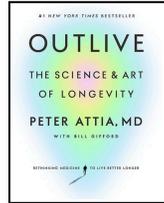


Your Kindle Notes For:



Outlive: The Science and Art of Longevity

Peter Attia MD and Bill Gifford

188 Highlight(s) | 0 Note(s)

Location: 254

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.

Location: 264

Unfortunately, in today's unhealthy society, “normal” or “average” is not the same as “optimal.”

Location: 270

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.

Location: 286

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).

Location: 298

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.

Location: 312

The time to repair the roof is when the sun is shining. —John F. Kennedy

Location: 389

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.

Location: 495

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.

Location: 586

Strategy without tactics is the slowest route to victory. Tactics without strategy is the noise before defeat. —Sun Tzu

Location: 610

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?

Location: 649

Moreover, when you do begin to decline, the descent is steep but relatively brief. This is called squaring the longevity curve.

Location: 652

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.

Blue highlight | Location: 662

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.

Location: 741

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.

Location: 766

In Medicine 3.0, our tactics must become interwoven into our daily lives. We eat, breathe, and sleep them—literally.

Blue highlight | Location: 779

We want to maintain physical strength, stamina, stability across a broad range of movements, while remaining free from pain and disability.

Location: 831

But our supporting framework must shift, from exclusively evidence-based to evidence-informed, risk-adjusted precision medicine.

Location: 903

The Older You Get, the Healthier You Have Been

Location: 938

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.

Location: 949

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

Location: 1,013

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.

Location: 1,108

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.

Location: 1,199

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.

Location: 1,264

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.

Location: 1,511

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.

Location: 1,526

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.

Location: 1,553

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 spillover.

Location: 1,568

Individual fat-storage capacity seems to be influenced by genetic factors.

Location: 1,579

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.

Location: 1,620

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.

Location: 1,637

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.

Location: 1,688

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.

Location: 1,718

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.

Blue highlight | Location: 1,722

These biomarkers help give us a clearer picture of a patient's overall metabolic health than HbA1c, which is not very specific by itself. But the first thing I look for, the canary in the coal mine of metabolic disorder, is elevated insulin.

Location: 1,751

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.

Location: 1,801

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).

Location: 1,899

“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.”

Location: 1,907

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.

Location: 1,950

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.

Location: 2,034

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.)

Location: 2,101

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]

Location: 2,182

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”? Then nobody is at low risk.

Location: 2,194

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.

Location: 2,202

“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:

Location: 2,214

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.

Location: 2,252

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.

Location: 2,255

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.

Location: 2,271

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.

Location: 2,325

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.

Location: 2,343

Our benchmark for success in a patient, or remission, is typically five-year survival, nothing more. We don't dare utter the word cure.

Location: 2,360

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.

Location: 2,364

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.

Location: 2,407

The game is won by killing cancers while sparing the normal cells. Selective killing is the key. Traditional chemotherapy occupies a fuzzy region between poison and medicine;

Location: 2,420

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).

Location: 2,460

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."

Location: 2,465

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]

Location: 2,473

The American Cancer Society reports that excess weight is a leading risk factor for both cancer cases and deaths, second only to smoking.

Location: 2,485

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.

Location: 2,502

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.

Location: 2,547

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.

Location: 2,617

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. All Nobel Prizes are impressive, but I'm pretty biased toward this one.

Location: 2,674

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.

Location: 2,718

Again, just as with immunotherapy treatment, it's a numbers game: the fewer cancerous cells we have, the greater our likelihood of success.

Location: 2,735

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.

Location: 2,740

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.

Location: 2,754

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.

Location: 2,777

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]

Location: 2,871

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.

Blue highlight | Location: 2,884

read Charles Graeber's 2018 book, Breakthrough, which goes into greater detail about Jim Allison's work with checkpoint inhibitors.

Location: 3,160

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.

Location: 3,190

Exercise is the only intervention shown to delay the progression of Parkinson's.

Location: 3,219

The key insight was that robust blood flow seemed to be critical to maintaining brain health.

Location: 3,220

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.

Blue highlight | Location: 3,227

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.

Location: 3,336

stress. 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

Location: 3,342

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.

Location: 3,346

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.)

Location: 3,354

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.

Location: 3,380

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).

Location: 3,394

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.

Blue highlight | Location: 3,397

Broadly, our strategy should be based on the following principles: 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. WHAT’S GOOD FOR THE LIVER (AND PANCREAS) IS GOOD FOR THE BRAIN. Metabolic health is crucial to brain health. 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. 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.

Location: 3,418

Absorb what is useful, discard what is useless, and add what is specifically your own. —Bruce Lee

Location: 3,430

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.

Location: 3,440

Our genes no longer match our environment.

Location: 3,459

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?

Location: 3,485

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.

Location: 3,522

We range widely and pick and choose and test tactics that will hopefully work for us. We are open to changing our minds.

Blue highlight | Location: 3,525

We adapt our tactics on the basis of our changing needs and our changing understanding of the best science out there.

Location: 3,526

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.

Location: 3,535

I never won a fight in the ring; I always won in preparation. —Muhammad Ali

Location: 3,557

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.

Blue highlight | Location: 3,565

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.

Location: 3,596

It turns out that peak aerobic cardiorespiratory fitness, measured in terms of VO2 max, is perhaps the single most powerful marker for longevity.

Location: 3,618

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 VO2 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.

Location: 3,649

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.”

Location: 3,653

But I can say with a very high degree of certainty that having a higher VO2 max is better for your overall health and longevity than having a lower VO2 max. Period.

Location: 3,669

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.

Location: 3,688

The data demonstrating the effectiveness of exercise on lifespan are as close to irrefutable as one can find in all human biology.

Location: 3,709

Muscle helps us survive old age. 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.

Location: 3,717

Eight hundred thousand older people are hospitalized for falls each year, according to the CDC.

Location: 3,724

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.

Location: 3,773

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.

Location: 3,783

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.

Location: 3,839

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.

Location: 3,846

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.

Location: 3,872

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.)

Location: 3,882

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.

Location: 3,898

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.

Location: 3,953

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.

Location: 3,985

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.

Location: 4,010

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.

Location: 4,017

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.

Location: 4,039

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.

Location: 4,068

Keep in mind, increasing your VO₂ 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 VO₂ 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.

Location: 4,088

Our goal is to become elite athletes of aging.

Location: 4,090

One study found that boosting elderly subjects' VO₂ max by 6 ml/kg/min, or about 25 percent, was equivalent to subtracting twelve years from their age.

Location: 4,146

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.

Location: 4,161

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.

Location: 4,168

it is very difficult to put on muscle mass later in life.

Location: 4,206

This frames how I view strength training in general. It's largely about improving your ability to carry things.

Location: 4,215

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;

Location: 4,225

(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.)

Location: 4,253

Grip strength is important at all ages.

Location: 4,255

If our grip is weak, then everything else is compromised.

Location: 4,269

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.)

Location: 4,358

All of the above, the research and my own experience, support my first commandment of fitness: First, do thyself no harm. How do we do this? I think stability is the key ingredient.

Location: 4,373

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.

Location: 4,377

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.

Location: 4,392

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.

Blue highlight | Location: 4,433

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.

Blue highlight | Location: 4,459

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.” —

Location: 4,466

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.

Blue highlight | Location: 4,471

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.

Location: 4,535

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.

Location: 4,545

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]

Location: 4,565

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.

Location: 4,605

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.)

Location: 4,669

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.

Location: 4,839

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.

Location: 4,867

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).

Blue highlight | Location: 4,872

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.

Location: 4,902

The problem is that epidemiology is incapable of distinguishing between correlation and causation.

Location: 5,006

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.

Location: 5,009

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.

Blue highlight | Location: 5,011

Most people confuse these and therefore fail to appreciate this nuance of clinical trials.

Location: 5,222

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.

Location: 5,294

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.

Location: 5,296

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? Let's now look at each of the four macronutrients in more detail.

Location: 5,331

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.

Location: 5,363

It's currently fairly easy for a nondiabetic to obtain a CGM from one of several online metabolic health start-ups.

Location: 5,388

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.)

Location: 5,430

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.

Location: 5,461

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.

Location: 5,472

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.

Location: 5,524

You could make the case that protein is a performance-enhancing macronutrient.

Location: 5,532

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.

Location: 5,614

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.

Location: 5,686

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.

Location: 5,726

moving our thinking toward a Nutrition 3.0 mindset, based on feedback and data rather than labels and trends and ideology.

Location: 5,730

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.

Location: 5,739

Protein is actually the most important macronutrient, the one macro that should not be compromised.

Location: 5,747

(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.)

Blue highlight | Location: 5,749

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.

Location: 5,866

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.

Location: 5,885

evolutionarily, sleep is non-negotiable.

Location: 5,889

We now know that sleep is as fundamental to our health as stability is fundamental to strength.

Location: 5,899

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.

Location: 5,906

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]

Location: 5,938

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.

Blue highlight | Location: 5,942

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.

Location: 5,947

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.

Location: 5,976

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.

Location: 6,024

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.

Location: 6,164

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,

Location: 6,184

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.

Location: 6,200

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.

Location: 6,206

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.

Location: 6,226

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).

Blue highlight | Location: 6,235

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.

Location: 6,316

Every man is a bridge, spanning the legacy he inherited and the legacy he passes on.
—Terrence Real

Location: 6,400

The substance-abuse crisis has created a longevity crisis, because it is really a mental health crisis in disguise.

Location: 6,478

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.

Location: 6,480

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?

Location: 6,614

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.

Location: 6,687

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."

Location: 6,723

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.

Location: 6,757

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."

Location: 6,847

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.