at that moment. I couldn’t do it. I just sat there seething. By Wednesday or Thursday, it had almost become a joke. We had all heard at least bits and pieces of everyone else’s story, but nobody knew anything about mine. At one point someone said, “C’mon, dude, are you like a serial killer or something? Like, what’s up?”

起初，我閉嘴了。一天中我最害怕的部分是每天兩次的情緒檢查，我們應該準確地描述我們當時的感受。我做不到。我只是坐在那裡沸騰。到了周三或週四，這幾乎成了一個笑話。我們都至少聽過其他人

的故事，但沒有人知道我的故事。有一次有人說：「來吧，夥計，你像個連環殺手還是什麼的？比如，怎麼了？」

I said nothing. I don't think my roommate slept well that night.

我什麼都沒說。我認為我的室友那天晚上睡得不好。

Finally, after four or five days, I could no longer remain silent. They had set aside almost an entire day when we were all supposed to tell our life stories from the beginning. We had an hour each, and we were supposed to prepare. So I was finally telling my life story for the first time to this group of perfect strangers—not even Jill had heard the whole thing—but I was telling it in a way that was very matter-of-fact: this happened when I was five, that happened when I was seven, and so on. Some of it was sexual; some of it was physical. But it was not all bad, I explained. These events, terrible as they were, had led me to take up boxing and martial arts at age thirteen. I got to punch bags, and people, and that channeled my anger. I learned how to protect myself, but I also gained discipline and focus, qualities that proved invaluable when, at around age nineteen, I pivoted from pugilism to mathematics.

終於，四、五天過去了，我再也無法保持沉默了。他們留出了幾乎一整天的時間，讓我們從頭開始講述自己的人生故事。我們每人有一小時的時間，我們應該做好準備。所以我終於第一次向這群完全陌生的人講述我的人生故事——連吉爾都沒有聽過整件事——但我是以一種非常實事求是的方式講述的：這發生在我五歲，那是我七歲時發生的事，依此類推。其中有些是性的；有些則與性有關。其中一些是身體上的。但這並不全然是壞事，我解釋。這些事件儘管很可怕，卻促使我在十三歲時開始學習拳擊和武術。我必須打沙袋和人，這可以發洩我的憤怒。我學會瞭如何保護自己，但我也獲得了自律和專注，當我在十九歲左右從拳擊轉向數學時，這些特質被證明是無價的。

Terrible as it was, my past was also what had set me on the path to becoming a doctor, I continued, growing somewhat defensive. Throughout college, I volunteered at a shelter for sexually abused teenagers, and I became close to many of them over four years, including one young woman who had been abused by her father. When she attempted suicide—one of many

attempts—I went to visit her in the hospital. I was a senior by then, and I had already applied to the top PhD programs in aerospace engineering. But I wasn't really sure it was my calling. Spending so much time in the hospital with her helped lead to the epiphany that I was meant to care for people, not solve equations.

儘管這很可怕，但我的過去也讓我走上了成為醫生的道路，我繼續說道，變得有些防禦。在整個大學期間，我在一個為遭受性虐待的青少年收容所做志願者，四年來我與他們中的許多人變得很親近，其中包括一名曾被父親虐待的年輕女子。當她試圖自殺時——這是眾多嘗試之一——我去醫院探望她。那時我已經是大四生，我已經申請了航空航天工程領域的頂尖博士課程。但我不太確定這是我的使命。和她一起在醫院待了這麼長時間，讓我頓悟到我應該照顧別人，而不是解方程式。

So do you see? I concluded. Parts of my past may have been bad, but in a way they also ended up setting me on a course toward a better life. Some of the kids I grew up with and boxed with, meanwhile, were getting arrested for armed robbery, and getting girls pregnant in high school, and all kinds of other stuff. That could easily have been me. So in a way, I said, my abuse may have actually saved my life—I don't really even need to be here!

那你看到了嗎？我得出結論。我的過去的某些部分可能很糟糕，但在某種程度上，它們最終也讓我走上了通往更好生活的道路。同時，一些和我一起長大、一起拳擊的孩子因持械搶劫、讓高中女孩懷孕以及其他各種事情而被捕。那很可能就是我。所以在某種程度上，我說，我的虐待實際上可能拯救了我的生命——我甚至不需要在這裡！

Right then, one of our therapists, Julie Vincent, cut me off. There are many rules at the Bridge, and one of the most important ones is *no minimizing*. You are not allowed to minimize anything that someone else is saying, and you are especially not allowed to minimize your own experiences. But she didn't flag me for that. Instead, she asked a simple question: "You were five years old when this first happened to you, right?"

就在那時，我們的一位治療師朱莉·文森特打斷了我。橋牌有很多規則，其中最重要的規則之一就是不能最小化。你不可以貶低別人所說的任何話，尤其不可以貶低你自己的經驗。但她並沒有因此而標記我。相反，她問了一個簡單的問題：“當這件事第一次發生在你身上時，你才五歲，對嗎？”

“That’s right,” I replied.

「沒錯，」我回答。

“And your son Reese is almost five years old now, right?”

“你的兒子里斯現在快五歲了，對吧？”

I nodded.

我點了頭。

“So you’re saying it’s okay that this happened to you when you were his age—but would you be okay with people doing that to Reese now?”

“所以你是說，當你在他這個年紀的時候，這種事發生在你身上是可以接受的——但是你現在可以接受人們對里斯這樣做嗎？”

Another rule at the Bridge is that you’re not supposed to hand anyone a Kleenex when they’re crying. They’re supposed to get up and fetch it themselves. Now it was my turn to stand up and walk over to the Kleenex box. It all came pouring out of me and, finally, I was able to embrace why I was there and begin the hard work of unpacking the last forty years of my life.

橋牌的另一個規則是，當任何人哭泣時，你不應該給他們紙巾。他們應該自己起身去拿。現在輪到我站起來走向紙巾盒了。這一切都從我的內心傾瀉而出，最後，我能夠接受我在那裡的原因，並開始努力解開我生命的最後四十年。

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One framework that the therapists at the Bridge work with, and that I found helpful, is called the Trauma Tree. The idea behind it is that certain undesirable behaviors that we manifest as adults, such as addiction and

uncontrolled anger, are actually adaptations to the various types of trauma we suffered in childhood. So while we only see the manifestation of the tree above the ground, the trunk and branches, we need to look underground, at the roots, to understand the tree completely. But the roots are often very well hidden, as they were with me.

橋樑治療師使用的一個框架（我發現它很有幫助）稱為「創傷樹」。背後的想法是，我們作為成年人表現出的某些不良行為，例如成癮和不受控制的憤怒，實際上是對我們在童年時期遭受的各種類型的創傷的適應。因此，雖然我們只看到樹在地面上的表現，樹幹和樹枝，但我們需要看看地下，看看樹根，才能完全了解樹。但根源往往隱藏得很好，就像我一樣。

Trauma generally falls into five categories: (1) abuse (physical or sexual, but also emotional or spiritual); (2) neglect; (3) abandonment; (4) enmeshment (the blurring of boundaries between adults and children); and (5) witnessing tragic events. Most of the things that wound children fit into these five categories.

創傷通常分為五類：（1）虐待（身體或性虐待，也包括情緒或精神虐待）；（2）疏忽；（三）遺棄；（4）糾纏（成人與兒童之間的界線變得模糊）；（5）目睹悲慘事件。大多數傷害兒童的事情都屬於這五類。

Trauma is a pretty loaded word, and the therapists at the Bridge were careful to explain that there can be “big-T” trauma or “little-t” traumas. Being a victim of rape would qualify as a big-T trauma, while having an alcoholic parent might subject a child to a host of little-t traumas. But in large enough doses over a long enough time, little-t traumas can shape a person’s life just as much as one major terrible event.

創傷是一個含義豐富的詞，橋樑的治療師小心翼翼地解釋說，可能存在“大T”創傷或“小T”創傷。成為強暴的受害者可能會受到嚴重的創傷，而父母酗酒可能會讓孩子遭受許多輕微的創傷。但在足夠大的劑量和足夠長的時間內，小小的創傷可以像一次重大的可怕事件一樣影響一個人的生活。

Both types can do tremendous damage, but little-t trauma is more challenging to address—in part, I suspect, because we are more inclined to dismiss it. Jeff English, one of the therapists I was working with, offered a useful blanket definition: Trauma, big T or little t, means having experienced moments of perceived helplessness. The situations in question may or may not have been life-or-death, he explained, “but to a child with an undeveloped brain, it may have seemed that way.”

這兩種類型都會造成巨大的損害，但小創傷更難以解決——我懷疑，部分原因是我們更傾向於忽視它。與我一起工作的治療師之一傑夫·英格利希 (Jeff English) 提供了一個有用的籠統定義：創傷，無論是大 T 還是小 t，都意味著經歷了感知到的無助時刻。他解釋說，所討論的情況可能是生死攸關的，也可能不是，“但對於一個大腦尚未發育成熟的孩子來說，情況可能就是這樣。”

This perfectly described how I had felt at certain times in my childhood. The feeling of powerlessness was a large source of my pain (and in later life, my anger). But I also want to make an important distinction between trauma and adversity. They are not the same. I am not suggesting that it is ideal for children to grow up without experiencing any adversity at all, which sometimes seems to be a primary goal of modern parenting. Many stressors can be beneficial, while others are not. There is no bright line between trauma and adversity; terrible as it was, my own experience had made me stronger in some ways. Julie's question is a pretty good litmus test: Would I want my child to experience it? If my daughter finished dead last in a cross-country race (for example), and didn't get a medal, that would be okay. Sure, she might feel upset in the moment, but it could also motivate her to train harder and give her a better appreciation for the joy of placing in the top three one day. What would not be okay is if I had then screamed at her, in front of the other runners, for getting beaten by the shortest kid on the team.

這完美地描述了我童年時期某些時候的感受。無能為力的感覺是我痛苦的一大根源（在後來的人生中，也是我憤怒的根源）。但我也想對創傷和逆境做出重要的區分。他們不一樣。我並不是說孩子們在沒有經歷任何逆境的情況下成長是理想的，這有時似乎是現代育兒的首要

目標。許多壓力源可能是有益的，而有些則不然。創傷和逆境之間沒有明顯的界線；儘管這很糟糕，但我自己的經歷在某些方面讓我變得更堅強。朱莉的問題是一個很好的試金石：我想讓我的孩子經歷它嗎？如果我的女兒在越野比賽中名列最後（例如），並且沒有獲得獎牌，那也沒關係。當然，她此刻可能會感到沮喪，但這也可以激勵她更加努力地訓練，讓她更好地體會有一天進入前三名的喜悅。如果我當時在其他跑者面前對她大喊大叫，因為她被隊裡最矮的孩子打敗了，那就不好了。

Just as an aside, a 2019 study provides an elegant demonstration of the principle that setbacks can be net positive. The researchers looked at junior scientists who had applied for NIH grants and separated them into two groups: One group had scored just above the threshold for funding, while the other had scored just below the funding line, meaning their grants were not funded. While the near-miss group were more likely to drop out of science in the immediate aftermath, those who stuck with it eventually outperformed their peers who had received funding on their first try. The early setback had not impaired their careers but may have had an opposite effect.

順便說一句，2019 年的一項研究完美地證明了「挫折可以帶來正面影響」這項原則。研究人員觀察了申請美國國立衛生研究院資助的初級科學家，並將他們分為兩組：一組的得分略高於資助門檻，而另一組的得分略低於資助線，這意味著他們的資助沒有得到資助。雖然僥倖成功的那組人更有可能在事後立即退出科學研究，但那些堅持下來的人最終表現優於那些在第一次嘗試時就獲得資助的同齡人。早期的挫折並沒有損害他們的職業生涯，但可能產生了相反的影響。

The most important thing about childhood trauma is not the event itself but the way the child adapts to it. Children are remarkably resilient, and wounded children become adaptive children. The problems begin when these adaptive children grow up to become maladaptive, dysfunctional adults. This dysfunction is represented by the four branches of the trauma tree: (1) addiction, not only to vices such as drugs, alcohol, and gambling, but also to socially acceptable things such as work, exercise, and perfectionism (check); (2) codependency, or excessive psychological reliance on another person; (3)

habituated survival strategies, such as a propensity to anger and rage (check); (4) attachment disorders, difficulty forming and maintaining connections or meaningful relationships with others (check). These branches are often fairly obvious and easy to spot; the tricky part is digging down to the roots and beginning to disentangle them. All of this is highly individual; everyone responds and adapts to trauma in a unique way. And it's not as if there is some sort of pill that can make someone's trauma, or their adaptations to it, simply go away. It requires hard work—and, as I would come to understand, it can also take a very long time.

關於童年創傷，最重要的不是事件本身，而是孩子適應它的方式。孩子的適應力非常強，受傷的孩子會成為適應性強的孩子。當這些適應性強的兒童長大後成為適應不良、功能失調的成年人時，問題就開始出現了。這種功能障礙表現為創傷樹的四個分支：（1）成癮，不僅是對毒品、酒精和賭博等惡習的成癮，而且是對工作、運動和完美主義等社會可接受的事物的成癮（檢查）；（2）相互依賴，或對他人過度的心理依賴；（3）習慣性的生存策略，例如憤怒和暴怒的傾向（勾選）；（4）依附障礙，難以與他人建立和維持連結或有意義的關係（勾選）。這些分支通常相當明顯且容易發現；棘手的部分是深入挖掘根源並開始理清它們。所有這些都是高度個性化的；每個人都以獨特的方式來應對和適應創傷。並不是有某種藥丸可以讓某人的創傷或對創傷的適應消失。這需要艱苦的工作——而且，據我了解，這也可能需要很長時間。

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This is yet another realm where Medicine 2.0 too often falls short. Most therapists diagnose patients based on the bible of mental health, the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5), a 991-page-long compendium of every conceivable psychological condition. The DSM is a valiant attempt to organize and codify all of the myriad forms of mental disorders—to scientize it, in effect, and also to facilitate insurance reimbursement. But in reality, as Paul Conti observes, our stories and our conditions are really unique to each of us. Not all of them fall into tidy

diagnostic categories. Everyone is different; everyone's story is different. No person is a "code." Therefore, he believes, such rigorous codification "presents an obstacle to *actually understanding the person*."

這是另一個醫學 2.0 經常無法達到的領域。大多數治療師根據心理健康聖經《精神疾病診斷與統計手冊》第 5 版 (DSM-5) 來診斷患者，該手冊長達 991 頁，涵蓋了每種可以想像的心理狀況。《精神疾病診斷統計手冊》是一次勇敢的嘗試，旨在將各種形式的精神障礙組織起來並編纂成法——實際上是為了使其科學化，同時也為了促進保險報銷。但事實上，正如保羅·孔蒂所觀察到的那樣，我們的故事和我們的處境對我們每個人來說都是獨一無二的。並非所有這些都屬於整齊的診斷類別。每個人都是不同的；每個人的故事都不同。沒有人是「代碼」。因此，他認為，如此嚴格的編纂「給真正理解人帶來了障礙」。

This is also what makes it difficult to offer blanket advice to everyone about this topic; every reader will have their own emotional makeup, their own history, and their own issues to address. Yet one difficulty that we all share is that Medicine 2.0 is set up to treat mental and emotional health in pretty much the same way that it treats everything else: diagnose, prescribe, and, of course, bill. While antidepressants and other psychoactive medications have helped many patients, including me, finding a complete solution is rarely simple. For one thing, this is primarily a disease-based model, which is how Medicine 2.0 addresses and solves other problems, such as infections and acute illnesses: treat the symptoms and send the patient home. Or if the situation is more serious, as it was with me, send the patient off for a couple of weeks at a place like the Bridge, and then send them home—*voilà*, problem solved.

這也是很難向每個人提供有關該主題的全面建議的原因；每個讀者都有自己的情感構成、自己的歷史、自己要解決的問題。然而，我們都面臨的一個困難是，醫學 2.0 的設計目的是治療心理和情緒健康，其方式與治療其他一切疾病幾乎相同：診斷、開藥，當然還有賬單。雖然抗憂鬱藥物和其他精神活性藥物已經幫助了包括我在內的許多患者，但找到完整的解決方案絕非易事。一方面，這主要是一種基於疾

病的模型，這就是醫學 2.0 處理和解決其他問題的方式，例如感染和急性疾病：治療症狀並將患者送回家。或者，如果情況更嚴重，就像我的情況一樣，請將患者送到橋這樣的地方幾週，然後送他們回家——瞧，問題解決了。

One reason this approach has proved less effective in the psychological realm is that mental health and emotional health are not the same thing. Mental health encompasses disease-like states such as clinical depression and schizophrenia, which are complex and difficult to treat but do present with recognizable symptoms. Here, we are more interested in *emotional health*, which incorporates mental health but is also much broader—and less easy to codify and categorize. Emotional health has more to do with the way we regulate our emotions and manage our interpersonal relationships. I did not have a mental *illness*, per se, but I did have serious issues with my emotional health that impaired my ability to live a happy, well-adjusted life—and potentially did put my life in danger. Medicine 2.0 has a harder time dealing with situations such as this.

這種方法在心理領域被證明不太有效的原因之一是心理健康和情緒健康不是一回事。心理健康包括臨床憂鬱症和精神分裂症等類似疾病的狀態，這些狀態複雜且難以治療，但確實會出現可識別的症狀。在這裡，我們對情緒健康更感興趣，它包含心理健康，但範圍也更廣，而且更不容易編碼和分類。情緒健康更與我們調節情緒和管理人際關係的方式有關。我本身並沒有患有精神疾病，但我的情緒健康確實存在嚴重問題，這損害了我過著幸福、良好調整生活的能力，並可能使我的生命處於危險之中。醫學 2.0 處理此類情況會更加困難。

Taking care of our emotional health requires a paradigm shift similar to the shift from Medicine 2.0 to Medicine 3.0. It's about long-term prevention, just like our approach to preventing cardiovascular disease. We have to be able to recognize potential problems early and be willing to put in hard work to address these problems over a long period of time. And our approach must be tailored to each individual, with their unique history and set of issues.

照顧我們的情緒健康需要一種範式轉變，類似於從醫學 2.0 到醫學 3.0 的轉變。這是長期預防，就像我們預防心血管疾病的方法一樣。我們

必須能夠及早認識到潛在的問題，並願意長期努力解決這些問題。我們的方法必須針對每個人獨特的歷史和問題進行量身定制。

Our Medicine 3.0 thesis is that if we address our emotional health, and do so early on, we will have a better chance of avoiding clinical mental health issues such as depression and chronic anxiety—and our overall health will benefit as well. But there is rarely a simple cure or a quick fix, any more than we have a quick fix for cancer or metabolic disease.

我們的醫學 3.0 理論是，如果我們儘早解決情緒健康問題，我們將有更好的機會避免憂鬱和慢性焦慮等臨床心理健康問題，而且我們的整體健康也會受益。但很少有簡單的治癒方法或快速解決方法，就像我們對癌症或代謝疾病沒有快速解決方法一樣。

Addressing emotional health takes just as much constant effort and daily practice as maintaining other aspects of our physical health by creating an exercise routine, following a nutritional program, adhering to sleep rituals, and so on. The key is to be as proactive as possible, so that we can continue to thrive in all domains of healthspan, throughout the later decades of our lives.

解決情緒健康問題與其他透過制定運動計畫、遵循營養計畫、遵守睡眠習慣等來維持身體健康的方面一樣，需要持續的努力和日常練習。關鍵是要盡可能積極主動，這樣我們才能在生命的後幾十年，在健康壽命的各個領域繼續蓬勃發展。

What makes dealing with emotional health harder than physical health, I suspect, is that we are often less able to recognize the need to make changes. Few people who are overweight and out of shape fail to realize they need to make a change. Making the change might be another story. But countless people are in desperate need of help with their emotional health, yet fail to recognize the signs and symptoms of their condition. I was the poster child for this group.

我懷疑，處理情緒健康比處理身體健康更困難的原因是我們往往不太能夠認識到做出改變的必要性。很少有超重和身材走樣的人沒有意識到他們需要做出改變。做出改變可能是另一回事了。但無數人迫切需

要情緒健康方面的幫助，卻未能認清自己病情的跡象和症狀。我是這個群體的典型代表。

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After two weeks, I left the Bridge. My therapists there were uneasy about letting me go so soon; they wanted me to stay for another month, but I felt that I had made tremendous progress in that relatively short time. Acknowledging my past felt like a huge deal to me. I felt hopeful, and they finally agreed that I could leave. So I flew home the day before Christmas.

兩週後，我離開了大橋。我的治療師對這麼快讓我離開感到不安。他們想讓我再待一個月，但我覺得我在相對較短的時間內取得了巨大的進步。承認我的過去對我來說是一件大事。我感到充滿希望，他們終於同意我可以離開。所以我在聖誕節前一天飛回家。

This was probably a mistake.

這可能是個錯誤。

I wish I could say that this marked the end of the story, the point where Old Peter said goodbye, with his selfishness and his anger, and New Peter took his place, and we all lived happily ever after. Alas, that was not the case; it was, at best, only the end of the beginning.

我希望我可以說，這標誌著故事的結束，老彼得帶著他的自私和憤怒告別了，新彼得取代了他的位置，從此我們都幸福地生活在一起。唉，事實並非如此。這充其量只是開始的結束。

I had a lot of work to do when I came home, to process what had been unearthed at the Bridge and to begin to try to heal my relationships with my wife and my children. With the help of two wonderful therapists, Esther Perel (alone) and Lorie Teagno (with my wife), I made slow progress as the weeks and months went by. Lorie and Esther both felt I needed a male therapist, one who could model healthy male emotions. I tried out several good male therapists, but I did not feel a connection to any of them the way I had felt connected to Jeff English, my primary therapist at the Bridge.

當我回到家時，我有很多工作要做，要處理在橋上出土的東西，並開始嘗試修復我與妻子和孩子的關係。在兩位出色的治療師埃絲特·佩雷爾（Esther Perel）（獨自）和洛里·蒂格諾（Lorie Teagno）（和我的妻子）的幫助下，幾周和幾個月過去了，我取得了緩慢的進步。洛里和艾絲特都覺得我需要一位男性治療師，一個能塑造健康男性情緒的人。我嘗試過幾位優秀的男性治療師，但我感覺與他們中的任何一個都沒有像我與我在 Bridge 的主要治療師傑夫·英格利希 (Jeff English) 的聯繫那樣。

I was ready to give up when Esther suggested that I read Terrence Real's book *I Don't Want to Talk About It*, a groundbreaking treatise on the roots of male depression. Once I started, I could not put it down. It was almost creepy that this guy seemed to be writing *about me*, despite never having met me. His main thesis is that with women, depression is generally overt, or obvious, but men are socialized to conceal their depression, channeling it inward or into other emotions, such as anger, without ever wanting to discuss it. (Hence the title.) I could relate to the stories that he shared about his patients. So I began to work with Terry as well. After having gone far too long without any therapy at all, I was now seeing three therapists.

當艾絲特建議我讀泰倫斯·雷亞爾的書《我不想談論它》時，我正準備放棄，這是一本關於男性憂鬱症根源的開創性論文。一旦開始，我就無法愛不釋手。令人毛骨悚然的是，這個傢伙似乎在寫我，儘管他從未見過我。他的主要論點是，對女性來說，憂鬱症通常是公開的或明顯的，但男性在社交中會隱藏自己的憂鬱症，將其向內或轉化為其他情緒，例如憤怒，而不想討論它。（因此有了這個標題。）我可以理解他分享的關於他的病人的故事。所以我也開始和特里一起工作。在沒有接受任何治療太久之後，我現在去看了三位治療師。

Terry had grown up working-class in Camden, New Jersey, with a father whom he describes as a “loving, smart, and brutally violent man.” It turned out that the driving force was his father's hidden depression, which he had adeptly handed on to Terry. “My father beat his depression into me with a strap,” he told me. Trying to cope with his father's anger and violence was what had

pushed him in the direction of studying psychotherapy. “I needed to make sense of my father and his violence, so I would not repeat it,” he said.

特里在新澤西州卡姆登的工人階級家庭長大，他的父親被他形容為「充滿愛心、聰明且殘暴的暴力分子」。原來，驅動力是父親隱藏的憂鬱症，他巧妙地將這種憂鬱症遺傳給了特里。「我父親用一條帶子把憂鬱症強加給我，」他告訴我。試圖應對父親的憤怒和暴力促使他走上心理治療的道路。「我需要理解我的父親和他的暴力行為，所以我不會重複它，」他說。

Terry helped me continue to connect the dots between my own childhood and the kinds of dysfunction that had marked my adolescence and my life as an adult. Looking back at my teenage self, and the way I was in college, I realize now that I was morbidly depressed—clinically, off-my-rocker depressed. I just didn’t know it at the time. I had the classical symptoms of covert male depression, which were a tendency to isolate myself and, above all, a propensity to anger, perhaps my most potent addiction. One of the first things I wrote in my journal, after an early discussion with Terry, still resonates today: “90% of male rage is helplessness masquerading as frustration.”

特里幫助我繼續將自己的童年與標誌著我青春期和成年生活的各種功能障礙聯繫起來。回顧青少年時期的自己，以及我在大學時的情況，我現在意識到我患有病態憂鬱症——臨床上是一種瘋狂的憂鬱症。我當時只是不知道。我有隱性男性憂鬱症的典型症狀，這是一種孤立自己的傾向，最重要的是，有憤怒的傾向，這也許是我最嚴重的癮。在與特里進行早期討論後，我在日記中寫下的第一句話至今仍然引起共鳴：“90%的男性憤怒是偽裝成挫敗感的無助。”

Terry helped me make sense of the helplessness that I still felt. I came to understand that the crucial factor for me was the shame I felt about having been victimized. As is the case with many men, I had flipped that shame into a feeling of grandiosity. “Shame feels bad; grandiosity feels good,” he told me. “It is central to masculinity and traditional manhood, this flip from the one-down victim to the one-up avenger. What’s devilish about flipping from shame

into grandiosity like this is that it works. It makes you feel better in the short run, but it just creates havoc in your life in the long run.”

特里幫助我了解我仍然感到的無助感。我開始明白，對我來說最重要的因素是我對自己成為受害者感到羞恥。和許多男人的情況一樣，我把這種羞恥感變成了一種自大的感覺。「羞恥感很糟糕；宏偉的感覺很好，」他告訴我。「這是男子氣概和傳統男子氣概的核心，從一個倒下的受害者到一個向上的復仇者的轉變。像這樣從羞恥轉變為浮誇的可怕之處在於它有效。從短期來看，它會讓你感覺更好，但從長遠來看，它只會給你的生活帶來嚴重破壞。」

Even worse was the realization of what my behavior had been doing to my family, especially my kids. I was not so delusional as to think I was being a particularly good dad, at that point, but I took at least some modicum of pride in the fact that I could protect my kids from the trauma I had suffered. I was a great “provider” and “protector.” They would never have to suffer my specific childhood shame. But I knew they saw my overflowing anger, even though it was rarely directed toward them or Jill.

更糟的是意識到我的行為對我的家人，尤其是我的孩子造成的影響。那時，我並沒有妄想自己是一個特別好的父親，但我至少有一點自豪，因為我可以保護我的孩子免受我所遭受的創傷。我是一個偉大的「提供者」和「保護者」。他們永遠不會遭受我童年特有的羞恥。但我知道他們看到了我滿溢的憤怒，儘管這種憤怒很少是針對他們或吉爾的。

At the Bridge, I learned that children don't respond to a parent's anger in a logical way. If they see me screaming at a driver who just cut me off, they internalize that rage as though it were directed to them. Second, trauma is generational, although not necessarily linear. Children of alcoholics are not inevitably destined to become alcoholics themselves, but one way or another, trauma finds its way down the line.

在橋樑，我了解到孩子不會以合乎邏輯的方式回應父母的憤怒。如果他們看到我對著剛剛超車的司機大喊大叫，他們就會將這種憤怒內化，就好像這憤怒是針對他們的。其次，創傷是代代相傳的，儘管不

一定是線性的。酗酒者的孩子本身並不一定注定會成為酗酒者，但無論如何，創傷都會隨之而來。

As Terry had written: “Family pathology rolls from generation to generation like a fire in the woods taking down everything in its path until one person, in one generation, has the courage to turn and face the flames. That person brings peace to his ancestors and spares the children that follow.”

正如特里所寫：「家庭病態一代又一代地蔓延，就像樹林裡的一場大火，摧毀了它所經過的一切，直到一代人中的一個人有勇氣轉身面對火焰。這個人給他的祖先帶來了和平，並饒恕了後代。」

I wanted to be that person.

我想成為那個人。

—

Slowly, with the help of Terry as well as Esther and Lorie, I began to pick up some tools to help me deal with my past and to guide my day-to-day behavior onto a better path. One helpful model that Terry had taught me was to think about my relationships as akin to a delicate ecosystem, a kind of emotional ecology. Why would I want to poison the environment in which I had to live?

慢慢地，在特里、艾絲特和洛里的幫助下，我開始拿起一些工具來幫助我處理我的過去，並引導我的日常行為走上更好的道路。特里教給我的一個有用的模型是將我的人際關係視為一個微妙的生態系統，一種情緒生態。為什麼我要毒害我所居住的環境？

This sounds so basic, but it took some thought and consideration, and even strategizing, to put into practice. It meant pulling back from the little things that used to make me mad at the people around me, on a daily or even hourly basis; that, I now recognized, was poisoning the drinking well. I had to learn new ways of dealing with day-to-day problems and frustrations. This is an important stage in Terry's framework, the stage of teaching: *This is how you do it right. This is how you listen to your partner's complaint and be compassionate.*

這聽起來很基本，但需要一些思考和考慮，甚至制定策略才能付諸實行。這意味著每天甚至每小時都要從那些曾經讓我對周圍的人生氣的小事中抽身出來；我現在認識到，這正在毒害飲水井。我必須學習處理日常問題和挫折的新方法。這是特里框架中一個重要的階段，即教學階段：這就是你正確做事的方式。這就是你傾聽伴侶的抱怨並表現出同情心的方式。

“These are all skills,” Terry told me. “And like all the skills you have tried to master over your life, you can learn these, also.”

「這些都是技能，」特里告訴我。“就像你一生中試圖掌握的所有技能一樣，你也可以學習這些。”

Some of the changes I made seem like no-brainers. I made sure to spend time with my kids—one on one, no phones—every day that I was home. I would check in with Jill on her experience (not “events”) each day. I limited my phone time and my work hours to a strict window. One day a week, typically Saturday or Sunday, I would refrain from doing any work at all, something that went against decades of ingrained habit. Even more amazing, Jill and I went on an actual vacation for the first time in years, just the two of us, no kids.

我所做的一些改變似乎是理所當然的。我每天在家時都會確保與孩子們共度時光——一對一，不玩手機。我每天都會向吉爾詢問她的經歷（而不是「事件」）。我嚴格限制我的打電話時間和工作時間。每周有一天，通常是周六或週日，我會完全不做任何工作，這違背了幾十年來根深蒂固的習慣。更令人驚訝的是，吉爾和我多年來第一次真正去度假，只有我們兩個人，沒有孩子。

One skill I worked on that is a bit more complicated is called “reframing.” Reframing is basically the ability to look at a given situation from someone else’s point of view—literally reframing it. This is an incredibly difficult thing for most of us to do, as David Foster Wallace explained in his now famous 2005 commencement address to the graduating class at Kenyon College, “This Is Water”:

我研究的一項技能有點複雜，叫做「重構」。重構基本上是從別人的角度看待特定情況的能力——字面上的重構。對我們大多數人來說，這是一件極其困難的事情，正如大衛·福斯特·華萊士(David Foster Wallace) 在2005 年凱尼恩學院(Kenyon College) 畢業典禮上發表的著名畢業演說《這就是水》中所解釋的：

Everything in my own immediate experience supports my deep belief that I am the absolute center of the universe; the realest, most vivid and important person in existence. We rarely think about this sort of natural, basic self-centeredness because it's so socially repulsive. But it's pretty much the same for all of us. It is our default setting, hard-wired into our motherboards at birth.

我自己的直接經驗中的一切都支持我的堅定信念：我是宇宙的絕對中心；現存最真實、最生動、最重要的人。我們很少思考這種自然的、基本的自我中心，因為它在社會上是令人排斥的。但這對我們所有人來說幾乎都是一樣的。這是我們的預設設置，一出生就硬連線到我們的主機板上。

Think about it: there is no experience you have had that you are not the absolute center of. The world as you experience it is there in front of YOU or behind YOU, to the left or right of YOU, on YOUR TV or YOUR monitor. And so on. Other people's thoughts and feelings have to be communicated to you somehow, but your own are so immediate, urgent, real.

想想看：在你所經歷的一切經驗中，你都不是絕對的中心。您體驗到的世界就在您的前面或後面，在您的左側或右側，在您的電視或顯示器上。等等。別人的想法和感受必須以某種方式傳達給你，但你自己的想法和感受卻是如此直接、緊迫、真實。

I could relate. This had certainly been my own default setting, for as long as I could remember. It's tempting to try to pin it on my own history of

trauma, and my need to adapt to protect myself, but obviously it had stopped serving me so well. Easier described than accomplished, reframing entails taking a step back from a situation and then asking yourself, What does this situation look like through the other person's eyes? How do *they* see it? And why is your time, your convenience, or your agenda any more important than theirs?

我可以理解。從我記事起，這肯定是我自己的預設。我很想把它歸咎於我自己的創傷史，以及我需要適應以保護自己，但顯然它已經不再為我服務了。描述起來容易做起來難，重構需要從某種情況後退一步，然後問自己，從別人的角度來看，這種情況是什麼樣的？他們怎麼看？為什麼你的時間、你的便利或你的議程比他們的更重要？

This comes in handy almost every single day. For example, if my wife comes home and snips at me because I didn't help put away the groceries, my tendency might be to think, *Hey, I'm working really hard and I can't always pitch in.* And that sense of entitlement would sneak up inside me because, well, I am working very hard, and someone else can put away the groceries.

這幾乎每天都會派上用場。例如，如果我的妻子回家並因為我沒有幫忙收拾雜貨而批評我，我可能會想，嘿，我工作真的很努力，但我不能總是參與其中。權利的感覺會悄悄地潛入我的內心，因為，好吧，我工作非常努力，而其他人可以把雜貨收起來。

But then I ask myself, *Wait, what has Jill's day been like today?*

但後來我問自己，等等，吉爾今天過得怎麼樣？

She had to pick up our boys from school and take them to the grocery store, where they probably fought like wild animals and made everyone in the store think Jill is the worst mother on the planet because she can't control her spoiled little brats, while she stood in line at the deli counter just to get me the perfectly sliced deli meat that can't be found with the prepackaged deli meat, and then on the way home she hit every single red light while the boys threw Lego bricks at each other.

她必須接我們的男孩放學，帶他們去雜貨店，他們可能像野生動物一樣打架，讓店裡的每個人都認為吉爾是世界上最糟糕的母親，因為她

無法控制她被寵壞的小孩子，她在熟食櫃檯前排隊，只是為了給我買一塊切片完美的熟食肉，而預先包裝的熟食肉是找不到的，然後在回家的路上，她撞到了每一個紅燈，而男孩們則向每個人丟樂高積木。其他。

And you know what? When I view it through her lens, I quickly get over myself and realize that I'm the one who's being selfish and that next time I have to do better. That's the power of reframing. You realize that you have to step back from a situation, temper your reflexive reaction, and try to see what is actually happening.

你知道嗎？當我透過她的鏡頭來看這一切時，我很快就克服了自己，意識到我是那個自私的人，下次我必須做得更好。這就是重構的力量。你意識到你必須從某種情況中退一步，緩和你的反射反應，並試著看看到底發生了什麼事。

Somewhere along the line, in a random airport on a long work trip, I had picked up David Brooks's book *The Road to Character*. On the plane, I read the part where Brooks makes a key distinction between “résumé virtues,” meaning the accomplishments that we list on our CV, our degrees and fellowships and jobs, versus “eulogy virtues,” the things that our friends and family will say about us when we are gone. And it shook me.

在一次長途出差的途中，在一個隨機的機場，我拿起了大衛布魯克斯（David Brooks）的書《性格之路》。在飛機上，我讀到了布魯克斯對“簡歷美德”（即我們在簡歷、學位、獎學金和工作中列出的成就）與“悼詞美德”（我們的朋友和家人所列出的東西）之間做出關鍵區分的部分。當我們離開時會談論我們。這讓我震驚。

For my entire life, I had been accumulating mostly résumé virtues. I had plenty of those. But I had also recently attended a funeral for a woman about my age who had died of cancer, and I was struck by how lovingly and movingly her family had spoken about her—with hardly a mention of her impressive professional or educational success. What mattered to them was the person she had been and the things she had done for others, most of all her children.

在我的一生中，我主要是在履歷中累積美德。我有很多這樣的。但我最近也參加了一位與我年齡相仿、死於癌症的女性的葬禮，她的家人對她的談論是多麼親切和感人，這讓我印象深刻——幾乎沒有提到她令人印象深刻的職業或教育成就。對他們來說，重要的是她曾經為人以及她為他人（尤其是她的孩子）所做的事情。

Would anyone be speaking that way about me when it was my turn in the casket?

輪到我進棺材時，會有人這樣說我嗎？

I doubted it. And I decided that that had to change.

我對此表示懷疑。我決定必須改變這種情況。

—

I began using these tools and strategies on a daily basis, forming an emotional health routine of sorts. I focused on eulogy virtues, not résumé virtues. I worked on being more relational, more present with my family. I tried to practice reframing. But something still felt off. Even as I worked on my relationships with those closest to me, I still had a major blind spot: my relationship with myself. I had become a much better husband and father, but inside, I was just as hard on myself as ever. My deep self-hatred and loathing still contaminated most of my thoughts and emotions, and I didn't even realize it—nor did I understand why it was happening.

我開始每天使用這些工具和策略，形成情緒健康習慣。我關注的是悼詞美德，而不是履歷美德。我努力與家人建立更親密的關係，並且更陪伴家人。我嘗試練習重構。但還是覺得有些不對勁。即使當我努力處理與最親近的人的關係時，我仍然有一個主要的盲點：我與自己的關係。我已經成為一個更好的丈夫和父親，但在內心，我對自己一如既往的嚴格。我深深的自我憎恨和厭惡仍然污染著我的大部分思想和情感，我甚至沒有意識到，也不明白為什麼會發生這種情況。

I know I was not alone in this feeling. I was speaking with a patient of mine once, an incredibly successful and well-known person, and he said

something that stunned me. “I need to be great,” he said, “in order to feel like I’m not worthless.”

我知道我並不孤單有這種感覺。我曾經和我的一位病人交談過，他是一位非常成功和知名的人，他說了一些讓我震驚的話。“我需要變得偉大，”他說，“這樣才能感覺自己不是一文不值。”

That stunned me. Even *he* feels this way?

這讓我大吃一驚。連他也有這樣的感覺嗎？

Yet my own insecurity and self-hatred still gnawed at me. While I was getting better at dealing with other people—that constituted some progress—I was as hard on myself as ever. Anger still ruled me, even when I was supposedly having fun. Simply missing a shot at archery or spinning out of a turn in my driving simulator would send me into a seething, self-loathing rage. I would constantly lose my temper with myself and throw tantrums, yelling out loud and even snapping an arrow across my thigh if I missed a shot. That hurt a lot, but I kept doing it.

然而我自己的不安全感和自我憎恨仍然折磨著我。雖然我在與他人打交道方面做得越來越好——這構成了一些進步——但我對自己一如既往的嚴格。憤怒仍然統治著我，即使我本來應該玩得很開心。在我的駕駛模擬器中，光是射箭失敗或是在轉彎時打滑就會讓我陷入一種沸騰、自我厭惡的憤怒之中。我常常對自己發脾氣，發脾氣，大聲喊叫，如果射不中，甚至會用箭穿過大腿。這很痛苦，但我還是堅持要這樣做。

It was as if I had my own personal Bobby Knight, the Indiana University basketball coach who was famed for his red-faced sideline meltdowns (and who ultimately lost his job because of them), living inside my head. Whenever I made a mistake or felt I performed poorly, even in tiny ways, my own personal Coach Knight jumped up from the bench to scream at me. Make a mistake cooking dinner? *How do you not know how to grill a fucking steak?* Flub the intro recording to a podcast? *You are a worthless sack of shit who has no business being alive, let alone having a podcast!*

就好像我自己的私人鮑比奈特（Bobby Knight）住在我的腦海裡，他是印第安納大學的籃球教練，因在場邊的紅臉崩潰而聞名（並最終因此丟掉了工作）。每當我犯了錯誤或感覺自己表現不佳時，即使是很小的地方，我自己的私人教練奈特也會從板凳上跳起來對我大喊大叫。做晚餐時犯了錯？怎麼不知道怎麼烤牛排？弄亂播客的介紹錄音？你就是一個毫無價值的廢物，沒有活著的意義，更不用說擁有播客了！

The crazy part is that I actually believed that voice served me well. This rage and self-doubt had fueled much of my personal drive and whatever success I had enjoyed, I told myself. It was simply the price I had to pay. But in reality, all it had produced was more résumé virtues. And I wasn't even all that proud of my résumé. It would never be good enough.

最瘋狂的是，我實際上相信聲音對我很有幫助。我告訴自己，這種憤怒和自我懷疑極大地激發了我的個人動力以及我所取得的成功。這只是我必須付出的代價。但實際上，它所產生的只是更多的履歷優點。我甚至對我的簡歷並不感到自豪。它永遠都不夠好。

For the first time in my life, I had a radical thought: *Who cares how well you perform if you're so utterly miserable?*

我一生中第一次有了一個激進的想法：如果你這麼痛苦，誰會在乎你表現得如何呢？

During this time, Paul Conti, who continued to keep tabs on my declining emotional health as a friend, sensed another rising storm. He began suggesting that I go into another residential treatment facility. The Bridge had helped me greatly, and without it I would have lost my family. But Paul felt I had left the Bridge too soon, staying for only two weeks, and thus had not yet scratched the surface when it came to examining and healing my relationship with myself. But I stubbornly refused. *I'll be fine.*

在此期間，保羅·孔蒂（Paul Conti）作為朋友繼續關注我日益惡化的情緒健康狀況，他感覺到另一場風暴即將來臨。他開始建議我去另一家住院治療機構。這座橋給了我很大的幫助，沒有它我就會失去我的家人。但保羅覺得我離開這座橋太早了，只待了兩週，因此在審視和治

癒我與自己的關係時還沒有觸及表面。但我固執地拒絕了。我會沒事兒的。

Something had to give, and soon enough, it did.

必須放棄一些東西，很快，它就放棄了。

—

I imagine that if 2020 had been like any other year, I could have kicked the can down the road for a few more years and just gotten by somehow. But there is nothing like a crisis to bring every other simmering issue right to a full boil.

我想，如果 2020 年和其他年份一樣，我可能會再擱置幾年，然後以某種方式度過。但沒有什麼比危機更能讓其他所有醞釀已久的問題徹底沸騰的了。

When COVID hit, our practice was already maxed out. We bring on most of our new patients in the first two quarters of each year, so I had already committed my ancillary bandwidth to learning the ins and outs of the new patients. COVID instantly doubled or tripled our workload. There were daily calls with the research team to discuss everything we could find out about the disease, starting very early in the morning, as well as a new and daunting slate of COVID-related podcasts. I gave up my morning meditation practice in order to field the countless calls from patients, who were understandably panicked and looking for reassurance.

當新冠疫情來襲時，我們的練習已經達到極限。我們在每年的前兩個季度引進大部分新患者，因此我已經投入了我的輔助頻寬來了解新患者的來龍去脈。新冠疫情立即使我們的工作量增加了一倍或三倍。每天一大早就開始與研究團隊通電話，討論我們能找到的有關這種疾病的一切信息，以及一系列令人畏懼的新冠相關播客。我放棄了早上的冥想練習，以便接聽無數病人的電話，他們感到恐慌並尋求安慰，這是可以理解的。

As March bled into April it became clear there was no end in sight. One day in late April 2020, I was on a routine morning call with my practice manager when I couldn't take it anymore and started venting. I've lost control, I told her. I can't keep my patients' stories straight anymore. Was it patient X or patient Y who just last week told me about his daughter's struggle at school? Was it patient A or patient B whom I needed to reach out to that evening about an issue she was having? She tried to soothe me, saying I was doing the best I could under the circumstances and that our patients were grateful. But the more she talked, the angrier I got.

隨著三月進入四月，很明顯，事情還沒結束。2020年4月下旬的某天，當我與業務經理進行例行晨間通話時，我再也無法忍受並開始發洩。我告訴她，我失去了控制。我不能再讓病人的故事保持原樣了。上週剛剛向我講述他女兒在學校的掙扎的人是X患者還是Y患者？那天晚上我需要聯絡A患者還是B患者來解決她遇到的問題？她試圖安撫我，說我在這種情況下已盡力而為，我們的病人很感激。但她越說我就越生氣。

And just like that, I spun into a radical, self-destructive episode, one like I've never experienced before or since. Even remembering it now is terrifying. I threw a table across our living room. I tore my T-shirt to pieces. I screamed, in rage and pain. My wife begged me to leave the house for fear I would harm her or the kids. I thought about driving myself into a bridge abutment or other structure fast enough that I'd be killed. I was convinced that I was broken, defective; when they autopsied my brain, they would discover just how screwed up I was. I was beyond fixing. Nothing could make it right.

就這樣，我陷入了一場激進的、自我毀滅的事件，這是我以前或之後從未經歷過的。現在想起來都讓人毛骨悚然。我把一張桌子丟到客廳對面。我把T恤撕成了碎片。我尖叫起來，憤怒又痛苦。我的妻子懇求我離開家，因為擔心我會傷害她或孩子。我曾想過以足夠快的速度將自己撞到橋台或其他結構上，以至於我會被殺。我確信我是破碎的、有缺陷的；當他們對我的大腦進行屍檢時，他們會發現我有多糟糕。我已經無法修復了。沒有什麼可以讓它變得正確。

I ended up holed up in a motel, on the phone with Paul, Esther, and Terry.

They insisted that I needed to go back to a place like the Bridge. Now. True to form, I stubbornly disagreed, claiming that I could fix this with just a little more time and support, if only I could go home and get some rest. After pleading with them for forty-eight hours, I finally relented. In the middle of the night, I drove myself to Phoenix, Arizona, to be admitted to a place called Psychological Counseling Services, or PCS.

我最後躲在汽車旅館裡，與保羅、艾絲特和特里通電話。他們堅持我需要回到像大橋這樣的地方。現在。一如既往，我固執地不同意，聲稱只要多一點時間和支持，我就可以解決這個問題，只要我能回家休息一下就好了。經過四十八小時的懇求，我終於心軟了。半夜，我開車去了亞利桑那州的菲尼克斯，去一家名為心理諮商服務中心（PCS）的地方就診。

Terry had been telling me about PCS for nearly a year. He said it was a place that worked miracles, healing wounds that seemed beyond permanent. I asked how he could be so sure. He said I just needed to trust him.

特里向我講述 PCS 已近一年了。他說這是一個創造奇蹟的地方，治癒似乎無法永久的傷口。我問他怎麼能這麼肯定。他說我只需要相信他。

—

Just as with my visit to the Bridge two and a half years earlier, it took a few days to get settled in. Because it was the beginning of the pandemic, I was alone, dealing with therapists remotely on Zoom for twelve hours each day while I sat in a tiny Airbnb a few miles from the facility.

就像我兩年半前訪問大橋時一樣，花了幾天時間才適應。因為那是大流行的開始，我獨自一人，每天在 Zoom 上與治療師遠程交流 12 個小時，同時我坐在距離該設施幾英里的一個小 Airbnb 裡。

It was not until the second week that I began to make progress. Slowly, I came to accept that I had built a structure of perfectionism and workaholism on the pillars of performance-based esteem. This structure rested on a

foundation of my shame, some of which was brought on by trauma and some of which was inherited, as children take on the shame of those around them. But all of it was exacerbated by my own vicious cycle of self-loathing and guilt for my actions. It's not a coincidence that I have gravitated toward sports that demand perfection, like archery and driving race cars.

直到第二週我才開始有進步。慢慢地，我開始接受這樣的事實：我在基於績效的尊重的支柱上建立了一個完美主義和工作狂的結構。這種結構建立在我的羞恥感的基礎上，其中一些是由創傷造成的，有些是遺傳的，因為孩子們承受著周圍人們的羞恥感。但我自己的自我厭惡和對自己行為的愧疚的惡性循環加劇了這一切。我喜歡射箭和駕駛賽車等要求完美的運動，這並非巧合。

I ended up spending three weeks at PCS—twenty-one agonizing, uninterrupted days—finishing the work I had begun at the Bridge and going far beyond what I had imagined was possible. We covered an enormous amount of ground, but one task absolutely stymied me. On my second day, I was assigned to write out a list of forty-seven affirmations, representing one positive statement about myself for each year of my life. I made it to about five or six before I got completely stuck. For days and days, I couldn't come up with anything good to say about myself. My perfectionism and my shame did not permit me to believe anything nice about myself. I just couldn't do it.

我最終在 PCS 度過了三個星期——二十一天，痛苦而又不間斷——完成了我在大橋開始的工作，遠遠超出了我的想像。我們涵蓋了很多領域，但有一項任務絕對阻礙了我。第二天，我被指派寫出一份包含四十七個肯定的清單，代表我生命中每一年對自己的正面陳述。在我完全陷入困境之前，我已經做到了大約五到六點。幾天來，我想不出任何關於自己的好話。我的完美主義和羞恥感不允許我相信自己有任何優點。我就是做不到。

Finally, on the nineteenth day—a blistering hot Wednesday morning—it happened. One of my therapists, Marcus, was pushing deeper and deeper into a story I had told him earlier about how I had stopped wanting to celebrate my birthdays when I was about seven; in fact, I revealed, I would keep my birthday a “secret” until well into my twenties. His questions made it clear that

this was not something a healthy child would do, and it likely masked something more deeply wrong. He just kept digging and would not let it go.

最後，在第十九天——一個酷熱的星期三早晨——事情發生了。我的一位治療師馬庫斯正在深入探討我之前告訴他的一個故事，關於我如何在七歲左右不再想要慶祝自己的生日；事實上，我透露，我會保守我的生日“秘密”，直到二十多歲。他的問題清楚地表明，這不是一個健康的孩子會做的事情，而且很可能掩蓋了一些更嚴重的錯誤。他只是繼續挖，不肯放手。

That recognition pushed me into an emotional freefall. It had been two and a half years in the making, but I finally was able to let go and accept the truth about my past and how it had shaped me, without any excuses or rationalizations. All that I had become—good and bad—was in response to what I had experienced. It wasn't simply the big-T traumas, either; we uncovered many, many more little-t traumas, hidden in the cracks, that had affected me even more profoundly. I hadn't been protected. I hadn't felt safe. My trust had been broken by people who were close to me. I felt abandoned. All of that had manifested itself as my own self-loathing as an adult; I had become my own worst enemy. And I hadn't deserved any of it. This was the key insight. That little, sweet boy did not deserve any of it. And he was still with me.

這種認識讓我的情緒陷入了自由落體狀態。它已經醞釀了兩年半，但我終於能夠放手並接受關於我的過去以及它如何塑造我的真相，沒有任何藉口或合理化。我所發生的一切——無論好壞——都是對我所經歷的事情的回應。這也不僅僅是大T創傷那麼簡單。我們發現了許多許多隱藏在裂縫中的小創傷，這些創傷對我的影響更為深遠。我沒有受到保護。我覺得不安全。我的信任被與我親近的人打破了。我感到被拋棄了。這一切都表現為我作為一個成年人的自我厭惡；我已經成為自己最大的敵人。而我根本不配得到這些。這是關鍵的見解。那個可愛的小男孩不值得這樣。而他仍然和我在一起。

Once I had accepted all this, it was easy to write out the forty-seven affirmations.

一旦我接受了這一切，寫出四十七個肯定句就很容易了。

I am flawed, but not defective.

我有缺陷，但不是缺陷。

I am a good husband and father.

我是一個好丈夫、好父親。

I am a good cook.

我是個好廚師。

I am not my shame.

我不是我的恥辱。

I will find a way to love myself.

我會找到一種方式來愛自己。

They just poured out of me. It reminded me of this observation by Jacob Riis, the great Danish American journalist and social reformer: “When nothing seems to help, I go back and look at a stonecutter hammering away at his rock perhaps a hundred times without as much as a crack showing in it. Yet at the hundred-and-first blow it will split in two, and I know it was not the last blow that did it, but all that had gone before.”

他們只是從我身上傾瀉而出。這讓我想起了偉大的丹麥裔美國記者和社會改革家雅各布·里斯（Jacob Riis）的評論：“當似乎沒有任何幫助時，我會回頭看一個石匠錘擊他的岩石也許一百次，卻沒有出現任何裂縫。在裡面。然而，在第一百零一擊時，它就會分裂成兩半，我知道這不是最後一擊造成的，而是之前發生的一切造成的。”

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Looking back on all this, one of the most important lessons that I learned is that the type of change I describe in this chapter is not possible unless we are

equipped with a set of effective tools and sensors with which to monitor, maintain, and restore our emotional equilibrium. These tools and sensors are not innate; for most of us, they must be learned, and refined, and practiced daily. And neither are they quick fixes.

回顧這一切，我學到的最重要的教訓之一是，除非我們配備了一套有效的工具和感測器來監控、維護和恢復，否則我在本章中描述的變革類型是不可能的我們的情緒平衡。這些工具和感測器並不是與生俱來的，而是與生俱來的。對我們大多數人來說，它們必須每天學習、完善和練習。它們也不是快速解決辦法。

Yes, medications such as antidepressants and mood stabilizers matter and can help. Yes, a mindfulness meditation practice can make all this easier. Yes, molecules such as MDMA and psilocybin, when used with skilled guidance and in the correct setting, can be powerful; I have used both at critical points in my recovery, with remarkable results. But too often I see people tethering their hopes of transformation *solely* to a ketamine trip or a journey to the jungles of Peru with a shaman to guide them through the mind-blowing experience of an ayahuasca journey, or some other singular experience (or even, as in my case, thinking that two weeks in a facility such as the Bridge is enough, after which we can continue as though nothing fundamental has changed).

是的，抗憂鬱藥物和情緒穩定劑等藥物很重要並且可以提供幫助。是的，正念冥想練習可以讓這一切變得更容易。是的，MDMA 和裸蓋菇素等分子，如果在熟練的指導下並在正確的環境下使用，可以發揮強大的作用；我在康復的關鍵時刻使用了這兩種藥物，並取得了顯著的效果。但我經常看到人們把他們的轉變的希望僅僅寄託在氯胺酮之旅或秘魯叢林之旅上，由薩滿引導他們完成令人興奮的死藤水之旅，或其他一些奇異的經歷（甚至，就像我的情況一樣，我認為在橋樑這樣的設施中待兩週就足夠了，之後我們可以繼續下去，就好像沒有什麼根本性的改變一樣）。

All of these modalities are powerful and potentially useful, but we need to think of them as merely adjuncts to the deep and often very unpleasant, uncomfortable, at times very slow—at other times too fast—self-exploration

that is required in real psychotherapy. True recovery requires probing the depths of what shaped you, how you adapted to it, and how those adaptations are now serving you (or not, as in my case). This also takes time, as I found out the hard way; the biggest mistake of all is to believe that you're "cured," by a few months on a drug or a handful of therapy sessions, when in fact you're not even halfway there.

所有這些方式都很強大並且可能有用，但我們需要將它們視為真正心理治療所需的深層自我探索的輔助手段，而且常常非常不愉快、不舒服，有時非常慢，有時又太快。真正的康復需要深入探究是什麼塑造了你，你如何適應它，以及這些適應現在如何為你服務（或沒有，就像我的例子）。這也需要時間，我經過慘痛的教訓才發現：最大的錯誤是相信你已經「治癒」了，只需幾個月的藥物或幾次治療，而事實上你甚至還沒有治愈一半。

My progress upon returning from PCS was rooted in daily action, much of it uncomfortable. My most pressing challenge was quite simply to avoid having another one of my meltdowns, like the one that had led to me going to PCS in the first place. I had had other, lesser episodes leading up to it, but this one had felt like the explosion of the space shuttle *Challenger*, which blew up over the Atlantic Ocean just after launch in 1986.

從 PCS 回來後，我的進步植根於日常行動，其中大部分都是不舒服的。我最迫切的挑戰很簡單，就是避免再次陷入崩潰，就像當初導致我選擇 PCS 的那次崩潰一樣。在此之前我還經歷過其他較小的事件，但這次感覺就像挑戰者號太空梭的爆炸，它在 1986 年發射後不久在大西洋上空爆炸。

At the time, that disaster seemed completely unexpected, but a lengthy investigation revealed that was not the case at all. There had been warning signs and system failures building up inside the space shuttle program for years prior. These problems had been documented by the engineers, but they were ignored or covered up by management, because doing so seemed "easier" than delaying the launch. The result was a catastrophe that could have been prevented. My goal was to learn to understand the warning signs and the systems failures that could lead to a blow-up in my own life, to prevent it from

ever happening again. The idea is somewhat similar to what we've been talking about with Medicine 3.0, only applied to emotional health: spotting potential problems early and taking preventive action as soon as possible.

當時，這場災難似乎完全出乎意料，但經過長時間的調查後發現事實並非如此。幾年前，太空梭計畫中就已經出現過警訊和系統故障。這些問題已被工程師記錄下來，但被管理層忽視或掩蓋，因為這樣做似乎比推遲發布「更容易」。結果就是一場本來可以避免的災難。我的目標是學會理解可能導致我自己的生活崩潰的警告信號和系統故障，以防止它再次發生。這個想法有點類似我們一直在談論的醫學3.0，只適用於情緒健康：及早發現潛在問題並儘快採取預防措施。

The way in which I do this, the tools that I use, derive from a school of psychology known as dialectical behavior therapy, or DBT, developed in the 1990s by Marsha Linehan. Based on the principles of cognitive behavioral therapy, which seeks to teach patients new ways of thinking about or acting on their problems, DBT was developed to help individuals with more serious and potentially dangerous issues, such as an inability to regulate their emotions and a propensity to harm themselves or even attempt suicide. These people are lumped into something called borderline personality disorder, which is a bit of a catch-all diagnosis, but DBT has also been found to be helpful in patients with less dramatic and dangerous emotional health issues, a category that encompasses many more of us. I liken it, naturally, to Formula One: the race circuit is a high-stakes, high-risk laboratory where car manufacturers develop and test technologies that trickle down to our everyday street cars.

我這樣做的方式和使用的工具源自心理學派，稱為辯證行為療法

（DBT），由 Marsha Linehan 在 1990 年代開發。DBT 旨在幫助患者解決更嚴重和潛在危險的問題，例如無法調節自己的情緒和傾向。傷害自己，甚至企圖自殺。這些人被歸類為邊緣性人格障礙，這是一種包羅萬象的診斷，但 DBT 也被發現對那些不太嚴重和危險的情緒健康問題的患者有幫助，這一類別涵蓋了我們更多的人。我很自然地把它比作一級方程式：賽道是一個高風險、高風險的實驗室，汽車製造商在這裡開發和測試技術，這些技術滲透到我們日常的街道汽車中。

One thing I like about DBT is that it is backed up by evidence: clinical

trials have found it to be effective in helping suicidal and self-harming patients stop their dangerous behavior. Another thing that draws me to DBT is that it is skills-based, not just theoretical. Practicing DBT means literally working through a workbook with a DBT therapist, doing exercises every day. I'm better at doing than thinking sometimes. The practice of DBT is predicated on learning to execute concrete skills, repetitively, under stress, that aim to break the chain reaction of **negative stimulus → negative emotion → negative thought → negative action**.

我喜歡 DBT 的一件事是它有證據支持：臨床試驗發現它可以有效幫助自殺和自殘患者停止危險行為。DBT 吸引我的另一個原因是它是基於技能，而不僅僅是理論。練習 DBT 意味著與 DBT 治療師一起完成工作簿，每天練習。有時我更擅長做而不是想。DBT 的實踐是基於學習在壓力下重複執行具體技能，旨在打破負面刺激 → 負面情緒 → 負面想法 → 負面行動的連鎖反應。

DBT consists of four pillars joined by one overarching theme. The overarching theme is mindfulness, which gives you the ability to work through the other four: *emotional regulation* (getting control over our emotions), *distress tolerance* (our ability to handle emotional stressors), *interpersonal effectiveness* (how well we make our needs and feelings known to others), and *self-management* (taking care of ourselves, beginning with basic tasks like getting up in time to go to work or school). The first two—emotion regulation and distress tolerance—are the ones I need to work on most, so that's where I've focused with my DBT therapist, Andy White.

DBT 由四個支柱組成，並由一個總體主題連接起來。首要主題是正念，它使您能夠解決其他四個問題：情緒調節（控制我們的情緒）、痛苦承受能力（我們處理情緒壓力源的能力）、人際交往效率（我們如何很好地滿足我們的需求和感受）為他人所知）和自我管理（照顧好自己，從基本任務開始，例如準時起床去上班或上學）。前兩者——情緒調節和痛苦承受能力——是我最需要努力的，所以這就是我和我的 DBT 治療師 Andy White 重點關注的領域。

I visualize my distress tolerance as a window that opens and closes vertically. The narrower this window becomes, the more likely I am to

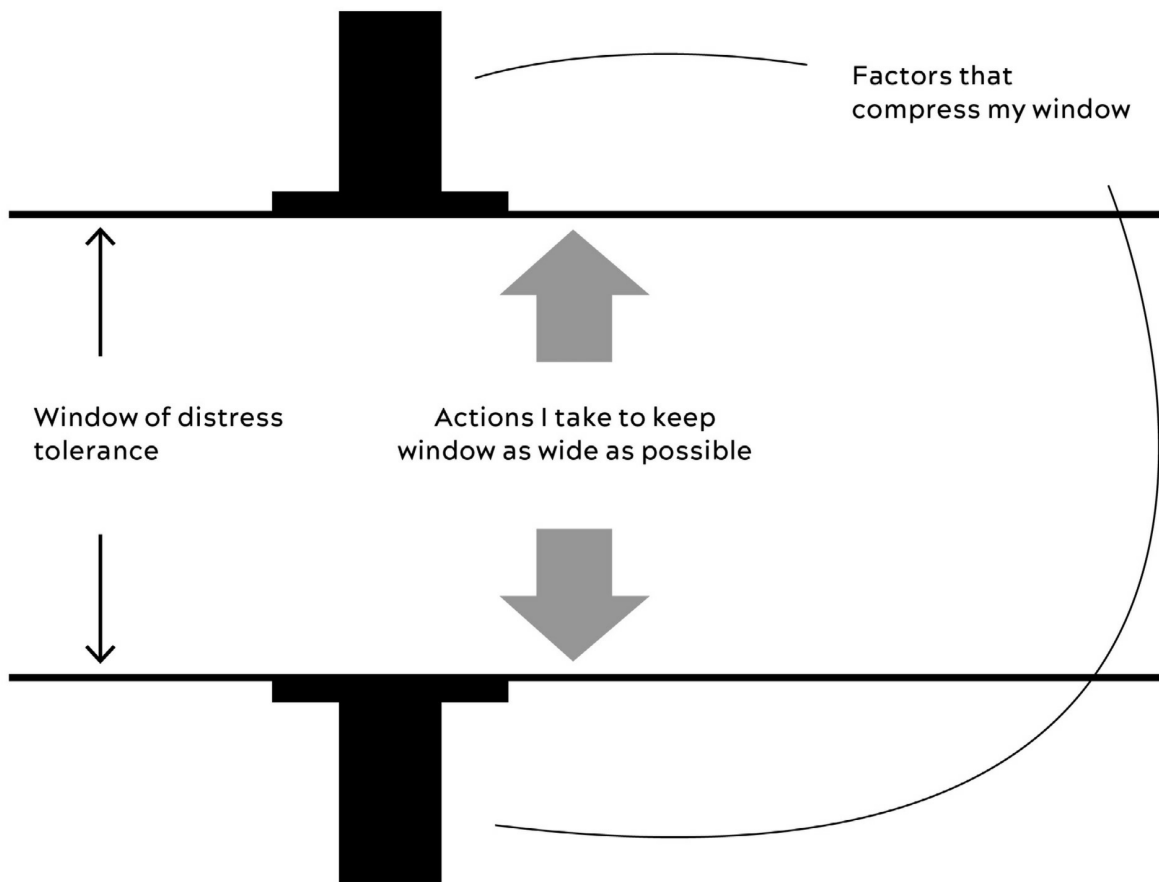
become dysregulated. My goals are to keep this window as wide as possible and to be very attentive to anything that might narrow it, even factors outside my control (see [figure 15](#)).

我將我的抗壓能力想像成一扇垂直打開和關閉的窗戶。這個視窗越窄，我就越有可能變得失調。我的目標是保持這個視窗盡可能寬，並非常注意任何可能縮小視窗的因素，甚至是我無法控制的因素（見圖 15）。

Many behaviors expand this window: exercise, sound sleep, good nutrition, time with my family, medications such as antidepressants or mood stabilizers, deep social connections, spending time in nature, and recreational activities that do not emphasize self-judgment. These are the things I have control over. I don't have as much control over the things that compress my window, but I still have some—for example, overcommitting to projects and saying yes to more than I should. Managing this window (in part by learning to say no) and trying to keep it as wide as possible is something I think about and work on almost every day.

許多行為都擴大了這個窗口：運動、良好的睡眠、良好的營養、與家人相處的時間、抗憂鬱藥物或情緒穩定劑等藥物、深厚的社會關係、花時間在大自然中，以及不強調自我判斷的娛樂活動。這些是我可以控制的事情。我對那些壓縮我的視窗的事情沒有太多的控制權，但我仍然有一些控制權——例如，過度致力於專案和對超出我應該做的事情說「是」。管理這個視窗（部分是透過學會說「不」）並嘗試使其盡可能寬，是我幾乎每天都在思考和工作的事情。

Figure 15. Managing Distress Tolerance



This is how I visualize my daily efforts to maintain and increase my distress tolerance, represented by the “window” or gap shown here. I try to focus on doing whatever I can to keep this window as wide open as possible.

這就是我如何想像我每天為維持和提高抗壓能力所做的努力，由此處顯示的“窗口”或差距表示。我盡力集中精力，盡我所能，讓這個窗口盡可能敞開。

They are linked: I needed to increase my distress tolerance in order to regain control over my emotions. And the better I regulate my emotions, the less I need to rely on that distress tolerance window. I found that as I worked on those two, my interpersonal effectiveness, which was obviously far from perfect, improved naturally. Self-management has never really been an issue

for me, but someone else might have different needs; DBT is highly adaptable.

它們是相互連結的：我需要提高我的痛苦承受能力，以便重新控制我的情緒。我越好調節自己的情緒，就越不需要依賴痛苦容忍窗口。我發現，當我在這兩點上努力時，我明顯遠非完美的人際交往能力自然而然地提高了。自我管理對我來說從來都不是一個真正的問題，但其他人可能有不同的需求；DBT具有很強的適應性。

DBT is rooted in mindfulness, which is one of those mushy buzzwords that I'd always despised until I began to understand it was a really effective tool to create distance between my thoughts and myself, to wedge even a sliver of space between some stimulus and my knee-jerk response. I needed that.

DBT 植根於正念，這是我一直鄙視的那些糊塗的流行詞之一，直到我開始明白它是一種真正有效的工具，可以在我的思想和我自己之間拉開距離，在一些刺激和刺激之間插入哪怕是一小片空間。我下意識的反應。我需要那個。

I had been practicing mindfulness meditation since I left the Bridge, with obviously mixed results, but I did begin to develop occasional flashes of insight, moments when I was able to detach myself from my thoughts and emotions. It's not complete detachment in the sense that we're checking out, but we want to create enough of a gap between stimulus and response so that we are not simply reacting reflexively to things that happen, like a driver who cuts us off in traffic or angry or distressing thoughts that we might have. That gap, in turn, allows us to process the situation in a calmer and more rational way. Do we really need to honk and curse, and potentially make the situation worse (even if the guy deserves it)? Or is it better to simply accept what happened and move on? Mindfulness helps us reframe it: The other driver may be rushing to the hospital with a sick child, for all we know.

自從我離開橋以來，我一直在練習正念冥想，結果顯然好壞參半，但我確實開始偶爾閃現出頓悟，那些時刻我能夠將自己從思想和情感中抽離出來。從我們正在檢查的意義上來說，這並不是完全的脫離，但我們希望在刺激和反應之間創造足夠的差距，這樣我們就不會簡單地

對發生的事情做出條件反射性的反應，例如司機在交通中搶道或我們可能有的憤怒或痛苦的想法。反過來，這種差距使我們能夠以更冷靜、更理性的方式處理這種情況。我們真的需要按喇叭和咒罵，並可能使情況變得更糟（即使那傢伙活該）？還是簡單地接受發生的事情並繼續前進更好？正念幫助我們重新建構它：據我們所知，另一位司機可能正帶著生病的孩子趕去醫院。

Another way in which mindfulness helps is by reminding us that when we are suffering, it is rarely because of some direct cause, like a rock that is crushing our leg at this very moment. Much more often, it is because we are thinking about some painful event that occurred in the past or worrying about something bad that may occur in the future. This, too, was an enormous revelation to me. Simply put, I experience less pain because I am able to recognize when the source of that pain is inside my own head. This was not an original insight, but it was nevertheless profound. I was about 2,500 years behind the Buddha, who said that “your worst enemy cannot harm you as much as your own unguarded thoughts.” Seneca improved on that in the first century AD, observing that “we suffer more often in imagination than in reality.” And later, in the sixteenth century, Shakespeare’s Hamlet noted, “There is nothing either good or bad, but thinking makes it so.”

正念的另一種幫助方式是提醒我們，當我們遭受痛苦時，很少是因為某些直接原因，例如此時此刻一塊岩石壓碎了我們的腿。更多時候，這是因為我們正在思考過去發生的一些痛苦事件或擔心未來可能發生的不好的事情。這對我來說也是一個巨大的啟示。簡而言之，我經歷的疼痛較少，因為我能夠辨識出疼痛的根源何時在我自己的腦海中。這不是一個原創的見解，但仍然是深刻的。我比佛陀落後大約 2,500 年，佛陀說：“你最大的敵人不可能像你自己不加防範的思想那樣傷害你。”塞內卡在公元一世紀對此進行了改進，他指出「我們在想像中比在現實中更容易受苦」。後來，在十六世紀，莎士比亞的《哈姆雷特》指出：“沒有什麼好壞之分，而是思想使然。”

One obvious way this applies is in how we think about ourselves. What does our inner dialogue sound like? Is it kind and forgiving and wise, or is it harsh and judgmental, like my inner Bobby Knight? One of the most powerful

exercises I learned was to simply listen to my self-talk. I would record voice memos to myself on my phone, after I did anything that could produce self-judgment, such as archery or driving my race-car simulator, or even just cooking dinner, and send each one to my therapist. My instinct in these situations was typically to scream at myself for failing somehow. My therapist at PCS told me to imagine instead that my best friend had performed exactly as I had done. How would I speak to him? Would I berate him the way I often berated myself? Of course not.

一個明顯的應用方式是我們如何看待自己。我們內心的對話聽起來是什麼樣的？是善良、寬容、明智，還是嚴厲、挑剔，就像我內心的鮑比奈特？我學到的最有效的練習之一就是簡單地傾聽我的自言自語。在我做了任何可以產生自我判斷的事情之後，例如射箭或駕駛我的賽車模擬器，甚至只是做飯，我都會在手機上給自己錄製語音備忘錄，然後將每一條都發送給我的治療師。在這些情況下，我的本能通常是因為某些原因而對自己尖叫。我在 PCS 的治療師告訴我，想像一下我最好的朋友的表現與我完全一樣。我該如何跟他說話呢？我會像我常常責備自己一樣責備他嗎？當然不是。

This was a slightly different take on reframing, forcing me to step outside myself and really see the disconnect between my “mistakes” (minor) and the way I talked to myself about those mistakes (brutal). I did this multiple times a day, every single day, for about four months; you can imagine how much space it took up on my phone. Over time, my inner Bobby Knight became fainter and fainter, and today it’s almost hard for me to remember what that voice used to sound like.

這是一種略有不同的重構方式，迫使我走出自我，真正看到我的「錯誤」（輕微）和我對自己談論這些錯誤的方式（殘酷）之間的脫節。我每天都會這樣做多次，持續了大約四個月；你可以想像它在我的手機上佔了多少空間。隨著時間的推移，我內心的鮑比奈特變得越來越微弱，今天我幾乎很難記住那個聲音以前聽起來是什麼樣的。

Another important goal of DBT is to help people learn to regulate their emotions. When I arrived at the Bridge, I had very little ability to recognize how I was feeling, let alone change or manage my emotional state. All I knew

was overflowing anger. This came to a head with me at the beginning of COVID, where I became so overloaded and so overwhelmed that I just exploded. I lost the ability to regulate my emotions, up and down. My close friend Jim Kochalka, a clinical psychologist, calls this type of emotional dysregulation “the inflammation of the psyche,” which feels about right to me.

DBT 的另一個重要目標是幫助人們學習調節自己的情緒。當我到達大橋時，我幾乎沒有能力識別自己的感受，更不用說改變或管理我的情緒狀態了。我只知道滿溢的憤怒。在新冠疫情剛開始的時候，我就遇到了這種情況，我的負荷如此之大，不知所措，以至於我簡直要爆炸了。我失去了調節情緒的能力。我的密友吉姆·科查爾卡（Jim Kochalka）是一位臨床心理學家，他將這種情緒失調稱為“心靈的發炎”，這對我來說是正確的。

This anger had long been an obstacle in my personal relationships, even with my family. As Terry Real had pointed out long ago, this anger was rooted in shame, but very often my anger would also *create* more shame. If I yell at my kids, for example, especially when I do it because I’m upset about something else, I feel shame. That shame then becomes an obstacle to my ability to reconcile with them, so I feel more shame. It’s like I’m digging myself into a hole, and it’s not only with my kids. Until I can reconcile and own my behavior, I can’t move on. This used to be a much bigger problem, but at least now I can usually spot it in real time, before the hole gets too deep.

這種憤怒長期以來一直是我個人關係的障礙，甚至是我與家人的關係。正如特里·雷亞爾很早之前指出的，這種憤怒源自於羞恥，但很多時候我的憤怒也會帶來更多的羞恥。例如，如果我對我的孩子大喊大叫，尤其是當我因為其他事情而生氣時，我會感到羞恥。這種羞恥感會成為我與他們和解的障礙，所以我感到更羞恥。這就像我給自己挖了一個洞，而且不只是我的孩子。在我能夠調和並承認自己的行為之前，我無法繼續前進。這曾經是一個更大的問題，但至少現在我通常可以在洞變得太深之前即時發現它。

DBT teaches a variety of techniques to enable people to maintain and improve their distress tolerance, and to recognize and cope with their emotions—and not be controlled *by* them, as I had been for so long. One

simple tactic that I use to cope with mounting emotional distress is inducing an abrupt sensory change—typically, by throwing ice water on my face or, if I'm really struggling, taking a cold shower or stepping into an ice bath. This simple intervention stimulates an important cranial nerve, the vagus nerve, which causes our heart rate and respiratory rate to slow and switches us into a calm, parasympathetic mode (and out of our fight-or-flight sympathetic mode). Interventions like these are often enough to help refocus and think about a situation more calmly and constructively. Another technique I have grown very fond of is slow, deep breathing: four seconds to inhale, six seconds to exhale. Repeat. As the breath goes, the nervous system follows.

DBT 教授各種技巧，使人們能夠保持和提高他們的痛苦耐受力，並認識和應對他們的情緒，而不是像我長期以來那樣被情緒控制。我用來應對日益嚴重的情緒困擾的一個簡單策略是引發突然的感官變化——通常是將冰水潑在臉上，或者，如果我真的很掙扎，就洗個冷水澡或進入冰浴。這種簡單的干預會刺激重要的腦神經，即迷走神經，導致我們的心率和呼吸頻率減慢，並將我們轉變為平靜的副交感神經模式（並擺脫戰鬥或逃跑的交感神經模式）。像這樣的干預措施通常足以幫助重新集中注意力並更冷靜和建設性地思考情況。我非常喜歡的另一個技巧是緩慢、深呼吸：吸氣四秒，吐氣六秒。重複。隨著呼吸的進行，神經系統也跟著進行。

It is also important to note that DBT is not a passive modality. It requires conscious thought and action on a daily basis. One tactic that I've found especially helpful is called *opposite action*—that is, if I feel like doing one thing (generally, not a helpful or positive thing), I'll force myself instead to do the exact opposite. By doing so, I also change the underlying emotions.

同樣重要的是要注意 DBT 不是一種被動方式。它需要每天有意識的思考和行動。我發現一種特別有用的策略稱為相反行動，也就是說，如果我想做一件事（通常不是一件有幫助或積極的事情），我會強迫自己做完全相反的事情。透過這樣做，我也改變了潛在的情緒。

The first time I experienced this was a pleasant Sunday afternoon shortly after we moved to Austin. I had made a commitment to my wife that I would take one day off each week, presumably Sunday, to be with the family.

Sunday rolled around and I was drowning in work. I was stressed out and grumpy, and I didn't want to see or hear anyone. I just wanted to grind through my work. All too conditioned to my selfish ways, Jill barely pushed back when I said I was too busy to take the kids to a nearby creek. But as I watched her piling the kids into the minivan, I spotted a perfect chance to put theory into practice. I ran out to the van, hopped in the front seat, and said, "Let's go." We got to Barton Creek and really didn't do anything special beyond walking around, skipping rocks across the water, and seeing who could hop from boulder to boulder without getting wet. Much to my surprise, my mood completely changed. I even insisted we stop for burgers and fries (!) on the way home.

我第一次經歷這種情況是在我們搬到奧斯汀後不久的一個愉快的周日下午。我向妻子承諾，我每週休息一天，大概是星期日，與家人在一起。週日過去了，我正沉浸在工作中。我壓力很大，脾氣暴躁，不想看到或聽到任何人。我只是想努力完成我的工作。當我說我太忙而無法帶孩子們去附近的小溪時，吉爾太習慣了我自私的方式，幾乎沒有反駁。但當我看著她把孩子們塞進小型貨車時，我發現了一個將理論付諸實踐的絕佳機會。我跑到貨車旁，跳進前座，說：“我們走吧。”我們到了巴頓溪，除了四處走走、在水面上跳過石頭、看看誰能在不被淋濕的情況下從一塊巨石跳到另一塊巨石之外，實際上沒有做任何特別的事情。令我驚訝的是，我的心情完全改變了。我甚至堅持要在回家的路上停下來吃漢堡和薯條（！）。

This is an easy example, obviously. Who wouldn't want to play with their kids instead of working? But for Old Peter, it would have been impossible. This small lesson, which I have implemented countless times since, taught me something very important: changing the behavior can change the mood. You do not need to wait for your mood to improve to make a behavior change. This is also why cognitive therapies alone sometimes come up short; simply thinking about problems might not help if our thinking itself is disordered.

顯然，這是一個簡單的例子。誰不想一邊工作一邊陪孩子玩耍呢？但對老彼得來說，這是不可能的。這個小教訓，我已經實施了無數次，它教會了我一些非常重要的東西：改變行為可以改變情緒。您不需要

等到心情好轉才做出行為改變。這也是為什麼單獨的認知療法有時會出現不足的原因。如果我們的思維本身是混亂的，那麼僅僅思考問題可能無濟於事。

Exercise is another important component of my overall emotional health program, particularly my practice of rucking, discussed in chapter 12. I find that spending time moving in nature, simply enjoying the feeling of the wind in my face and the smell of the budding spring leaves (and a heavily loaded pack on my back) helps me cultivate what Ryan Holiday calls “stillness,” the ability to remain calm and focused amid all the distractions that our world offers and that we create for ourselves. When my family comes along, it’s important bonding time. When I’m alone, rucking serves as a mindfulness practice, a kind of walking meditation. No phone, no music, no podcasts. Just the sounds of nature, and of my heavy breathing. This is another example of how action can lead us into a better mental state. And as Michael Easter pointed out to me, there is actual research suggesting that exposing oneself to the fractal geometric patterns in nature can reduce physiological stress, and that these effects show up on an EEG.

運動是我整體情緒健康計劃的另一個重要組成部分，尤其是在第12章中討論的鍛煉練習。我發現花時間在大自然中活動，只是享受微風拂面的感覺和初綻春葉的氣味（以及我背上的沉重的背包）幫助我培養瑞安·霍利迪所說的“平靜”，即在我們的世界提供的以及我們為自己創造的所有乾擾中保持冷靜和專注的能力。當我的家人出現時，這是一個重要的親密時間。當我獨自一人時，翻身是一種正念練習，一種步行冥想。沒有電話，沒有音樂，沒有播客。只有大自然的聲音和我粗重的呼吸聲。這是行動如何引導我們進入更好的精神狀態的另一個例子。正如邁克爾·伊斯特（Michael Easter）向我指出的那樣，有實際研究表明，將自己暴露在自然界的分形幾何圖案中可以減輕生理壓力，並且這些影響會顯示在腦電圖上。

The most important “tactic” by far is my regular weekly therapy session (down from three or four per week when I left PCS). This is not optional. Each session begins with a physical check-in: How am I feeling? How have I slept (a big one)? Am I in physical pain? Am I in conflict? Then we dissect

and discuss the events and issues of the week in minute detail. No topic is too insignificant. If, for example, I found myself getting really upset at a TV show or movie, this might be worth exploring. But we also tackle big-picture issues, the ones that propelled me into crisis in the first place. I complement my therapy sessions by writing in my journal, a place where I can practice articulating my emotions and understanding them, holding nothing back. I feel strongly that there is no substitute for this kind of work with a trained therapist.

到目前為止，最重要的「策略」是我每周定期接受治療（從我離開 PCS 時每週三到四次減少）。這不是可選的。每次治療都從身體檢查開始：我感覺怎麼樣？我睡得怎麼樣（一大覺）？我有身體疼痛嗎？我有衝突嗎？然後我們詳細剖析和討論本週的事件和問題。沒有一個話題是太微不足道的。例如，如果我發現自己對電視節目或電影感到非常沮喪，那麼這可能值得探索。但我們也解決大局問題，這些問題先將我推入危機。我透過在日記中寫作來補充我的治療課程，在日記中我可以練習表達自己的情緒並理解它們，毫無保留。我強烈感覺到，與訓練有素的治療師一起進行這種工作是無可取代的。

Most days, I try to stick to my “green-light” behaviors, even when I don’t automatically want to or feel too busy, or whatever. Every day I make mistakes, and every day I try to forgive myself for them. Some days are better than others, but over time I’ve made tangible progress. It’s important to note that my list of go-to activities and behaviors might not be the same as someone else’s, and even mine are not the same today as they were in the six months after I left PCS; there’s a line in the DBT literature about how it’s important to seek pleasurable activities “consistent with your own values.” Everyone has different problems and a different mental makeup, and everyone can find their own unique solutions. The techniques of DBT are adaptable and flexible, which is what makes them useful to a wide range of people.

大多數時候，我都會嘗試堅持我的「綠燈」行為，即使我不自覺地想要或感覺太忙，或其他什麼。我每天都會犯錯，每天我都試著原諒自己。有些日子比其他日子好，但隨著時間的推移，我取得了實際的進

步。值得注意的是，我的首選活動和行為清單可能與其他人的有所不同，甚至我現在的活動和行為清單也與我離開 PCS 後六個月時的有所不同；DBT 文獻中有一句話講述了尋求「與你自己的價值觀一致」的愉快活動的重要性。每個人都有不同的問題和不同的心理素質，每個人都能找到自己獨特的解決方案。DBT 技術具有適應性和靈活性，這使得它們對廣泛的人群有用。

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If you take nothing else from my story, take this: *If I can change, you can change.* All of this has to begin with the simple belief that real change is possible. That's the most important step. I believed I was the most horrible, incorrigible, miserable son of a bitch that was ever shat into civilization. For as long as I could remember, I believed that I was defective and that my flaws were hard-wired. Unchangeable. Only when I at least entertained the notion that maybe I was not actually a monster was I able to start chipping away at the narrative that had nearly destroyed my life and everyone in my wake.

如果你從我的故事中沒有學到什麼，那就看這篇：如果我能改變，你也能改變。這一切都必須始於一個簡單的信念：真正的改變是可能的。這是最重要的一步。我相信我是有史以來最可怕、最不可救藥、最悲慘的混蛋，被丟進文明社會了。從我記事起，我就相信自己是有缺陷的，而且我的缺陷是與生俱來的。不可改變的。只有當我至少接受了這樣一個想法：也許我實際上並不是一個怪物時，我才能夠開始削弱幾乎摧毀了我的生活和我身後的每個人的敘述。

This is the key step. You have to believe you can change—and that you deserve better.

這是關鍵的一步。你必須相信你可以改變——並且你值得更好。

Yet it can be a very difficult step for many people to take, for a number of reasons—the social stigma that persists around mental and emotional health, to name just one. It's difficult for many people, myself included at one point, to recognize that they have a problem, admit that they need help, and then

take action, particularly if it means talking about it openly with others, or taking time off work, or dealing with the expense of treatment.

然而，對許多人來說，這可能是一個非常困難的步驟，原因有很多——僅舉一例，圍繞著心理和情緒健康持續存在的社會恥辱。對許多人來說，包括我自己在內，很難認識到自己有問題，承認自己需要幫助，然後採取行動，特別是當這意味著與他人公開談論這個問題，或者請假，或者處理問題時。加上治療費用。

This is part of the shift in our mindset that needs to happen if we are to begin to address the epidemic of emotional health disorders, along with the attendant drug use, alcohol abuse, eating disorders, suicide, and violence that goes along with it. We have to make it okay to be vulnerable, to ask for and receive help.

如果我們要開始解決情緒健康障礙的流行，以及隨之而來的吸毒、酗酒、飲食失調、自殺和暴力等問題，那麼這是我們思維方式轉變的一部分，我們需要進行這種轉變。我們必須讓自己變得脆弱、尋求和接受幫助。

I resisted seeking help for the longest time. It was only when I was confronted with unbearable choices—losing my family, or even losing my life at my own hands—that I reluctantly agreed to do what I should have done much sooner, and to pay as much attention to my emotional health as I had always paid to my physical health.

我在很長一段時間裡拒絕尋求幫助。直到我面臨難以承受的選擇——失去家人，甚至失去自己的生命——我才勉強同意做我應該早點做的事情，並像我一樣關注自己的情緒健康。我一直都在為自己的身體健康付出代價。

As I settled into the next phase of my recovery, I began to notice something I had never experienced before: I found more joy in *being* than in *doing*. For the first time in my life, I felt that I could *be* a good father. I could *be* a good husband. I could *be* a good person. After all, this is the whole point of living. And the whole point of *outliving*.

當我進入復原的下一階段時，我開始注意到一些我從未經歷過的事情：我發現存在比做事更快樂。我有生以來第一次覺得我可以成為一個好父親。我可以成為一個好丈夫。我可以成為一個好人。畢竟，這就是生活的全部意義。以及生存的全部意義。

There's a quote from Paulo Coelho that I think about often: "Maybe the journey isn't so much about becoming anything," he writes. "Maybe it's about unbecoming everything that isn't really you, so you can be who you were meant to be in the first place."

我經常想起保羅·科埃略的一句話：「也許這段旅程並不是要成為什麼，」他寫道。 “也許是為了讓一切不屬於你的東西變得不相稱，這樣你就可以成為你本來就應該成為的人。”

EPILOGUE

結語

It was only after much reflection on this whole experience that I really began to understand how emotional health relates to longevity, and how my journey helped redefine my perspective.

只有在對整個經歷進行了深入思考之後，我才真正開始理解情緒健康與長壽之間的關係，以及我的旅程如何幫助重新定義了我的觀點。

I had long subscribed to a kind of Silicon Valley approach to longevity and health, believing that it is possible to hack our biology, and hack it, and hack it, until we become these perfect little humanoids who can live to be 120 years old. I used to be all about that, constantly tinkering and experimenting with new fasting protocols or sleep gadgets to maximize my own longevity. Everything in my life needed to be optimized. And longevity was basically an engineering problem. Or so I thought.

我長期以來一直認同矽谷的長壽和健康方法，相信有可能破解我們的生物學，破解它，破解它，直到我們成為這些可以活到 120 歲的完美小類人生物。我曾經熱衷於此，不斷修改和試驗新的禁食方案或睡眠設備，以最大限度地延長自己的壽命。我生活中的一切都需要優化。長壽基本上是工程問題。或者說我是這麼想的。

It took five years, two stints in inpatient treatment centers, and the near loss of my marriage and my kids to change my mind. What I eventually realized, after this long and very painful journey, is that longevity is meaningless if your life sucks. Or if your relationships suck. None of it matters if your wife hates you. None of it matters if you are a shitty father, or

if you are consumed by anger or addiction. Your résumé doesn't really matter, either, when it comes time for your eulogy.

我花了五年時間，在住院治療中心住過兩次，並且差點失去了婚姻和孩子，改變了我的想法。經過這段漫長而痛苦的旅程後，我最終意識到，如果你的生活很糟糕，那麼長壽就沒有意義。或者如果你的人際關係很糟糕。如果你的妻子討厭你，那一切都沒關係。如果你是個糟糕的父親，或者如果你被憤怒或毒癮所吞噬，這些都無關緊要。當需要致悼詞時，你的履歷也並不重要。

All these need to be addressed if your life is to be worth prolonging—because the most important ingredient in the whole longevity equation is the *why*. Why do we want to live longer? For what? For whom?

如果你想讓你的生命值得延長，所有這些都需要解決——因為整個長壽方程式中最重要的因素就是「為什麼」。我們為什麼想活得更久？為了什麼？為了誰？

My obsession with longevity was really about my fear of dying. And something about having children was making my obsession with longevity ever more frenetic. I was running away from dying as fast as I could. Yet at the same time, ironically, I was also avoiding actually living. My tactics might have succeeded in my living longer, with optimal glucose regulation and ideal lipoprotein levels, but my strategy was unquestionably accumulating more regrets. My physical and cognitive health were great, but my emotional health was tanking.

我對長壽的執著其實是因為我對死亡的恐懼。有了孩子，我對長壽的執著變得更加瘋狂。我正在以最快的速度逃離死亡。但諷刺的是，同時，我也在逃避實際的生活。我的策略可能成功地延長了我的壽命，實現了最佳的血糖調節和理想的脂蛋白水平，但我的策略無疑是積累了更多的遺憾。我的身體和認知健康狀況都很好，但我的情緒健康狀況卻每況愈下。

My biggest regret is that so much of the misery that I've experienced, and the pain that I have inflicted on other people, could have been avoided if I had reached a better understanding of this sooner in life, preferably much sooner.

The saddest part is that I wasted so much time being so detached, so miserable, and so misguided. So much time pursuing an empty goal.

我最大的遺憾是，如果我早點、最好早點更好地理解這一點，我所經歷的那麼多痛苦以及我給他人帶來的痛苦都是可以避免的。最可悲的是，我浪費了太多的時間，如此超然、如此痛苦、如此被誤導。這麼多時間追求一個空洞的目標。

But as my recovery progressed, I noticed that my preoccupation with dying began to fade away. And my quest for longevity no longer felt like a grim, desperate task; now the things I did every day felt welcome, necessary. I was enhancing my life and looking forward to the future. My journey to outlive finally had clarity, purpose, and meaning.

但隨著我康復的進展，我注意到我對死亡的關注開始消失。我對長壽的追求不再感覺是一項嚴峻、絕望的任務；現在我每天所做的事情都感到受歡迎、必要。我正在改善我的生活並展望未來。我的生存之旅終於有了清晰、目標和意義。

It brought me back to something my dear friend Ric Elias had said to me. Ric had been one of 155 passengers on the US Airways flight that emergency-landed in the Hudson River in January of 2009. As the plane was coming down, Ric and most of the other passengers were certain that they were going to die. Only the pilot's skill and more than a little luck prevented disaster. If the plane had been going a little bit faster, it would have broken apart on impact; a few miles per hour slower, and the nose would have tipped forward and it would have sunk into the river. A handful of tiny factors like that made the difference between everyone on that plane living and many or most (or all) of them dying.

這讓我想起了我親愛的朋友里克·埃利亞斯對我說過的話。里克是 2009 年 1 月緊急降落在哈得遜河的全美航空航班上的 155 名乘客之一。當飛機即將墜落時，里克和大多數其他乘客都確信他們會死。只有飛行員的技術和一點運氣才避免了災難。如果飛機速度再快一點，它就會在撞擊時解體；每小時慢幾英里，機頭就會向前傾斜並沉入河中。諸

如此類的一些微小因素，就決定了飛機上的每個人都活著，還是許多或大多數（或全部）人死去。

That day changed Ric's outlook on longevity in a way that really resonates with me. All that time, I had been obsessed about longevity for the wrong reason. I was not thinking about a long, healthy life ahead; instead, I was mourning the past. I was trapped by the pain that my past had caused and was continuing to cause. I wanted to live longer, I think, only because deep down I knew I needed more runway to try to make things right. But I was only looking backward, not forward.

那天改變了里克對長壽的看法，這引起了我的共鳴。一直以來，我都因為錯誤的原因而沉迷於長壽。我並沒有想過未來的長壽、健康的生活；我只想著未來的生活。相反，我在哀悼過去。我被我的過去所造成的痛苦所困，並且仍在繼續造成痛苦。我想，我想活得更久，只是因為我內心深處知道我需要更多的跑道來嘗試讓事情變得正確。但我只是向後看，沒有向前看。

“I think people get old when they stop thinking about the future,” Ric told me. “If you want to find someone's *true* age, listen to them. If they talk about the past and they talk about all the things that happened that they did, they've gotten old. If they think about their dreams, their aspirations, what they're still looking forward to—they're young.”

「我認為當人們不再思考未來時，他們就會變老，」里克告訴我。

「如果你想知道某人的真實年齡，就聽聽他們的說法。如果他們談論過去，談論他們所做的所有事情，他們就已經老了。如果他們思考他們的夢想、他們的抱負、他們仍然期待什麼——他們還年輕。」

Here's to staying young, even as we grow older.

這是為了保持年輕，即使我們變老了。

For my patients.

為了我的病人。

And for Jill, Olivia, Reese, and Ayrton...for your patience.

感謝吉爾、奧莉維亞、里斯和艾爾頓.....感謝你們的耐心。

ACKNOWLEDGMENTS

致謝

This book came perilously close to never seeing the light of day. In early 2020, after my book agent and publisher fired me for failing to deliver a manuscript that was already a year late, I was in no mood to put any additional effort into it and decided to scrap the whole project. The draft sat untouched for about nine months until my friend Michael Ovitz asked if he could read it. A couple of weeks later, Michael called to tell me that he thought it had great potential and that it needed to be published. He suggested that my coauthor Bill Gifford and I send a cleaned-up version to his friend, Diana Baroni, at Penguin Random House. Had Michael not forced the issue, making the introduction to Diana and consummating the agreement with Penguin Random House, *Outlive* might still be a random Google doc seen only by Bill and me and a handful of others. I'm grateful for Diana's ability to see what that somewhat ragged manuscript could become, and, more importantly, for her guidance in helping us get it there.

這本書差一點就面世了。2020年初，我的圖書代理商和出版商因未能交付已經遲到一年的手稿而解雇了我，我沒有心情為此付出任何額外的努力，並決定放棄整個專案。草稿大約九個月沒有動過，直到我的朋友邁克爾·奧維茨問他是否可以閱讀。幾週後，麥可打電話告訴我，他認為它有很大的潛力，需要出版。他建議我和合著者比爾·吉福德（Bill Gifford）向他在企鵝蘭登書屋的朋友戴安娜·巴羅尼（Diana Baroni）發送清理後的版本。如果邁克爾沒有強迫這個問題，向戴安娜做介紹並與企鵝蘭登書屋簽訂協議，*Outlive* 可能仍然是一個隨機的Google 文檔，只有比爾和我以及其他一些人才能看到。我很感激戴安

娜能夠看到這份有些粗糙的手稿會變成什麼樣子，更重要的是，感謝她的指導幫助我們實現了目標。

Long before that, this book would have died on the vine without Bill's help. In mid 2017, after I had written about 30,000 words on my own, my then publisher said my draft was too technical and lacked any sense of me as a person and my own journey to understanding the importance of longevity. They suggested I find a coauthor, and so began a long search that led to Bill. I had read a story Bill wrote in 2015 about rapamycin, as well as his book *Spring Chicken*, and had a hunch that he was the right person to help me navigate a very delicate task: to convey this complex subject matter accurately and with attention to nuance and detail, while making it readable and accessible to a broader audience. As Bill put it, he is my translator. In the process, Bill also became a close friend and someone who, at times, saw the worst in me, but I hope also the best.

早在這之前，如果沒有比爾的幫助，這本書就已經夭折了。2017年年中，當我自己寫了大約3萬字後，當時的出版商說我的草稿太技術性，缺乏對我作為一個人的認識，也缺乏我自己理解長壽重要性的旅程。他們建議我找一位合著者，於是我開始了漫長的搜索，最後找到了比爾。我讀過比爾在2015年寫的一篇關於雷帕黴素的故事，以及他的書《春雞》，並預感到他是幫助我完成一項非常微妙的任務的合適人選：準確地傳達這個複雜的主題，並注意細微差別和細節，同時使其可供更廣泛的受眾閱讀和理解。正如比爾所說，他是我的翻譯。在這個過程中，比爾也成為了我的親密朋友，他有時看到我最壞的一面，但我也希望看到最好的一面。

I cannot imagine having written this book without the help of Bob Kaplan. Bob was my head of research from 2015 through 2021, and he played an essential role in not only gathering and poring through all the studies that went into this book, but also pushing back on ideas and forcing me to be more rigorous in my thinking. If that wasn't enough, Bob came out of retirement in 2022 to take on the Herculean task of organizing the notes. Bob, along with Vin Miller, also did most of the fact-checking, while Rachel Harrus, Sam Lipman, and Kathryn Birkenbach helped with some of the research.

我無法想像如果沒有鮑伯卡普蘭的幫助，我會寫出這本書。鮑伯(Bob)從2015 年到2021 年擔任我的研究主管，他不僅在收集和深入研究本書中的所有研究方面發揮了重要作用，而且在反駁想法並迫使我更加嚴謹的思考方面發揮了重要作用。如果這還不夠，鮑伯在 2022 年復出，承擔整理筆記的艱鉅任務。鮑勃和文·米勒也完成了大部分事實查核工作，而雷切爾·哈勒斯、山姆·利普曼和凱瑟琳·伯肯巴赫則幫助完成了部分研究。

One thing that really surprised me about this process was how generous people were with their time and expertise. I sent many sections of the manuscript to experts for feedback. Without a single exception, every person that I asked said yes. My gratitude to the following people cannot be overstated: Kellyann Niotis and Richard Isaacson (neurodegenerative diseases), Matt Walker and Vik Jain (sleep), Lew Cantley and Keith Flaherty (cancer), Layne Norton, David Allison, and Kevin Bass (nutrition), Steve Austad (caloric restriction), Nir Barzilai (centenarians), Matt Kaeberlein and David Sabatini (rapamycin, mTOR), Tom Dayspring (atherosclerosis), and Beth Lewis, who was immensely helpful as I tried (and tried, and tried) to write about stability in a way that made sense.

對於這個過程，真正令我驚訝的一件事是人們對他們的時間和專業知識的慷慨。我將手稿的許多部分發送給專家以尋求回饋。我問過的每個人無一例外都說是。我對以下人員的感激之情怎麼強調都不為過：Kellyann Niotis 和Richard Isaacson（神經退化性疾病）、Matt Walker 和 Vik Jain（睡眠）、Lew Cantley 和Keith Flaherty（癌症）、Layne Norton、David Allison和Kevin Bass（營養）、Steve Austad（熱量限制）、Nir Barzilai（百歲老人）、Matt Kaeberlein 和David Sabatini（雷帕黴素、mTOR）、Tom Dayspring（動脈粥樣硬化）和Beth Lewis，當我在嘗試（並嘗試、嘗試）時，他們提供了極大的幫助。以有意義的方式寫下穩定性。

So much of what I've written about in this book is rooted in my interactions with my patients and with my podcast guests. My patients' experiences comprise the substrate for this book, the raw material, and they remind me constantly of the need to be continually learning. This is why my

podcast, *The Drive*, exists: It's a forcing function that requires me and my staff to learn at a breakneck pace. The knowledge I gain each week through interviewing experts has also informed much of what you have just read.

我在本書中所寫的大部分內容都源自於我與患者和播客嘉賓的互動。我的病人的經驗構成了這本書的基礎，原料，他們不斷提醒我需要不斷學習。這就是我的播客《The Drive》存在的原因：它是一種強制功能，要求我和我的員工以極快的速度學習。我每週透過採訪專家所獲得的知識也為您剛剛讀到的內容提供了大量資訊。

As indebted as I feel to the brilliant scientists and physicians who have mentored me throughout my career, I feel an equal if not greater debt to Paul Conti for forcing me to go to the Bridge, and to the therapists who saved my life: Esther Perel, Terry Real, Lorie Teagno, Katy Powell, Andy White, Jeff English, and entire team at PCS.

正如我對在我的職業生涯中指導過我的傑出科學家和醫生的感激之情一樣，我也對保羅·康蒂（Paul Conti）感到同樣的感激，甚至更多，因為他們迫使我去橋，以及拯救了我生命的治療師：埃絲特·佩雷爾（Esther Perel）、Terry Real、Lorie Teagno、Katy Powell、Andy White、Jeff English 以及 PCS 的整個團隊。

Several friends also read early sections of this book and provided great feedback: Rosie Kurmaniak, Deb and Hugh Jackman, David Buttarro, Jason Fried, and Judith Barker.

一些朋友也閱讀了本書的前幾部分，並提供了很好的回饋：Rosie Kurmaniak、Deb 和 Hugh Jackman、David Buttarro、Jason Fried 和 Judith Barker。

You might not know this about me (although maybe you do by now), but I'm kind of a particular guy, so getting the cover just "right" was no easy task. Thankfully, Rodrigo Corral and his team were able to come in and design a cover that Bill and I felt really represented the work inside. They remained incredibly patient with my micromanaging of every detail of this process without so much as a chirp.

你可能不了解我（儘管也許你現在已經了解了），但我是一個特別的人，所以讓封面「正確」並不是一件容易的事。值得慶幸的是，羅德里戈·科拉爾和他的團隊能夠進來設計一個封面，比爾和我覺得它真正代表了裡面的作品。他們對我對這個過程的每個細節的微觀管理都保持著令人難以置信的耐心，沒有發出任何吱吱聲。

One of the hardest things about writing this book was simply finding time to work on it. The clinical team at Early Medical worked overtime to enable me to spend large blocks of time uninterrupted. Lacey Stenson manages almost every facet of my personal and professional life and executed some very big lifts to make this book happen. Without Lacey, none of the trains run on time. Nick Stenson not only manages every aspect of our digital and podcast content, but he also oversaw the entire launch strategy and execution for this book, which turned out to be much more involved than he or I ever expected.

寫這本書最困難的事情之一就是找到時間來寫它。Early Medical 的臨床團隊加班加點，讓我能夠不間斷地度過大部分時間。萊西·斯滕森（Lacey Stenson）幾乎管理我個人和職業生活的方方面面，並執行了一些非常大的任務來使這本書得以出版。沒有萊西，所有火車都不會準時行駛。尼克·斯滕森不僅管理我們數位和播客內容的各個方面，而且還監督這本書的整個發布策略和執行，結果比他或我預期的要複雜得多。

Lastly, and most importantly, I want to thank Jill. She lived through the highs and lows and never—not one single moment—stopped supporting me, even when any reasonable person would have been justified in kicking me to the curb. You never let go of the rope. Olivia, Reese, and Ayrton saw too much of their daddy in front of a computer screen on nights and weekends and repeatedly asked that I work less. Now that this book is done, I can finally give them more of what they rightly deserve.

最後，也是最重要的，我要感謝吉爾。她經歷了高潮和低谷，但從未——沒有一刻——停止支持我，即使任何理智的人都會有理由把我踢到路邊。你永遠不會鬆開繩子。奧莉維亞、里斯和艾爾頓在晚上和週

末經常在電腦螢幕前看到他們的爸爸，並一再要求我少工作。現在這本書已經完成了，我終於可以給他們更多他們應得的東西。

Bill Gifford

比爾·吉福德

I would like to thank Martha McGraw for her kindness, coaching, and support throughout this long and sometimes arduous project. I wouldn't have made it without you. Thanks also to Bob Kaplan for the massive research downloads and helping me make sense of many complex topics. And to my friend Stephen Dark for all the walks.

我要感謝瑪莎·麥格勞在這個漫長且有時艱鉅的計畫中給予的善意、指導和支持。沒有你我就不可能成功。也要感謝鮑勃卡普蘭 (Bob Kaplan) 提供的大量研究下載並幫助我理解許多複雜的主題。感謝我的朋友史蒂芬·達克 (Stephen Dark) 的所有散步。

NOTES

筆記

Introduction

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The reality was: Yamamoto et al. (2015).

現實是：山本等人。（2015）。

[GO TO NOTE REFERENCE IN TEXT](#)

[前往註釋中的參考文獻](#)

Chapter 1. The Long Game

第 1 章 持久戰

In 1900, life expectancy: Kinsella (1992).

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Chapter 2. Medicine 3.0

第2章醫學3.0

“First, do no harm”: Sokol (2013).

「首先，不要傷害」：索科爾（2013）。

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as Steven Johnson points out: S. Johnson (2021).

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Chapter 5. Eat Less, Live Longer?

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Chapter 7. The Ticker

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第8章 失控的細胞

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Chapter 10. Thinking Tactically

第 10 章 戰術思考

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Chapter 16. The Awakening

第16章 覺醒

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第 17 章. 正在進行的工作

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INDEX

指數

The page numbers in this index refer to the printed version of the book. Each link will take you to the beginning of the corresponding print page. You may need to scroll forward from that location to find the corresponding reference on your e-reader.

本索引中的頁碼指的是本書的印刷版。每個連結都會將您帶到相應列印頁面的開頭。您可能需要從該位置向前滾動才能在電子閱讀器上找到相應的參考。

Note: Page numbers in *italics* indicate figures and tables.

註：斜體頁碼表示圖和表。

[A](#) [B](#) [C](#) [D](#) [E](#) [F](#) [G](#) [H](#) [I](#) [J](#) [K](#) [L](#) [M](#) [N](#) [O](#) [P](#) [Q](#) [R](#) [S](#) [T](#) [U](#) [V](#) [W](#) [X](#) [Y](#)
[Z](#)

A

accidental deaths, [226–227](#), [227](#), [381–382](#)

意外死亡, 226–227, 227, 381–382

ACHIEVE (Aging and Cognitive Health Evaluation in Elders), [203](#)

ACHIEVE（老年人的衰老和認知健康評估），203

adoptive cell therapy (adoptive cell transfer; ACT), [163–164](#)

過繼性細胞療法（過繼性細胞轉移；ACT），163–164

aducanumab, [183](#)

阿杜卡單抗，183

aerobic fitness. *See* [cardiorespiratory fitness](#)

有氧健身。查看心肺健康

aging process, [43–45](#), [71](#), [143–144](#), [143](#), [363–364](#)

老化過程, 43–45, 71, 143–144, 143, 363–364

alanine aminotransferase (ALT), [91–92](#), [91n](#)

丙胺酸轉氨酶 (ALT), 91–92, 91n

alcohol

酒精

Alzheimer's disease and, [201](#), [321](#)

阿茲海默症和, 201, 321

anesthesia considerations, [89](#)

麻醉注意事項，89

centenarians and, [59–60](#), [61](#)

百歲老人和, 59–60, 61

liver disease and, [89–90](#)

肝臟疾病, 89–90

recommendations, [320–321](#)

建議, 320–321

research on, [302](#)

研究, 302

sleep and, [321](#), [371–372](#), [374](#)

睡覺, 321, 371–372, 374

Ali, Muhammad, [41–44](#), [72](#), [216](#)

穆罕默德·阿里, 41–44, 72, 216

Allingham, Henry, [59](#)

亨利·阿林厄姆, 59 歲

Allison, David, [300–301](#)

大衛·艾莉森, 300–301

Allison, James, [160–161](#), [160n](#)

艾利森, 詹姆斯, 160–161, 160n

Alzheimer, Alois, [181](#), [182](#), [185](#)

阿茲海默症, 阿洛伊斯, 181, 182, 185

Alzheimer's disease

阿茲海默氏症

amyloid hypothesis, [182–185](#)

澱粉樣蛋白假說, 182–185

amyloid hypothesis alternatives, [194–197](#)

澱粉樣蛋白假說替代方案, 194–197

APOE gene variants (*e2*, *e3*, *e4*), [67–69](#), [178–179](#), [180](#), [189](#), [196](#), [197–199](#)

APOE 基因變異 (*e2*、*e3*、*e4*)、67–69、178–179、180、189、196、197–199

background, [83](#), [102](#), [180–186](#)

背景, 83, 102, 180–186

conclusion, [204–205](#)

結論, 204–205

early detection strategy, [178–179](#), [180](#)

早期檢測策略, 178–179, 180

Medicine 2.0 vs. Medicine 3.0 approaches, [188](#), [190](#)

醫學 2.0 與醫學 3.0 的比較, 188, 190

prevention strategy, [186–193](#), [199–204](#), [225](#), [321](#), [326](#), [363](#)

預防策略, 186–193, 199–204, 225, 321, 326, 363

risk factors, [17](#), [71–72](#), [109](#), [188–189](#), [196](#)

風險因子, 17, 71–72, 109, 188–189, 196

treatments targeting amyloid, [183–184](#)

針對澱粉樣蛋白的治療, 183–184

Alzheimer's Treatment, Alzheimer's Prevention (Isaacson), [187](#)

阿茲海默症的治療，阿茲海默症的預防（艾薩克森），187

Ambien, [364](#), [365](#), [366](#)

安必恩、364、365、366

AMP-activated protein kinase (AMPK), [82](#)

AMP 活化蛋白激酶 (AMPK), 82

amyloid-beta, [182–185](#), [195–196](#), [362–363](#)

β 澱粉樣蛋白，182–185、195–196、362–363

amyotrophic lateral sclerosis (ALS; Lou Gehrig's disease), [83](#), [179](#)

肌萎縮側索硬化症（ALS；盧伽雷氏症），83, 179

Andrews, Peter, [104–105](#)

彼得安德魯斯，104–105

APOE gene variants (e2, e3, e4), [67–69](#), [178–179](#), [180](#), [189](#), [196](#), [197–199](#)

APOE 基因變異（e2、e3、e4）、67–69、178–179、180、189、196、197–199

apolipoprotein A (apoA), [117](#), [120](#)

載脂蛋白 A (apoA), 117, 120

apolipoprotein B (apoB), [117](#), [117n](#), [120](#), [121](#), [133–134](#), [137](#)

載脂蛋白 B (apoB)、117、117n、120、121、133–134、137

apolipoprotein B (apoB) test, [126–127](#), [130–131](#), [132](#)

載脂蛋白 B (apoB) 測試, 126–127, 130–131, 132

apolipoprotein E (APOE), [67–68](#), [197–198](#)

載脂蛋白 E (APOE), 67–68, 197–198

Aretaeus of Cappadocia, [102](#)

卡帕多西亞的阿雷泰烏斯, 102

arterial plaque, [122](#), [124–125](#)

動脈斑塊, 122, 124–125

Ashkenazi Jewish centenarians, [61](#)

德系猶太人百歲老人, 61 歲

ashwagandha, [366](#)

阿什瓦甘達, 366

atherosclerotic cardiovascular disease (ASCVD). See [cardiovascular disease](#)

動脈粥狀硬化性心血管疾病（ASCVD）。參見心血管疾病

atherosclerotic plaque, [122](#), [124–125](#)

動脈粥狀硬化斑塊, 122, 124–125

Atlas of Atherosclerosis Progression and Regression (Stary), [119](#)

動脈粥狀硬化進展和消退圖（Stary），119

automobile accident analogy, [212–213](#)

車禍類比, 212–213

autophagy, [82–83](#), [341](#)

自噬, 82–83, 341

B

Bacon, Francis, [27](#)

法蘭西斯培根, 27 歲

balloon analogy, [101](#), [108](#)

氣球比喻, 101, 108

“Barry Get-Up” fitness assessment, [290](#)

「Barry Get-Up」健身評估, 290

Barzilai, Nir, [61](#), [64](#), [87](#)

巴爾齊萊, 尼爾, 61, 64, 87

bathtub analogy, [98](#)

浴缸比喻, 98

B-cell lymphoma, [160](#)

B 細胞淋巴瘤, 160

bempedoic acid (Nexletol), [138](#)

bempedoic 酸 (Nexletol) , 138

Betts, James, [344](#)

詹姆斯貝茨, 344

Blessed, Garry, [181](#), [184](#), [194](#)

有福的加里, 181, 184, 194

blood pressure. *See* [high blood pressure](#)

血壓. 看 高血壓

blood test for cancer (liquid biopsy), [145](#), [172–175](#), [172n](#)

癌症血液檢查（液體切片）, 145, 172–175, 172n

Boorstin, Daniel J., [177](#)

丹尼爾·布爾斯廷, 177

borderline personality disorder, [400](#)

邊緣性人格障礙, 400

Bowers, Mildred, [60](#)

米爾德里德鮑爾斯, 60 歲

Bradford Hill, Austin, [222n](#), [298](#)

布拉德福德山, 奧斯汀, 222n, 298

Bradford Hill criteria, [298–299](#), [298n](#)

布拉德福德希爾標準, 298–299, 298n

brain-derived neurotrophic factor (BDNF), [225](#)

腦源性神經營養因子 (BDNF), 225

brain glucose metabolism, [194–196](#)

腦葡萄糖代謝, 194–196

breast cancer, [33n](#), [146–147](#), [152](#), [153](#), [167](#), [167n](#), [168](#), [303](#), [303n](#)

乳癌, 33n, 146–147, 152, 153, 167, 167n, 168, 303, 303n

breathing, [272–277](#), [276n](#)

呼吸, 272–277, 276n

Bridge to Recovery, [377–380](#), [383–388](#), [397](#)

恢復之橋, 377–380, 383–388, 397

Brooks, David, [394](#)

大衛布魯克斯, 394

Brooks, George, [238](#), [241](#)

喬治布魯克斯, 238、241

Buddha, [403](#)

佛陀, 403

Burns, Ken, [158](#)

肯·伯恩斯, 158

C

caffeine, [372–373](#)

咖啡因, 372–373

calcium score, [113–114](#), [124–126](#), [124n](#), [128](#), [135–136](#), [136n](#)

鈣評分, 113–114, 124–126, 124n, 128, 135–136, 136n

Calment, Jeanne, [59–60](#), [61](#)

珍妮·卡爾門特, 59–60, 61

calorie restriction (CR), [79–83](#), [152–153](#), [309](#), [310](#), [311–316](#)

熱量限制 (CR)、79–83、152–153、309、310、311–316

cancer, [140–176](#). *See also specific types of cancer*

癌症, 140–176。另請參閱特定類型的癌症

background, [102](#), [140–142](#)

背景, 102, 140–142

centenarians and, [63](#)

百歲老人, 63

conclusion, [175–176](#)

結論, 175–176

demographics, [142–144](#), [143](#)

人口統計, 142–144, 143

genetic mutations and, [145–147](#), [150–151](#)

基因突變和, 145–147, 150–151

meat and, [299–300](#)

肉和, 299–300

Medicine 2.0 vs. Medicine 3.0 approaches, [167](#), [176](#)

醫學 2.0 與醫學 3.0 的比較, 167, 176

risk factors, [53–54](#), [72](#), [107–108](#), [109](#)

風險因子, 53–54, 72, 107–108, 109

strategy: early detection (background), [145](#), [165–167](#)

策略：早期檢測（背景），145, 165–167

strategy: early detection (future directions), [86](#), [172–175](#)

策略：早期檢測（未來方向），86, 172–175

strategy: early detection strategy (trade-offs), [167–172](#), [172n](#)

策略：早期檢測策略（權衡），167–172, 172n

strategy: overview, [144–145](#)

策略：概述，144–145

strategy: treatment (dietary interventions), [154–158](#)

策略：治療（飲食幹預），154–158

strategy: treatment (immunotherapy), [158–165](#), [160n](#)

策略：治療（免疫療法），158–165, 160n

strategy: treatment (overview), [145](#), [147–149](#)

策略：治療（概述），145, 147–149

The Cancer Genome Atlas, [146–147](#)

癌症基因組圖譜，146–147

Cantley, Lew, [151](#), [152–153](#), [154–155](#), [156](#)

盧·坎特利, 151, 152–153, 154–155, 156

car accident analogy, [212–213](#)

車禍類比, 212–213

carbohydrates, [318](#), [322–330](#), [347](#)

碳水化合物, 318, 322–330, 347

cardiorespiratory fitness

心肺健康

background, [216–218](#)

背景, 216–218

benefits of, [201–202](#), [219–223](#), [222n](#), [222](#), [224n](#), [225](#)

201–202、219–223、222n、222、224n、225 的好處

maximum aerobic output, [220–221](#), [223](#), [244–252](#), [246](#), [250–251n](#), [250](#)

最大有氧輸出, 220–221, 223, 244–252, 246, 250–251n, 250

overview, [236](#)

概述, 236

power of, [287–290](#)

的幂, 287–290

preparation overview, [236](#)

準備概述, 236

sleep and, [354–355](#), [355n](#)

睡眠, 354–355, 355n

zone 2 training, [237–244](#)

2 區訓練, 237–244

cardiovascular disease, [111–139](#)

心血管疾病, 111–139

background, [15–16](#), [111–115](#), [209](#)

背景, 15–16, 111–115, 209

centenarians and, [63](#)

百歲老人, 63

cholesterol and, [115–119](#)

膽固醇和, 115–119

demographics, [112–113](#), [142–143](#)

人口統計, 112–113, 142–143

excess fats and, [98](#), [99](#)

多餘的脂肪和, 98, 99

lipid-lowering medications for, [129–130](#), [130n](#), [133–134](#), [136–139](#)

降血脂藥物, 129–130、130n、133–134、136–139

Lp(a) and, [127–130](#)

Lp(a) 和, 127–130

Medicine 2.0 vs. Medicine 3.0 approaches, [29](#), [130](#), [137](#)

醫學 2.0 與醫學 3.0 方法, 29, 130, 137

progression of, [119–125](#), [134–137](#)

進展, 119–125, 134–137

risk factors, [71–72](#), [109](#), [125–127](#), [196](#)

風險因子, 71–72, 109, 125–127, 196

risk reduction, [130–139](#)

降低風險, 130–139

sleep and, [357](#), [358–359](#)

睡覺, 357, 358–359

CAR-T (chimeric antigen receptor T cells), [159–160](#)

CAR-T（嵌合抗原受體 T 細胞），159–160

Case, Anne, [382](#)

凱斯，安妮，382

causation

因果關係

in clinical trials, [302–306](#)

臨床試驗, 302–306

in epidemiology, [53](#), [53n](#), [297–302](#)

流行病學, 53, 53n, 297–302

CCGA (Circulating Cell-free Genome Atlas), [174–175](#)

CCGA（循環無細胞基因組圖譜），174–175

Centenarian Decathlon

百歲十項全能

background, [229–230](#)

背景, 229–230

maximum aerobic output, [220–221](#), [223](#), [244–252](#), [246](#), [250–251n](#), [250](#)

最大有氧輸出, 220–221, 223, 244–252, 246, 250–251n, 250

overview and questions to ask, [231–234](#)

概述與要問的問題, 231–234

preparation overview, [235–237](#)

準備概述, 235–237

strength foundation training, [255–262](#), [263–290](#). *See also* [stability training](#)

肌力基礎訓練, 255–262、263–290。另請參閱穩定性訓練

zone 2 training, [237–244](#)

2 區訓練, 237–244

centenarians

百歲老人

genetics of, [62](#), [66–70](#)

62、66–70 的遺傳學

Medicine 2.0 vs. Medicine 3.0 approaches, [65–66](#)

醫學 2.0 與醫學 3.0 的對比, 65–66

phase shift of, [63–66](#), [71–72](#)

相移, 63–66, 71–72

research on, [51–52](#), [60–62](#)

研究, 51–52, 60–62

“secrets” to living longer, [59–60](#), [70–72](#)

長壽的“秘訣”, 59–60、70–72

Centers for Disease Control (CDC), [93](#)

疾病管制中心 (CDC), 93

central adiposity, [94](#)

中央肥胖, 94

cerebrovascular disease (stroke), [63](#), [112–113](#), [195–196](#), [224](#)

腦血管疾病（中風）, 63, 112–113, 195–196, 224

cervical cancer, [167](#), [171](#)

子宮頸癌, 167, 171

CGM (continuous glucose monitoring), [31](#), [323–330](#), [323n](#), [324n](#)

CGM（連續血糖監測）、31、323–330、323n、324n

Chandel, Navdeep, [74–75](#)

錢德爾，納維迪普，74–75

checkpoint inhibitors, [160–162](#), [160n](#), [163](#)

檢查點抑制劑, 160–162、160n、163

chemotherapy, [148–149](#)

化療, 148–149

chimeric antigen receptor T cells (CAR-T), [159–160](#)

嵌合抗原受體 T 細胞 (CAR-T), 159–160

cholesterol, [16](#), [68](#), [71–72](#), [115–119](#), [197–198](#)

膽固醇, 16, 68, 71–72, 115–119, 197–198

cholesterol efflux, [123](#)

膽固醇流出, 123

chronotypes, [368–369](#), [368n](#)

時間類型, 368–369, 368n

Circulating Cell-free Genome Atlas (CCGA), [174–175](#)

循環無細胞基因組圖譜 (CCGA), 174–175

cirrhosis, [92–93](#)

肝硬化, 92–93

clinical trials, [297](#), [302–306](#)

臨床試驗, 297, 302–306

Coelho, Paulo, [408](#)

保羅·科埃略, 408

cognitive behavioral therapy, [400](#)

認知行為療法, 400

Cognitive Behavioral Therapy for Insomnia (CBT-I), [376](#)

失眠認知行為治療 (CBT-I) , 376

Coley, William, [158–159](#)

威廉·科利, 158–159

colon cancer, [153](#), [161–162](#), [166](#), [166n](#), [169–171](#), [169–171nn](#)

結腸癌, 153, 161–162, 166, 166n, 169–171, 169–171nn

The Comfort Crisis (Easter), [256–257](#)

舒適危機 (復活節) , 256–257

concentric loading, [257](#), [260](#)

同心裝載, 257, 260

Conti, Paul, [380](#), [388](#), [395–396](#), [397](#)

保羅·孔蒂, 380, 388, 395–396, 397

continuous glucose monitoring (CGM), [31](#), [323–330](#), [323n](#), [324n](#)

連續血糖監測 (CGM), 31, 323–330, 323n, 324n

Corby, Patricia, [203](#)

派翠西亞·科比, 203

Cornaro, Alvise, [79–80](#)

阿爾維斯·科爾納羅, 79–80

Cornaro, Luigi, [312](#)

路易吉·科爾納羅, 312

correlation

相關性

in clinical trials, [302–306](#)

臨床試驗, 302–306

in epidemiology, [297–302](#)

流行病學, 297–302

COVID-19, [28](#), [43–44](#), [242n](#), [396–397](#), [404](#)

新冠肺炎 (COVID-19)、28、43–44、242n、396–397、404

Crick, Francis, [150](#)

弗朗西斯·克里克, 150

crime scene analogy, [119–121](#), [124](#)

犯罪現場類比, 119–121, 124

CT angiogram, [124](#), [124n](#), [135–136](#), [136n](#)

CT 血管攝影、124、124n、135–136、136n

cytokines, [86](#), [98](#), [225](#)

細胞激素, 86, 98, 225

D

Dayspring, Tom, [114](#), [128](#), [344–346](#)

黎明, 湯姆, 114, 128, 344–346

Dayvigo (lemborexant), [365–366](#)

Dayvigo (lemborexant) , 365–366

DBT (dialectical behavior therapy), [400–407](#)

DBT (辯證行為治療) , 400–407

DeAngelo, James, [140–141](#), [164](#)

詹姆斯·德安吉洛, 140–141, 164

Deaton, Angus, [382](#)

安格斯·迪頓, 382

decathlon. *See* [Centenarian Decathlon](#)

十項全能。查看百歲十項全能

de la Torre, Jack, [194–195](#)

傑克·德拉托雷, 194–195

dementia. *See* [neurodegenerative diseases](#)

失智.參見神經退化性疾病

dementia with Lewy bodies, [179](#)

路易氏體癡呆, 179

dental health, [203](#)

牙齒健康, 203

depression, [196](#), [203](#), [390–392](#)

憂鬱症, 196, 203, 390–392

Deter, Auguste, [181](#), [182](#), [185](#)

奧古斯特·德特, 181, 182, 185

DHA, [200](#), [336–337](#), [340](#)

Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5), [388](#)

精神疾病診斷與統計手冊，第五版 (DSM-5)，388

dialectical behavior therapy (DBT), [400–407](#)

辯證行為治療 (DBT)，400–407

Diehn, Max, [172–173](#)

馬克斯·迪恩，172–173

dietary restrictions (DR), [309](#), [310](#), [317–320](#). *See also specific diets*

飲食限制 (DR)，309、310、317–320。另請參閱具體飲食

diffusion-weighted imaging MRI, [171–172](#)

擴散加權成像 MRI，171–172

“Discourses on the Sober Life” (Cornaro), [80](#)

「關於清醒生活的論述」（科爾納羅），80

distress tolerance, [401](#), [402](#), [404–405](#)

抗壓性, 401, 402, 404–405

DNS (dynamic neuromuscular stabilization), [270–271](#), [272](#), [275](#), [280n](#)

DNS（動態神經肌肉穩定），270–271, 272, 275, 280n

Dog Aging Project, [85–86](#)

狗衰老項目, 85–86

Down syndrome, [182](#)

唐氏綜合症, 182

Dunning-Kruger curve, [293–294](#), [293](#)

鄧寧-克魯格曲線, 293–294, 293

DWI MRI, [171–172](#)

DWI 磁振造影, 171–172

dynamic neuromuscular stabilization (DNS), [270–271](#), [272](#), [275](#), [280n](#)

動態神經肌肉穩定 (DNS), 270–271, 272, 275, 280n

E

early-onset Alzheimer's disease, [182](#), [185](#)

早發性阿茲海默症, 182, 185

Easter, Michael, [256–257](#)

復活節, 邁克爾, 256–257

Easter Island (Rapa Nui), [73–76](#), [87n](#)

復活節島（拉帕努伊），73–76, 87n

eccentric loading, [257](#), [260–261](#)

偏心負載, 257, 260–261

effectiveness tests, [304](#)

有效性測試, 304

efficacy tests, [304](#)

功效測試, 304

eggs, [118](#)

雞蛋, 118

Elias, Ric, [410–411](#)

里克·埃利亞斯, 410–411

emergency landing on Hudson River, [410–411](#)

哈德遜河緊急迫降, 410–411

emotional health, [377–408](#)

情緒健康, 377–408

conclusion, [399–400](#), [407–408](#)

結論, 399–400, 407–408

COVID-19 and, [396–397](#), [404](#)

COVID-19 和, 396–397, 404

importance of, [17](#), [380–383](#)

17、380–383 的重要性

inpatient treatment, [377–380](#), [383–388](#), [397–399](#), [400](#)

住院治療, 377–380, 383–388, 397–399, 400

as longevity tactic, [47](#)

作為長壽策略, 47

male depression, [390–392](#)

男性憂鬱症, 390–392

medications, [399](#), [401](#)

藥物, 399, 401

Medicine 2.0 vs. Medicine 3.0 approaches, [388–389](#)

醫學 2.0 與醫學 3.0 方法, 388–389

mental health comparison, [388–389](#)

心理健康比較, 388–389

nutritional biochemistry and, [401](#)

營養生化, 第 401 章

overview, [49](#), [50](#)

概述, 49, 50

tools for, [361–362](#), [392–396](#), [398–399](#), [400–407](#)

工具, 361–362, 392–396, 398–399, 400–407

trauma and, [384–388](#)

創傷和, 384–388

The Emperor of All Maladies (Mukherjee), [155](#), [156](#), [158](#)

萬病王（慕克吉），155、156、158

endometrial cancer, [152](#), [153](#)

子宮內膜癌, 152, 153

endothelium, [119–123](#), [122](#), [128](#)

內皮細胞, 119–123, 122, 128

endurance exercise. *See* [cardiorespiratory fitness](#)

耐力鍛鍊。查看心肺健康

English, Jeff, [386](#), [390](#)

英語, 傑夫, 386, 390

EPA, [336–337](#), [340](#)

美國環保局, 336–337, 340

epidemiology, [53](#), [53n](#), [297–302](#)

流行病學, 53, 53n, 297–302

Epworth Sleepiness Scale, [368](#), [368n](#)

Epworth 嗜睡量表, 368, 368n

esophageal cancer, [152](#), [153](#)

食道癌, 152, 153

ethyl eicosapentaenoic acid (Vascepa), [139](#)

乙基二十碳五烯酸 (Vascepa), 139

eulogy virtues, [394](#), [410](#)

悼詞美德, 394, 410

everolimus, [76](#), [84](#)

依維莫司, 76, 84

evidence-based medicine, [50–51](#)

實證醫學, 50–51

evolution, [66–67](#), [103–106](#), [198](#), [353](#), [362n](#)

進化, 66–67, 103–106, 198, 353, 362n

exercise

鍛鍊

background, [48](#), [216–218](#)

背景, 48, 216–218

benefits of, [17](#), [47](#), [48](#), [100](#), [201–202](#), [218–228](#), [222n](#), [222](#), [224n](#),
[254–256](#)

17、47、48、100、201–202、218–228、222n、222、224n、
254–256 的優點

continuous glucose monitoring and, [329](#), [330](#)

連續血糖監測, 以及, 329, 330

emotional health and, [401](#), [405–406](#)

情緒健康, 401、405–406

Medicine 2.0's approach to, [219](#)

醫學 2.0 的方法, 219

power of, [287–290](#)

的幂, 287–290

sleep and, [354–355](#), [355n](#), [373](#), [374](#)

睡眠與, 354–355, 355n, 373, 374

training recommendations, [229–234](#). *See also* [centenarian decathlon](#)

訓練建議, 229-234。另請參閱百歲十項全能

types of, [237–262](#). *See also* [cardiorespiratory fitness](#); [strength training](#)

類型, 237-262。另請參閱心肺健康; 肌力訓練

Extra Life (Johnson), [28](#)

額外的生命 (約翰遜), 28

ezetimibe (Zetia), [138](#), [138n](#)

依折麥布 (Zetia), 138, 138n

F

fasting, [156–157](#), [309](#), [310–311](#), [340–346](#)

禁食, 156–157, 309, 310–311, 340–346

fasting glucose test, [31](#), [94](#), [101](#), [323](#)

空腹血糖測試, 31, 94, 101, 323

fats (dietary), [304–306](#), [318](#), [329–330](#), [335–336n](#), [335–340](#), [347](#)

脂肪 (飲食)、304–306、318、329–330、335–336n、335–340、347

fat storage, [96–100](#), [104](#), [107n](#), [237](#), [238–239](#)

脂肪儲存, 96–100, 104, 107n, 237, 238–239

“fatty streak,” [121–122](#), [122](#)

“脂肪條紋”，121–122, 122

Ferriss, Tim, [74–75](#)

提姆·費里斯，74–75

Feynman, Richard, [27](#), [291](#), [292](#)

理查·費曼，27, 291, 292

“First, do no harm,” [23–24](#), [23n](#), [88](#)

「首先，不要傷害」23-24, 23n, 88

Flaherty, Keith, [157](#)

基斯·弗拉哈蒂，157

flossing, [203](#)

使用牙線，203

foam cells, [121](#), [122](#), [123](#), [124](#)

泡沫單元，121、122、123、124

follicular lymphoma, [159–160](#)

濾泡性淋巴瘤，159–160

food frequency questionnaire, [299](#), [299n](#)

食物頻率問卷, 299, 299n

food supply safety, [210n](#)

食品供應安全，210n

Foreman, George, [41–43](#), [72](#)

喬治·福爾曼, 41–43, 72

Four Horsemen. *See* [cancer](#); [heart disease](#); [metabolic dysfunction and metabolic syndrome](#); [neurodegenerative diseases](#)

四騎士。參見癌症；心臟病；代謝功能障礙和代謝症候群；神經退化性疾病

FOXO3 gene, [69–70](#)

FOXO3 基因, 69–70

frailty, [253–255](#)

虛弱, 253–255

Franklin, Rosalind, [150](#)

富蘭克林, 羅莎琳德, 150

fructose, [104–107](#), [210](#), [329](#)

果糖, 104–107, 210, 329

G

Galleri (Grail test), [174–175](#)

Galleri（聖杯測試），174–175

Galpin, Andy, [252–253](#)

安迪加爾平, 252–253

Gandhi, Mahatma, [349](#)

聖雄甘地, 349

Gay, Nathan, [163](#)

內森同性戀, 163

genetics. *See also specific genes*

遺傳學。另請參見特定基因

Alzheimer's disease and, [67–69](#)

阿茲海默症, 67–69

of cancer cells, [145–147](#), [150–151](#), [159n](#)

癌細胞數量, 145–147, 150–151, 159n

fat-storage capacity, [98–99](#)

脂肪儲存能力, 98–99

of longevity, [62](#), [66–70](#), [123–124](#)

長壽, 62, 66–70, 123–124

of metabolic dysfunction, [199](#)

代謝功能障礙, 199

gentamicin, [20–21](#)

慶大霉素, 20–21

ghrelin, [358](#)

胃飢餓素, 358

glioblastoma, [147](#)

膠質母細胞瘤, 147

glucose metabolism

葡萄糖代謝

APOE and, [68](#)

APOE 和, 68

in brain, [194–196](#)

在大腦中, 194–196

of cancer cells, [149–154](#), [156](#)

癌細胞, 149–154, 156

carbohydrates and, [322–330](#)

碳水化合物, 322–330

exercise and, [237](#), [238–239](#), [241–243](#)

練習與, 237, 238–239, 241–243

fructose comparison, [106–107](#), [106–107n](#)

果糖比較, 106–107, 106–107n

sleep and, [357–358](#)

睡覺, 357–358

storage of glucose, [96–97](#)

葡萄糖的儲存, 96–97

glycogen, [96–97](#)

肝醣, 96–97

Gonzalez-Lima, Francisco, [192](#)

岡薩雷斯利馬, 弗朗西斯科, 192

Gordon, Robert J., [28](#)

戈登·羅伯特·J., 28 歲

gout, [102](#), [104](#), [106](#)

痛風, 102, 104, 106

Grail test (Galleri), [174–175](#)

聖杯測試 (Galleri), 174–175

grandiosity, [391](#)

宏偉, 391

Griffin, John, [216–217](#), [218](#)

約翰·格里芬, 216–217, 218

grip strength, [201](#), [202](#), [256–257](#), [258–260](#)

握力, 201, 202, 256–257, 258–260

growth hormone, [364](#)

生長激素, 364

H

Hamlet (Shakespeare), [403](#)

哈姆雷特（莎士比亞），403

Hanahan, Douglas, [149](#)

道格拉斯·哈納漢，149

Harper, Bob, [128–129](#)

鮑勃哈珀，128–129

Hawthorne effect, [325–326](#), [330](#)

霍桑效應，325–326, 330

HDL (“good”) cholesterol, [94](#), [116](#), [120](#), [123–124](#), [123n](#), [132–133](#)

HDL（「好」）膽固醇，94、116、120、123–124、123n、132–133

healthcare reimbursement system, [33–34](#)

醫療報銷制度，33–34

healthspan

健康壽命

of centenarians, [64–65](#)

百歲老人，64–65

defined, [10–11](#)

定義，10–11

deterioration vectors, [45–47](#)

惡化向量，45–47

Four Horsemen and. *See* [cancer](#); [heart disease](#); [metabolic dysfunction](#)

[and metabolic syndrome](#); [neurodegenerative diseases](#)

四騎士和。參見癌症；心臟病；代謝功能障礙和代謝症候群；神經退化性疾病

Marginal Decade vs. Bonus Decade, [36–40](#), [39](#), [65](#)

邊際十年與獎金十年, 36–40, 39, 65

Medicine 2.0 vs. Medicine 3.0 approaches, [33](#), [38–40](#), [39](#), [65](#)

醫學 2.0 與醫學 3.0 方法, 33, 38–40, 39, 65

strategy for extension of, [41–47](#)

擴展策略, 41–47

tactics for expansion of, [47–50](#)

擴張策略, 47–50

Healthy Aging and Body Composition Study, [334](#)

健康老化與身體組成研究, 334

healthy user bias, [193](#), [301–302](#), [301n](#), [321](#)

健康的使用者偏見, 193、301–302、301n、321

hearing loss, [203](#)

聽力損失, 203

heart attack. *See* [heart disease](#)

心臟病發作.參見心臟病

heart disease. *See* [atherosclerotic cardiovascular disease](#)

心臟病.參見動脈粥狀硬化性心血管疾病

hemoglobin A1c (HbA1c) test, [13–14](#), [13n](#), [31](#), [108](#)

糖化血紅蛋白 (HbA1c) 測試, 13–14、13n、31、108

high blood pressure

高血壓

as Alzheimer's disease risk factor, [196](#)

作為阿茲海默症的危險因素, 196

as cardiovascular risk factor, [120–121](#), [126](#), [133](#)

作為心血管危險因子, 120–121, 126, 133

centenarians and, [63](#)

百歲老人, 63

metabolic dysfunction and, [94](#), [104](#), [106](#)

代謝功能障礙和, 94, 104, 106

sleep and, [357](#), [369n](#)

睡覺, 並且, 357, 369n

high-density lipoproteins. *See* [HDL \(“good”\) cholesterol](#)

高密度脂蛋白。請參閱 HDL (“好”) 膽固醇

high-fructose corn syrup, [105n](#)

高果糖玉米糖漿, 105n

hip-hinging movements, [258](#), [261–262](#), [268–271](#), [269](#), [285–287](#)

髖部鉸鏈運動, 258, 261–262, 268–271, 269, 285–287

Hippocrates, [23–24](#), [23n](#), [25–26](#), [79](#), [88](#)

希波克拉底, 23–24, 23n, 25–26, 79, 88

Hitchens, Christopher, [148–149](#)

克里斯多福·希欽斯, 148–149

Hodgkin's lymphoma, [143](#)

霍奇金淋巴瘤, 143

Holiday, Ryan, [406](#)

假日, 瑞安, 406

homocysteine, [108](#), [132](#), [132n](#), [204](#)

同型半胱氨酸、108、132、132n、204

Honjo, Tasuku, [161](#)

本莊佐, 161

Horner, Jack, [73](#)

傑克霍納, 73 歲

Horsemen. *See* [cancer](#); [heart disease](#); [metabolic dysfunction and metabolic syndrome](#); [neurodegenerative diseases](#)

騎兵。參見癌症；心臟病；代謝功能障礙和代謝症候群；神經退化性疾病

HRT (hormone replacement therapy), [32–33](#), [33n](#), [204](#), [254–255](#)

HRT（荷爾蒙替代療法）、32–33、33n、204、254–255

Huntington's disease, [179](#)

亨廷頓舞蹈症, 179

hypertension. *See* [high blood pressure](#)

高血壓。看高血壓

I

I Don't Want to Talk About It (Real), [390](#)

我不想談論它（真實），390

IGF-1 (insulin-like growth factor), [153–155](#)

IGF-1（類胰島素生長因子），153–155

immunosuppression, [84–87](#)

免疫抑制，84–87

immunotherapy, [140–142](#), [149](#), [158–165](#), [160n](#)

免疫療法，140–142, 149, 158–165, 160n

infectious (contagious) disease, [26–28](#), [28](#), [198](#)

傳染病，26–28, 28, 198

inflammation, [85–86](#), [98](#)

發炎，85–86, 98

injury prevention, [263–265](#). *See also* [stability training](#)

傷害預防，263–265。另請參閱穩定性訓練

Inman, Thomas, [23n](#)

托馬斯·英曼, 23n

insomnia, [363](#), [365–366](#), [373](#), [376](#)

失眠, 363, 365–366, 373, 376

Insomnia Severity Index, [368](#), [368n](#)

失眠嚴重程度指數, 368, 368n

insulin, [97](#), [99](#), [108–109](#), [152–154](#), [156](#), [196–197](#), [340](#)

胰島素, 97, 99, 108–109, 152–154, 156, 196–197, 340

insulin resistance

胰島素抗性

as Alzheimer’s disease risk factor, [196–197](#)

作為阿茲海默症的危險因素, 196–197

as cancer risk factor, [154](#)

作為癌症危險因素, 154

as cardiovascular risk factor, [126](#)

作為心血管危險因素, 126

defined, [100–101](#)

定義, 100–101

Medicine 2.0’s approach to, [109–110](#)

醫學 2.0 的方法, 109–110

metabolic dysfunction and, [98](#), [99](#), [100–102](#)

代謝功能障礙和, 98, 99, 100–102

prevention through exercise, [224](#)

透過運動預防, 224

sleep and, [356–357](#), [358](#)

睡覺, 356–357, 358

type 2 diabetes cause, [109](#)

2 型糖尿病原因, 109

intermittent fasting, [310–311](#)

間歇性斷食, 310–311

intersections-car accident analogy, [212–213](#)

十字路口-車禍類比, 212–213

intra-abdominal pressure (IAP), [275–276](#)

腹內壓 (IAP), 275–276

Ioannidis, John, [224](#), [224n](#), [300](#)

約翰·約安尼迪斯, 224, 224n, 300

ipilimumab (Yervoy), [161](#)

易普利瑪 (Yervoy), 161

Isaacson, Richard, [186–187](#), [191](#), [192](#)

理查德·艾薩克森, 186–187, 191, 192

J

Johnson, Rick, [104–105](#)

約翰遜，里克，104–105

Johnson, Steven, [28](#)

史蒂文約翰遜，28 歲

Joslin, Elliott, [102](#)

喬斯林，艾利歐特，102

Joyner, Mike, [221](#)

喬伊納，麥克，221

K

Kaeberlein, Matt, [84](#), [85–86](#)

馬特·卡伯萊因，84, 85–86

Kennedy, John F., [20](#)

約翰甘迺迪，20

ketogenic diet, [133](#), [155–156](#), [200–201](#), [292–293](#), [319–320](#), [339n](#)

生酮飲食，133, 155–156, 200–201, 292–293, 319–320, 339n

Keys, Ancel, [118](#)

鑰匙，安塞爾，118

Keytruda, [162](#)

Keytruda, 162

kidney (renal) cancer, [152](#), [153](#), [159](#), [159n](#)

腎癌, 152, 153, 159, 159n

King Lear (Shakespeare), [181](#)

李爾王（莎士比亞），181

Klickstein, Lloyd, [84](#)

勞埃德·克里克斯坦，84 歲

Klotho (*KL*) gene, [180](#), [199](#)

Klotho (KL) 基因，180, 199

Knauss, Sarah, [61](#)

莎拉諾斯，61 歲

Knight, Bobby, [395](#), [403–404](#)

鮑比奈特，395, 403–404

Koch, Robert, [26](#), [26n](#)

羅伯特·科赫，26, 26n

Kochalka, Jim, [404](#)

吉姆·科查爾卡，404

Krauss, Ron, [114](#)

羅恩·克勞斯，114

Kübler-Ross, Elisabeth, [23](#)

庫伯勒-羅斯，伊莉莎白，23

L

lactate, [151](#), [151n](#), [240–242](#)

乳酸, 151, 151n, 240–242

LaLanne, Jack, [234](#)

拉蘭，傑克，234

Layman, Don, [333–334](#)

外行，唐，333–334

Lazar, Mitch, [99](#)

拉扎爾，米奇，99

LDL (“bad”) cholesterol

低密度脂蛋白（「壞」）膽固醇

as cancer risk, [53–54](#)

作為癌症風險，53–54

as cardiovascular risk factor, [116](#), [120–121](#), [137](#)

作為心血管危險因素，116, 120–121, 137

levels of (LDL-C), [123–124](#), [123n](#), [126](#), [127](#), [131–132](#), [131n](#), [133n](#)

(LDL-C)、123–124、123n、126、127、131–132、131n、133n
水平

liver and, [133n](#)

肝臟和, 133n

Lp(a) and, [128](#)

Lp(a) 和, 128

LDL receptors (LDLR), [133n](#), [134](#)

低密度脂蛋白受體 (LDLR), 133n, 134

Lee, Bruce, [209](#)

李布魯斯, 209

leptin, [107n](#), [358](#)

瘦素, 107n, 358

leukemia, [142](#), [143](#), [160](#)

白血病, 142, 143, 160

Lewis, Beth, [262](#), [268–270](#), [272–279](#), [281–284](#), [288–290](#)

路易斯, 貝絲, 262、268–270、272–279、281–284、288–290

Lewy, Friedrich, [185](#)

弗里德里希·路易, 185

Lewy body dementia, [179](#), [185](#), [189](#)

路易氏體失智症, 179, 185, 189

Libby, Peter, [131](#), [137–138](#)

彼得·利比, 131, 137–138

lifespan, [38–40](#), [39](#), [44–45](#), [65](#)

壽命, 38–40, 39, 44–45, 65

Linehan, Marsha, [400](#)

萊恩漢, 瑪莎, 400

lipid-lowering medications, [128–129](#), [130n](#), [133–134](#), [136–139](#)

降血脂藥物, 128–129, 130n, 133–134, 136–139

lipid management, [133–134](#)

血脂管理, 133–134

lipoproteins, [68](#), [108](#), [116–117](#), [117n](#). *See also* [HDL \(“good”\) cholesterol](#); [LDL \(“bad”\) cholesterol](#)

脂蛋白, 68、108、116–117、117n。另請參閱 HDL（“好”）膽固醇；低密度脂蛋白（「壞」）膽固醇

liquid biopsies, [145](#), [172–175](#), [172n](#)

液體活檢, 145, 172–175, 172n

Lister, Joseph, [26](#), [26n](#), [27](#)

約瑟夫李斯特, 26、26n、27

liver

肝

alcohol metabolism in, [321](#)

酒精代謝, 321

cholesterol and, [116](#)

膽固醇和, 116

fasting and, [340](#)

第340章

glucose metabolism and, [96](#)

葡萄糖代謝, 96

LDL receptors and, [133n](#), [134](#)

LDL 受體和, 133n, 134

metabolic dysfunction and, [88–93](#), [98](#), [99](#), [107–108](#)

代謝功能障礙, 88–93, 98, 99, 107–108

regeneration potential of, [92](#)

再生潛力, 92

liver cancer, [147](#), [152](#), [153](#)

肝癌, 147, 152, 153

longevity, [59–72](#). *See also* [centenarians](#)

長壽, 59–72。另見百歲老人

author's quest to understand, [14–19](#), [50](#), [73–75](#)

作者對理解的追求, 14–19, 50, 73–75

defined, [9–11](#)

定義, 9–11

from evidence-based to evidence-informed, [50–55](#)

從基於證據到以證據為依據, 50–55

Four Horsemen and. *See* [cancer](#); [heart disease](#); [metabolic dysfunction and metabolic syndrome](#); [neurodegenerative diseases](#)

四騎士和。參見癌症；心臟病；代謝功能障礙和代謝症候群；神經退化性疾病

Medicine 2.0 vs. Medicine 3.0 approaches, [11–14](#), [33–34](#), [47–51](#), [71](#)
醫學 2.0 與醫學 3.0 方法, 11–14, 33–34, 47–51, 71

objective of, [36–40](#), [46–47](#)

目標, 36–40, 46–47

outlook on, [409–411](#)

展望, 409–411

rapamycin and, [73–79](#), [77n](#), [83–87](#)

雷帕黴素和, 73–79, 77n, 83–87

rethinking, [17–19](#), [20–35](#). *See also* [paradigm shift](#)

重新思考, 17-19、20-35。另請參見範式轉變

slow deaths, [7–9](#)

緩慢死亡, 7-9

strategy for, [41–47](#), [50–55](#), [70–72](#)

策略, 41–47, 50–55, 70–72

tactics for expansion of, [47–50](#), [209–215](#). *See also* [emotional health](#); [exercise](#); [nutritional biochemistry](#); [sleep](#); *specific medications and supplements*

擴張策略, 47-50, 209-215。另請參閱情緒健康; 鍛煉; 營養
生物化學; 睡覺; 特定藥物和補充劑

Longo, Valter, [156–157](#)

瓦爾特·隆戈, 156–157

Lou Gehrig's disease (ALS), [83](#), [179](#)

盧伽雷氏症 (ALS), 83, 179

low-density lipoproteins. *See* [LDL \(“bad”\) cholesterol](#)

低密度脂蛋白。請參閱低密度脂蛋白（“壞”）膽固醇

Lp(a), [127–130](#), [130n](#), [131](#), [131n](#), [137](#)

Lp(a)、127–130、130n、131、131n、137

Lunesta, [365](#)

盧內斯塔, 365

lung cancer, [13](#), [147](#), [163](#), [171–172](#)

肺癌, 13, 147, 163, 171–172

lymphomas, [143](#), [159–160](#)

淋巴瘤, 143, 159–160

Lynch syndrome, [161–162](#)

林奇症候群, 161–162

M

macronutrients. See [alcohol](#); [carbohydrates](#); [fats \(dietary\)](#); [protein](#)

宏量營養素。參見酒精；碳水化合物；脂肪（餐）；蛋白質

macrophages, [121](#), [122](#), [123](#)

巨噬細胞, 121, 122, 123

Mannick, Joan, [84](#)

瓊·曼尼克, 84 歲

Marginal Decade, [37–40](#), [39](#), [65](#)

邊緣十年, 37–40, 39, 65

maximum aerobic output, [220–221](#), [223](#), [244–252](#), [246](#), [250–251n](#), [250](#)

最大有氧輸出, 220–221, 223, 244–252, 246, 250–251n, 250

MCI (mild cognitive impairment), [190](#), [363](#)

MCI（輕度認知障礙）, 190, 363

McKinsey & Company, [22–23](#)

麥肯錫公司, 22–23

Mediterranean diet, [200](#), [304–306](#), [305n](#)

地中海飲食, 200, 304–306, 305n

melanomas, [146](#), [159](#), [159n](#), [161](#)

黑色素瘤, 146, 159, 159n, 161

melatonin, [202–203](#)

褪黑激素, 202–203

Mendelian randomization (MR), [53–54](#), [53n](#), [302](#)

孟德爾隨機化 (MR), 53–54, 53n, 302

Merrill, Thomas, [284](#)

湯瑪斯·梅里爾, 284

metabolic dysfunction and metabolic syndrome, [88–110](#)

代謝功能障礙與代謝綜合徵, 88–110

as Alzheimer's disease risk factor, [72](#), [109](#), [196–197](#), [199](#), [200–201](#)

作為阿茲海默症的危險因素, 72, 109, 196–197, 199, 200–201

background, [17](#), [88–90](#)

背景, 17, 88–90

biomarkers for, [108–109](#)

生物標誌物, 108–109

as cancer risk factor, [72](#), [107–108](#), [109](#), [152–153](#)

作為癌症危險因素, 72、107–108、109、152–153

as cardiovascular risk factor, [17](#), [72](#), [109](#)

作為心血管危險因素, 17, 72, 109

criteria for, [93–96](#)

標準, 93–96

evolution and, [103–105](#)

進化和, 103–105

fat storage and, [96–100](#), [99](#)

脂肪儲存和, 96–100, 99

fructose and, [104–107](#)

果糖, 104–107

genetics of, [199](#)

遺傳學, 199

insulin resistance and, [100–102](#)

胰島素阻抗, 100–102

liver and, [88–93](#), [98](#), [99](#), [107–108](#)

肝臟和, 88–93, 98, 99, 107–108

Medicine 2.0 vs. Medicine 3.0 approaches, [14](#), [31](#), [108–110](#)

醫學 2.0 與醫學 3.0 方法, 14, 31, 108–110

obesity comparison, [93–94](#), [95](#)

肥胖比較, 93–94, 95

sleep and, [356–358](#)

睡覺, 356–358

as type 2 diabetes risk factor, [72](#), [99](#), [102–103](#)

作為第 2 型糖尿病危險因素, 72, 99, 102–103

metastatic cancer, [140–142](#), [144](#), [146](#), [147–149](#), [165–167](#)

轉移性癌症, 140–142, 144, 146, 147–149, 165–167

metastatic melanoma, [165](#)

轉移性黑色素瘤, 165

metformin, [87](#)

二甲雙胍, 87

mild cognitive impairment (MCI), [190](#), [363](#)

輕度認知障礙 (MCI), 190, 363

mindfulness mediation practice, [399](#), [402–403](#), [406](#)

正念冥想練習, 399, 402–403, 406

“miraculous” survivors, [155](#), [158–159](#)

「奇蹟般的」倖存者, 155, 158–159

mismatch-repair deficiency, [162](#)

錯配修復缺陷, 162

mitochondria, [224](#), [237](#), [238–242](#), [242n](#)

粒線體, 224, 237, 238–242, 242n

mitochondrial biogenesis, [82](#)

粒線體生物發生, 82

monkey studies, [312–316](#), [314n](#)

猴子研究, 312–316, 314n

monounsaturated fats, [133](#)

單元不飽和脂肪, 133

mono-unsaturated fatty acids (MUFA), [335–336n](#), [335–340](#)

單元不飽和脂肪酸 (MUFA), 335–336n, 335–340

Morano, Emma, [60](#)

艾瑪·莫拉諾, 60 歲

Morningness/Eveningness Questionnaire (MEQ), [368n](#)

早上/晚上問卷 (MEQ), 368n

morphine, [365](#)

嗎啡, 365

Mortality (Hitchens), [148–149](#)

死亡率 (希欽斯), 148–149

MRI, for lung cancer screening, [171–172](#), [172n](#)

MRI, 用於肺癌篩檢, 171–172, 172n

mTOR (mechanistic target of rapamycin), [77–78](#), [77n](#), [82](#), [85](#), [341](#)

mTOR (雷帕黴素的機械標靶), 77–78, 77n, 82, 85, 341

Mukherjee, Siddhartha, [155](#), [156](#), [158](#)

悉達多·慕克吉, 155, 156, 158

multiple myeloma, [152](#), [153](#)

多發性骨髓瘤, 152, 153

muscle, [96](#), [97](#), [98](#), [99](#). *See also* [strength training](#)

肌肉、96、97、98、99。另請參閱肌力訓練

N

NAFLD (nonalcoholic fatty liver disease), [91](#), [92](#), [93](#), [98](#), [107–108](#), [109–110](#), [344](#)

NAFLD（非酒精性脂肪肝）、91、92、93、98、107–108、109–110、344

NASH (nonalcoholic steatohepatitis), [91](#), [92–93](#), [102](#), [344](#), [357](#)

NASH（非酒精性脂肪性肝炎），91, 92–93, 102, 344, 357

National Institutes of Health, [71](#), [187](#), [313–316](#), [314n](#)

美國國立衛生研究院，71, 187, 313–316, 314n

neurodegenerative diseases, [83](#), [177–180](#), [186–193](#), [204–205](#), [209](#), [363](#).

See also [Alzheimer's disease](#)

神經退化性疾病, 83, 177–180, 186–193, 204–205, 209, 363。另見阿茲海默症

New England Centenarian Study, [62](#), [63–65](#)

新英格蘭百歲老人研究，62, 63–65

nicotinamide riboside (NR), [79](#)

煙鹼醯胺核苷 (NR)，79

Niotis, Kellyann, [187](#), [191](#)

尼奧蒂斯、凱莉安, 187, 191

noncalcified plaques, [124](#), [125](#)

非鈣化斑塊, 124, 125

non-Hodgkin's lymphoma, [143](#)

非何杰金氏淋巴瘤, 143

nutritional biochemistry, [291–306](#)

營養生物化學, 291–306

alcohol, [320–321](#)

酒精, 320–321

background, [291–294](#)

背景, 291–294

caloric restriction, [309](#), [310](#), [311–316](#)

熱量限制, 309, 310, 311–316

with cancer treatments, [155–156](#)

癌症治療, 155–156

carbohydrates, [318](#), [322–330](#), [347](#)

碳水化合物, 318, 322–330, 347

conclusion, [346–348](#)

結論, 346–348

dietary restrictions, [309](#), [310](#), [317–320](#)

飲食限制, 309, 310, 317–320

emotional health and, [401](#)

情緒健康, 以及, 401

fasting (time-restricted eating), [156–157](#), [309](#), [310–311](#), [340–346](#)

禁食（限時進食）、156–157、309、310–311、340–346

fats, [304–306](#), [318](#), [329–330](#), [335–336n](#), [335–340](#), [347](#)

脂肪, 304–306, 318, 329–330, 335–336n, 335–340, 347

goals of, [294–296](#)

目標, 294–296

as longevity tactic, [48](#)

作為長壽策略, 48

overview, [17](#), [48–49](#)

概述, 17, 48–49

protein, [17](#), [318](#), [329–334](#), [330n](#)

蛋白質, 17, 318, 329–334, 330n

quantity and quality of food, [315–316](#)

食物的數量和質量, 315–316

research on, [296–306](#), [305n](#)

研究, 296–306, 305n

Standard American Diet, [308–311](#), [326–327](#)

標準美國飲食, 308–311, 326–327

nuts, [304–306](#), [337](#)

堅果, 304–306, 337

O

obesity, [93–94](#), [95](#), [107–108](#), [152](#), [153](#), [369n](#)

肥胖, 93–94, 95, 107–108, 152, 153, 369n

obstructive sleep apnea, [369](#), [369n](#)

阻塞性睡眠呼吸中止症, 369, 369n

O'Connor, Anahad, [127–128](#), [130](#)

奧康納, 阿納哈德, 127–128, 130

Ohsumi, Yoshinori, [83](#)

大隅良典, 83 歲

old-man blood, [356](#)

老人血, 356

olive oil, [304–306](#)

橄欖油, 304–306

Olshansky, S. Jay, [71](#)

奧尚斯基, S.傑伊, 71 歲

omega-3 fatty acids, [200](#), [204](#), [336–340](#)

omega-3 脂肪酸, 200、204、336–340

oral glucose tolerance test (OGTT), [109](#), [109n](#)

口服葡萄糖耐受試驗 (OGTT), 109, 109n

oral health, [203](#)

口腔健康, 203

orexin, [365–366](#)

食慾素, 365–366

ovarian cancer, [152](#)

卵巢癌, 152

Overton, Richard, [59](#)

理查德·奧弗頓, 59 歲

oxidative stress, [120–121](#)

氧化應激, 120–121

P

pancreas, [98](#), [99](#), [101](#)

胰臟, 98, 99, 101

pancreatic adenocarcinoma, [162](#)

胰臟腺癌, 162

pancreatic cancer, [2](#), [146–147](#), [152](#)

胰臟癌, 2, 146–147, 152

paradigm shift, [20–35](#)

典範轉移, 20–35

author's quest to understand, [20–25](#)

作者對理解的追求, 20-25

medical history eras, [23–28](#)

醫學史時代, 23-28

overview, [17–19](#)

概述, 17–19

risk assessment, [22–25](#)

風險評估, 22–25

parasympathetic nervous system, [272](#), [405](#)

副交感神經系統, 272, 405

Parkinson's disease, [83](#), [179](#), [185](#), [189](#), [190](#), [192–193](#)

帕金森氏症, 83, 179, 185, 189, 190, 192–193

Parsley, Kirk, [352–354](#)

歐芹, 柯克, 352–354

Pasteur, Louis, [26](#), [26n](#)

路易斯·巴斯德, 26, 26n

PCSK9 inhibitors, [129–130](#), [138](#)

PCSK9 抑制劑, 129–130, 138

PD-1, [161](#), [162](#)

pembrolizumab (Keytruda), [161](#)

派姆單抗 (Keytruda), 161

Perel, Esther, [50](#), [390](#), [392](#), [397](#)

埃絲特·佩雷爾, 50, 390, 392, 397

performance-based esteem, [394](#), [397](#), [410](#)

基於績效的尊重, 394, 397, 410

Perls, Thomas, [63](#), [64](#), [65](#)

湯瑪斯·佩爾斯, 63, 64, 65

P. gingivalis, [203](#)

牙齦卟啉單胞菌, 203

physical stamina. *See* [cardiorespiratory fitness](#)

體力。查看心肺健康

PI3-kinases (PI3K), [152–154](#)

PI3 激酶 (PI3K), 152–154

PI3K inhibitors, [154–155](#), [156](#)

PI3K 抑制劑, 154–155, 156

Pittsburgh Sleep Quality Index, [367–368](#), [367n](#)

匹茲堡睡眠品質指數, 367–368, 367n

plant-based protein, [333](#)

植物蛋白, 333

platinum-based chemotherapy, [163](#)

鉑類化療, 163

Plato, [180–181](#)

柏拉圖, 180–181

polyunsaturated fatty acids (PUFA), [335–336n](#), [335–340](#), [337n](#)

多元不飽和脂肪酸 (PUFA), 335–336n, 335–340, 337n

Pott, Percival, [297n](#)

珀西瓦爾·波特, 297n

Prasad, Vinay, [163](#)

普拉薩德, 維奈, 163

prediabetes. *See* [insulin resistance](#)

糖尿病前期。參見胰島素抗性

PREDIMED (PREvención con Dieta MEDiterránea) study, [304–306](#), [305n](#)

PREDIMED (PREvención con Dieta MEDiterránea) 研究, 304–306, 305n

prostate cancer, [147](#), [167](#), [168–169](#)

攝護腺癌, 147, 167, 168–169

protein (dietary), [17](#), [318](#), [329–334](#), [330n](#)

蛋白質（膳食）, 17, 318, 329–334, 330n

protein aggregates, [83](#)

蛋白質聚集體, 83

protein supplements, [333–334](#)

蛋白質補充劑, 333–334

PSEN1 mutation, [182](#), [185](#)

PSEN1 突變, 182, 185

psychedelics, [399](#)

迷幻藥, 399

Psychological Counseling Services, [397–399](#), [400](#)

心理諮商服務, 397–399, 400

PTEN gene, [145–146](#), [152](#)

PTEN 基因, 145–146, 152

pulling motions, [258](#), [261–262](#)

拉動, 258, 261–262

Q

Quviviq (daridorexant), [365–366](#)

Quviviq (daridorexant) , 365–366

R

race car analogy, [266–267](#), [277–278](#), [284](#)

賽車類比, 266–267, 277–278, 284

randomized controlled trials, [50–51](#), [54–55](#)

隨機對照試驗, 50–51、54–55

Rano Kau, [75](#)

拉諾·考, 75 歲

rapamycin, [74–79](#), [77n](#), [83–87](#)

雷帕黴素, 74–79, 77n, 83–87

Rapa Nui (Easter Island), [73–76](#), [87n](#)

拉帕努伊（復活節島），73–76, 87n

reactive oxygen species (ROS), [120–121](#)

活性氧 (ROS), 120–121

Real, Terrence, [377](#), [390–392](#), [404](#)

雷亞爾, 特倫斯, 377, 390–392, 404

Reaven, Gerald, [93–94](#), [109](#)

傑拉爾德·雷文, 93–94, 109

rectal cancer, [153](#), [167](#), [169–171](#), [169–171nn](#)

直腸癌, 153, 167, 169–171, 169–171nn

red meat, [299–300](#)

紅肉, 299–300

reframing, [392–394](#), [404](#)

重構, 392–394, 404

renal (kidney) cancer, [152](#), [153](#), [159](#), [159n](#)

腎癌, 152, 153, 159, 159n

resilience of centenarians, [72](#)

百歲老人的韌性, 72

résumé virtues, [394](#)

簡歷美德, 394

resveratrol, [78–79](#)

白藜蘆醇, 78–79

Rintala, Michael, [271](#), [276n](#)

邁克爾林塔拉, 271, 276n

risk assessment, [22–25](#), [53–55](#)

風險評估, 22–25, 53–55

The Road to Character (Brooks), [394](#)

品格之路（布魯克斯），394

Rosenberg, Steve, [140–142](#), [145](#), [156](#), [158–160](#), [320](#)

史蒂夫·羅森伯格, 140–142, 145, 156, 158–160, 320

rosuvastatin (Crestor), [137–138](#)

瑞舒伐他汀（Crestor），137–138

Roth, Martin, [181](#), [184](#), [194](#)

馬丁·羅斯, 181, 184, 194

Rowley, Theresa, [60](#)

特里薩羅利, 60 歲

rucking (carrying heavy stuff), [256–257](#), [405–406](#)

搬運（搬運重物），256–257, 405–406

S

Sabatini, David, [74–75](#), [76–78](#)

大衛·薩巴蒂尼，74–75、76–78

Sagan, Carl, [88](#)

卡爾·薩根，88

San Millán, Iñigo, [237–239](#), [240](#), [241](#), [242n](#), [243–244](#)

聖米蘭，伊尼戈，237–239, 240, 241, 242n, 243–244

saturated fatty acids (SFA), [118](#), [133](#), [133n](#), [335–336n](#), [335–340](#)

飽和脂肪酸 (SFA)、118、133、133n、335–336n、335–340

saunas, [204](#)

桑拿房, 204

scientific method, [27](#)

科學方法，27

Sehgal, Aji, [75–76](#)

阿吉·塞加爾，75–76

Sehgal, Suren, [75–77](#), [87n](#)

蘇倫·塞加爾，75–77, 87n

“self-driving” car analogy, [30](#)

「自動駕駛」汽車類比, 30

self-talk, [395](#), [403–404](#)

自言自語, 395, 403–404

Semmelweis, Ignaz, [26–27](#)

伊格納茲·塞梅爾維斯, 26–27

Seneca, [403](#)

塞內卡, 403

“senile dementia,” [181](#)

「老年癡呆症」181

sensitivity, [167–168](#)

靈敏度, 167–168

Shakespeare, William, [181](#), [403](#)

威廉·莎士比亞, 181, 403

shame, [391](#), [397](#), [404](#)

恥辱, 391, 397, 404

Shulman, Gerald, [97](#), [100](#)

傑拉德·舒爾曼, 97, 100

sleep, [349–376](#)

睡眠, 349–376

background, [349–352](#)

背景, 349–352

brain health and, [359–364](#)

大腦健康, 359–364

cardiovascular disease and, [358–359](#)

心血管疾病和, 358–359

conclusion, [376](#)

結論, 376

continuous glucose monitoring during, [327](#), [329](#), [330](#)

期間連續血糖監測, 327, 329, 330

emotional health and, [361–362](#), [401](#)

情緒健康, 361–362, 401

environment for improving, [369–374](#)

改善環境, 369–374

importance of, [47](#), [202–203](#), [352–354](#)

的重要性, 47, 202–203, 352–354

insomnia, [363](#), [365–366](#), [373](#), [376](#)

失眠, 363, 365–366, 373, 376

length of sleep cycle, [354–355](#)

睡眠週期長度, 354–355

medications for, [364–367](#)

藥物, 364–367

metabolic dysfunction and, [356–358](#)

代謝功能障礙, 356–358

overview, [49](#)

概述, 49

process for improving, [321](#), [367–369](#)

改進過程, 321, 367–369

rules for, [374–375](#)

規則, 374–375

stages of, [360–362](#), [362n](#)

階段, 360–362, 362n

sleep apnea, [369](#), [369n](#)

睡眠呼吸中止症, 369, 369n

sleep opportunity, [375](#)

睡眠機會, 375

sleep questionnaires, [367–368](#), [367n](#), [368n](#)

睡眠問卷, 367–368、367n、368n

sleep restriction, [373](#), [376](#)

睡眠限制, 373, 376

smoking, [59–60](#), [61](#), [120–121](#), [125–126](#), [133](#), [196](#)

吸菸, 59–60, 61, 120–121, 125–126, 133, 196

Sniderman, Allan, [114](#), [118–119](#), [136](#)

艾倫·斯尼德曼, 114, 118–119, 136

soda, [60](#), [107](#), [109](#), [109n](#), [292–293](#)

蘇打水, 60, 107, 109, 109n, 292–293

“soft” plaques, [124](#), [124n](#), [125](#)

「軟」斑塊, 124、124n、125

specificity, [167–168](#)

特異性, 167–168

spontaneous remission, [140–142](#), [158–159](#), [164](#)

自發性緩解, 140–142, 158–159, 164

stability training

穩定性訓練

background, [263–265](#)

背景, 263–265

breathing, [272–277](#), [276n](#)

呼吸, 272–277, 276n

caveats, [271–272](#), [283–284](#)

注意事項, 271–272、283–284

exercises, [261–262](#), [268–271](#), [269](#), [277–287](#)

練習, 261–262, 268–271, 269, 277–287

importance of, [265–268](#)

的重要性, 265–268

overview, [236](#)

概述, 236

power of, [287–290](#)

的幂, 287–290

preparation overview, [236](#)

準備概述, 236

slow down to go fast with, [284](#)

慢下來快走, 284

stability defined, [266](#)

穩定性的定義, 266

trainers and, [283–284](#)

培訓師和, 283–284

Standard American Diet (SAD), [308–311](#), [326–327](#)

標準美國飲食 (SAD), 308–311, 326–327

Stary, Herbert C., [119](#)

斯塔里, 赫伯特·C., 119

statins, [133–134](#), [136–139](#), [305](#), [305n](#)

他汀類藥物, 133–134, 136–139, 305, 305n

step-up exercise, [285–287](#)

升級練習, 285–287

stomach cancer, [140–142](#), [153](#)

胃癌, 140–142, 153

STOP-BANG questionnaire, [369](#), [369n](#)

STOP-BANG 問卷, 369, 369n

strength training

肌力訓練

background, [216–218](#), [252–253](#)

背景, 216–218, 252–253

benefits of, [201–202](#), [223–228](#), [254–256](#)

201–202、223–228、254–256 的好處

foundation training, [255–262](#)

基礎訓練, 255–262

overview, [236](#)

概述, 236

power of, [287–290](#)

的幂, 287–290

preparation overview, [236](#)

準備概述, 236

protein consumption and, [330](#), [330n](#)

蛋白質消耗量和, 330, 330n

Streptomyces hygroscopicus, [75](#)

吸水鏈黴菌, 75

stress, [202–203](#), [327](#), [329](#), [330](#), [357–358](#), [373](#), [374–375](#)

壓力, 202–203, 327, 329, 330, 357–358, 373, 374–375

stroke (cerebrovascular disease), [63](#), [112–113](#), [195–196](#), [224](#)

中風（腦血管疾病）, 63, 112–113, 195–196, 224

Stromsness, Michael, [269–270](#), [271](#), [284](#)

邁克爾·斯特羅姆斯內斯, 269–270, 271, 284

substance-abuse crisis, [381–382](#)

藥物濫用危機, 381–382

suicide, [381–382](#), [400](#)

自殺, 381–382, 400

Sun Tzu, [36](#), [41](#)

孫子, 36, 41

sympathetic nervous system, [272](#)

交感神經系統, 272

“Syndrome X,” [94](#)

“X綜合症”[94](#)

T

TAME (Targeting Aging with Metformin) trial, [87](#)

TAME（二甲雙胍抗衰老）試驗，[87](#)

Tanchou, Stanislas, [209](#)

坦丘，斯坦尼斯拉斯，[209](#)

tasks of daily living, [46](#), [64](#), [231–234](#), [401](#)

日常生活任務，[46](#), [64](#), [231–234](#), [401](#)

tau, [182](#), [183](#), [184](#), [362–363](#)

鈦，[182](#), [183](#), [184](#), [362–363](#)

Taylor, Linda, [159](#)

泰勒琳達，[159](#)

T cells, [158–161](#), [163–164](#)

T細胞，[158–161](#)、[163–164](#)

Teagno, Lorie, [390](#), [392](#), [397](#)

洛瑞·蒂格諾，[390](#), [392](#), [397](#)

Templeton, John, [235](#)

約翰·坦普爾頓，[235](#)

Thatcher, Margaret, [140](#)

柴契爾夫人，瑪格麗特，140

“This Is Water” (Wallace), [393](#)

「這就是水」（華萊士），393

Thompson, Craig, [151](#)

克雷格湯普森，151

time-restricted eating (TR), [156–157](#), [309](#), [310–311](#), [340–346](#)

限時飲食 (TR)、156–157、309、310–311、340–346

Tithonus, [10](#), [63](#)

提托努斯, 10, 63

TNF-alpha, [198](#)

腫瘤壞死因子- α ，198

toe yoga, [278–279](#), [279n](#)

腳趾瑜伽，278–279, 279n

Tomlinson, Bernard, [181](#), [184](#), [194](#)

伯納德·湯姆林森，181, 184, 194

TOR (target of rapamycin), [77n](#). *See also* [mTOR](#)

TOR（雷帕黴素靶點），77n。另請參見 mTOR

transcription factors, [69–70](#)

轉錄因子，69–70

The Transformed Cell (Rosenberg), [141](#)

轉化的細胞（羅森伯格），141

trauma, [384–388](#)

創傷, 384–388

Trauma Tree, [386](#), [387–388](#)

創傷樹, 386, 387–388

trazodone, [366](#), [366n](#)

曲唑酮, 366, 366n

triglycerides, [94](#), [98](#), [108](#), [126](#)

三酸甘油酯, 94, 98, 108, 126

Truman, Harry S., [111](#)

哈里·S·杜魯門, 111

tumor-infiltrating lymphocytes (TILs), [164](#), [164n](#)

腫瘤浸潤淋巴細胞 (TIL), 164, 164n

“tumor suppressor” genes, [146](#)

“腫瘤抑制”基因, 146

Tutu, Desmond, [7](#)

圖圖, 德斯蒙德, 7

type [2](#) diabetes

2型糖尿病

causes, [109](#)

原因, 109

as disease of civilization, [102](#), [209](#)

作為文明病, 102, 209

impact of, [152](#), [154](#), [196–197](#)

的影響, 152, 154, 196–197

Medicine 2.0's approach to, [13–14](#), [13n](#)

醫學 2.0 的方法, 13–14, 13n

risk factors, [72](#), [99](#), [102–103](#), [357](#)

風險因子, 72, 99, 102–103, 357

Tyson, Mike, [55](#)

麥克泰森, 55 歲

U

University of Wisconsin–Madison monkey study, [313–316](#), [314n](#)

威斯康辛大學麥迪遜分校猴子研究, 313–316, 314n

uric acid, [104–106](#), [108](#), [126](#)

尿酸, 104–106, 108, 126

US Airways emergency landing, [410–411](#)

全美航空緊急著陸, 410–411

V

Valium, [365](#)

安定, 365

van Cauter, Eve, [356–357](#), [358](#)

範考特, 夏娃, 356–357, 358

Vander Heiden, Matthew, [151](#)

范德海登, 馬修, 151

vascular dementia, [191](#), [196](#), [197](#)

血管性失智症, 191, 196, 197

vegan Standard American Diet, [308](#)

純素標準美國飲食, 308

very-early-onset Alzheimer's disease, [182](#)

極早發性阿茲海默症, 182

visceral fat, [98–100](#), [99](#), [126](#)

內臟脂肪, 98–100, 99, 126

vitamin B, [132n](#), [204](#)

維生素 B, 132n, 204

vitamin D, [204](#)

維生素 D, 204

VLDLs (very-low-density lipoproteins), [108](#), [117n](#), [131](#), [132](#), [137](#), [139](#)

VLDL（極低密度脂蛋白）、108、117n、131、132、137、139

VO₂ max, [220–221](#), [223](#), [244–252](#), [246](#), [250–251n](#), [250](#)

攝氧量₂ 最大、220–221、223、244–252、246、250–251n、250

W

Wallace, David Foster, [392–393](#)

大衛·福斯特·華萊士，392–393

Warburg, Otto, [149](#)

奧托·瓦爾堡，149

Warburg effect, [150](#), [151–152](#), [151n](#), [157](#)

瓦爾堡效應，150、151–152、151n、157

Watson, James, [150–151](#)

詹姆斯·沃森，150–151

weight training. *See* [strength training](#)

重量訓練。查看肌力訓練

Weinberg, Robert, [149](#)

羅伯特溫伯格，149

Weiss, Ethan, [342](#)

伊森·韋斯，342

Welles, Orson, [307](#)

威爾斯，奧森， 307

Whipple Procedure, [2](#)

惠普爾手術， 2

White, Andy, [401](#)

安迪懷特， 401

Whitehall II cohort study, [190](#)

白廳 II 隊列研究， 190

Wilkins, Maurice, [150](#)

莫里斯·威爾金斯， 150

Willcox, Bradley, [69](#)

威爾科克斯·布拉德利， 69

Women's Health Initiative (WHI), [303–304](#)

婦女健康倡議 (WHI)， 303–304

X

Xanax, [366](#)

阿普唑侖， 366

Y

Yassine, Hussain, [198](#)

侯賽因·亞辛, 198

Z

Zelman, Samuel, [90–91](#), [107](#)

塞繆爾·澤爾曼, 90–91, 107

zone 2 training, [237–244](#)

2 區訓練, 237–244

[A](#) [B](#) [C](#) [D](#) [E](#) [F](#) [G](#) [H](#) [I](#) [J](#) [K](#) [L](#) [M](#) [N](#) [O](#) [P](#) [Q](#) [R](#) [S](#) [T](#) [U](#) [V](#) [W](#) [X](#) [Y](#)
[Z](#)



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