

EXCERPT BOOKLET

OUTLIVE

THE SCIENCE & ART
OF LONGEVITY

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WITH BILL GIFFORD

RETHINKING MEDICINE TO LIVE BETTER LONGER



GREETINGS,

Thank you for your support and enthusiasm for my upcoming book: *OUTLIVE: The Science and Art of Longevity*. This book is the result of many years of research, writing, editing, rewriting, and re-editing, and to show my gratitude for your interest, I am excited to share with you a few select sections as an advanced preview.

This will almost certainly be the only book I write in my life, and in it I share the wisdom I've gained from the best and brightest in medicine, geroscience, and human performance, all of whom have provided me with the substrate to chart my own path into the world of human longevity. I've sought to synthesize the insights I've gathered into practical frameworks for the pursuit of a longer and better life, and *OUTLIVE* is the result of that effort.

My sincere hope is that through this book others may benefit from sharing in the knowledge that has changed how I approach my own health and that of my patients, and that it might guide readers on their own journeys toward a longer, healthier, and more fulfilling life. Providing you, my audience, with knowledge to benefit your life and health lies at the heart of what motivates me and my whole team, and this book would not have been possible without your continued interest in and enthusiasm for our work.

To give you even a small amount of gratitude for preordering, you'll see two different sections from *OUTLIVE* in this PDF, both of which have concepts that I believe are of paramount importance to extend your lifespan and healthspan.

- **Medicine 3.0:** In this section, you'll find a discussion of my approach to medicine, in which greater emphasis is placed on prevention of disease over treatment alone and on improving quality of life in addition to its duration. I explain the importance of treating each patient as a unique individual, and how risk—not only of doing something but also of not doing something—must be incorporated into each decision.
- **Centenarian Decathlon:** In this section, you'll read about my framework for helping patients approach their current physical fitness as the foundation for maintaining the physical abilities they wish to have in the later decades of their lives.

Thank you, again, for your preorder and I hope you enjoy the full version of *OUTLIVE* on March 28, 2023.

-PETER



TOWARD MEDICINE 3.0



Toward Medicine 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.

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.

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.

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.

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.

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.

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.

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.

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.

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.

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.

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.*

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.

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.

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?*

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.

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.*

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.

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.

Another, related issue is that longevity itself, and healthspan in particular, doesn't really fit into the business model of our current healthcare system.

* 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.

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.

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.”

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.

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.

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.

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.

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?

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.

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

THE CENTENARIAN DECATHLON



The Centenarian Decathlon

What in the world is the Centenarian Decathlon?

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.

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.

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.

I start by presenting my patients with a long list of physical tasks that might include some of the following:

1. Hike 1.5 miles on a hilly trail.
2. Get up off the floor under your own power, using a maximum of one arm for support.
3. Pick up a young child from the floor.
4. Carry two five-pound bags of groceries for five blocks.
5. Lift a twenty-pound suitcase into the overhead compartment of a plane.
6. Balance on one leg for thirty seconds, eyes open. (Bonus points: eyes closed, fifteen seconds.)
7. Have sex.

8. Climb four flights of stairs in three minutes.
9. Open a jar.
10. Do thirty consecutive jump-rope skips.

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?

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.

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?

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.

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.

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.

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:

11. Swim half a mile in twenty minutes.
12. Walk with a thirty-pound dumbbell in each hand for one minute.
13. Draw back and fire a fifty-pound compound bow.
14. Do five pull-ups.
15. Climb ninety steps in two minutes ($\text{VO}_2 \text{ max} = 32$).
16. Dead-hang for one minute.
17. Drive a race car within 5 to 8 percent of the pace I can do so today.
18. Hike with a twenty-pound backpack for an hour.
19. Carry my own luggage.
20. Walk up a steep hill.

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.

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, rac-

ing 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.

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.

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.

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.

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ON SALE 3.28.23



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