STRONGER AFTER 50

Building a Healthier Lifestyle

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Stronger After 50: Building a Healthier Lifestyle

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A Note Before You Start

Ten weeks. That's how long it took the lifters in a study of a hundred nursing home residents, average age eighty-seven, to more than double the strength in their legs. Some of them were in their nineties. Nobody handed them a peptide or optimized their hormones. They lifted weights three times a week, in a trial published in the New England Journal of Medicine in 1994, and their bodies did what bodies do at any age when you give them a reason.

I've owned health clubs for more than thirty years, and I've watched that happen to people in their sixties and seventies more times than I can count. I've also watched the opposite, which is most people. They get to fifty, decide their body is a car with too many miles on it, and drive it gently to the scrapyard. This book is about the first group, and what separates them from the second isn't genetics, money or willpower. It's two things that cost almost nothing, and a way of thinking about everything else that I'm going to teach you.

I'm not a doctor. A lot of what's in this book touches on things you should not do without a medical professional involved, and I'll say so every time.

Here's what I am. I'm sixty-four years old. I've been lifting weights since I was about twelve. I've owned health clubs for more than thirty years. Parkway Athletic Club has six Northern Nevada locations at the time I'm writing this, and my companies own and run four of them, in South Reno, Downtown Reno, Sparks and Carson City. Fernley and Fallon are affiliated clubs. I have an MBA in finance, which has nothing to do with your bench press but has everything to do with how I read a study, because finance teaches you to look at the number behind the claim and ask who's selling what.

And I experiment on myself constantly. I check my glucose twice a day and my blood pressure and my pulse multiple times a day. I get full blood work every month, not every year, and everything

that goes in my mouth gets logged into an app. I'm in the gym at least an hour and a half, at least five days a week. I weigh about 175 pounds and I run between 12 and 14% body fat.

So when I tell you something worked for me, I'm not guessing. I have the labs. They show me what changed, even when they can't prove why.

Where I'm coming from

This book is written from a functional and holistic point of view. That phrase gets used loosely, so here's what I mean by it.

I mean that I'm more interested in why something is happening than in what to name it. When somebody's blood pressure is up and their A1c is drifting and they're exhausted and they're carrying forty extra pounds, I don't see four problems. I see one system that's been getting the wrong inputs for twenty years, showing up in four places.

I mean that the body is connected. Your gut affects your immune system, your sleep affects your hormones, your muscle mass affects your blood sugar and your stress affects your gut.

I mean that the person matters more than the average. I spend an entire chapter on why that's a rigorous position and not a lazy one, because it's the idea this whole book stands on.

I don't mean that science is the enemy. You'll find hundreds of studies cited in here. What I mean is that research gives you base rates and starting points, and it very often doesn't describe the specific person standing in your shoes. I'll show you how often, with numbers, in Chapter 2.

A few more things you should know going in

I changed my mind about a lot of stuff. When I started personal training, I gave everybody advice through the lens of my own body. I told people not to eat avocados and to avoid fat. Some of these people were forty years older than me and had completely different physiology. I was confidently wrong. If you catch me

contradicting something I said in a video three years ago, you probably caught me correcting an error.

I checked the research for this book, and some of it embarrassed me. There are claims I've repeated on my channel that don't hold up as well as I thought. There are also things my own camp believes that don't survive contact with the evidence, and I've named those too, because a book that only criticizes the other side isn't worth reading. There's a whole chapter near the end listing what I got wrong.

The peptide chapters are going to be more careful than you expect. I talk about peptides publicly and I've used them. But there's a difference between a drug that's been through phase 3 trials with twenty thousand people and a powder that some website will ship you in an unmarked envelope with "research use only" printed on the label. I'm going to keep those two separated, because the sloppiest thing happening in this space right now is people treating them like they're the same.

Nothing here is a prescription. That goes for the training, the food, and absolutely the drugs. Talk to your doctor. If you don't like what your doctor says, go get a second opinion from someone who specializes in what you're asking about. But go get one. Don't just take the advice of a guy on YouTube, including me.

Where to start. You don't have to read this book in order. If you want to get moving this week, read Chapter 5 for the two non-negotiables, Chapter 8 for how to train and Chapter 16 for the protein rule. Then go straight to Chapters 52 to 54: a week of training, a day of eating and your first 90 days. The supplement, hormone and peptide chapters are there when you want them. They come after the basics, not before. If you have kidney disease, take diabetes medication, have fallen recently or have a painful tendon, read Chapters 19, 22, 13 and 14 first.

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Every chapter stands on its own. If you only read three, make them Chapter 2, Chapter 5 and Chapter 56.

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PART I — THE GROUND RULES

Chapter 1 — Everyone Is Different (And Why That's Not a Cop-Out)

I'm starting here because if you get this one wrong nothing else in the book will help you, and almost everybody gets it wrong.

Go on social media right now and search anything about diet. You'll find a thousand people telling you, with total certainty, that you must eat carbs, and a thousand more telling you, with equal certainty, that carbs are killing you. You'll find people who say fasting fixed their life and people who say fasting wrecked their hormones.

It took me thirty years to fully understand that most of them are telling the truth. They're telling the truth about themselves, and that's the problem. They found something that worked in their body, and because it worked so well, they assumed it was a law of nature instead of a fact about them.

This is not the soft version of that claim

"Everyone is different" is what people say when they don't want to be pinned down. That's not what I mean. I mean something specific and measurable, and there's hard science behind it.

Researchers in Israel took 800 people, put continuous glucose monitors on them, and recorded about 1.5 million glucose measurements across nearly 47,000 meals (Zeevi and colleagues, Cell, 2015). Then they gave everybody the same standardized piece of bread, an identical 50 grams of carbohydrate.

The average blood sugar response was 44. That number is the extra glucose above baseline over the two hours after eating, measured in mg/dL-hours. The bottom tenth of people averaged under 15. The top tenth averaged above 79.

That's more than a five-fold spread in response to the exact same food.

And this wasn't noise. When they repeated the same meal in the same person, the response was highly reproducible. The variation between people is real signal.

A bigger study out of the UK (PREDICT 1, over a thousand people, published in Nature Medicine in 2020) found the same thing across the board. Between-person variation in response to identical meals: triglycerides 103%, glucose 68%, insulin 59%.

The part that surprised me is what explained that variation:

What explained the response	Blood fat	Blood sugar
The meal itself	3.6%	15.4%
Gut microbiome	7.1%	6.0%
Genetics	0.8%	9.5%

Genetics explained under 1% of the fat response and under 10% of the glucose response.

That finding cuts two ways. It supports personalization, because the differences between people are large and real, and general advice averages them away.

And it cuts hard against genetic testing as the way to personalize. If your DNA explains under 10% of how you respond to a meal, a spit-kit is not going to tell you what to eat.

You don't find out about yourself by reading a gene panel. You find out by measuring yourself.

What "everyone is different" actually means

It doesn't mean nothing is knowable. That's the lazy version. A better way to think about it is in three tiers.

Tier one: things that are true for basically everybody. Resistance training builds strength at every age that's been tested, including in ninety-year-olds in nursing homes. Protein is required to build and keep muscle. Cardiorespiratory fitness tracks with how long you live. Sleep matters.

Tier two: things that are true on average but vary enormously person to person. That covers how many carbs you tolerate, how you respond to fasting and how much training volume you recover from. The average tells you where to start. It doesn't tell you where you'll end up.

Tier three: things nobody knows yet. That's way more of this field than anybody admits, especially in supplements and peptides. We'll get there.

Most of the screaming online is people from tier two acting like they're in tier one.

The nutritionist conversation

I had a nutritionist named Nicole on my channel a while back, and she said something that stuck with me. I asked her: what's the first thing you say to somebody who tells you they need to go on a diet?

She said: "It's all of them and none of them."

Somebody comes to her having done carnivore for thirty days with no weight loss, feeling like they failed. But maybe carnivore is wrong for that person. She doesn't start with the diet. She starts with what's going on in the body. Is there an autoimmune condition or a thyroid problem? Are they absorbing nutrients at all? Is there fatty liver in somebody who doesn't drink, or perimenopause with hormones all over the place? You can't take a woman whose immune system is attacking her thyroid and put her on the same plan as a forty-year-old guy with a clean panel and expect the same result.

That's not mysticism. That's paying attention to the person in front of you instead of the average of ten thousand people who aren't in the room.

So what do you do with this?

You run experiments on yourself, and you run them properly. That means:

One change at a time. If you start creatine, drop your carbs, add a fasting window and change your training split all in the same week, and you feel different, you've learned nothing. You don't know which one did it.

Long enough to matter. Two weeks minimum for most dietary changes. Eight to twelve weeks for training changes. Your body doesn't reorganize itself in four days.

Measured, not remembered. Your memory of how you felt last month is fiction. Write it down.

With actual data where you can get it. That means blood work, body composition, numbers in the gym and blood pressure. It doesn't mean the mirror, the scale by itself, or vibes.

The formal name for this is an n-of-1 trial, and it's a legitimate research methodology with an entire government manual written about it. Some evidence hierarchies rank a well-conducted n-of-1 trial above a randomized controlled trial for making a decision about one specific person, because it was run on that person.

The one thing I'll be dogmatic about

There are exactly two things in this book I'm going to tell you are non-negotiable: lift weights and eat enough protein. Those two are tier one, and we have data going back decades in populations from twenty-year-old athletes to ninety-six-year-old nursing home residents. I'll show you that data in Chapter 5. Everything else, including the diet style, the cardio format, the supplements and the timing, is yours to test.

Chapter 2 — Why the Research Might Not Be About You

I'm going to spend the next two hundred pages citing trials at you. So I need to tell you up front what those trials can and can't do, because the single biggest mistake people make with health research is assuming that a finding from a study is a finding about them. Most of the time it isn't, and I can prove that with numbers.

The people in the trials are not the people reading this book

Researchers went through 305 randomized controlled trials across 31 different physical conditions and calculated what percentage of real-world patients with those conditions would have been excluded from the trials meant to treat them (Trials, 2020).

The median exclusion rate was 77.1%.

In the typical trial, more than three out of four actual patients with the condition would not have been allowed in the study.

It gets worse when you look at the details:

- About one in four trials excluded more than 90% of patients.
- More than half excluded at least 75%.
- Four out of five excluded at least half.
- Asthma trials excluded 96% of real asthma patients. COPD, 84%. Hypertension, 83%. Type 2 diabetes, 82%.

And what got you excluded? The top three reasons:

- Having another medical condition: 68.4% of trials
- Your age: 49.4% of trials
- Taking other medications: 32.2% of trials

The authors' own conclusion was that most people with any of the conditions studied would be excluded from most trials treating those conditions.

Specifically about your age

A systematic review published in JAMA in 2007 sampled 283 randomized trials from the highest-impact medical journals in the world.

- 72.1% excluded people on the basis of age.
- 38.5% specifically excluded older adults.
- Conditions related to being female were grounds for exclusion in 39.2%.
- Only 47.2% of those exclusions were even strongly justified.

A larger review of 4,341 trials in the four best medical journals found that 29% had an upper age limit, and 93% of those gave no reason for it.

Put that together

Picture a woman of sixty-four. She has high blood pressure that's controlled on a medication and some arthritis in one knee. Her kidney function is a little below where it was at forty. She takes four prescriptions.

She would have been excluded from most of the trials that generated the guidelines being used to treat her. That's not because anybody was careless. Trials are designed to isolate one variable, and the way you do that is by removing everything that complicates it. Comorbidity, age and other medications all complicate it.

The clean answer you get from a clean trial is an answer about clean people. And after fifty, almost nobody is clean.

This isn't a conspiracy theory or anti-science. Every number in this chapter comes from mainstream medical journals, published

by researchers who believe in clinical trials, pointing out a structural limitation of their own field.

The average hides both the benefit and the harm

There's a second, deeper problem. When a trial reports a result, it reports an average, and the average can be actively misleading about what happens to any individual person in it.

Suppose a treatment cuts everybody's risk by the same percentage. Your actual benefit still depends on how much risk you had to begin with, and if the treatment carries any harm at all, the people at low risk can come out behind while the people at high risk come out well ahead. The average across both groups describes neither of them.

In one real heart disease trial, RITA-3, the highest-risk eighth of patients had about eight times the event rate of the lowest-risk quarter and got substantial benefit. The lowest-risk groups got nothing meaningful. The published result was one number, and it concealed that completely.

That's not a flaw in that study. That's true of nearly every trial ever run, and it's almost never reported.

What "evidence-based" was supposed to mean

You'll hear that if something hasn't been proven in a randomized trial it isn't real, and that this is what "evidence-based medicine" means. It isn't. David Sackett, the man who defined the term in the BMJ in 1996, defined it as the best external evidence combined with the clinician's judgment and the patient's own values, and he wrote plainly that the evidence may simply not apply to the person in front of you. Eighteen years later three insiders published a paper in the same journal titled "Evidence based medicine: a movement in crisis?" Their prescription was individualized evidence, shared decisions, and judgment over rule-following. That is the argument my side of the fence has been making for thirty years. It just happens to be in the BMJ.

The version that means “if it’s not in a trial it doesn’t count” is a caricature. When somebody uses it to dismiss what you’ve observed in your own body, they’re being lazy in a way that sounds rigorous.

What I actually want you to take from this

I don’t want you to take from this that research is worthless. I’m citing hundreds of studies in this book and I believe in them. Research gives you base rates, and it’s the best starting point available. It is not a verdict about you.

And I’ll go one step further, because this is what I believe: too much deference to the average will hold you back. I’ve watched it happen. Somebody feels terrible, gets a panel back, and gets told everything is normal, so they stop looking. Somebody’s told at sixty that they should stick to light weights because that’s what the guidance says for their age group. Somebody gets told there’s no evidence for what they’re experiencing, when what’s true is that nobody has studied it in people like them.

Absence of evidence is not evidence of absence. Most of the time it just means nobody ran the trial, or ran it in a population you don’t belong to.

One limit on all of this, because it’s the obvious way to misuse it

“Nobody has studied this in people like me” is a reason to run your own experiment. It is not a reason to inject something. The difference is what happens if you’re wrong.

If I try a diet for six weeks and it doesn’t work, I’ve lost six weeks and I have the labs to prove it. If I change my training and it makes my elbow hurt, I stop, and I’ve learned something. Both are cheap and reversible, and I find out.

If I take a compound with no toxicology data, no known therapeutic window, and no biomarker anybody can name to watch, then there is no mechanism by which I find out I was wrong until something has already happened to me.

Absence of evidence buys you room to experiment in proportion to how cheaply and how quickly you could discover you were mistaken. That's a lot of room for food, light, sleep and training, and almost none for an unidentified powder from a website.

In Part V you'll watch me apply that rule hard against things I've used myself and against people I agree with.

And there's a companion rule that arrives in the next chapter and does most of the work: skepticism about the average is earned by being rigorous about yourself.

So here's the posture

Neither "the studies say so, therefore" nor "I don't trust studies." It's this:

Start where the evidence points. Then measure what actually happens in you. When those two disagree, you are the one standing in your body.

Chapter 3 — Root Cause, Not Symptom

Here's a story I've watched a hundred times in thirty years of owning gyms.

Somebody comes in at fifty-eight, carrying forty extra pounds. They're on a blood pressure medication, a statin, something for reflux, and they've just been told their A1c is creeping up, so there's a fourth prescription coming. They're tired all the time and sleeping badly. Their doctor gave them twelve minutes and a printout.

Every one of those prescriptions is treating a number. Not one of them is treating why the numbers moved. That's the whole argument of this chapter.

The system is good at the wrong thing

I'm not interested in doctor-bashing. Modern medicine is extraordinary at acute care. If I have a heart attack tonight, I want a cardiologist and a cath lab, not a smoothie. Emergency medicine, trauma, infectious disease and surgery are genuine triumphs, and anyone who tells you otherwise is selling something.

It is structurally bad at chronic disease. That's not because doctors are bad. It's because the model is built for something else.

A fifteen-minute visit optimized for coding and prescribing cannot deliver behavior change. Physicians get very little training in nutrition or exercise. Reimbursement flows toward procedures and prescriptions, not toward the forty-five-minute conversation about why somebody isn't sleeping. And nobody's actual job, in the sense of being paid and measured for it, is keeping you well.

That's not a fringe complaint. That's the health services research consensus, and even people who are sharply critical of functional medicine concede this point.

What “root cause” actually means

The functional framework says: don’t start with the diagnosis. Start with the person and work backward.

The Institute for Functional Medicine, founded in 1991 by the biochemist Jeffrey Bland, organizes it into three questions:

Antecedents. What predisposed this person? Genetics, family history, what happened to them early in life.

Triggers. What kicked it off? An infection, an injury, a divorce, a job change, a course of antibiotics, a period of terrible sleep.

Mediators. What’s keeping it going? Inflammation, a disrupted gut, chronic stress hormones, poor sleep, not enough muscle.

Then it looks across systems instead of one organ at a time: how you digest, how you make energy, how you clear things out, how the parts talk to each other. Underneath all of it are the five inputs that move the needle: sleep, movement, food, stress, and who you spend your time with.

That framework has never been validated as a diagnostic instrument, and it doesn’t need to be. It’s a way of taking a proper history. The pieces of it that matter (that the systems are connected, that lifestyle is the biggest lever, that you have to look at the whole timeline) are things basically nobody disputes.

What the outcome data actually shows

The Cleveland Clinic opened a Center for Functional Medicine in 2014, and in 2019 they published results in JAMA Network Open (Beidelschies and colleagues).

They matched functional medicine patients to conventional primary care patients at the same institution. At six months the functional medicine group was doing better on physical and mental health scores, by a small but real margin. At twelve months the difference was gone. And the initial functional visits ran 60 to 75 minutes against a conventional visit a fraction of that length, so the study cannot separate “functional medicine” from

"more time with a clinician." A follow-up found that group appointments worked at least as well as individual ones, at lower cost.

Most people in my camp skip past what that means. The likeliest explanation for both results is that time, relationship and accountability change behavior, which is a well-established finding in behavioral medicine and has nothing to do with any supplement protocol. That doesn't bother me at all. If the mechanism is "spend more time with people and hold them accountable," that's the finding, and it's a good one. Keep the delivery model and the content separate in your head and you keep your credibility.

The single best example of root-cause thinking

Josh Holyfield put something in a video that I thought was the clearest version of this idea I've heard.

Before I quote him, this book has a rule about conflicts and I'm not going to exempt somebody I agree with. He's a content creator, not a clinician or a researcher, and at the time I'm writing he has commercial interests in the supplement and peptide space. That's the same disclosure I'd want made about me, since I own gyms and this book has my name on it. I'm citing him for a framing I think is right and for cautions I think are excellent.

He was talking about obesity, and he said the problem usually isn't that somebody has too much fat. It's that they don't have enough muscle. They're under-muscled, not over-fat.

Skeletal muscle is the largest organ in your body by mass, and it accounts for something like 75 to 80% of insulin-stimulated glucose disposal, which is the sugar your body clears out of your blood when insulin tells it to. (You'll see that figure quoted as "80% of the glucose from a meal," including by people I respect. That's not quite what it measures, because after a real meal a big share goes to the liver and gut too. The point stands either way.) Muscle is your glucose sink. The more of it you carry, the more sugar your body can pull out of your blood and put somewhere useful.

Less muscle means more glucose staying in your blood and more insulin released to deal with it. Over time, that means insulin resistance. And insulin resistance sits underneath an enormous amount of what goes wrong after fifty: the blood pressure, the triglycerides, the belly fat, the A1c creeping up, the fatigue.

So you can treat the blood pressure. You can treat the A1c. Or you can go after the thing sitting underneath both of them.

That's root-cause thinking, and notice that it doesn't require believing anything unproven. Every link in that chain is established physiology.

He said something else I want to quote, because it's the most useful sentence I've read on this: you don't heal your metabolism. You change the inputs and your body recalibrates.

Your metabolism isn't broken and it doesn't need fixing. It's doing what it's designed to do, which is reflecting what your body thinks it needs based on what you're giving it: sleep, protein, muscle mass, activity, stress.

What everybody in this world actually agrees on

If you read across the prominent functional and holistic voices (Gabrielle Lyon on muscle, Peter Attia on longevity, Ben Bikman on insulin, Robert Lustig on processed food, Stacy Sims on women, Josh Holyfield on protein and peptides), they disagree loudly about plenty: saturated fat, carbohydrate limits, fasting, seed oils, whether you should wear a glucose monitor.

But strip out the arguments and there's a convergent core that every one of them holds, and it's more defensible than any individual's version of it:

1. Resistance training is non-negotiable, and it's the intervention conventional medicine most under-prescribes.
2. Protein above the RDA benefits adults over 50.
3. Cardiorespiratory fitness is one of the strongest modifiable predictors of mortality we have.

4. Metabolic health is measurable and detectable years earlier than standard care detects it.
5. Ultra-processed food drives overconsumption, and this one has a randomized controlled feeding trial behind it, not just epidemiology.
6. Sleep is a primary variable, not a secondary one.
7. Individual variation is real, and guidelines are population averages.
8. A fifteen-minute visit cannot deliver behavior change.

That list is the spine of this book. Every item on it is well supported. And notice how little you have to believe beyond it. You don't need a single claim about toxins, seed oils, detoxification or adrenal fatigue to get all of it.

Gabrielle Lyon calls her version "muscle-centric medicine," and I think that's the single best framing anybody in this space has produced: muscle is the organ of longevity. It's not a cosmetic outcome. It's an organ, with metabolic responsibilities, that you can grow or lose depending on what you do.

The trap on my own side of the fence

Here's the failure mode in my world, and Holyfield named it better than I would have. A lot of people in this space say they hate big pharma. They don't want drugs treating the side effects of other drugs. And then they do exactly that with peptides and supplements.

If your hair is falling out or your hormones are off, there's a peptide for that. If your gut's a mess, here's a five-supplement protocol.

That's not root-cause medicine. That's the same treadmill with a different label on it. And the incentives are identical. A lot of clinics and companies make more money the longer you stay on the stack, which means nobody in the transaction is paid to solve the underlying problem.

I've seen this from the inside. I'll come back to it hard in Part V.

The test I'd apply, to any protocol including my own: is this fixing the input, or is it managing the output? Both have their place. But if everything you're doing is in the second category, you're not doing functional medicine. You're doing pharmacology with better marketing.

What this means for how to read the rest of the book

Every part of this book is organized around going underneath the symptom.

You're losing strength: the root cause is motor units, disuse and protein, not age itself.

You're gaining fat: look at muscle, activity, protein, food engineered to be eaten fast, sleep and medications. Any of them can play a part.

Your blood pressure is up: look at sodium and potassium together, at body composition, at sleep, at alcohol.

You're tired: look at your thyroid, your iron, your B12, your sleep architecture, and how much muscle you're carrying, before you look at a stimulant.

And the order of operations never changes: training, then food, then sleep, then everything else. The last category is where most people start, and it's why most people fail.

One caveat before we go further

I'm going to spend this book telling you that the research often doesn't apply to you, and that you have to find out about yourself. That cuts both ways, and I know it.

The same reasoning that says "the trial doesn't capture my situation" can be used to justify literally anything. If the standard is "I feel like it works," then everything works. That's how people end up on fourteen supplements, three unapproved compounds and a protocol that costs them six hundred dollars a month and does nothing.

So here's the discipline I try to hold, and I'd ask you to hold it too: skepticism about the average is earned by being rigorous about yourself.

You get to say "that study doesn't describe me" if you're measuring yourself: written down, changed one at a time, over enough weeks to mean something.

If you're not doing that, then "everyone is different" isn't a scientific position. It's just an excuse to believe whatever you already wanted to believe.

Chapter 4 — What Actually Happens To You After 50

Let me tell you what's happening under the hood, because most people over fifty have a vague sense that things are "slowing down" without knowing what's changing. It matters, because the thing that's changing fastest is not the thing most people worry about.

You lose strength faster than you lose muscle

This is the fact to hold onto from this chapter, and almost every fitness article gets it wrong.

There's a big study called Health ABC: 1,880 older adults, tracked for three years, looking at both muscle mass and muscle strength (Goodpaster and colleagues, published in the Journals of Gerontology in 2006).

Leg lean mass dropped about 1% per year.

Knee extensor strength dropped 2.6% to 4.1% per year, depending on the group.

So strength was falling roughly three times faster than mass. A review by Narici and colleagues in 2012 put the gap even wider. They concluded strength declines two to five times faster than size.

In that Health ABC study, the people who gained lean mass over the three years did not hold onto their strength. The statistics on that were flat, with no relationship at all. You can add muscle and still get weaker.

Which means the scale and the mirror are both lying to you

You've probably heard the number "you lose 3 to 8 percent of your muscle per decade after thirty." I've probably said it myself. When I went looking for where that figure comes from, I couldn't find a primary source for it.

There's a related figure, "1 to 2% per year," which works out to 10 to 20% per decade, and Narici's group states outright that that one is misattributed in the literature.

The real version, from longitudinal studies where they followed the same people over years, is about 1% of leg lean mass per year in adults over 70. When it starts is argued about. You'll see 27, 45, or 60 depending on how the study was designed.

But mass isn't the number to watch anyway.

Strength predicts death and muscle size doesn't. That comes from the same cohort in a different paper: Newman and colleagues, 2006, 2,292 people aged 70 to 79, followed about five years, 286 deaths.

Quadriceps strength: for every standard deviation lower, men had a 51% higher risk of dying, women 65% higher.

Muscle size, measured by CT scan and by DXA, was not strongly related to mortality at all. And adjusting for it barely moved the strength relationship.

This isn't a fringe finding anymore. In 2019 the European Working Group on Sarcopenia formally rewrote its diagnostic criteria to make low strength the primary criterion instead of low mass.

I find this liberating. Most people over fifty are chasing size and getting frustrated because they're not filling out their sleeves like they did at thirty. You're chasing the wrong number. Get strong. The size that comes with it comes with it.

Why you're losing strength: your wiring, not just your meat

You have motor units, each one a nerve cell and all the muscle fibers it controls. By around age 71, healthy people have roughly 40% fewer motor units than young adults (McPhee and colleagues, 2016). The nerve cell bodies stay pretty stable until about 60, then start dropping off. Past 75, some people are under 50% of young counts, and in extreme cases under 10%.

Your body compensates. Surviving motor units sprout new connections and take over orphaned fibers, and the surviving low and moderate threshold units get about 50% bigger. That's why you don't feel like you've lost 40% of anything.

But the units you lose first are disproportionately the fast, high-threshold ones, the ones that produce power, which is force produced fast. That's why the thing that goes first isn't your ability to lift a heavy thing slowly. It's your ability to catch yourself when you trip.

The researchers themselves flag that this evidence base is limited: no long-term longitudinal studies, small samples, and a lot of the work done on small hand and foot muscles because those are easy to measure. So hold the exact numbers loosely. The direction is solid.

Your aerobic capacity falls, and it accelerates

VO2max, the maximum amount of oxygen your body can use, is the best single number we have for cardiorespiratory fitness. And it goes down.

And the rate of decline accelerates. The Baltimore Longitudinal Study of Aging tracked 810 people aged 21 to 87 for a median of about eight years (Fleg and colleagues, Circulation, 2005). In your twenties and thirties, VO2max declines 3 to 6% per decade. In your seventies and beyond, it's over 20% per decade. And the decline is larger in men than women from the forties onward.

Most people don't know this because most of the numbers you see quoted come from cross-sectional studies, comparing 40-year-olds to 70-year-olds at one point in time. Those studies systematically underestimate the decline, because the 70-year-olds you can find to test are the survivors. The flat "about 10% per decade" figure you see everywhere is an artifact of that.

The functional floor, for reference, is around 17.5 mL/kg/min, about 5 METs (five times the energy you use sitting at rest). Below that, independent living gets hard. Below 3 METs, just keeping

your body running at rest eats more than 30% of your total capacity.

Your tendons change too

Collagen accumulates cross-links as you age (advanced glycation end-products), and they build up faster if your blood sugar runs high. The collagen gets stiffer and more brittle. Meanwhile the cells that build and repair connective tissue slow down. Aged human fibroblasts take roughly three times longer to divide than young ones.

The practical version: your tendons repair slower and tolerate less. Tendinopathy affects roughly a quarter of adults and accounts for about half of all reported musculoskeletal injuries.

The evidence here is thin, and Chapter 14 says so at length. A lot of what's written about tendon aging mixes rabbit, rat, horse and human data together without separating them. But if you're over fifty and lifting, you already know this in your elbows.

And your sleep changes — but probably not the way you think

Total sleep time drops. Deep slow-wave sleep drops. REM drops. Time awake in the middle of the night goes up. Sleep efficiency goes down.

Here's the correction, from a meta-analysis of 65 studies covering 3,577 healthy people from age 5 to 102 (Ohayon and colleagues, 2004): only sleep efficiency keeps significantly declining after 60. Everything else largely plateaus.

That means most of the "sleep gets worse as you age" damage happens between young adulthood and sixty. If your sleep is getting noticeably worse at 68 compared to 62, the odds are good that's not normal aging. That's sleep apnea, or your prostate, or a medication, or pain, or depression, something with a name and often a treatment. Go find out.

The summary

- Strength falls 2–5× faster than muscle size.

- In the big cohorts, strength predicts survival. Size doesn't.
- The loss is substantially neural. You're losing motor units, especially fast ones.
- Aerobic capacity falls, and it falls faster every decade.
- Tendons stiffen and repair slower.
- Sleep degrades mostly before sixty, not after.

None of that is a death sentence. Every single one of those systems responds to training, which is the next chapter and the next part of this book. But you need to know what you're fighting, and it's not your waistline.

Chapter 5 — The Two Non-Negotiables

I said I'd only be dogmatic about two things. Here they are, and here's why.

Non-negotiable one: lift weights

I don't mean "stay active," "get your steps in" or "do some yoga." I mean lift heavy things against progressive resistance, at least twice a week, for the rest of your life.

I'm going to spend all of Part II on how. Right now I want to establish why, with a level of evidence that should end the argument.

In 1990, Maria Fiatarone and colleagues published a study in JAMA on ten frail nursing home residents, with a mean age of 90.2 years and a range of 86 to 96. They did eight weeks of knee extensions, three times a week, working up to 80% of their one-rep max.

Knee extensor strength went up 174%.

That number gets thrown around constantly and it's misleading. It was ten people, with no control group, for eight weeks, on one single exercise. And they had an extraordinarily deconditioned starting point. When you start near zero, percentage gains are enormous.

So look at the follow-up instead. Fiatarone's team ran a controlled version in 1994, published in the New England Journal of Medicine: one hundred frail nursing home residents, mean age 87.1, ten weeks, with proper control groups.

- Strength: +113% in the exercise groups versus +3% in the non-exercisers.
- Gait velocity: +11.8% versus a small decline.
- Stair-climbing power: +28.4% versus +3.6%.

If it works at 87 in a nursing home, your "I'm too old to start" is not a real argument. I'm sorry.

And here's the twist in that study

Thigh muscle area in the 1994 trial went up 2.7%, and that result wasn't even statistically significant.

Strength was up 113%. Size was up 2.7%, and not reliably.

That tells you something profound about what's happening when an older person starts lifting. The early gains are overwhelmingly neural. You're not building new meat. You're relearning how to recruit the meat you already have. Your nervous system is switching motor units back on that it had stopped bothering to call.

This shows up in the pooled data too. Borde and colleagues meta-analyzed 25 randomized trials with 819 healthy older adults, mean age 70. Effect size for strength: 1.57, which is large. Effect size for muscle size: 0.42, which is small.

The authors were honest about their own limitations: average study quality was poor (4.6 out of 10 on the PEDro scale) and heterogeneity was high. Take the exact numbers with salt. Take the pattern seriously.

What about people who aren't frail?

Nursing home residents have enormous room to improve. What about a healthy 65-year-old?

The best-controlled answer I found is Phillips and colleagues, 2017, in JCI Insight. It had forty-eight people in three age groups (18–28, 45–55, and 65–75), roughly half men and half women. They did twenty weeks of supervised whole-body resistance training, identical program, 70% of one-rep max.

Strength: all three age groups improved by a similar relative amount. The absolute numbers were lower in the older group, but the percentage gain was comparable.

Size: strongly age-dependent. Whole-body lean mass went up 5.24% in the young group and was statistically significant. In the

middle-aged group: 1.12%, not significant. In the older group: 1.33%, not significant. Leg lean mass increased only in the young.

Muscle quality (strength per unit of size) improved equally in all three groups.

So here's the accurate, and I think encouraging, framing: you can still get strong. You just won't get as big. And since strength is what predicts survival and function, that's a fine trade.

One more detail from that study: the 45–55 group was already almost as blunted as the 65–75 group. The drop-off in your ability to add size doesn't wait for retirement.

Does it actually make you live longer?

Momma and colleagues pooled 16 cohort studies in the British Journal of Sports Medicine in 2022. Individual studies ranged from about 4,000 to 480,000 people.

Muscle-strengthening activity was associated with 10–17% lower risk of all-cause mortality, cardiovascular disease, total cancer, diabetes and lung cancer. Combined with aerobic activity: 40% lower all-cause mortality, 46% lower cardiovascular, 28% lower cancer.

That analysis also found a J-shape, and I've seen it misused. Benefit peaked around 30–60 minutes a week of strength work and apparently declined above about 130–140 minutes. People have used that to argue you shouldn't lift much.

Don't buy it. That's self-reported activity data from a small number of cohorts. The more likely explanation is measurement error and reverse causation: people with health problems reporting more activity, or people who lift a lot misreporting. I don't know of any convincing mechanism by which three hours of lifting a week starts killing you. But the J deserves the same caution as the benefit, because both come from observational data. It's not a reason to cap your training.

Non-negotiable two: at least 1 gram of protein per pound of desired body weight

I'll do the full treatment in Part III. Here is the rule, and then the short version of why.

At least 1 gram of protein per pound of desired body weight, every day. That's my rule. If you want to weigh 175, that's at least 175 grams. If you weigh 250 and want to weigh 185, that's at least 185 grams. That's per pound of the body you're building, not per pound of what the scale says today. If you have kidney disease, or your doctor has given you a different number for a medical reason, use your doctor's number (Chapter 19).

You cannot build or hold muscle without the raw material, and after fifty your body responds less to the protein you eat. That's a measured phenomenon called anabolic resistance. Feed a twenty-two-year-old 20 grams of protein and his muscle-building machinery switches on. Feed a seventy-year-old the same 20 grams and the response is blunted. In the study that pooled the dose-response data, older men needed about 0.4 grams per kilogram in a single meal to get the full response, against 0.24 for young men. Two-thirds more, per meal, just to get the same signal. Measured against lean mass the gap was wider still: 0.6 against 0.25.

Now do the arithmetic everybody skips. Four real meals a day at 0.4 grams per kilogram already puts you at 1.6 grams per kilogram, which is where the biggest meta-analysis of protein and lifting put its plateau. Run the same four meals at the lean-mass dose and you're at 2.4 grams per kilogram of lean mass, which for somebody at 15 percent body fat is about 2 grams per kilogram of body weight. A gram per pound is that arithmetic with a small margin on top.

The RDA is 0.8 grams per kilogram. Every research group working on aging and muscle thinks that's too low for older adults, and the two expert bodies that have looked at it put the floor at 1.0 to 1.2 for healthy older adults and at least 1.2 if you're training. Those

are floors, set so you don't lose ground. I'm not interested in not losing ground.

I run the rule myself. I weigh 175, I eat at least 175 grams, and most days I'm over 200. That's real food, planned on purpose, and it does not happen by accident. Chapter 16 has the evidence, the limits of the evidence, and what my monthly labs say about it. Chapter 17 has the per-meal dose.

Why these two and nothing else

Because everything else in this book is contingent.

Creatine works, but you'll be fine without it. Zone 2 versus intervals is a real debate with real evidence on both sides. Fasting works great for some people and badly for others. The peptide chapters are full of things I'd never tell you that you need.

But if you're sixty and you don't lift and you don't eat enough protein, nothing else you do is going to stop you from getting weak. And getting weak is the thing that takes your independence.

Everything else is optimization. These two are the foundation.

Chapter 6 — Measure, Don't Guess

I check my glucose twice a day, and my blood pressure and pulse multiple times a day. I get a full blood panel every month and log every gram of food.

People think that's obsessive, and maybe it is. But I'm running experiments on my own body, and an experiment without measurement isn't an experiment. It's a story you tell yourself afterward.

The mirror lies

We got a body composition scanner at the Carson City club. It's a 3D scanner that puts you on a turntable, rotates you for about forty seconds, and gives you body fat percentage plus measurements at dozens of specific points.

The most useful thing about it isn't the accuracy. It's the consistency. You cannot take your own bicep measurement in exactly the same spot twice. The machine can. It still has measurement error, so one small change doesn't prove much. A trend over several scans is real information, not tape-measure drift.

And what I've seen over and over with members is that people think they're leaner than they are. Somebody's convinced they're at 15% and they scan at 19. That's just human nature. You look in the mirror in the good light with good posture.

I got scanned at 13.7% at age 62. I'll take that. But the reason I know it's 13.7 and not "pretty good, I think" is that I measured.

I did a test once when I was a couple pounds lighter than the previous scan, and my body fat percentage was higher. I was lighter on the scale with worse composition. If I'd only had a bathroom scale I'd have concluded I was making progress. That made me look hard at whether I was losing muscle.

How to do it so the numbers mean something

Whatever you use (scanner, DXA, calipers, bioimpedance, tape measure), the method matters less than the consistency.

Use the same time of day, the same clothes, the same state (fasted or not, but the same either way) and the same relationship to your last workout. Then the differences you see are much more likely to be real, not noise from a big dinner and a hard leg day.

And don't test too close together. Body composition doesn't move meaningfully in a week. Once a month is plenty.

The numbers I actually watch

I'll give you the full protocol in Chapter 50 with the specific blood markers. For now, the short list of what I think everyone over fifty should be tracking:

In the gym. Your working weights on three or four main lifts. Write them down. This is your single best real-time indicator that things are going right or wrong, and it's free. If your numbers are climbing, or holding while you diet, you're doing okay. If they're falling and you didn't plan for that, something's wrong.

Blood pressure. A cheap cuff, taken consistently. This is the highest-value fifty dollars you will ever spend on health equipment. It is not a substitute for your doctor, but it will show you patterns nobody sees in one annual visit.

Body composition, monthly. Whatever method you can access consistently.

Blood work, at least twice a year. More if you're changing something significant. I do monthly because I'm always changing something.

Grip strength, if you can. More on this in Chapter 7. It's a shockingly good marker.

Resting heart rate. Any watch does this now. Trends matter more than any single reading.

What measurement is not

It's not control. I want to be careful here, because I've watched people get unwell chasing numbers: weighing food to the gram at a restaurant, refusing to eat with their family, spiraling when the scale moves two pounds.

The numbers are there to tell you whether your experiment is working. If tracking is making you miserable or making you weird about food, that's a real cost and you should count it. Some people do better with loose tracking, or with tracking only protein, or with a two-week audit twice a year instead of daily logging forever.

I log everything because I like it and because I'm running experiments I want answers to. That's my choice, not a requirement I'm handing you.

The one habit that beats all of it

Write down what you changed and when. I mean the changes, not the results: date, what you started or stopped, dose, why. Six weeks from now when something feels different, you're going to try to reconstruct what you did and you're going to get it wrong. Everybody does.

A single note on your phone is enough. It costs nothing and it's the difference between having data and having anecdotes.

PART II — TRAINING

Chapter 7 — The Cheapest Test in Medicine

Squeeze a device. That's the test.

Grip strength is the most absurdly good predictor of how long you're going to live, relative to how easy it is to measure, of anything I've come across.

The numbers

The PURE study, published in The Lancet in 2015 (Leong and colleagues), followed 139,691 people aged 35 to 70 across seventeen countries at every income level.

For every 5 kilograms of lower grip strength:

- All-cause mortality: 16% higher
- Cardiovascular mortality: 17% higher
- Non-cardiovascular mortality: 17% higher
- Stroke: 9% higher
- Heart attack: 7% higher

And the headline that made everybody sit up: grip strength predicted all-cause death better than systolic blood pressure did.

Then UK Biobank replicated it. Celis-Morales and colleagues, BMJ, 2018: 502,293 people, completely different population, different continent, different methods. Per 5 kilograms lower grip: 16% higher all-cause mortality in men, 20% in women.

Two enormous studies, different populations, essentially the same number. In this field, that's about as good as convergent evidence gets.

Now let me talk you out of half of it

Grip strength did not predict everything. In PURE, it was not associated with incident diabetes or with respiratory hospitalization. And in high-income countries, higher grip went with slightly higher cancer rates. That link wasn't found in middle- or low-income countries, and it probably reflects body

size and detection patterns, not a real effect. UK Biobank found the opposite direction on cancer. That relationship is not settled.

Blood pressure still wins for predicting heart disease. Grip beat blood pressure for dying of anything. But for predicting whether you'll develop cardiovascular disease, systolic blood pressure was better (1.39 versus 1.21). Don't throw out your cuff.

Median follow-up in PURE was four years. That's short enough that reverse causation is a serious concern. Some of those weak-grip people were weak because they were already sick with something undiagnosed.

And most importantly, there is no trial showing that training your grip specifically reduces your mortality. It's the same story for quadriceps strength in the Health ABC data.

So what is grip strength actually doing? It's a biomarker. It's a cheap, fast readout of your whole neuromuscular system, your nutrition status, your inflammatory burden, and how much other disease you're carrying. It's a dashboard light, not the engine.

Squeezing a hand gripper while watching TV will not extend your life. Getting systemically stronger might, and grip is how you check.

What the numbers should be

From the European sarcopenia criteria, the thresholds for "weak" are under 27 kg for men, under 16 kg for women. If you're below that, that's a clinical finding, and it's worth a conversation with your doctor.

For reference on where you started: peak grip is about 51 kg for men in their thirties, 31 kg for women in their late twenties to early forties, from a pooled British dataset of nearly 50,000 people (Dodds and colleagues, 2014).

Decline from fifty onward is close to linear, roughly 0.59 kg per year for men and 0.31 kg for women. That one's from a separate Danish study of 8,342 people (Frederiksen and colleagues, 2006).

By eighty, about 23% of men and 27% of women fall into the "weak" category.

The other tests worth doing

Grip is the famous one, but there are three more that take no equipment and tell you a lot.

Five-times sit-to-stand. Arms crossed over your chest, stand up and sit down five times as fast as you can. Over 15 seconds is a sarcopenia flag.

Gait speed. Time yourself walking four meters at normal pace. Under 0.8 meters per second is a flag.

Timed Up and Go. Stand from a chair, walk three meters, turn, come back, sit. Over 20 seconds is a flag.

All of them are used clinically. And unlike the mirror, they don't flatter you.

What I'd actually do with this

Test yourself today or this week, and write the numbers down.

Then retest every six months. The number itself isn't magic, but the trend is information you cannot get any other way. A drop in grip strength or sit-to-stand speed over a year, in someone who's training consistently, is a signal that something else is going on, and it'll show up before you feel it.

It's an early warning system that costs nothing.

Chapter 8 — How To Actually Train After 50

Here's where I have to fight my own instincts, because what I do isn't necessarily what I should tell you to do.

I train an hour and a half, five days a week, and I've done some version of that since I was twelve. That's fifty years of accumulated tolerance for training volume. If you're fifty-eight and you've been out of the gym for fifteen years, copying my program is a good way to get hurt in about three weeks.

So here's what the evidence supports, and where I differ from it and why.

You don't need a special "over 50" program

There's a whole industry built on the opposite claim, but the evidence doesn't support a fundamentally different program for older adults. It supports the same variables with a different risk weighting.

You lift heavy things and you progress. You don't train to complete failure very often, and you leave a little more margin than a twenty-five-year-old would. That's the difference.

Frequency: two to three times a week

- Borde's meta-analysis found 2 sessions per week optimal for strength gains, 3 for size.
- The NSCA position statement recommends 2–3 times per week per muscle group on non-consecutive days, with 1 time per week as the minimum to prevent losing ground.
- ACSM's 2026 update, an umbrella review of 137 systematic reviews and over 30,000 participants, says at least twice a week for all major muscle groups.

Two full-body sessions a week, done consistently for a year, will beat a five-day split you abandon in March. I've watched it happen in my clubs for three decades.

Intensity: heavier than you think

This is where a lot of over-50 training advice goes badly wrong. Somebody turns 55 and switches to the lightest dumbbells on the rack and sets of twenty, and then wonders why nothing happens.

The evidence:

- 70–79% of your one-rep max was optimal for strength in Borde's analysis.
- The NSCA recommends 70–85% of 1RM for maximal strength, dropping to 40–60% when you're specifically training power.
- ACSM 2026 puts strength work around 80% of 1RM.
- The LIFTMOR bone trial (covered in Chapter 12) used over 85% of 1RM in postmenopausal women with low bone mass and had essentially no adverse events.

In practical terms, 70–85% of your max is a weight you can do roughly 6 to 12 reps with. If you're stopping sets of twenty because you're bored rather than near your limit, you're not training strength.

One technique point that matters more after fifty than it did at thirty: **do not hold your breath under a heavy load.** Exhale through the hard part of the rep. Breath-holding against a closed glottis spikes blood pressure sharply, and if you have hypertension, an aneurysm, or eye or cerebrovascular disease, that spike is the risk, not the weight.

Volume: two to three sets, and here's a live argument

The classic recommendation is 2–3 sets per exercise, 6–12 reps, with 8–10 exercises total covering the whole body. That's Borde, the NSCA, and most of the field.

ACSM's 2026 update puts hypertrophy at around 10 sets per muscle group per week.

But this isn't settled. In 2025, Radaelli and colleagues published a network meta-analysis in Sports Medicine covering 151

randomized trials and 6,306 older adults. They found that for hypertrophy and lean body mass, low volume was most effective, ahead of both moderate and high.

That directly contradicts Peterson's 2011 meta-analysis, which found higher volume produced greater lean mass gains, and basically the entire younger-adult literature, where more volume up to a point means more growth.

My read is that the low-volume arms in older-adult trials are probably better supervised, better adhered to, and applied to more deconditioned people. That's confounding, not physiology. But I could be wrong, and so could the researchers on either side.

In practice, don't stress about volume. If you're doing 2–3 hard sets per exercise, twice a week, you're inside the range where all the evidence agrees you'll make progress.

Failure: probably don't, but the reason isn't what you think

The NSCA's position is explicit: avoid repetitions to failure. Perform about 50–70% of the maximum reps you could do, and leave meaningful reps in the tank.

ACSM 2026 says training to failure "is not strictly necessary."

When I dug into this I was surprised. There's essentially no randomized trial testing failure versus non-failure specifically in adults over 50. The NSCA's recommendation is expert consensus plus safety reasoning, extrapolated from younger populations. It's prudent, but it rests on indirect evidence and expert judgment, not direct trials in older adults, and I think you deserve to know the difference.

My own practice is to go close to failure on machine work and isolation stuff where getting stuck isn't dangerous, and to stay two or three reps away on anything heavy and free-weight where failure means the bar lands on me. That's a risk judgment, not a physiology judgment, and I'd suggest the same to you.

Rest between sets

The recommendations conflict, so I'll show you both.

Borde's meta-regression found 60 seconds optimal for strength, but the effect size on that finding was 4.68, which is implausibly large and driven by very few studies. Don't trust it.

The NSCA recommends 1.5 to 3 minutes.

I rest until I feel ready for the next set, which on heavy compound work is usually 2 to 3 minutes and on smaller stuff is a minute or less. That's fifty years of doing it, not science, but it lines up with the NSCA, and the NSCA has better reasoning behind it than a meta-regression artifact.

Machines or free weights?

ACSM 2026, reviewing 137 systematic reviews: no consistent difference. Bodyweight, bands and home routines came out equally effective.

The NSCA recommends machines for beginners and frail adults, and I agree completely. Machines aren't better, but the failure mode is safer and the learning curve is shorter.

I use both. If you're coming back after a long layoff, start on machines, build a base for eight to twelve weeks, then add free-weight compounds if you want them. If you never do, you'll still get most of the benefit.

Power work: worth doing, oversold

Power training (moving lighter weights fast) gets promoted hard as the thing older adults specifically need. The logic is good: the fast motor units are the ones you lose first, and power is what catches you when you stumble.

The evidence is real but modest. Balachandran and colleagues, JAMA Network Open, 2022, pooled 20 randomized trials with 566 older adults. Power training beat traditional strength training on physical function with an effect size of 0.30, which is small.

Translated to clinical terms, that's about 0.62 seconds better on the Timed Up and Go and about half an extra stand on the chair-stand test. Certainty of the evidence: low.

So the popular claim that power training is dramatically superior for older adults overstates it. Include some, but don't reorganize your life around it.

Practically, take a few sets each week at 40–60% of your max and move the concentric (the lifting part) as fast as you safely can. Leg press, chest press, med ball throws. That's enough.

Eccentric work

This means lowering the weight slowly, or emphasizing the lowering phase. Čretnik and colleagues pooled 19 papers in adults 55 to 80.

Eccentric training beat conventional on Timed Up and Go (effect size −0.68), on 30-second sit-to-stand (0.81), and on a 2-minute step test (0.53).

It did not beat conventional on isometric knee strength, ankle strength, 6-minute walk, lean leg mass or body fat.

So it's useful for functional performance, particularly the anaerobic functional tests, and it has a lower cardiovascular cost per unit of force, which matters if you've got cardiac limitations. It isn't a miracle.

Does cardio ruin your lifting?

This is the "interference effect," and everybody worries about it.

Khalafi and colleagues, 2025, pooled 53 studies with 2,873 participants aged 51 to 82.

Concurrent training versus aerobic alone: lean body mass +0.51 kg favoring concurrent.

Concurrent training versus resistance alone: lean body mass difference −0.10 kg, which was not significant. Fat mass, not significant. Body fat percentage, not significant.

In this age group, then, doing cardio doesn't cost you muscle. Concurrent training was as good as lifting for muscle and as good as cardio for fat. That's a well-powered and reassuring finding. It's one meta-analysis of 53 fairly heterogeneous studies, so it's not the last word, but it's enough that I'd stop worrying about it.

What happens if you stop

Grgic's 2022 meta-analysis on detraining in older adults:

- 12 to 24 weeks off: not a statistically significant loss.
- 31 to 52 weeks off: significant loss (effect size −1.11).

With three to six months off, the small studies didn't detect a significant loss. That's not a guarantee you keep everything, but you haven't lost it all. With a year off you clearly lose ground.

The evidence base is thin (six studies), but the practical message is useful and reassuring. If you have surgery, or a family crisis, or you just fall off for a season, come back.

A template you can actually use

Before you start: if you have known cardiovascular disease, uncontrolled hypertension, a recent surgery or joint replacement, osteoporosis, or you have been sedentary for more than a year, get cleared by your physician first. This is not a formality.

Two full-body days a week is the floor, and it's a good floor.

Each session:

- One lower-body push (squat pattern, leg press, or hack squat)
- One lower-body hinge or pull (deadlift variation, hip thrust, leg curl)
- One upper-body push (chest press, overhead press)
- One upper-body pull (row, pulldown)
- One carry or core piece

Do 2–3 sets of 6–12 reps each, with a weight that leaves you 2–3 reps short of failure. Rest 90 seconds to 3 minutes on the big stuff.

Add weight when you can hit the top of your rep range on all sets with clean form, and not before.

If you want a third day, add it. If you want to split it into upper/lower across four days, do that. The specific arrangement isn't where your results come from. They come from showing up in year three.

Chapter 9 — Strength, Size, and Power Are Three Different Things

People use these words interchangeably and then get frustrated when their training doesn't do what they expected. They're separate qualities that adapt on different timelines, and after fifty they diverge more than they did at twenty-five.

Strength is maximum force: can you move the heavy thing at all? Size (hypertrophy) is how much muscle tissue you have. Power is force times speed: can you move the thing fast?

At twenty-five, training any one of them drags the other two along. After fifty, that coupling loosens.

You saw the evidence in Chapter 5: equal relative strength gains in every age group, size gains that faded after forty-five, and 87-year-olds who doubled their strength with almost no change in thigh size.

Strength adapts through your nervous system first and your muscle second, which is why it improves fast and at any age. Size requires building tissue, which requires a hormonal and nutritional environment that gets less cooperative with age.

Power is its own thing again, and it declines fastest of the three, because the motor units you lose first are the fast ones.

What this means for you

If your goal is function and independence, train strength and power. Size will do what it does.

If your goal is looking better, you still train strength, because strength progress is what drives size in practice, and this program is built on progressive load, not on chasing "the pump." But adjust your expectations. Don't expect to add fifteen pounds of muscle at sixty. You might add three or four over a couple of years of good work, and combined with fat loss that will change how you look substantially.

If your goal is not falling down, train power and balance. I'll cover balance in Chapter 13.

The reframe that helped me

I spent decades chasing size, because that's what I learned at twelve and never questioned. Somewhere in my late fifties I switched to chasing strength and body composition instead, and I was happier and got better results.

The reframe works because size is a slow, blunt, discouraging metric after fifty, and strength is a fast, precise, encouraging one. You can add five pounds to a lift this month. You probably won't add a visible pound of muscle this month, and if the scale says you did, a lot of it is water and glycogen.

Chapter 10 — The Number That Predicts How Long You Live

If I could make you care about one number besides your strength, it's this one.

VO2max (your cardiorespiratory fitness) is one of the strongest predictors of all-cause mortality, and it shows up consistently across large populations. In one of the biggest studies of it, low fitness carried a larger adjusted hazard than smoking, diabetes, or known coronary artery disease.

I'll show you that comparison and then how far you can push it, because it's the most quoted and most abused statistic in this field.

The study

Mandsager and colleagues, JAMA Network Open, 2018. 122,007 people who underwent treadmill testing at the Cleveland Clinic. Mean age 53. Median follow-up 8.4 years, 1.1 million person-years, 13,637 deaths.

They sorted people into fitness categories by METs and ran the hazard ratios.

Elite fitness versus Low fitness: hazard ratio 0.20. Flip it around and Low versus Elite is 5.04. The least fit group had five times the adjusted mortality risk of the most fit.

Now here's the comparison that should stop you cold. Same model, same population, same adjustments:

Risk factor	Adjusted hazard ratio
End-stage renal disease	2.78
Smoking	1.41
Diabetes	1.40
Coronary artery disease	1.29
Hypertension	1.21

Risk factor	Adjusted hazard ratio
Low fitness (vs. elite)	5.04

Being in the least-fit group carried a bigger adjusted hazard than smoking, than diabetes, and than end-stage kidney disease.

And there's no ceiling

The second finding kills a myth I've heard a hundred times.

You'll hear people say there's a U-shaped curve, that too much exercise becomes cardiotoxic, that extreme endurance athletes are damaging their hearts. In this dataset, Elite still beat High (hazard ratio 0.77, and statistically significant). More fitness kept being better all the way to the top of the distribution, and no ceiling was observed.

Let me caveat this properly

I'm not going to hand you a 5.04 without telling you where it's soft.

This is a clinically referred population: people who got sent for a treadmill test, usually because a doctor was worried about something. That's not the general public, and selection bias cuts in multiple directions.

It's observational. Some of those low-fitness people were unfit because they were already sick with something undiagnosed. That reverse causation inflates the low-fitness hazard, and there's no way to fully adjust it away.

Those disease hazard ratios are covariates in the same model, not a head-to-head randomized comparison. Saying "unfitness is worse than smoking" makes a great headline, and in this one model the numbers do point that way. But it's not the same as saying being unfit causes 3.5 times the death risk that smoking causes.

But it replicates

Kokkinos and colleagues, Journal of the American College of Cardiology, 2022. Over 750,000 US veterans, mean age 61, median follow-up 10.2 years. About 15% were in their seventies and 3.6% in their eighties.

Least fit versus extremely fit: hazard ratio 4.09. Per 1-MET increase in fitness: hazard ratio 0.86.

The relationship held across the entire spectrum of age, sex and race, including the oldest groups.

The meta-analysis that produced the number everybody quotes is Kodama and colleagues, JAMA, 2009, 33 studies, 102,980 participants. Each 1-MET increase in fitness: 13% lower all-cause mortality. That's where "1 MET = 13%" comes from and it's well supported.

Can you actually improve it after sixty?

Yes.

Huang and colleagues pooled 41 controlled trials with 2,102 participants, mean age 60 and up, starting VO2max between 14.7 and 31.5 mL/kg/min.

Pooled improvement: +3.78 mL/kg/min. That's roughly a 12–26% relative improvement, or about one MET.

Now, it's tempting to chain that to the Kodama number and say you've bought yourself 13% lower mortality. Don't, and neither will I. Kodama measured the association between the fitness level people have and how long they live. Huang measured how much fitness people gain from training. Those are different questions, and gluing them together produces a causal claim neither study makes.

What you can say is that people who sit one MET higher have about 13% lower mortality in cohort data, and training reliably moves you about one MET. Whether moving yourself up buys the

same thing as being up there is a reasonable inference and not a demonstrated one.

Programs longer than 20 weeks did better. The typical dose was three sessions a week, averaging 38 minutes, which is under two hours a week. That's a very large return on the time.

The floor you don't want to go below

Around 17.5 mL/kg/min (about 5 METs) is roughly where independent living starts to get difficult. Below 3 METs, just running your body at rest consumes more than 30% of your total aerobic capacity, which means everything feels hard because for you, everything is hard.

Remember from Chapter 4 that VO2max decline accelerates, to over 20% per decade in your seventies. That means the buffer you build in your fifties and sixties is what keeps you above the functional floor in your eighties.

You're not training for now. You're training for then.

Chapter 11 — Zone 2 Versus Intervals

This is the argument I get asked about most, and it's the one where the gap between what people say online and what the research shows is widest.

The claim

Zone 2 (easy aerobic work, conversational pace, roughly 60–70% of max heart rate) is supposed to be uniquely good at building mitochondria, improving fat oxidation, and extending lifespan. You'll hear that most of your cardio should be Zone 2, often in an 80/20 split with high intensity.

I've repeated versions of this, and so have a lot of smart people.

The problem

In 2025, Storoschuk and colleagues published a review in Sports Medicine titled (I love this) "Much Ado About Zone 2." They went looking for the evidence base, and here's what they found.

On acute signaling: Zone 2 produces "small and inconsistent" metabolic stress, with negligible-to-small changes in the cellular energy ratios that trigger adaptation. It does not increase AMPK activity in endurance-trained men. There was no change in PGC-1α gene expression (the master regulator of mitochondrial biogenesis) at 30 minutes or 90 minutes.

Work-matched training above Zone 2 produced greater energy-ratio changes, greater CaMKII activation, and greater PGC-1α expression.

On chronic training: four weeks of Zone 2 training did not increase citrate synthase activity or mitochondrial respiration. Five months of primarily Zone 2 training failed to improve citrate synthase activity.

They cite a meta-analytic threshold: exercise below roughly 60% of maximum work rate is not expected to improve mitochondrial content or respiratory capacity at all.

On cardiorespiratory fitness: studies comparing Zone 2 to vigorous training in untrained people show either no difference, or greater improvement with higher intensity, or improvement only with higher intensity. In already-active and trained people, fitness only increased with intensities above Zone 2.

Their conclusion, quoted about as directly as I can put it: current evidence does not support Zone 2 as the optimal intensity for improving mitochondrial or fat-oxidative capacity. And they failed to find substantive evidence that Zone 2 is superior to higher intensities.

And the structural problem they identify is the biggest one: almost no study has explicitly examined the effect of Zone 2 training as such. The entire popular case is inference from studies that happened to use similar intensities without testing the question.

The HIIT side

Liang and colleagues, 2024, pooled 44 randomized trials with 1,863 older adults, mean ages 60 to 81.

HIIT versus no exercise:

- Cardiorespiratory fitness: g = 0.77 (large)
- Muscular strength: g = 0.47
- Muscular endurance: g = 0.65
- Systolic BP: −0.29
- Resting heart rate: −0.36
- Body fat %: −0.26
- Balance (Timed Up and Go): −0.79

HIIT versus other forms of exercise:

- Cardiorespiratory fitness: g = 0.23 (small but statistically significant)
- Everything else: not significant

And the tolerability data matters: attendance was 80% or better in 17 of 20 studies that reported it, and dropout was mostly under

20%. Sixty-to-eighty-year-olds tolerate interval training fine in supervised settings.

The gap: adverse events were not systematically reported. That's a real hole.

The one trial that tried to answer it with deaths

Generation 100, published in the BMJ in 2020 (Stensvold and colleagues). This is the only randomized trial of exercise intensity with mortality as the primary outcome.

1,567 older adults in Trondheim, Norway. Mean age 72.8. Randomized to HIIT (about 90% peak heart rate), moderate continuous training (about 70%), or a control group following national activity guidelines. Five years.

Result: no significant difference in all-cause mortality for exercise versus control.

- HIIT vs control: hazard ratio 0.63 (not significant)
- MICT vs control: hazard ratio 1.24 (not significant)
- HIIT vs MICT: hazard ratio 0.51 (not significant)

Mortality: control 4.7%, HIIT 3.0%, MICT 5.9%.

VO2peak at five years: HIIT was 0.7 mL/kg/min higher than both other groups. All three groups prevented the expected age-related decline.

The authors' own limitations are severe: the control group stayed highly active and performed more HIIT than the moderate-intensity group did. Only about half the HIIT participants met the strict intensity criteria. And 87.5% of participants reported good health at baseline with 80% already moderately to highly active.

The correct interpretation is that this trial couldn't answer the question, because it had too few deaths in a healthy cohort and a contaminated control. It is not evidence that intensity doesn't matter. The MICT group having the highest mortality of the three is almost certainly noise.

So what do I actually think?

Here's my synthesis, separated by confidence.

Well supported:

- Any cardio beats no cardio, by a lot. Huang's +3.78 mL/kg/min in older adults came mostly from moderate-intensity programs.
- Higher intensity produces more fitness gain per unit of time invested.
- HIIT is tolerated by people in their sixties, seventies and eighties.
- Total volume of activity matters enormously.

Not supported:

- That Zone 2 has unique mitochondrial properties.
- That Zone 2 is the optimal intensity for anything.
- That you should avoid going above Zone 2.
- That the 80/20 polarized model is validated for health. That distribution comes from elite endurance performance research and got extrapolated.

Not resolved:

- Whether higher intensity actually reduces mortality more. Generation 100 was the only real attempt and it couldn't tell us.

What I do, and what I'd suggest

This is a judgment call built on incomplete evidence, but here's what I'd suggest:

Do most of your aerobic work at whatever intensity you'll actually keep doing. Volume is the thing you can control and it's clearly beneficial. If that's walking, walk. If it's easy cycling, cycle. The Zone 2 crowd oversold the mechanism but they didn't hurt anybody by getting people to move more.

Add one or two harder sessions a week: intervals, hills, whatever format you like, as long as it gets you breathing hard for repeated bouts. That's where the time-efficient fitness gain lives.

Don't be afraid of intensity because you're over fifty. The tolerability data is good. Get cleared by your doctor first if you have any cardiac history (that's a real caution, not a formality) and then go.

What I do is a mix, and most of my conditioning comes as a byproduct of how I lift rather than from dedicated cardio sessions. That works for me because I've got fifty years of base. It's not what I'd tell a beginner.

Chapter 12 — Bones

If you're a woman past menopause, or a man past about sixty-five, this chapter might matter more than any other in the book, because a hip fracture at eighty is frequently the beginning of the end.

And most of what you've been told about exercise for bone is wrong.

"Weight-bearing exercise builds bone" is too vague to be true

Here's what a 2025 review in Current Osteoporosis Reports found when it sorted exercise types by what they actually do to bone density:

- Moderate-to-low intensity progressive resistance training: failed to produce lumbar spine BMD gains.
- Low-impact exercise like walking: no positive BMD effect.
- Non-weight-bearing exercise like cycling and swimming: no positive BMD effect.
- High-intensity resistance training above 80% of 1RM, plus impact: the most robust gains, around 2–3% at the lumbar spine.

Walking is wonderful. It's good for your heart, your mood, your joints, your blood sugar and your life. It does not build bone.

The trial that changed the guidelines

LIFTMOR. Watson and colleagues, Journal of Bone and Mineral Research, 2018.

The subjects were 101 postmenopausal women with an average age of 65. All of them had a T-score below −1.0, meaning osteopenia or osteoporosis. That's exactly the population that had been told for decades to avoid heavy lifting and spinal loading.

The protocol was 8 months of twice-weekly, 30-minute supervised sessions: five sets of five reps at over 85% of one-rep max in the

deadlift, overhead press and back squat, plus a jumping chin-up with a drop landing.

Results versus a home-based low-intensity control group:

	Training group	Control
Lumbar spine BMD	+2.9%	−1.2%
Femoral neck BMD	+0.3%	−1.9%
Femoral neck cortical thickness	+13.6%	+6.3%
Height	+0.2 cm	−0.2 cm

They got taller.

Adverse events across the entire trial: one, a minor lower back spasm. Compliance in the training group was 92%.

The safety result is as important as the density result. This overturned standing clinical advice.

LIFTMOR-M followed it up in 93 men averaging 67, and got +4.1% lumbar spine BMD, plus +1.5% lean mass against a −2.4% loss in controls, with 5 minor adverse events total. One caveat on that one: it was semi-randomized. The 26-man control group was a non-randomized matched group rather than a randomized arm. That's a weaker design than LIFTMOR and you should weight it accordingly.

Now the part almost nobody tells you

The total hip doesn't respond.

Look at that LIFTMOR table again. Lumbar spine was +2.9%, and femoral neck was +0.3%, which is really prevention of loss, not gain.

And it's not just LIFTMOR. The Osteocise trial (162 people, 12 months): modest 1.0–1.1% gains at spine and femoral neck, no change at total hip. ACTLIFE-RCT (13 months): significant lumbar spine effect, no total hip improvement.

Every single trial shows lumbar spine gains and a flat total hip. That's a genuine and underreported problem, because hip fractures can be devastating.

Nobody has a solution to that. It's one of the biggest open gaps in this field. What I'd say is that the trials show strength, function, balance and lean mass all improving alongside the spine BMD, and preventing the fall is a legitimate way to prevent the hip fracture even if you can't thicken the bone.

The other caveats you deserve

These were surrogate outcomes, because BMD is a proxy. LIFTMOR was not powered to detect fractures and did not measure them.

The trial ran eight months, and we don't have long-term data from these protocols.

It was fully supervised by exercise physiologists, which is not the same as you doing 5×5 deadlifts in your garage off a YouTube video.

And the population most likely to be reading this chapter is the one that wasn't studied. LIFTMOR excluded people with a vertebral fracture in the previous twelve months. If that's you, this chapter's protocol has not been tested on you. Talk to your doctor, and find a physical therapist who knows this literature.

It doesn't stick if you stop. One trial extension found lumbar spine gains were lost when adherence dropped below 50%, and detraining studies suggest BMD drifts back toward baseline within about a year of stopping. Interestingly, femoral neck gains persisted better.

One thing this chapter must not be read as saying. If you have **diagnosed osteoporosis** (not osteopenia, not a family history, a diagnosis), then drug treatment is the evidence-based therapy, and it is what the fracture trials were run on. Bisphosphonates, denosumab, and the anabolic agents have randomized evidence for preventing fractures that no exercise program in this

literature comes close to. Heavy resistance training is an adjunct to that treatment. It is not a substitute for it, and nothing in this chapter is a reason to decline or stop a prescription. Lift *and* take the medication your physician prescribes. See also Chapter 37 on menopausal hormone therapy, which is one of the few interventions in this book with a randomized fracture reduction behind it.

What to actually do

If you have osteopenia or osteoporosis and no recent vertebral fracture, and your doctor clears you:

- Get supervised by a trainer or physio who understands loading for bone. This is not optional.
- Progress to heavy compound lifts (deadlift, squat, overhead press) with low reps and high load.
- Add impact if your joints tolerate it, even something as simple as heel drops or a small hop.
- Twice a week, for at least a year. The trials that worked ran 8–13 months.
- Keep doing it. When adherence drops below 50%, the spine gains disappear.

And know what you're getting: better spine density, better strength, better function, better balance, and probably not better hip density. That's the deal.

Chapter 13 — Balance, and Not Falling Down

I'll open this chapter with the finding that surprised me most in all the research I did for this book.

Strength training alone hasn't been shown to prevent falls.

I believed the opposite for years, and I've said the opposite. I was wrong, and here's the data.

The Cochrane review

Sherrington and colleagues, Cochrane Database, 2019. 108 randomized trials, 23,407 participants, 25 countries. Average age 76.

Overall exercise: 23% reduction in the rate of falls. High-certainty evidence. That's about 195 fewer falls per 1,000 people per year.

Fall-related fractures: 27% reduction. (Lower certainty, from 10 studies.)

Now the breakdown by type of exercise, which is where the picture changes:

Exercise type	Rate ratio for falls	Certainty
Balance & functional training	0.76 — 24% reduction	High
Multiple exercise types combined	0.66 — 34% reduction	Moderate
Tai Chi	0.81 — 19% reduction	Low
Resistance training alone	1.14 — no clear benefit	Very low
Walking programs	1.14 — no clear benefit	Very low
Dance	1.34 — no clear benefit	Very low

Balance and functional training had high-certainty evidence and a meaningful reduction. Resistance training on its own showed no clear benefit, from very low-certainty evidence.

Let me not overstate the correction either

That resistance-training estimate rests on five studies and 327 people, rated very low certainty. That's an absence of evidence, not strong evidence of absence. The confidence interval is enormous.

So the claim isn't "lifting is useless for falls." It's that strength training is necessary but not sufficient. You have to train balance specifically, and nobody does.

You can be strong and still fall. Being strong helps you survive the fall and get up afterward, but it doesn't stop the fall from happening.

What kind of balance training

This is the second thing that surprised me. Lesinski and colleagues pooled 23 randomized trials with 1,220 community-dwelling adults over 65, and broke balance down into types:

Balance domain	Effect size
Static steady-state (standing still)	0.51 — moderate
Dynamic steady-state (walking)	0.44 — small
Proactive balance (anticipating reaching, stepping)	1.73 — large
Reactive balance (recovering from a shove or trip)	1.01 — large

The big effects are on proactive and reactive balance, which makes sense, because those are the domains that determine whether a stumble becomes a fall.

Programs built around standing on one leg are training the thing that improves least.

The optimal dose from that analysis: 11–12 weeks, 3 sessions a week, 31–45 minutes each, about 90–120 minutes a week.

What proactive and reactive training actually looks like

Proactive means you know the perturbation is coming and you prepare:

- Stepping over and around obstacles
- Reaching outside your base of support to pick something up
- Tandem walking, heel-to-toe, forward and backward
- Stepping onto and off boxes of varying heights
- Carrying something awkward while navigating

Reactive means someone or something disturbs you and you recover. Learn these with a physical therapist or a qualified trainer, with something solid to grab. If you've already fallen or you feel unsteady, don't do nudges or unstable-surface work on your own:

- A partner giving you gentle unexpected nudges while you stand
- Catching and throwing a ball while standing on an unstable surface
- Deliberately stepping to recover from a controlled lean
- Anything that produces a genuine, unrehearsed correction

That second category is the one almost nobody trains, and it's the one that maps directly onto real falls. You don't fall because you couldn't stand still. You fall because your foot caught something and your body couldn't reorganize fast enough.

This is where power training and balance training meet. Recovering from a trip is a power problem, because you need force fast.

The mobility trial

The LIFE study (Pahor and colleagues, JAMA, 2014) is the biggest and best causal evidence that exercise prevents functional decline.

1,635 sedentary adults aged 70 to 89. Randomized to a structured physical activity program (walking toward 150 min/week, plus lower-body strength with ankle weights, plus balance and flexibility) or to health education workshops. Mean follow-up 2.6 years.

- Major mobility disability (losing the ability to walk 400 meters): 30.1% versus 35.5%. Hazard ratio 0.82.
- Persistent mobility disability: 14.7% versus 19.8%. Hazard ratio 0.72.
- Serious adverse events: no increase.

That's real and it's causal, but look at the absolute numbers: 30% of the exercise group still became mobility disabled. It's an 18% relative reduction, not a rescue. Exercise substantially improves your odds, but it doesn't make you immune.

The Otago number I don't believe

You'll see it cited constantly: the Otago home exercise program reduces mortality by 55%.

That's from Thomas and colleagues, 2010: 7 trials, 1,503 participants, average age 81. Falls: RR 0.68, a 32% reduction. That number I believe. Mortality: RR 0.45.

A 55% mortality reduction from a home exercise program in twelve months is not plausible. That's a bigger effect than any drug in cardiology. It rests on small numbers of deaths across a handful of trials, and it's almost certainly selection and publication bias.

Cite the falls result, and treat the mortality result with visible skepticism when you run into it.

The practical prescription

Add 10 minutes of balance work to the end of every training session, three times a week. Focus on proactive and reactive, not static standing.

Ten minutes is a starting dose, not the 90–120 minutes a week the analysis found works best, so build toward more if you can. For anyone over seventy, few ten-minute blocks in this book pay back more, and virtually nobody does it. Until I looked at this research, that included me.

Chapter 14 — Tendons, Joints, and Training Around the Damage

Before I start, you should know this is the weakest evidence area in the book. Much of what gets written about tendon aging comes from animal studies presented as if it were human data. I'll flag where I'm on solid ground and where I'm reasoning.

The good news: aging tendon still adapts

Epro and colleagues, Journal of Experimental Biology, 2017. 34 women aged 60 to 75. Achilles tendon loading protocol: 90% of maximum voluntary contraction, 5 sets of 4 reps, isometric plantarflexion, 3 seconds loading and 3 seconds relaxation. Three times a week for 14 weeks, then twice a week out to 18 months. Twenty-one women trained and thirteen were controls, and only 12 kept going to 18 months, so the long-term column is a small group.

Measure	Baseline	14 weeks	1.5 years
Achilles tendon stiffness	488 N/mm	598 (+22%)	610
Young's modulus	1.37 GPa	1.63 (+19%)	1.66
Tendon cross-section	~65 mm^2	~69 (+6%)	~69
Plantarflexor strength	~109 Nm	~133 (+22%)	~137

One: aging tendon is mechanosensitive. It gained 22% stiffness in 14 weeks in women in their sixties and seventies. It isn't inert.

Two: essentially all the adaptation happened in the first 14 weeks, and nothing further accrued over the next 16 months. You get the tendon adaptation early and then you're maintaining it.

What loading tendon actually requires

Look at that protocol again, because it's different from what builds muscle.

It's very high load, long duration per rep, isometric, and low total volume: twenty reps a session at 90% of max, holding three seconds.

That's a different stimulus from 3 sets of 10 at 70%. And be clear about what the study shows: healthy older Achilles tendons adapt to a carefully controlled heavy isometric program. It's not a do-it-yourself fix for a painful tendon. If an Achilles or patellar tendon has been cranky for weeks, get it assessed and have a clinician set the load.

The mismatch problem

Karamanidis and colleagues, 2018, found that very old adults (eighties) have lower tendon stiffness than the merely old (sixties), and that short-term conventional resistance training which improves muscle does not change tendon in the very old.

Which suggests muscle and tendon adapt on different timescales, and you can end up with a mismatch: a muscle that can generate more force than its tendon has adapted to handle.

That's a plausible injury mechanism, but it's an inference. No trial has tested a tendon-aware progression scheme against a conventional one for injury outcomes in adults over fifty. I'm reasoning, not citing.

But the reasoning is good enough that I'd act on it.

Why your tendons changed

One cause is advanced glycation end-products (AGEs), which are sugar molecules cross-linking your collagen. They accumulate with age and they accumulate faster with higher blood sugar. That's the mechanistic case for why metabolic health and tendon health are connected, and it's a reason to care about your glucose beyond diabetes risk.

The cells that build and repair connective tissue divide about three times slower in aged human tissue. That figure comes from fibroblast work, and a lot of the tendon-specific literature pools animal data, which is the problem I flagged at the top of this chapter.

Meanwhile, tendinopathy affects roughly 25% of adults and accounts for about half of all reported musculoskeletal injuries.

Is lifting actually dangerous?

A 2023 systematic review of 28 studies covering 13,127 resistance-training practitioners found injury rates per 1,000 hours:

Modality	Injuries per 1,000 hours
Traditional strength training	under 1.0
Weightlifting	3.2
CrossFit / high-intensity functional training	4.2
Powerlifting	4.0
Strongman	5.5

Traditional strength training is, by these numbers, one of the safest things you can do with your body.

The catch: the average age in that review was 28.7. The authors state explicitly that there's no specific data on older adults.

So look at the actual older-adult trial data instead:

- LIFTMOR: one minor adverse event across 8 months of supervised >85% 1RM training in osteoporotic women.
- LIFTMOR-M: five minor events across the 67 men who actually trained (the other 26 were non-training controls), averaging 67 years old.
- LIFE: serious adverse events not increased in 818 people aged 70–89 over 2.6 years.

Supervised heavy resistance training in older adults has a remarkably clean safety record. The caveat is that trials are

supervised, screened, and progressed by professionals, which is an argument for getting supervision, not an argument against lifting.

If you have a hip or knee replacement

Resistance training is strongly indicated after joint replacement and the strength data is good. But range of motion, impact and loading are surgeon-specific and implant-specific. Deep flexion, high-impact plyometrics and end-range loading may or may not be appropriate for your prosthesis. Get the specific restrictions from your surgeon, in writing, and give them to whoever supervises your training.

How I'd train around aging connective tissue

This section is judgment, informed by evidence but not proven by it.

Ramp load slowly, slower than you think you need to. Your muscle will be ready before your tendon is, which is the whole mismatch problem.

Heavy isometrics are the one part of this section with direct evidence in older adults, and that evidence is narrow: healthy Achilles tendons in women aged 60 to 75, on a carefully controlled near-maximal protocol. If you want to use them, have a physical therapist or another qualified professional design the loading for your tendon and build it up gradually. If a tendon is already painful, get it assessed before you load it hard.

Full range where you can tolerate it. Loaded stretch positions appear to be where the connective tissue adaptation lives, though the human data here is thinner than the enthusiasm.

Warm up longer than you did at thirty. I don't have a study for that, but everybody over fifty who lifts will tell you the same thing.

Manage your blood sugar. The AGE cross-linking mechanism is one of the few places where your metabolic health and your joints connect directly.

Don’t train through sharp pain. Achy is usually fine. Sharp, localized, and worse the next morning is not. Your connective-tissue cells divide about three times slower now, so you don’t have the recovery margin you had at thirty-five.

If something’s been hurting for more than six weeks, go see somebody. Tendon problems that get chronic are far harder to fix than tendon problems caught early. I have learned this the expensive way more than once.

Chapter 15 — Recovery, Sleep, and Time Off

Let me start by knocking down something I've believed and repeated for years.

"Older adults need more recovery time" is not well supported

Hayes and colleagues published a systematic scoping review in Sports Medicine Open in 2023 covering 27 studies in adults 65 and over, looking at recovery from resistance exercise.

Here's what they found comparing older to younger adults:

In men: four out of five studies showed older males had smaller changes in muscle damage markers than younger men. The older men were damaged less, not more.

In women: older women showed greater strength decrements and slower recovery than younger women, but creatine kinase and soreness didn't differ.

The authors' own verdict was essentially that the available data make it hard to give clear recommendations. And they flagged that data in women is badly lacking compared to men.

So the folk wisdom ("you're older, you need more days off") is not supported in men and is weakly supported in women from a small literature.

What the data does show about recovery timelines in older adults generally:

- Strength decrements peak 0–48 hours and require more than 72 hours for full recovery in most studies.
- Soreness peaks 24–48 hours and largely resolves by 3–5 days.

Treat seventy-two hours as a rough guide, not a rule. The reviewers themselves said the data were too inconsistent for clear recommendations. It fits training a given muscle group about

twice a week rather than four times, with your own performance and soreness as the tiebreaker.

Sleep

I covered the architecture in Chapter 4. Here's the practical layer.

Sleep duration and mortality in older adults is U-shaped, with the low point at 7–8 hours (Niu and colleagues, 2020, pooling 28 cohorts and 95,259 adults over 60).

But look at the asymmetry:

Sleep duration	Hazard ratio
≤5 hours	1.06
≤6 hours	1.05
≤7 hours	1.04
≥8 hours	1.24
≥9 hours	1.31
≥10 hours	1.45

The long-sleep association is far stronger than the short-sleep association in this population.

Please do not read that as "sleeping 9 hours will kill you." In older adults, long sleep is much more likely a marker of something (occult illness, depression, sleep-disordered breathing, medication effects) than a cause of anything. If you're sixty-eight and suddenly needing ten hours, the useful response is to find out why, not to set an alarm.

Sleep and muscle: borrowed evidence

You've heard that poor sleep wrecks your gains and tanks your testosterone. Here's what those claims rest on.

Sleep restriction and muscle protein synthesis: Saner and colleagues, 2020. Five nights of restricted sleep reduced myofibrillar protein synthesis, and high-intensity interval exercise partially rescued it. That was in healthy young men.

Acute sleep deprivation: Lamon and colleagues, 2021. One night of total deprivation reduced muscle protein synthesis and altered the testosterone/cortisol environment. That was in young men too.

The famous testosterone stat: Leproult and Van Cauter, JAMA, 2011. One week of 5-hour sleep dropped testosterone 10–15%. That was ten young men, and it gets cited in approximately every article about sleep ever written.

There's no equivalent data in adults over fifty. Every claim connecting sleep to training adaptation after fifty (including claims I've made) is extrapolated from young cohorts.

I still think sleep matters enormously, and I sleep like it's a priority. But I'm telling you the evidence is borrowed, because you should know when a confident-sounding claim is standing on ten young men.

Time off is not a failure

From Chapter 8, remember the detraining numbers: three to six months completely off did not produce a statistically significant loss of muscle in older adults, and thirty-one to fifty-two weeks did.

That's six small studies, a thin evidence base. But if you get sick, or have surgery, or life falls apart for a season, you probably have more of a buffer than you fear. Come back when you can. You are not starting over.

What I actually do

I do two hard lower-body sessions a week, never on consecutive days. Upper body I can push harder and more often because it beats me up less. I take full days off when I feel beat up, which I've gotten much better at honoring than I was at forty.

I protect seven to eight hours of sleep and keep the same wake time. The wake time is the one sleep habit I'd defend against all comers, because it's the thing that stabilizes everything else.

And I take an easy week roughly every eight to ten weeks, with lighter weights, the same movements, and no attempt to progress. I have no trial to cite for that. It's fifty years of noticing that when I don't do it, something eventually hurts.

PART III — FOOD

Chapter 16 — Protein: The Number That Changes Everything

If you only change one thing about how you eat after fifty, change this.

The official number is probably too low

The RDA for protein is 0.8 grams per kilogram of body weight per day. For a 180-pound person that's about 65 grams. That number was set to prevent deficiency in the average adult. It was never designed to optimize muscle in a 65-year-old who lifts.

Two major expert bodies have said so.

The PROT-AGE study group (Bauer and colleagues, 2013) recommends 1.0–1.2 g/kg for healthy older adults, 1.2–1.5 with illness, and up to 2.0 with severe illness or malnutrition.

ESPEN, the European clinical nutrition society, recommends at least 1.0 g/kg for older people, with Grade B evidence and 100% consensus among the panel.

Notice those two don't fully agree. PROT-AGE is more aggressive. When two authoritative bodies land in different places, you're in tier two (the range where reasonable people differ) and you should know it.

Why the RDA is questioned

The RDA was built on nitrogen balance studies, and that method has real problems. It tends to overestimate what goes in and underestimate what comes out, producing implausibly positive results. It also clusters test intakes near zero balance, and the efficiency of protein use falls near zero balance, so the regression systematically underestimates requirement. Plus urea pools need five to seven days to equilibrate, and many of the old studies ran shorter.

When researchers reanalyzed the same data with better statistics, they got 0.91–1.0 g/kg, not the 0.66 the RDA was built on.

A newer method called indicator amino acid oxidation (IAAO) gave higher numbers still: an RDA-equivalent of 1.29 g/kg for women over 65 and 1.24 for men over 65 (roughly 55–60% above the current RDA).

Now the part that matters. Those IAAO studies had twelve women and six men. They're 24-hour tracer studies with no clinical outcomes, using a method that's never been validated against long-term health. The direction is corroborated by the nitrogen-balance reanalysis. The precision implied by "1.29 grams per kilogram" is false precision.

The number everybody quotes, and what it really means

Morton and colleagues, British Journal of Sports Medicine, 2018. Forty-nine randomized trials, 1,863 participants. This is the source of "1.6 g/kg."

What they found:

- Protein supplementation on top of resistance training added +2.49 kg to 1RM strength, about 9% more than training alone.
- Added +0.30 kg of fat-free mass, about 27% more than training alone.
- Breakpoint at 1.62 g/kg/day, above which no further contribution to fat-free mass.

That's where the number comes from. Now three caveats you rarely see.

One: the confidence interval on that breakpoint is 1.03 to 2.20 g/kg. The data are compatible with the plateau being anywhere from just above the RDA to nearly triple it. "1.6" is a point estimate of a meta-regression breakpoint. It is not a demonstrated optimum.

Two: the absolute effect is small. It's three hundred grams of extra fat-free mass and two and a half kilos of extra 1RM, across the entire literature. Protein is an adjunct to lifting, not a substitute for it.

Three: only 13 of the 49 studies enrolled anybody over 45, and in those older participants the average supplemental dose was just 20 grams a day. Extrapolating 1.6 g/kg to a seventy-year-old is inference.

And here's the finding that cuts directly against how this gets sold: the benefit of supplementation declined with age instead of increasing. It declined by about 0.01 kg per year of age, and that was statistically significant.

The rule: at least 1 gram per pound of desired body weight

Here's my rule, then the case for it, then the limits of the case, because you deserve all three.

At least 1 gram of protein per pound of desired body weight, every day. Want to weigh 175? Eat at least 175 grams. Weigh 240 and want to weigh 180? Eat at least 180. In metric, that's at least 2.2 grams per kilogram of desired body weight. If you have kidney disease, or your doctor has given you a different number for a medical reason, use your doctor's number (Chapter 19).

Why that high? Start with Morton's number. The breakpoint was 1.62 grams per kilogram, but the confidence interval ran from 1.03 to 2.20, and the authors wrote, in the paper itself, that it may be prudent to recommend about 2.2 grams per kilogram for anyone trying to get the most out of lifting. Two point two per kilogram is a gram per pound. I didn't pick the number to be aggressive. I picked the top of the range that the largest analysis in the field called prudent.

Then add what you read in Chapter 4 and will read in Chapter 17. Your muscle responds less to each meal than it did at thirty. Moore's pooled analysis found older men needed about 0.4 grams per kilogram per meal to get the full synthesis response, and 0.6 per kilogram of lean mass. Yang's trial in seventy-one-year-olds found that 40 grams after training beat 20, where in young men 20 is the ceiling. Four meals a day at the lean-mass dose works out to 2.4 grams per kilogram of lean mass, which for somebody at 15 percent body fat is about 2 grams per kilogram of body weight. A gram per pound is that arithmetic with a small margin on top.

The rule is not a number I happen to like. It's the daily total you get when every meal is big enough to make older muscle listen.

Then add the deficit, because most people reading this want to lose fat, and protein matters more in a deficit, not less. Longland's trial ran 2.4 grams per kilogram against 1.2 through a brutal 40 percent deficit with training. The high-protein group gained 1.2 kilograms of lean mass while losing more fat. The low-protein group gained nothing. Those were young men, so hold the size of that effect loosely, but the direction is what every review of dieting athletes has found: the leaner you are and the harder you cut, the more protein per pound of lean mass it takes to keep the muscle. The sports nutrition position stands put that at 2.3 to 3.1 grams per kilogram of lean mass. My rule is the low end of it.

Why goal weight? Protein need scales with the tissue you're keeping and building, not with the fat you're carrying. That's why Moore's cleaner number was the one measured per kilogram of lean mass, and why the athlete guidelines dose per kilogram of lean mass too. Goal weight is the practical version of that for somebody without a DXA scan. A 250-pound man who wants to weigh 175 doesn't need 250 grams. He needs 175, which is about 1.5 grams per kilogram of what he weighs today, squarely inside the research range, and 2.2 per kilogram of the body he's building. Somebody already at goal weight gets the full rule. Nobody gets a number they can't eat.

Is it safe? Devries pooled 28 trials in 2018 and found no effect of high protein on kidney function in healthy adults. Antonio's group ran trained men at over 3 grams per kilogram for a full year with no change in blood lipids, liver or kidney markers. Chapter 19 covers the real exceptions: kidney disease, or any medical reason your doctor has for setting a different target. If either applies, follow your doctor's number before you push. Everyone else should still know their eGFR and urine albumin, and have their doctor read them. My own kidney markers, checked monthly for years at more than 175 grams a day, have never moved.

The limits, stated plainly. No randomized trial has tested a gram per pound in people over sixty-five. Nunes' 2022 meta-analysis found benefit in the over-65 group at 1.2 to 1.6 grams per kilogram and had no trials at all above 1.6 in that age group. Not negative ones. None. Morton's older subgroup didn't gain more from extra protein, though those trials gave older people only about 20 grams a day on top of a baseline already at 1.2. And there's the Levine finding at the end of this chapter. So the evidence firmly puts your floor at 1.2 to 1.6. Above that, the rule stands on the per-meal physiology, on the deficit data, on the safety data, and on thirty years of watching what happens to people over fifty who run the floor versus people who run the rule. The floor keeps you from getting weaker. The rule is for getting stronger, and it's the one I'd bet my own body on. I do, every month, with labs.

Treat it as non-negotiable. Tracked, every day, not when you feel like it. That's the part most people get wrong, and it's why the person who "eats plenty of protein" is usually at 90 grams when they finally count.

The thing that actually matters more than the number

Protein without lifting doesn't do much.

The cleanest demonstration is Verreijen and colleagues, 2017 (a 2×2 factorial trial in 100 adults aged 55 to 80). Four groups: high protein or normal protein, with or without resistance exercise.

No significant main effect of protein on fat-free mass. No protein-by-exercise interaction.

Only the high-protein-plus-exercise group showed a significant gain in fat-free mass on its own: +0.6 kg. But the trial didn't show that protein itself made a significant difference.

Exercise is the load-bearing variable. Protein is permissive: it lets the training work. On its own, it hasn't been shown to do much.

I want that to land, because there's an entire industry selling protein powder to older adults on the implication that drinking it

will keep them strong. It won't. It'll keep them from being limited by protein while they do the work, which is the training.

What about bone?

You may have heard that high protein leaches calcium from your bones (the "acid-ash hypothesis").

It's wrong, and the evidence points the other way. A 2019 systematic review found a positive relationship between protein intake above the recommended level and higher femoral neck and total hip bone density, plus an 11% reduction in hip fractures with higher protein intake. Other work associates protein around 1.1 g/kg with 1.8% higher hip BMD, 6% higher lumbar spine BMD, and 64% lower vertebral fracture risk over five years.

All of that is observational. Nobody has randomized people to a higher protein intake and then counted fractures. The 64% figure in particular is an association from a cohort, not an effect from a trial, and I'd hold it loosely.

But given how hard it is to improve hip bone density with exercise (Chapter 12), a consistent association running in the opposite direction from the old acid-ash story is at least worth knowing about.

One more thing you should hear from me rather than from a headline

There's a study you may run into: Levine and colleagues, Cell Metabolism, 2014, using NHANES data on about 6,380 people. It reported that high protein intake in people aged 50 to 65 was associated with substantially higher all-cause and cancer mortality.

Here's the fuller picture. The association reversed above 65: in the older group, higher protein was associated with lower cancer and total mortality. It's observational. Diet was assessed from a single 24-hour recall, which is a very thin instrument for characterizing someone's habitual eating. And it couldn't separate protein

source, so the animal-protein signal is tangled up with everything else that travels with a high-meat diet.

It's a real finding and it hasn't been replicated in trials. My position is that the intervention evidence (protein plus resistance training preserving lean mass and function) is what I'd act on, and I'd lean toward getting a meaningful share of that protein from fish, dairy, eggs and plants rather than all of it from red meat. But you should know the study exists, and you should know nobody has settled it.

Chapter 17 — Anabolic Resistance and the Per-Meal Dose

Here's a phenomenon that explains a lot about why eating like you did at thirty stops working.

Your muscle stops listening as well

Feed a young man 20 grams of protein and his muscle protein synthesis ramps up. Feed an older man the same 20 grams and the response is blunted. The signaling machinery (mTOR and the pathways downstream) responds less.

That's anabolic resistance. It was first described by Cuthbertson and colleagues in 2005, and it's been replicated repeatedly since.

The consequence: the dose that used to be enough isn't anymore.

How much more?

Moore and colleagues pooled the dose-response data across studies and found the per-meal breakpoint:

	Per kg body mass	Per kg lean mass
Older men (~71)	0.40 g/kg	0.60 g/kg
Younger men (~22)	0.24 g/kg	0.25 g/kg

Older men needed roughly 67% more per kilogram of body weight and 140% more per kilogram of lean mass.

Practically: about 0.4 grams per kilogram per meal. For an 80-kilogram (176-pound) person, that's about 32 grams per meal.

Caveat, stated plainly: that's a retrospective pooled breakpoint analysis, not a prospective trial. The body-weight comparison came out at $p = 0.055$, which is not conventionally significant. And the standard deviations are large.

The best direct evidence

Yang and colleagues, 2012. Thirty-seven men, average age 71. They did unilateral leg resistance training, with one leg worked and one leg rested, and were then given whey protein at 0, 10, 20 or 40 grams.

At rest: only 20 g and 40 g produced significant increases in muscle protein synthesis. 10 grams did nothing.

After resistance exercise: 20 g and 40 g both beat 0 and 10, and critically, 40 g beat 20 g.

That's the key contrast. In young men, the response plateaus around 20 grams. In these older men, the exercised leg kept responding all the way to 40 grams.

If there's one study that justifies eating more protein per sitting after fifty, especially around training, that's it.

Leucine

Leucine is the amino acid that acts as the trigger. There's a threshold you have to cross to flip the switch, and it's higher in older muscle.

Katsanos and colleagues showed a small essential amino acid dose with 26% leucine failed to stimulate muscle protein synthesis in elderly subjects while working fine in the young. Raise leucine to 41% of the mixture and the elderly response came back.

PROT-AGE translates this to 2.5–2.8 grams of leucine per meal, which is roughly what's in 25–30 grams of high-quality animal protein.

But here's the correction. Leucine is a trigger, not a substrate. Meta-analytic work shows leucine reliably raises acute muscle protein synthesis but does not consistently translate into actual lean mass over weeks to months. Selling leucine or BCAA supplements on the basis of acute synthesis data is an overstatement. HMB has the same problem, with lots of acute marker data and thin outcome data.

Get your leucine from food. It comes free with the protein.

Do you have to spread it evenly?

You've heard you should eat 30 grams at every meal, evenly spread. It's messier than it sounds.

For it: Mamerow and colleagues, 2014, a crossover study where the same 90 grams of daily protein was given as 30/30/30 or as 10/15/65. The even pattern produced 25% greater 24-hour muscle protein synthesis. But the sample size was eight people, it ran seven days, and muscle protein synthesis is a surrogate.

Against it: Kim and colleagues, 2018, an 8-week randomized trial in older adults testing distribution patterns. It was null on every endpoint, with no difference in anabolic response, lean mass, strength or function.

Hudson and colleagues reviewed the whole literature in 2020 and found five longitudinal trials: one favored even distribution (a non-significant trend, $p = 0.056$), three were null, and one, in hospitalized older adults, favored the skewed pattern.

(One of those null trials showed a non-significant trend toward the skewed pattern preserving more lean mass during energy restriction, $p = 0.067$. I'm not counting it, because 0.067 doesn't clear the conventional 0.05 bar, and neither does the 0.056 on the other side. If I counted it as a win for the skewed side I'd be doing exactly what I criticize other people for doing in Chapter 35.)

Their conclusion, near enough verbatim: the available evidence is too limited and inconsistent to conclude anything definitive, and "it appears more important to ensure adequate total daily protein intake."

They do endorse a practical compromise: at intakes of 0.8–1.3 g/kg, make sure at least one meal has enough protein to maximally stimulate synthesis, regardless of the overall split.

The myth I want to kill

"You can only absorb 20 to 30 grams of protein at a time. The rest is wasted."

This is false in two separate ways.

One: absorption is near-complete for much larger doses. Your gut is not throwing protein away. What plateaus at 20–30 grams is the acute myofibrillar synthetic response (a specific measurement of one thing), not absorption.

Two: large boluses do useful work. A hundred grams of casein produces prolonged amino acid availability and sustained whole-body anabolism, even if the acute synthesis spike doesn't scale linearly.

The defensible version of the claim is much weaker: per-meal doses around 0.4 g/kg maximize the acute synthetic response in older adults, and hitting your daily total matters more than how you split it.

If your life works better with two big meals, eat two big meals. Just hit the number.

What I actually do

I eat three or four times a day. On a four-feed day the three non-training meals run 40 to 60 grams each. On a three-feed day the other two have to be 50 to 60 to still clear my 175-gram floor. The pre-training feed is one of the three or four, not an extra one on top, and it's bigger, about 75 grams of protein along with carbs (120 to 150 grams of them while I was on retatrutide; Chapter 40).

That's higher than the research requires per meal. It's what works for my training and my appetite. If you can only manage 30 grams at breakfast, 30 at lunch and 60 at dinner, you're doing fine, as long as the day adds up to your number.

Chapter 18 — Protein Quality, and Why Collagen Doesn't Count

Not all protein is the same, and after fifty the differences matter more than they used to.

How quality gets measured

The old system is PDCAAS. It's truncated at 1.0, which means it literally cannot distinguish whey from egg from soy. They all score a perfect 1.00 and the scale runs out.

The newer system is DIAAS, adopted by the FAO in 2013. It measures true digestibility at the end of the small intestine, amino acid by amino acid, and it isn't truncated, so it can rank things.

FAO categories: a DIAAS of 1.00 (100%) or above is "excellent." 0.75 to 0.99 is "good." Below 0.75, you can't make a quality claim at all.

Here's roughly where common proteins land:

Protein	DIAAS
Whole milk / milk protein	1.14–1.43
Egg	1.12–1.13
Beef	1.09–1.22
Chicken breast	1.08
Whey protein isolate	0.96–1.09
Casein	0.90–1.20
Tofu	0.97
Soy protein isolate	0.90–0.92
Pea protein	0.66–0.82
Rice protein	0.37–0.52
Oats	0.44
Wheat / gluten	0.39–0.40

Protein	DIAAS
Hydrolyzed collagen / gelatin	0

Values vary a bit by lab and reference pattern, so don't treat any single number as gospel. The tiers are what matter.

Collagen scores zero. It contains no tryptophan at all. It's also short on methionine, isoleucine and threonine, while being loaded up with glycine, proline and hydroxyproline.

Because it's missing an essential amino acid entirely, it cannot support muscle protein synthesis.

Two trials prove it directly:

Oikawa and colleagues, 2020: healthy older women, average age 69, given 30 grams of whey or collagen twice daily for six days, matched for nitrogen and calories. Whey delivered 3.5 grams of leucine per dose, and collagen delivered about 0.6.

Whey significantly raised muscle protein synthesis at rest and after exercise. Collagen did not significantly raise it at rest, and the integrated six-day measurement showed collagen was not elevated above baseline at all, in the rested leg or the exercised leg. Whey beat collagen with $p < 0.001$.

(Sample size caveat: 22 randomized, final analysis on 8 and 7. Very small.)

McKendry and colleagues, 2024: 31 healthy older males, double-blind, controlled diet at the RDA plus 50 grams a day of whey, pea, or collagen.

Whey and pea both enhanced myofibrillar protein synthesis. Collagen did not.

Note that pea performed like whey at that dose. Plant protein at sufficient quantity did the job.

So never count collagen toward your protein target

If you're drinking collagen in your coffee and logging it as 20 grams of protein, you're logging 20 grams that do almost nothing for your muscle. Collagen is protein, but it's incomplete (it's missing an essential amino acid) and it performed poorly for muscle building in the trials. It's the most common protein-tracking error I see.

But collagen might do something else

There is a plausible niche, and it's connective tissue, not muscle.

Shaw and colleagues, 2017: 8 healthy young men, randomized crossover. Vitamin-C-enriched gelatin, 5 or 15 grams, taken one hour before six minutes of rope-skipping, three times a day for three days.

15 grams one hour pre-exercise doubled serum PINP, a marker of collagen synthesis. And engineered ligament constructs grown in the subjects' serum showed increased collagen content and better mechanical properties.

The mechanism is sensible. Gelatin delivers glycine and proline, vitamin C is a cofactor for collagen synthesis, and brief loading drives blood flow to the tendon at the right moment.

Now the caveats, and they're big. It was eight young men for three days, measuring a blood marker plus a lab-grown tissue model. There was no hard clinical endpoint at all: no tendon healing, no injury rates, no pain, no function. And there's no older-adult data. It's promising, but it isn't proven.

Whey versus casein

Whey digests faster, has more leucine, and produces a bigger acute spike. Pennings and colleagues showed whey beat both casein hydrolysate and micellar casein for postprandial muscle protein accretion in older men.

But the advantage is largely acute and kinetic. Over weeks, with adequate total protein and resistance training, whey-versus-

casein differences in actual lean mass are small and inconsistently demonstrated.

Casein's slow release may make it better before bed. That's a reasonable use.

Animal versus plant

Reid-McCann and colleagues, 2025: 43 randomized trials, 30 of them meta-analyzed.

Overall muscle mass: small effect favoring animal protein (SMD −0.20).

But in adults 60 and over specifically: SMD −0.05, not significant.

Soy versus milk protein: no difference at all.

The animal advantage came mostly from comparisons against non-soy plant isolates, the low-DIAAS stuff like rice protein.

Muscle strength across 14 trials and physical performance across 5 trials: no significant differences.

If you eat plant-based, the practical implication is to eat more total protein (maybe 20 to 30% more) from complementary or blended sources, not to abandon plant eating.

One warning for plant-based eaters over 50

EPIC-Oxford followed 54,898 people for an average of 17.6 years.

Hip fracture, adjusted for BMI, versus meat eaters: vegetarians 25% higher; vegans 131% higher (about 15 extra hip fractures per 1,000 people over 10 years).

Total fractures: vegans 43% higher.

The associations stayed significant after adjusting for calcium and protein, though they attenuated.

This is observational, and the vegans in that cohort had lower BMI, lower calcium and lower protein intakes. So it reads best as a

warning about poorly constructed vegan diets rather than an indictment of plant-based eating.

But it's a real and clinically meaningful signal for anyone over fifty. If you're vegan past fifty: get your protein up, get your calcium in, get B12 and vitamin D handled, and lift.

The vegan chapter of my own life

I did vegan for a couple of months once. My blood work came back beautiful.

I don't recommend it for me. It wasn't the best fit. But when I ate vegan, I planned the protein and the essential amino acids deliberately, instead of just cutting out animal products. That's the part most people skip.

That's the difference between a designed plant-based diet and a diet that just happens to have no animals in it. Subtraction is where people get in trouble after fifty.

Chapter 19 — The Kidney Myth (and the Real Exception)

You've heard it. Your doctor may have told you. High protein damages your kidneys.

What the evidence says

Devries and colleagues, Journal of Nutrition, 2018. Twenty-eight studies, 1,358 participants: healthy adults, obese adults, people with type 2 diabetes and hypertension. Anyone with diagnosed kidney disease was excluded.

High protein was defined as 1.5 g/kg or more, or 20%+ of calories, or 100+ grams a day.

Change in GFR between high-protein and normal-protein interventions: no significant adverse difference.

The authors were about as blunt as researchers get. Devries, the lead author: there is simply no evidence linking a high-protein diet to kidney disease in healthy people or those at risk. Phillips, the senior author: protein causing kidney damage lacks any support.

The most current synthesis (Silva and colleagues, 2026, 22 randomized trials with over 1,400 people, testing intakes around 2.0 g/kg or higher) found:

- eGFR increased (SMD 0.39), with high heterogeneity
- Serum creatinine: no significant change
- Body fat percentage down, fat-free mass unchanged

Their language: eGFR rises "without consistent biochemical evidence of renal injury," and the rise probably reflects short-term hemodynamic adaptation.

That's the kidney doing more work, which is what it does when you give it more work. It's not the kidney being damaged.

The limit of what we know

Here's what I won't tell you: that it's proven safe forever.

These trials are mostly six to twenty-four months. Nobody has run a twenty-year randomized trial of 2 grams per kilogram. "No evidence of harm over one to two years in healthy kidneys" is a real finding. It is not "proven safe for life."

I've been eating high protein for decades and my kidney markers are fine. That's an anecdote with monthly labs behind it, which is better than a plain anecdote, but it's still one person.

The exception that actually matters after fifty

Chronic kidney disease prevalence rises steeply with age. This is not a rare condition in the over-fifty population, and plenty of people have it without knowing.

PROT-AGE's guidance:

- eGFR below 30 and not on dialysis: restrict to 0.8 g/kg. This is the real restriction, and it's important.
- On dialysis: above 1.2, ideally 1.5 g/kg. More, not less.

The newer kidney guideline (KDIGO, 2024) is more cautious than PROT-AGE. For anyone with chronic kidney disease at stage 3 or worse, which means an eGFR under 60, it suggests about 0.8 g/kg. It says to avoid going above 1.3 g/kg if your kidney disease is at risk of getting worse. It also allows more protein for older people who are frail or losing muscle. That's a call for your doctor to make, not me.

So here's my actual advice, and it's the practical takeaway of this whole chapter:

Before you push protein hard after fifty, know your eGFR and your urine albumin (uACR).

Both are cheap. eGFR is on a standard metabolic panel. uACR is a simple urine test, so ask for it. Have your doctor read the results with you, because kidney disease can be there even with an eGFR

above 60. If the results look normal in context, the evidence in this chapter says go ahead. If either one is off, or you've been told you have kidney disease, don't push protein until your doctor sets your number. Same if your doctor has any other medical reason for a different target. That's my rule: kidney disease means your doctor signs off on the number.

That's the whole thing. Get the numbers, have them read in context, and then stop worrying about it.

Chapter 20 — Pick Your Diet

Now we're back to Chapter 1, because this is the area where "everyone is different" does the most work.

The trial that should have settled the personalization argument

DIETFITS. Gardner and colleagues, JAMA, 2018. 609 people aged 18 to 50. I'll flag that age range immediately, because a book about being over fifty leaning on a trial that enrolled nobody over fifty is exactly the move I criticize elsewhere. It's the best test of the personalization question anyone has run, but it is not an older-adult trial. Hold it accordingly.

Twelve months, randomized to low-fat or low-carb, with both groups coached to maximize food quality.

Weight loss at 12 months: low-fat −5.3 kg, low-carb −6.0 kg. Difference between groups: 0.7 kg, not significant.

But here's the part that matters more. They had pre-specified hypotheses that people with certain genotypes would do better on one diet, and that people with different insulin secretion patterns would do better on another. Those were the headline hypotheses of the whole study.

Diet by genotype interaction: $p = 0.20$. Diet by insulin secretion: $p = 0.47$.

Both failed. This was the single best test of "match your diet to your biology" using the two most plausible markers, and neither one predicted anything.

DIETFITS doesn't refute what I've said all through this book, that everyone is different. What it refutes is the claim that we can currently predict, from a genetic test or an insulin panel, which diet you should be on. We can't, and the commercial tests selling you that are selling you nothing.

What DIETFITS doesn't rule out is that individuals still respond differently for reasons we can't measure yet: appetite, adherence,

food preference, gut symptoms, medical conditions, life circumstances. Those are real and they're why the average difference of 0.7 kg tells you almost nothing about you specifically.

You still have to test it on yourself. You just can't shortcut it with a spit kit.

The one thing the diets have in common

Both arms were coached to maximize food quality: more vegetables, fewer refined foods, less added sugar, mostly whole food. That's the variable both arms shared, and that's probably where the results came from.

The lipid trade-off

DIETFITS also showed the metabolic trade-off cleanly:

Change (mg/dL)	Low-carb	Low-fat
LDL cholesterol	+3.62	−2.12
Triglycerides	−28.20	−9.95
HDL	+2.64	+0.40

Low-carb: better triglycerides, better HDL, worse LDL. Low-fat: the reverse on LDL, less improvement elsewhere.

Which matters more for you depends on your starting lipid picture and your cardiovascular risk. That's a conversation with your doctor holding your actual numbers, not something a book can answer.

The carbohydrate mortality curve

Seidelmann and colleagues, Lancet Public Health, 2018. The ARIC cohort (15,428 people followed a median of 25 years, 6,283 deaths) plus a meta-analysis of 8 cohorts totaling 432,179 people.

The relationship was U-shaped, with the lowest mortality around 50–55% of calories from carbohydrate.

- Under 30% of calories from carbs: 37% higher mortality
- Over 70%: 16% higher mortality

Modeled life expectancy at fifty: 33.1 more years on moderate carbs, 29.1 on low-carb, 32.0 on high-carb.

But the real finding is the substitution analysis, and this is the part that gets left out:

- Replacing carbs with animal-derived protein and fat: 18% higher mortality
- Replacing carbs with plant-derived protein and fat: 18% lower mortality

It's the same carbohydrate reduction with the opposite outcome. What you replace the carbs with matters far more than the carbohydrate percentage.

Observational data, food frequency questionnaires at two visits over 25 years, and the low-carb eaters in that cohort smoked more and moved less. So hold it loosely. But the substitution finding is consistent with everything else we know.

What I actually eat, and how it changed

For years I ran a keto-style diet. Fifty grams of carbs a day, maybe seventy at the maximum, usually less. My body was well adapted to running on fat. I felt great.

Then I used a peptide, and my carbohydrate needs changed dramatically. While I was on it, I went from 50 grams of carbs to 400 grams a day, and I hit a wall twenty minutes into a workout if I didn't eat 120 to 150 grams of carbs beforehand. Today I'm around 200 grams.

I'll tell that whole story in Chapter 40. I bring it up here because I was certain about my diet, and I was right about it, and then my body changed and the answer changed with it. The right diet for you at fifty-two might not be the right diet for you at sixty-three. Mine wasn't.

How to actually pick

Start with total protein. At least 1 gram of protein per pound of desired body weight (Chapter 16). (Kidney disease, or a different number from your doctor? Use your doctor's.) That's non-negotiable and it's independent of which diet style you pick. Build around it.

Then pick the style you can live with. That's the one you'll still be doing in two years, which may not be the one with the best studies. Adherence is the whole game.

Then test it properly, for two weeks minimum and ideally four to six, one change at a time. Track how you feel, how you train, what your body composition does, and if you can, what your blood work does.

Then adjust. And accept that you'll do this again in a few years.

On dirty versions of clean diets

Somebody tells me they've been doing keto for years, and my first question is: keto, or dirty keto?

Because there's a version of every diet where you follow the letter and ignore the point. Dirty keto is processed junk that happens to be low in carbs. Junk-food vegan is candy and chips that happen to have no animal products. Both technically comply, and neither works.

Being vegan isn't an excuse to eat junk, and neither is keto. If you're going to run a diet, run it properly, with real food, deliberately chosen. Otherwise you're not testing the diet, you're testing whether you can lose weight eating garbage in a specific macronutrient ratio.

Chapter 21 — What Actually Has Outcome Data

Here's a question almost nobody asks about a diet: has anybody ever tested whether it makes you live longer or keeps you out of the hospital?

For most diets, the answer is no. They've been tested on blood markers, weight, and short-term measurements, but not on whether you die.

Let me sort the field by that standard, because after fifty it's the standard that matters.

Mediterranean — the only one with hard endpoint trials

PREDIMED is the famous one, and I need to tell you the whole story, because it's a good lesson in how to read research.

The original 2013 paper was retracted in 2018.

Here's what happened. A statistician named John Carlisle analyzed the baseline data and flagged that the randomization looked implausible. An investigation found three specific problems: over 400 participants were household members enrolled without independent randomization; at one of eleven sites, whole clinics were allocated instead of individual patients, affecting over 450 people; and there was apparently inconsistent use of randomization tables at another site.

In total, 1,588 of 7,447 participants, about 21%, had group assignments that departed from proper randomization.

The New England Journal of Medicine retracted the paper and republished it the same day with two reanalyses: one statistically correcting for the clustering, and one simply deleting all 1,588 affected participants.

The republished results:

- 7,447 people aged 55–80 at high cardiovascular risk, median follow-up 4.8 years

- Mediterranean diet plus extra-virgin olive oil: 8.1 versus 11.2 events per 1,000 person-years. Hazard ratio 0.69.
- Mediterranean diet plus nuts: 8.0 versus 11.2. Hazard ratio 0.72.

The conclusions were essentially unchanged after both reanalyses.

Now the fair criticisms, which the "the diet was vindicated" narrative glosses over:

- 21% of participants weren't properly randomized. The trial is best described as partially randomized. Results being unchanged is reassuring, but it isn't exculpatory.
- The control arm was weak. For the first three years it was a leaflet, upgraded to matched-intensity counseling only in 2006. Some of the effect may be intervention intensity rather than diet composition.
- The intervention groups got free olive oil or nuts. The control got nothing.
- A hazard ratio of 0.69 sounds enormous. The absolute risk reduction is about three events per 1,000 patient-years, roughly 0.3% per year.

Then there's CORDIOPREV, which is cleaner. Published in The Lancet in 2022. 1,002 patients with established coronary heart disease, average age 59.5, seven years of follow-up. Mediterranean versus low-fat.

Primary composite outcome: 17.3% versus 22.2%. A 28% relative risk reduction after adjustment, $p = 0.024$.

Men benefited significantly. Women showed no significant reduction, but fewer than 18% of enrollees were women, so that's underpowered, not evidence of no effect.

Verdict: Mediterranean is the only dietary pattern with two randomized trials showing reductions in hard cardiovascular endpoints, one in primary prevention with a randomization asterisk and one in secondary prevention. That is the strongest hard-endpoint evidence base in all of nutrition, and it isn't close.

DASH — powerful on blood pressure, silent on outcomes

The DASH diet has excellent trial evidence for lowering blood pressure.

The original 1997 trial: 459 people, a controlled feeding trial where all food was provided, eight weeks. Sodium held constant across arms so the effect was the diet pattern, not salt.

DASH versus control: about −5.5 systolic / −3.0 diastolic overall, and about −11.4 / −5.5 in people who were already hypertensive.

The 2001 DASH-Sodium trial layered three sodium levels on top:

Combined effect of low-sodium DASH versus high-sodium control: −7.1 mm Hg systolic in non-hypertensive people, −11.5 in hypertensive people.

Those are drug-sized effects from food.

But DASH has never been tested against hard outcomes. Both trials were short, fully fed, and measured blood pressure only. The inference from “5 mm Hg lower” to “fewer strokes” is drawn from other literature (drug trials and cohort studies), not from DASH itself.

That’s still a reasonable inference from indirect evidence.

Low-carb — no hard outcome data at all

DIETFITS gave us twelve-month weight loss and lipids. Nothing on events.

There has never been a randomized trial of a low-carbohydrate diet with cardiovascular events or mortality as the outcome.

The observational data is the Seidelmann U-curve, with the substitution finding I described in the last chapter.

That doesn’t mean low-carb is bad. It means if somebody tells you low-carb has been proven to extend life, they are making it up.

Plant-based — strong observational, no primary-prevention trial

Vegetarian and vegan patterns have strong observational support (Adventist Health Study-2, EPIC, and others) for cardiovascular disease, type 2 diabetes and all-cause mortality.

But there is no primary-prevention randomized trial with hard endpoints. And for over-fifties there's the fracture signal I covered in Chapter 18.

The hierarchy

Tier one, hard endpoint RCT evidence: Mediterranean, and salt substitution, which I'll cover in Chapter 28. It reduced stroke, cardiovascular events and death in a trial of nearly 21,000 people, which puts it squarely in this tier even though it's a single change rather than a whole diet pattern. It's a short list.

Tier two, strong surrogate RCT evidence: DASH, for blood pressure.

Tier three, strong observational, no hard-endpoint RCT: plant-based patterns, fiber intake, avoiding ultra-processed food.

Tier four, short-term surrogate data only: low-carb, keto, carnivore, most fasting protocols, most everything else.

Being in tier four doesn't mean a diet doesn't work. It means nobody has checked whether it does the thing that matters.

If I were forced to pick a default for someone over fifty who didn't want to experiment, I'd say: Mediterranean pattern, at least 1 gram of protein per pound of desired body weight (unless kidney disease or your doctor says otherwise), and lift weights. That's the combination with the best evidence per unit of misery, and it isn't especially close.

Chapter 22 — Fasting: What's Real and What Isn't

I've done fasting and I've made videos about fasting. When I went through the research for this book, it didn't hold up the way I expected.

The trial that broke the hype

TREAT. Lowe and colleagues, JAMA Internal Medicine, 2020. 116 people, average age 46.5, twelve weeks. Time-restricted eating (eat noon to 8 pm, fast the rest) versus three structured meals a day.

Weight loss: TRE −0.94 kg. Structured meals −0.68 kg. Difference between groups: −0.26 kg, p = 0.63, not significant.

Twelve weeks of 16:8 produced about two pounds of weight loss, no better than eating normally.

No significant differences in fat mass, fasting glucose, fasting insulin, HbA1c, lipids, or estimated intake either.

Then came the finding that got everyone's attention: lean mass. Appendicular lean mass index dropped significantly more in the fasting group (p = 0.005). In the smaller group that had body scans, total lean mass fell 1.10 kg in the fasting arm and didn't significantly change in the control arm.

Roughly 65% of the weight lost in the time-restricted group's scanned subgroup was lean mass. That's the wrong two-thirds.

Be fair to both sides here. That lean mass result was a secondary outcome, measured by DXA in only 50 of the 116 participants, and it drew a formal letter in the same journal cautioning against overinterpretation. It has not been consistently replicated. Treat it as a credible warning signal, not a settled finding.

But the primary result, that time-restricted eating didn't beat normal eating for weight loss, is robust.

The twelve-month replication

Liu and colleagues, New England Journal of Medicine, 2022. 139 adults with obesity, twelve months.

Both groups were calorie restricted to about 75% of usual intake. The fasting group additionally restricted eating to an 8-hour window.

- Calorie restriction alone: −6.3 kg
- Calorie restriction plus time-restricted eating: −8.0 kg
- Difference: −1.8 kg, not significant.

No significant differences in body fat, lean mass, or metabolic risk factors.

When calories are matched, the eating window adds nothing. That's a clean result from a good trial.

The strongest pro-fasting trial

I'll give the other side its best shot.

Catenacci and colleagues, Annals of Internal Medicine, 2025. 165 adults, twelve months. A 4:3 protocol (80% energy restriction on three non-consecutive days a week) versus daily caloric restriction.

Weight: −7.6% with intermittent fasting versus −5.0% with daily restriction. 58% versus 47% achieved at least 5% loss. Better systolic blood pressure, total cholesterol, LDL and fasting glucose.

That's a real win for the fasting arm.

But read what it was. That's intermittent energy restriction, not time-restricted eating, and it does not validate 16:8. And both arms got group behavioral support and exercise recommendations. The most likely mechanism is that a 4:3 structure was easier to adhere to, producing a bigger actual deficit.

Which is the general conclusion about fasting: it works when it makes you eat less. It has no magic beyond that.

The specific concerns for people over fifty

A 2026 systematic review looked at 31 studies of intermittent fasting in adults 60 and over, though only 7 randomized trials were eligible for the meta-analysis, which is a very thin base.

Weight loss was modest: 16:8 produced about −1.92 kg versus usual diet. Cardiometabolic markers improved somewhat, with HbA1c down 0.12 to 0.2% and systolic BP down 5 to 13 mm Hg.

Interestingly, the 16:8 studies in this review consistently reported no lean mass loss, which contradicts TREAT.

But two signals in that review deserve your attention:

- Prolonged nocturnal fasting beyond about 12.4 hours was associated with 58% increased cardiovascular mortality.
- Eating windows of 10 hours or less were associated with lower cognitive test scores.

Both are observational, both from heterogeneous data, and both non-linear. Don't panic about them. But the review's authors recommended moderate fasting approaches in this population rather than extreme protocols, and I think that's right.

Notice that both signals point the same way, toward concern about longer fasts, and one of them overlaps the advice I'm about to give: a ten-hour eating window is a fourteen-hour overnight fast. Because the data are that soft, I'm not going to let either one set a hard number. What I take from them is that the extreme end is where the concern lives, not that there's a precise safe window.

Why I'm now cautious about fasting after fifty

Put the pieces together.

You have anabolic resistance, so you need a bigger per-meal protein dose to trigger muscle protein synthesis.

You need at least 1 gram of protein per pound of desired body weight (Chapter 16). (Kidney disease, or a different number from your doctor? Use your doctor's.)

And you're going to compress all of that into eight hours?

For someone with a 180-pound goal weight, that's 180 grams in two meals, ninety grams a sitting. It's doable, but it takes deliberate effort, and most people doing 16:8 are not planning it that carefully. They skip breakfast and eat what they were already eating.

Combine that with TREAT's lean mass signal, whatever its replication status, and the direction of concern is clear.

Fasting is a tool for eating less. If you're over fifty and your problem is that you're eating too much, it may help. If your problem is that you're losing muscle, it's pointed the wrong way.

And the autophagy thing

You'll hear that fasting triggers autophagy (cellular cleanup) and that this is why it extends life.

The autophagy data is almost entirely mechanistic and animal work. There is no human trial linking a specific fasting window to a clinical outcome via autophagy.

This is, in my opinion, the single most oversold claim in the entire fasting field. It has a real mechanism behind it in cells and mice, and the leap from there to "fast 16 hours and you'll live longer" is entirely unsupported in humans.

If you're going to fast after fifty

Some people eat less and feel better on a compressed window. Here's how I'd do it:

If you take insulin, a sulfonylurea such as glipizide, glyburide or glimepiride, or any other glucose-lowering drug, talk to your prescriber before you start a fasting protocol or a calorie deficit. Insulin and sulfonylureas are

the big ones: fasting or eating less on those can cause hypoglycemia (low blood sugar) at doses that were safe the week before, and the dose may need to come down first.

- Keep the window at ten hours or more, not eight and not six.
- Pair it with resistance training. That's non-negotiable.
- Deliberately target protein inside the window, with at least two meals hitting 0.4 g/kg. Plan it, don't wing it.
- Track your strength. If your lifts are falling, you're losing the thing you can't afford to lose. Stop.
- Don't do it because of autophagy. Do it because it helps you eat less, if it does.

Chapter 23 — Fiber

Fiber has good evidence

Reynolds and colleagues, The Lancet, 2019. 185 prospective studies covering 135 million person-years, plus 58 randomized trials with 4,635 adults.

Highest versus lowest fiber intake:

Outcome	Risk reduction
All-cause mortality	15%
Coronary heart disease mortality	31%
Coronary heart disease incidence	24%
Stroke incidence	22%
Type 2 diabetes incidence	16%
Colorectal cancer incidence	16%

Dose-response: about 7% lower all-cause mortality per additional 8 grams of fiber a day. Greatest benefits at 25–29 grams a day, with the curves suggesting continued benefit above 30 for cardiovascular disease and diabetes.

Most people over fifty are eating half that.

Now note the asymmetry

Those observational numbers are big, 15 to 31% risk reductions.

The randomized trial results on surrogates are tiny:

- Body weight: −0.37 kg (high quality evidence)
- Total cholesterol: −0.15 mmol/L (moderate)
- Systolic blood pressure: −1.27 mm Hg (moderate)

That gap tells you something. High-fiber whole foods travel with an entire healthy lifestyle. The claim is “fiber-rich whole foods are

consistently associated with better hard outcomes," not "a fiber supplement will cut your heart disease risk 31%."

Eat the food. The supplement is a distant second.

The glycemic index finding nobody publicizes

Same Lancet series. They also assessed glycemic index and glycemic load.

Low to very-low certainty evidence. Glycemic index showed minimal risk reduction for most outcomes. The type 2 diabetes reduction of 11% attenuated to 5% on sensitivity analysis. And trials showed "no consistent benefits" from changing dietary glycemic index.

The authors' conclusion: GI and glycemic load are less useful as measures of carbohydrate quality than dietary fiber.

That's a fairly direct undercutting of an entire industry. If you've been organizing your carbohydrate choices around glycemic index, the evidence says organize them around fiber instead.

The microbiome: what's actually established

Established:

- Diet changes your gut microbiota composition, quickly and reproducibly.
- Fermentable fiber increases the bacteria that produce short-chain fatty acids.
- Distinct microbiome signatures are associated with obesity, diabetes, inflammatory bowel disease and colorectal cancer.
- Fecal microbiota transplant for recurrent C. difficile infection works and is used clinically. That is essentially the only causally validated microbiome intervention in medicine.

What's not established, and this is most of what you read:

A 2020 review of the randomized trials found that 13 of 16 documented composition shifts after fiber interventions. But several trials found composition changed without any corresponding increase in measurable short-chain fatty acids. In one, 31 healthy people had altered composition and no change in fecal SCFAs or metabolic markers at all.

Metabolic benefits concentrated in metabolically impaired people, not healthy ones. In 44 overweight/prediabetic people, Bifidobacterium went up with a prebiotic, but fasting insulin, glucose and HOMA-IR didn't move. In 27 people with type 2 diabetes, a high-fiber diet did significantly reduce HbA1c.

And there's a diversity paradox: some studies showed metabolic improvement with reduced diversity, which undercuts "more diversity equals better health."

The reviewers' verdict: a firm causal conclusion between gut microbiota and metabolic regulation remains elusive.

The fermented food study

Wastyk and colleagues, Cell, 2021. 36 healthy adults, 10 weeks.

The fermented food arm (yogurt, kefir, kimchi, kombucha, brined vegetables, up to six servings a day) showed increased microbial diversity, dose-dependently, and all 19 measured inflammatory proteins decreased, including IL-6.

In the high-fiber arm, diversity did not increase and cytokines did not decrease. Responses were highly individual instead.

The authors' hypothesis for the fiber null was that ten weeks isn't long enough, and that industrialized microbiomes are depleted of the bacteria that can break fiber down in the first place.

Caveats: 36 people, 10 weeks, one site, healthy adults, and immune markers rather than clinical outcomes. This is an interesting hypothesis-generating study that got reported as if it proved fermented food prevents disease. It did not.

And there's a whole industry built on top of the microbiome: leaky gut, sensitivity panels, testing kits, probiotic protocols. That's the next chapter.

The safe version

Eat 25 to 30-plus grams of fiber a day from varied whole plant foods. Include some fermented foods.

The foods have outcome evidence. The mechanism is still speculative. Act on the foods, hold the mechanism loosely, and don't buy the test kit.

Chapter 24 — The Gut: What's Real and What's Sold to You

Nicole, the nutritionist I had on my channel, doesn't start with the diet. She starts with the gut. Autoimmune condition? Thyroid? Are you absorbing anything? Fatty liver in somebody who doesn't drink?

I think that instinct is right, and I also think this is the area where my side of the fence has done the most damage to its own credibility. So let me separate what's real from what's been sold to you.

What's actually established

Intestinal permeability is a real, measurable physiological property. Your gut lining is a barrier with tight junctions between cells, and how leaky that barrier is can be measured by differential sugar absorption tests, by electrophysiology on tissue samples, and by markers of bacterial products crossing into the blood.

And it is altered in specific conditions. A consensus review in BMC Gastroenterology (Bischoff and colleagues, 2014) lists them: inflammatory bowel disease (Crohn's and ulcerative colitis, with documented changes in the tight junction proteins), celiac disease, critical illness and trauma (where barrier breakdown leads to sepsis), food allergy, and IBS.

That's established biology, not fringe.

What's association only: obesity, metabolic disease, type 2 diabetes, fatty liver, and neurological conditions. Those associations are real. Whether increased permeability causes them, results from them, or just travels alongside them is not established. The consensus group's own words were that we have limited knowledge of what causes barrier dysfunction and what restores it.

Notice that the expert group deliberately avoids the term “leaky gut.” They distinguish “intestinal barrier” (the function) from “intestinal permeability” (the measurable feature). That’s because “leaky gut syndrome” has come to mean something much larger and much less supported than the physiology.

The zonulin problem

Here’s some bad news about a test a lot of people in my world order.

Zonulin was proposed as the protein that regulates tight junctions, the thing you could measure in blood to assess gut permeability. Commercial panels test for it. Hundreds of published studies used the test kit.

In 2018, a group published in Frontiers in Endocrinology what happened when they checked what the widely used commercial ELISA was detecting.

The theory said zonulin is a specific protein called pre-haptoglobin-2. If that’s true, then people with a particular genotype who cannot produce that protein at all should show zero zonulin. In 376 subjects, they didn’t. The readings were similar across all genotypes. That’s an immediate red flag.

So they ran the analysis properly, with antibody capture, mass spectrometry and Western blot. The kit was capturing complement C3 and its breakdown products, and most likely a protein called properdin.

Then the definitive test: they added purified recombinant zonulin at known concentrations. The kit didn’t detect it.

The proteins it does capture were elevated in obese and diabetic patients and did correlate with metabolic markers, so the assay measures something meaningful. But it isn’t measuring zonulin, and it is not a validated measure of gut permeability.

If somebody hands you a serum zonulin number from a commercial panel and builds a supplement protocol on it, that

protocol is built on an assay that doesn't detect the thing it says it detects.

IgG food sensitivity testing — and this one is unanimous

These tests are enormously popular and I think they do real harm.

The Canadian Society of Allergy and Clinical Immunology position statement puts it bluntly: they strongly discourage food-specific IgG testing for identifying or predicting adverse reactions to food.

Here's why. IgG to a food is a normal marker of exposure and immune tolerance. It's exactly what you see when oral immunotherapy succeeds. A positive IgG means you eat that food. That's what it's telling you.

It is not a marker of pathology. There is no body of research supporting its use to diagnose or predict adverse reactions to food.

The harms the allergy society lists are real:

- False diagnoses leading to unnecessary restriction, worse quality of life, and nutritional inadequacy
- Unnecessary cost and referrals
- And the dangerous one: somebody with a genuine IgE-mediated allergy may have low IgG to that allergen and be advised to reintroduce a food that could kill them

The American Academy of Allergy, Asthma and Immunology, the European academy, the National Institute of Allergy and Infectious Diseases, the British society and the College of American Pathologists all hold the same position. There is no legitimate dissent on this one.

I know people who've spent hundreds of dollars on a panel that came back with a list of nineteen foods to avoid, and then spent a year eating a miserably narrow diet. If that describes you, the good news is you can probably have most of it back.

SIBO — real condition, bad test

Small intestinal bacterial overgrowth is a genuine clinical entity. Classically it shows up after abdominal surgery, in motility disorders, with blind loops, in scleroderma. Rifaximin has FDA approval for IBS with diarrhea.

The problem is the testing.

The American College of Gastroenterology published a clinical guideline in 2020. Every single recommendation in it is "conditional" with "very low" or "low" quality evidence.

Breath test accuracy against the actual reference standard, culturing fluid from the small bowel:

Test	Sensitivity	Specificity
Lactulose breath test	31–68%	44–100%
Glucose breath test	20–93%	30–86%

Agreement between breath testing and aspirate culture: about 65%.

With sensitivity as low as 20 to 31% and specificity as low as 30 to 44%, these tests are close to uninformative in a general population. A positive lactulose breath test in somebody who just has bloating carries very little diagnostic weight. And lactulose speeds up transit, so an early hydrogen rise may just mean the sugar reached your colon, not that you have overgrowth in your small intestine.

And the elaborate stuff built on top of that (hydrogen versus methane versus hydrogen-sulfide "dominance," sequential herbal antimicrobial rounds, elemental diets, prokinetics) has no adequately powered trials at all. Recurrence rates are high.

Direct-to-consumer microbiome tests

The National Institute of Standards and Technology ran the obvious experiment: take identical samples of standardized

human fecal material and send them, in triplicate, to seven commercial microbiome services. Twenty-one tests of the same material.

- Only 3 bacterial genera were consistently detected across every sample. Just 17 appeared in all datasets, under 2% of the 1,208 taxa identified.
- Sequencing depth ranged from under 20,000 reads to over 10 million.
- For 17 of 18 common genera, the variability from the method was equal to or greater than the actual biological variability.
- Replicates of the identical sample were classified as both "healthy" and "unhealthy," with different recommendations.

An international consensus statement (69 specialists across 18 countries) concluded there is insufficient evidence to recommend routine microbiome testing. And it made one recommendation I want to highlight, because it applies far beyond this test:

The lab that sells you the test should not also sell you the protocol.

So what actually works for your gut?

Here's the part I can recommend without hedging.

Fiber, from food. I covered the evidence in Chapter 23: 25 to 30-plus grams a day from varied whole plants, with real outcome data behind it.

Fermented foods. The Wastyk fermented-food trial I described in Chapter 23 found increased microbial diversity and reduced inflammatory markers from six servings a day over ten weeks. It was a small study that measured immune markers rather than clinical outcomes, but it's food, it's cheap, and for most people the downside is small. Pick the ones you tolerate, and watch the sodium.

Low FODMAP (a diet low in certain fermentable carbohydrates), done properly, for IBS. This is the best-evidenced elimination

approach and it ranks highly in network meta-analyses for symptom improvement. But it has a reintroduction phase, and that phase is the point. Staying on it long-term risks depleting your microbiome and your nutrition. Elimination is a diagnostic tool, not a diet.

And here's one about gluten. A double-blind crossover study in 37 people who self-reported gluten sensitivity found gluten-specific effects in only 8% of participants, and those effects weren't reproduced on rechallenge. Symptoms improved on a low-FODMAP diet and got worse whether the participants were given gluten or whey. There was no dose-response.

For most people who feel better off wheat, the culprit appears to be the fermentable carbohydrates, not the gluten. That matters, because it means the useful intervention is different from the one people usually pick.

If you have celiac disease, none of that applies. Gluten is a genuine, lifelong, non-negotiable exclusion. Get tested before you go gluten-free, because the test doesn't work once you've already stopped eating it. I've watched people cut gluten for two years, feel better, and then be unable to get a definitive answer about whether they have celiac disease.

The elimination protocol I'd actually run

If you think a food is bothering you, don't buy a panel. Run the experiment.

One hard line first. This is for a food you suspect you don't tolerate, after you've talked to your doctor about symptoms that won't go away. It is not for allergies. If a food has ever given you hives, swelling or wheezing, or made you faint, don't test it at home. See an allergist. And if you have celiac disease, gluten doesn't get reintroduced. Ever.

Pick one food or one category, not nineteen.

Remove it completely for two to three weeks. Trace amounts defeat the point.

Then reintroduce it deliberately, on its own, in a meaningful quantity, and pay attention for 48 to 72 hours.

Write it down, both phases.

That costs nothing, it has no false positives from a bad assay, and it's the same n-of-1 logic that runs through this entire book. It's slower than a blood test, and it tells you more than a panel will. Symptoms come and go, though, and expecting a reaction can create one, so repeat it before you believe it.

Chapter 25 — Ultra-Processed Food

This one has an elegant experiment behind it.

The metabolic ward trial

Hall and colleagues, Cell Metabolism, 2019. Twenty weight-stable adults, average age 31, living inside a metabolic ward at the NIH, meaning every calorie in and out was measured. Randomized crossover, two weeks on each diet.

The diets were matched for presented calories, macronutrients, sugar, fiber and sodium. The big difference between them was processing level. And both diets were rated equally pleasant, so it wasn't a taste-preference confound.

Participants could eat as much as they wanted.

Result: they consumed 508 more calories a day on the ultra-processed diet. $p = 0.0001$.

Weight: +0.9 kg on ultra-processed, −0.9 kg on unprocessed. Weight change correlated with intake at $r = 0.8$.

The satiety hormone PYY was higher on the unprocessed diet. Ghrelin, the hunger hormone, was lower.

And here's the detail I find most interesting: participants ate about 17 calories per minute faster on the ultra-processed diet. They cleared the plate before their satiety signaling could catch up.

The caveats it deserves

It was twenty people, four weeks, average age 31.

The authors were explicit that the study was not designed to identify the cause of the difference. Subsequent analyses have argued that much of the 508 calories is explained by the ultra-processed meals being more energy dense and more palatable rather than by "processing" as a category, which would mean the

mechanism is a food property some processed foods share, not processing itself.

No older-adult replication exists.

It was the first randomized causal evidence in this area, which makes it important, and it's twenty young people, which makes it preliminary.

Since then there's been a bigger one. The UPDATE trial (Dicken and colleagues, Nature Medicine, 2025) gave 55 adults with overweight or obesity two eight-week diets at home: one minimally processed, one ultra-processed, both built to healthy-eating guidelines. Both groups lost weight, but they lost about twice as much on the minimally processed diet, about 2% of body weight versus 1%. Still short, still not older adults, and it says nothing yet about disease. But the direction held.

The observational weight

Lane and colleagues, BMJ, 2024. An umbrella review: 45 pooled meta-analyses from 14 reviews, about 9.9 million participants, 32 health outcomes.

Convincing evidence: cardiovascular-related mortality roughly 50% higher; anxiety and common mental disorders around 50% higher; type 2 diabetes 12% higher.

Highly suggestive: all-cause mortality 21% higher; heart-disease mortality 40–66% higher; obesity; depression 22% higher; sleep problems.

That's consistent, across millions of people, on multiple outcomes.

And it's all observational. The NOVA classification itself is contested. It groups whole-wheat supermarket bread and fortified breakfast cereal in the same category as soft drinks and candy. Residual confounding by income, education, smoking, activity and total calories is substantial.

What I take from it

The direction of evidence is consistent enough to act on, even though the mechanism and the precise numbers aren't established.

Practically, for someone over fifty: most of your food should be food you'd recognize as food. Meat, fish, eggs, dairy, vegetables, fruit, beans, nuts, whole grains, potatoes, rice.

That's not a moral position or a purity thing. The more of your diet comes from that list, the easier it is to hit your protein, hit your fiber, and not accidentally eat 500 extra calories because the food was engineered to go down fast.

I eat organic where I can, grass-fed and grass-finished beef, and I make my own burgers. I don't have a trial showing organic is better. That's a preference, and I'll label it as one. The whole-food part I'll defend. The organic part is me spending my own money on something the evidence doesn't require.

Chapter 26 — Alcohol After 50

I'm going to be direct: the story you were told about moderate drinking is dead.

What we used to believe

The J-curve. Non-drinkers had higher mortality than moderate drinkers, so a drink or two a day was protective. Red wine, resveratrol, the French paradox, all of it.

What killed it

Zhao and colleagues, JAMA Network Open, 2023. 107 cohort studies. 4,838,825 participants. 425,564 deaths.

Low-volume drinkers (up to about two standard drinks a day) versus lifetime non-drinkers, fully adjusted: relative risk 0.93, p = 0.07, which is not statistically significant.

And in the studies that were free of abstainer bias (using occasional drinkers as the reference, controlling for former drinkers, recruiting at younger ages), the risk was about 0.97, no protection at all.

Why the old J-curve existed: the older studies used current non-drinkers as the comparison group. That group includes people who quit drinking because they got sick. A contaminated reference group makes moderate drinkers look healthy by comparison. It's called the sick-quitter effect, and once you correct for it, the protection evaporates.

The genetic evidence

This is the part that really closes it.

Biddinger and colleagues, JAMA Network Open, 2022. UK Biobank, 371,463 people, average age 57.

Observationally, they saw the classic J-curve. Light-to-moderate drinkers looked healthier.

But those drinkers also had better self-reported health, smoked less, had lower BMI, and were more physically active. The apparent benefit largely disappeared after adjusting for lifestyle.

Then they ran Mendelian randomization, using genetic variants that predict alcohol consumption, which are assigned at conception. That cuts out a lot of lifestyle confounding, as long as the method's assumptions hold.

Per standard deviation increase in genetically predicted alcohol: hypertension odds ratio 1.3. Coronary artery disease odds ratio 1.4.

And the non-linear analysis found risk rising exponentially, with increases in disease risk even comparing light to moderate levels.

Their conclusion: the observed cardioprotective effects of light-to-moderate drinking are largely mediated by confounding lifestyle factors.

The thresholds

From the Zhao meta-analysis, where mortality risk becomes significantly elevated:

- Men: at 45 grams a day or more, about three-plus standard drinks.
- RR 1.15 at 45–64 g, RR 1.34 above 65 g.
- Women: at 25 grams a day or more, about two drinks. RR 1.21 at 25–44 g, rising to 1.61 above 65 g.

Women's threshold is roughly half of men's. And pooling all female drinkers versus female lifetime non-drinkers gave RR 1.22.

Let me also give the fair criticism

The Global Burden of Disease analysis concluded that zero alcohol minimizes health risk, and the "no safe level" framing went everywhere.

The fair pushback: the absolute risk difference between zero and one drink a day is very small. It's widely quoted as roughly 914 versus 918 events per 100,000 person-years, about a 0.5% relative

increase. Critics argued that "no safe level" overstates the practical significance of a tiny absolute increment.

I think that's a legitimate criticism. The framing is: there is no level of alcohol that improves your health, and at one drink a day the harm is real but small.

That makes it a personal cost-benefit judgment, not a medical emergency. It just means the health justification is gone. If you drink, drink because you enjoy it, not because it's good for your heart.

The over-50 specifics

Several things change with age that make the same drink hit differently:

- Lower lean body water, so the same drink produces a higher blood alcohol level
- Reduced first-pass metabolism in the liver
- Falls and fracture risk, when you're already dealing with declining balance and bone density
- Medication interactions: anticoagulants, benzodiazepines, NSAIDs, blood pressure drugs
- Atrial fibrillation risk
- Sleep architecture disruption. Alcohol reliably wrecks the second half of the night, and you already have less slow-wave sleep to spare

That last one is underrated. If you're training hard and drinking in the evening, you're compromising recovery in a way you probably weren't at thirty.

I don't drink much. That's a personal choice tied up with my faith as much as with the research. But I'd have made the same call on the research alone.

Chapter 27 — Losing Fat Without Losing Muscle

This is the chapter most people over fifty need, because most people over fifty who want to change their body want to lose fat. Doing that badly costs you things you can't easily get back.

The trial everyone over sixty should know about

Villareal and colleagues, New England Journal of Medicine, 2017. One hundred sixty obese adults, average age 70, randomized for 26 weeks to: control, diet plus aerobic exercise, diet plus resistance exercise, or diet plus both.

All three exercise arms lost about 8.5 to 9 kg, roughly 9% of body weight. Control lost under 1%.

Now look at what that weight was made of:

Group	Lean mass change	Total hip BMD	VO2peak	Strength	Physical function
Diet + aerobic	−2.7 kg (−5%)	about −3%	+18%	+4%	+14%
Diet + resistance	−1.0 kg (−2%)	about −0.5%	+8%	+19%	+14%
Diet + both	−1.7 kg (−3%)	about −1%	+17%	+18%	+21%

The aerobic-only group lost 2.7 kilograms of lean mass and about 3% of their hip bone density in six months.

Remember from Chapter 12 that essentially no exercise intervention reliably improves hip bone density.

The combination group won on the primary outcome, physical performance, beating aerobic alone ($p = 0.01$) and resistance alone ($p = 0.02$).

The message: intentional weight loss after seventy costs you lean mass and hip bone, and resistance training, not walking, is what cuts those losses.

Protein during a deficit

Verreijen and colleagues, 2015. Eighty obese older adults, average age 63, double-blind, 13 weeks, 600-calorie deficit, resistance training three times a week. One group got a whey-plus-leucine-plus-vitamin-D supplement.

Achieved protein: 1.11 versus 0.85 g/kg.

- Appendicular muscle mass: +0.4 kg in the supplemented group versus −0.5 kg in control, a difference of about 0.95 kg.
- Fat loss was the same in both groups.

They got the same fat loss and about a kilogram better lean mass from roughly 0.26 g/kg more protein plus lifting.

And the study that gets over-extrapolated

Longland and colleagues, 2016. Forty overweight men on a 40% energy deficit with resistance training and intervals six days a week, comparing 2.4 versus 1.2 g/kg of protein.

The high-protein group gained 1.2 kg of lean mass while losing 4.8 kg of fat, during a severe deficit. The low-protein group gained 0.1 kg.

It's a spectacular result, with caveats. The participants averaged 23 years old. The training volume was extreme and fully supervised. Dietary fat differed between arms (15% versus 35%), so protein wasn't cleanly isolated. It ran four weeks.

That study gets quoted as if it were run on sixty-year-olds. It wasn't, and the size of the effect won't transfer. The direction does, and it matches Verreijen's older-adult result above and the 2×2 trial from Chapter 16: more protein, with lifting, keeps more muscle in a deficit. Protein alone showed no significant effect in that 2×2. Protein plus resistance training was the only arm with a

significant gain on its own, though the trial couldn't show the protein itself made the difference.

A 2026 meta-analysis of high-protein diets found reduced body fat percentage but no significant effect on fat-free mass, meaning that in pooled trials without a strong training stimulus, protein's muscle-sparing effect isn't robust.

Protein helps, but training is what does the work.

The actual protocol

If you're over fifty and want to lose fat:

If you take insulin, a sulfonylurea such as glipizide, glyburide or glimepiride, or any other glucose-lowering drug, talk to your prescriber before you start a fasting protocol or a calorie deficit. Insulin and sulfonylureas are the big ones: fasting or eating less on those can cause hypoglycemia (low blood sugar) at doses that were safe the week before, and the dose may need to come down first.

1. Lift from day one, not "once I lose some weight first." Do two to three sessions a week, the template from Chapter 8.
2. Set protein at your number, at least 1 gram of protein per pound of desired body weight, and hold it. A deficit is where the rule earns its keep: the leaner you get and the harder you cut, the more protein it takes to keep the muscle (Chapter 16). (Kidney disease, or a different number from your doctor? Use your doctor's.)
3. Make the deficit moderate: 300 to 500 calories a day, not 1,000. You're not in a hurry, and aggressive deficits are where lean mass goes.
4. Track your lifts, not just the scale. If your working weights are holding or climbing while your waist shrinks, the deficit is working. If your lifts are falling off a cliff, you're cutting too hard or not eating enough protein.
5. Expect to lose some lean mass. The goal is minimization, not zero.

6. Get body composition measured, not just weight. Remember my scan: lighter on the scale, higher body fat. The scale by itself will lie to you about the thing you care about.
7. Watch your bone density if you're at risk, especially women post-menopause and especially if you're losing significant weight. This is a conversation to have with your doctor before you start, not after.

The uncomfortable truth about the deficit

I've watched a lot of people over fifty lose weight and end up looking worse: smaller, but soft and weak. The word people use is "skinny fat," and it's what happens when you lose weight without lifting and without protein.

You'll weigh less, but you'll be functionally weaker than when you started, with less bone, and you'll regain the weight as fat because you lowered your metabolic capacity in the process.

That can set you up for a worse trajectory into your seventies.

Losing fat after fifty is worth doing. Do it while lifting, with your doctor's OK, because lifting means you lose less muscle and bone along the way. If you can't lift, get a plan built for you.

Chapter 28 — Water, Salt, and Blood Pressure

Short chapter, but one finding here is important and almost nobody knows it.

Your thirst signal breaks

Three things change with age, and together they matter.

Thirst is blunted. Healthy older men deprived of water for 24 hours reported no significant increase in subjective thirst compared to younger controls. The response to a sudden osmotic load stays intact. What breaks is the response to slowly rising osmolality, which is what happens when you gradually get dehydrated over a day.

Kidney concentrating ability falls. Ages 60 to 79 show about a 20% reduction in maximum urinary concentrating ability. By 80, over 50% reduction from the youthful peak.

Total body water drops from about 75% in infancy to 50–60% in older people. Water turnover falls about 700 mL a day between 30 and 80.

But “eight glasses a day” is made up

The recommendation lacks solid evidence, and one finding shows how tightly your body regulates this:

People at the 10th percentile of water intake (1,694 mL a day) and people at the 90th percentile (7,934 mL a day) had plasma osmolality of 279 and 280 mmol/kg respectively.

That’s a nearly five-fold difference in intake with essentially identical blood concentration.

The clinical recommendations: ESPEN says at least 1.6 L a day for women, 2.0 L for men from beverages. EFSA says 2.0 L for women and 2.5 L for men, total, including water from food.

A practical warning: checking your urine color is standard advice, and it performs poorly in older adults. Clinical signs, skin turgor

and urine markers are all unreliable in this age group. Serum osmolality is the reference standard, and that requires a blood test.

The hydration-and-aging signal

Dmitrieva and colleagues, 2023 (the ARIC cohort, 11,255 people assessed over 30 years). They looked at serum sodium as a hydration proxy.

- Above 142 mEq/L: 10–15% increased odds of accelerated biological aging
- Above 144: about 50% increase
- Chronic disease risk up to 64% higher above 142
- Premature death 21% higher at 144.5–146

The authors said it plainly: the findings don't prove causation, and randomized trials are needed.

Serum sodium is an imperfect hydration proxy. It also reflects illness, medications like diuretics and SSRIs, and kidney function. Reverse causation is entirely plausible.

Interesting, but not actionable yet. Your sodium level is on a standard panel, so look at it, and if it's running above 142 consistently, mention it to your doctor.

What hydration interventions actually achieve

A recent review of the trials found:

- Skin: 2 L/day for 30 days increased skin hydration. Real, modest.
- Metabolic: 1.5 L/day for 6 weeks decreased a vasopressin surrogate and glucose in high-risk people.
- Kidney: one trial found increased water intake did not slow kidney function decline over a year in CKD patients, a clear null.
- Constipation: 1.5–2 L/day improved stool frequency in people already on a high-fiber diet. No trial has tested water alone.

- Cognition: heterogeneous, inconclusive.

The reviewers' own summary: major gaps remain regarding optimal water requirements in older adults, and we don't even have a good definition of a well-hydrated state.

Don't wait for thirst, and don't trust urine color alone, because after sixty both get unreliable. Drink regularly through the day. Don't force liters, and don't build an identity around it. If you have heart failure or kidney disease, or you've been told to limit fluids, your doctor sets the number, not me.

Now the finding that actually matters: salt substitution

This is the one: SSaSS, Neal and colleagues, New England Journal of Medicine, 2021.

20,995 people across 600 villages in rural China. 73% had a prior stroke. The rest were 60-plus with poorly controlled hypertension. Mean follow-up 4.74 years.

The intervention was simple: replace regular salt with a substitute that's about 75% sodium chloride and 25% potassium chloride. Same salty taste, less sodium, more potassium.

Results:

Outcome (rates per 1,000 person-years)	Salt substitute	Regular salt
Stroke	29.14	33.65
Fatal stroke	6.78	8.79
Major adverse cardiovascular events	49.1	56.3
All-cause mortality	39.28	44.61

That's a 14% reduction in stroke, a 23% reduction in fatal stroke and a 12% reduction in all-cause death, from changing the salt.

The safety concern, high potassium, didn't materialize: hyperkalemia 3.35 versus 3.30 per 1,000 person-years, p = 0.76. No significant increase.

Mean systolic blood pressure difference: only −3.3 mm Hg. That small change produced meaningful outcome differences across a large population.

This is the only trial showing that a sodium-lowering intervention reduces stroke, cardiovascular events and death, not just blood pressure. It's as much a potassium intervention as a sodium one, which I think is underappreciated.

The caveats: very high-risk rural Chinese population with very high baseline sodium intake, about 4.3 g/day versus roughly 3.5 in typical Western diets. Open-label. Critically, people with known kidney disease or on potassium-sparing drugs were excluded, so the reassuring potassium safety result does not transfer to people with impaired kidney function.

If you have normal kidney function and high blood pressure, switching to a potassium-based salt substitute is one of the lowest-effort changes you can make. Talk to your doctor first, especially if you're on an ACE inhibitor, an ARB, or a potassium-sparing diuretic. Those combinations can cause dangerous potassium levels.

And the counterpoint on sodium

The PURE study reported a J-shaped relationship between estimated sodium excretion and cardiovascular events, with apparent harm at both very low (<3 g/day) and high (>6 g/day) intakes.

That's been heavily criticized. It used spot-urine estimating equations that systematically bias low measurements upward and high measurements downward, and reverse causation is a real concern.

Whether very low sodium intake is harmful is unresolved. What's not controversial is that most people eat too much, and that potassium intake is too low.

The salt substitute addresses both at once, which is why I like it.

PART IV — SUPPLEMENTS

Chapter 29 — How To Think About Supplements

I take supplements, and I've made a lot of videos about them. This is the part of the book where I'll disappoint some people, including past versions of me.

Supplements are not approved by the FDA before they're sold

Under the 1994 law that governs them in the US, DSHEA, dietary supplements require no FDA approval before being sold. Medicines have to be approved first.

The manufacturer, not the FDA, is responsible for having evidence that the product is safe and the label is truthful. Any ingredient marketed before October 15, 1994 is grandfathered: it skips the new-ingredient notification. The manufacturer is still responsible for safety, but nobody checks first.

The FDA mostly acts after the fact. It can take action against any supplement that's adulterated or misbranded, with warning letters, recalls and other enforcement (mandatory recall authority came in with the Food Safety Modernization Act in 2011). But that usually comes once the product is on the shelf, and often after people have already swallowed it.

And the label is a marketing claim, not a measurement

Carry this sentence out of this chapter: the label is a marketing claim, not a measurement.

I used to back that up with a 2013 DNA study of herbal products in BMC Medicine. That paper was retracted in 2024 after an investigation found evidence of data fabrication, so I've dropped it.

Here's one that holds up. A 2023 JAMA analysis of 25 melatonin gummy products found 22 of 25 (88%) inaccurately labeled, with actual melatonin ranging from 74% to 347% of what the label said among the products that contained it. One contained no melatonin at all. Five also listed CBD, and the measured amounts ran a bit above the label.

There's ongoing analytical work finding unapproved pharmaceutical analogues in sports, weight-loss and "cognitive" supplements, including products still for sale months or years after FDA recalls.

Emergency department visits attributed to dietary supplements in the US run around 23,000 a year, with about 2,150 hospitalizations. In adults over 65, a notable share of those are choking and swallowing problems from the pills themselves.

So what do you do?

Buy third-party certified. The ones that mean something:

- NSF Certified for Sport: tests for banned substances, screens for contaminants
- Informed Sport tests every batch before release. Informed Choice buys products off the shelf and tests them at random, at least twelve batches a year
- USP Verified: verifies identity, potency, purity
- ConsumerLab: independent testing

The NIH is explicit that these seals do not guarantee a product is safe or effective. They only verify that what's in the bottle matches the label. But that alone puts you in a different risk category than an uncertified product.

Prefer single ingredients like creatine monohydrate, vitamin D3 and psyllium, not "Advanced Longevity Matrix." Proprietary blends are legally allowed to hide the individual amounts, so you can't know whether you're getting a clinical dose of anything or a dusting of everything.

Assume plant-based protein powders carry more heavy metals than whey. Analytical testing consistently finds lead, cadmium and arsenic at higher rates in plant powders, because plants take up what's in the soil.

My framework

I sort everything into three buckets, and I use them for the rest of this section.

WORKS. Randomized trials, meaningful effect sizes, replicated. It's a very short list.

MIGHT WORK. Plausible mechanism, some human data, either small or mixed or surrogate-only. Reasonable to try if you'll measure something.

HYPE. Mechanism sounds great, human evidence is absent, negative, or entirely funded by the people selling it.

Two rules before you buy anything

Rule one: supplements are the last 5%. If your training is inconsistent, your protein is at 60 grams a day, and you sleep five hours, no capsule will help you. The order of operations is training, then food, then sleep, then supplements. People run it backward because supplements are the easiest thing to buy.

Rule two: if you can't name what you'd measure, don't take it. Before you start something, decide what would tell you it's working: a lab value, a lift number, a symptom, a sleep score. If the answer is "I'd feel like I'm doing something," you're buying a feeling. There's nothing wrong with that as long as you know that's what you bought.

Chapter 30 — Creatine: The One That Actually Works

If I could put only one supplement in this book, it'd be this one.

The muscle evidence

Chilibeck and colleagues, 2017: a meta-analysis of 22 studies, 721 participants, mean ages 57 to 70, comparing creatine plus resistance training against placebo plus resistance training.

- Lean tissue mass: +1.37 kg (95% CI 0.97–1.76), $p < 0.00001$
- Chest press strength: SMD 0.35, $p = 0.0002$
- Leg press strength: SMD 0.24, $p = 0.01$

I should give you the range rather than the best number. Across the three meta-analyses, the lean mass figures come in at +0.94, +1.33 and +1.37 kg. Call it about 1.2 kilograms on average. I've seen people quote 1.37 as though it's the number (including me, in earlier drafts), and taking the highest of three is the cherry-picking I complain about elsewhere in this book.

That 1.2 kilograms comes on top of what training alone gave people in their sixties. Devries and Phillips found the same direction in 357 participants averaging 64 years old.

Put that number next to Chapter 5. Phillips's twenty-week study found no statistically significant lean mass gain at all in the 65–75 group from training alone. Adding roughly 1.2 kg on top of training in that population is a large effect in context.

Dosing — and you don't need to load

The NIH's guidance: 20 g/day (4 × 5 g) for 5–7 days, then 3–5 g/day, or simply 3–6 g/day for 3–4 weeks with no loading phase. Both reach the same saturation. Loading just gets you there faster.

In Chilibeck's 22 studies, only 8 used loading. The rest just took 3–5 grams a day.

Loading is optional, so skip it if it upsets your stomach. Take 5 grams a day, every day, and in a month you're saturated.

Timing doesn't matter much, so take it whenever you'll remember.

Buy creatine monohydrate, not HCl, not buffered, not "advanced." Monohydrate is what every study used, it's the cheapest form, and there's no evidence any other form is better. Look for Creapure or an NSF/Informed certification. Creatine tests cleaner than most supplement categories, but dicyandiamide and creatinine are known manufacturing impurities.

The kidney myth

You'll hear creatine damages your kidneys. It doesn't, and here's why people think it does.

A 2025 systematic review in BMC Nephrology (21 studies, with 440 participants in the creatinine analysis) found serum creatinine rose by a trivial 0.07 mg/dL and GFR showed no significant difference.

The authors' explanation: a modest, transient increase in serum creatinine, likely due to metabolic turnover rather than kidney impairment.

Creatine raises your serum creatinine without harming your kidneys. Serum creatinine is what your doctor uses to estimate GFR. If you're on creatine and you get a kidney panel, your eGFR will look worse than it is.

Tell your doctor you take creatine before the blood draw. If there's a real question about your kidney function, ask for cystatin C instead. It's a different marker that creatine doesn't affect.

I've watched people get scared into quitting creatine over a lab value that creatine caused directly and harmlessly.

Side effects

The main real effect is weight gain from water retention, usually 1 to 2 kilos in the first few weeks, intracellular. Some people notice, most don't. GI upset and cramping are anecdotal and uncommon.

Safety data extends out several years. It's one of the most-studied supplements in existence.

Now the parts where I have to correct myself

Creatine and your brain. Avgerinos and colleagues found effects on cognition in 2018 and it got a lot of coverage, including from me.

A 2024 meta-analysis broke it down by age. The attention benefit was significant in ages 18–60 and not significant above 60 ($p = 0.61$). Executive function was null overall.

The cognitive case, in the population reading this book, isn't made. The muscle case is excellent. Don't let one launder the other.

Creatine and bone. There's a meta-analysis specifically titled to say creatine does not increase bone mineral density in older adults, and a 2025 meta-analysis confirmed it ($p = 0.557$).

I've seen creatine promoted for bone health, but the evidence doesn't support it.

The verdict

WORKS, for muscle and strength, in exactly your demographic, at 3–5 grams a day of monohydrate, for about fifteen dollars a month.

The exceptions

All of the above is about healthy kidneys. If you have diagnosed chronic kidney disease, particularly an eGFR under 60, creatine has not been studied in you, and the fact that it shifts creatinine means you and your nephrologist lose a marker you need. Ask before you start. And if your doctor has any other medical reason for you to skip it, skip it. Same rule as Chapter 19: get the numbers first.

Chapter 31 — Vitamin D: The Honest Version Is Unflattering

I take vitamin D, and so do a lot of people over fifty. When I read the trial evidence for this book, it was worse than I expected.

It's a case study in how a supplement becomes universal without the evidence to support it.

The big trials found nothing

VITAL: Manson and colleagues, New England Journal of Medicine, 2019. 25,871 people, 2,000 IU a day of vitamin D3, median 5.3 years.

- Invasive cancer: hazard ratio 0.96, p = 0.47
- Major cardiovascular events: hazard ratio 0.97, p = 0.69
- All-cause mortality: hazard ratio 0.99

Nothing. Across nearly 26,000 people over five years.

VITAL fractures: LeBoff and colleagues, NEJM, 2022. Same trial, 1,991 fractures.

- Total fracture: hazard ratio 0.98
- Nonvertebral fracture: 0.97
- Hip fracture: 1.01

No effect modification by baseline vitamin D level, BMI, age, sex or race. There was no significant benefit by starting vitamin D level either, though this trial wasn't designed to settle treating real deficiency.

Supplementing unselected adults does nothing for fractures, the thing vitamin D is most commonly taken for.

D-Health: Neale and colleagues, Lancet Diabetes & Endocrinology, 2022. 21,315 people, 60,000 IU monthly for five years. Blood levels went from 77 to 115 nmol/L, so the dosing worked.

- All-cause mortality: hazard ratio 1.04, p = 0.47

- Cancer mortality: hazard ratio 1.15, and excluding the first two years, 1.24, p = 0.05

The authors invoked "the precautionary principle." That's researcher language for: this might be going the wrong direction.

DO-HEALTH: Bischoff-Ferrari and colleagues, JAMA, 2020. 2,157 adults aged 70 and over, testing vitamin D, omega-3 and strength training in a factorial design over three years.

All six primary endpoints were null: systolic and diastolic blood pressure, physical performance, cognition, nonvertebral fractures, infections.

One note on that trial: the exercise arm came up null too. Given everything in Part II, that tells you the population was too healthy and the exercise program too light to move anything. It's a negative trial about that specific protocol, not a refutation of exercise.

More is definitely not better

Two clean randomized trials found that higher doses caused harm.

Bischoff-Ferrari and colleagues, 2016. 200 adults aged 70-plus who'd already had a fall. Monthly dosing at 24,000 IU versus 60,000 IU versus 24,000 plus calcifediol.

The higher doses reliably raised blood levels, produced no improvement in lower-extremity function, and came with more falls: 66.9% and 66.1% in the high-dose groups versus 47.9% in the lower-dose group (p = 0.048).

Sanders and colleagues, JAMA, 2010. 2,256 women aged 70-plus given 500,000 IU once a year for 3–5 years.

- Falls: 15% more (p = 0.03)
- Fractures: 26% more (p = 0.047) (171 fractures on vitamin D versus 135 on placebo)

The risk clustered in the first three months after each dose.

The pattern is clear: bolus dosing (weekly, monthly, or annual megadoses) is what produces harm. Daily, modest dosing is what the evidence supports.

If your doctor has you on 50,000 IU weekly, that's a conversation worth having, not a decision you make on your own. There are legitimate reasons for it in documented deficiency, and it's usually a time-limited repletion course rather than a permanent regimen. Don't stop a prescribed dose without telling the person who prescribed it.

The "deficiency epidemic" is mostly a definition

Using the standard cutoff (under 30 nmol/L, or 12 ng/mL), only 2.9% of US adults aged 60 and over are actually deficient.

The "epidemic of vitamin D deficiency" you've heard about is largely an artifact of people using 30 ng/mL as the threshold instead of the official 20 ng/mL sufficiency line. Move the line and you turn most of the population into patients.

The official categories:

- Deficient: under 30 nmol/L (12 ng/mL)
- Inadequate: 30–50 nmol/L (12–20 ng/mL)
- Sufficient: 50 nmol/L and above (20 ng/mL and above)
- Excess: above 125 nmol/L (50 ng/mL)
- Toxicity: typically above 375 nmol/L (150 ng/mL)

RDA: 600 IU for ages 51–70, 800 IU above 70. Upper limit: 4,000 IU/day.

The US Preventive Services Task Force concluded with moderate certainty that vitamin D supplementation does not reduce falls or fall-related injuries in community-dwelling adults 65 and older.

Who actually benefits

Real deficiency is real, and correcting it matters. The people who benefit:

- Documented deficiency on a blood test

- Malabsorption (bariatric surgery, celiac, inflammatory bowel disease)
- Housebound or institutionalized
- Very dark skin at high latitude
- On anticonvulsants or glucocorticoids
- Significant obesity (vitamin D distributes into fat, diluting blood levels)

One more note: there's a signal that Black Americans may face greater risk of falls and fractures at intakes of 2,000 IU/day or more. That's from the NIH's own review.

What I'd do

Test. It's a cheap, standard blood test.

If you're below 20 ng/mL, supplement daily (1,000 to 2,000 IU is plenty for most people) and retest.

If you're above 20 ng/mL, the trial evidence says supplementing won't do anything for you. You can take it anyway. At reasonable daily doses it's cheap and safe. Just know you're buying insurance, not benefit.

Don't take bolus megadoses unless a doctor is treating documented deficiency and monitoring you.

I take 2,000 IU daily and my levels sit in a good range. I won't claim that's doing something the trials say it isn't.

Chapter 32 — Omega-3 and the Fish Oil Wars

This one's more interesting than vitamin D, because of an unresolved scientific controversy at its heart.

Primary prevention: nothing

VITAL again: the same 25,871 people, this time getting 1 gram a day of omega-3 (460 mg EPA + 380 mg DHA) for 5.3 years.

- Major cardiovascular events: hazard ratio 0.92, p = 0.24
- Invasive cancer: 1.03
- All-cause mortality: 1.02

There was a secondary finding (total heart attack, hazard ratio 0.72) that got a lot of coverage. But that's a secondary endpoint in a trial that missed its primary. Treat it as hypothesis-generating, not as a result.

ASCEND (15,480 people with diabetes, 1 gram a day, mean 7.4 years): no significant effect on serious vascular events.

For general prevention in healthy people, fish oil at 1 gram a day doesn't do anything measurable.

The controversy: REDUCE-IT versus STRENGTH

REDUCE-IT. Bhatt and colleagues, NEJM, 2019. 8,179 statin-treated patients with elevated triglycerides, given icosapent ethyl at 4 grams a day (a purified EPA drug, not a supplement) versus placebo. Median 4.9 years.

About a 25% relative reduction in the primary composite. Roughly 20% reduction in cardiovascular death, 28% in stroke, 31% in heart attack.

That's a big, drug-sized effect. Icosapent ethyl had already been approved in 2012 for severe hypertriglyceridemia, and REDUCE-IT supported adding cardiovascular risk reduction to the label in December 2019.

STRENGTH. Nissen and colleagues, JAMA, 2020. 13,078 patients, 675 sites, 22 countries. Omega-3 carboxylic acid at 4 grams a day versus corn oil.

Stopped early for futility. Primary hazard ratio 0.99, $p = 0.84$. 12.0% versus 12.2%.

It wasn't a dosing failure. Participants achieved EPA up 269% and DHA up 40%.

Two trials, both 4 grams a day of omega-3, one showing a 25% reduction and one showing exactly nothing.

The mineral oil problem

Nissen's argument is a good one.

REDUCE-IT used mineral oil as its placebo. In that placebo arm, over the trial:

- LDL cholesterol rose 10.2%
- ApoB rose 7.8%
- hs-CRP (an inflammation marker) rose 32%

None of that happened with corn oil in STRENGTH.

If the comparator group got worse, then part or all of the apparent 25% benefit could be an artifact of the placebo harming people rather than the drug helping them.

Bhatt and the manufacturer dispute this, arguing the biomarker shifts are too small to explain an effect that size.

This is unresolved, and the field hasn't decided who's right. But anyone presenting REDUCE-IT as settled proof isn't telling you the whole story.

The atrial fibrillation signal — this one's real

STRENGTH: atrial fibrillation 2.2% versus 1.3%. Hazard ratio 1.69, $p < 0.001$.

The NIH states it plainly: taking 4 grams a day of omega-3 supplements for several years slightly increased the risk of atrial fibrillation in people with cardiovascular disease or at high risk.

A pooled meta-analysis across seven cardiovascular outcome trials (roughly 81,000 participants) reported a hazard ratio around 1.25 for atrial fibrillation (AF), with a dose-response above about 1 gram a day.

REDUCE-IT itself showed more AF hospitalization on the drug.

This is a real, dose-dependent safety signal at high doses. If you're over fifty and taking 3–4 grams a day of fish oil because more seemed better, this is the thing to know about.

What omega-3 does do

Triglycerides: solidly established. 0.5–5 grams a day lowers triglycerides about 15%, roughly 5.9 mg/dL per gram. The prescription dose for severe hypertriglyceridemia is 4 grams a day and it works.

The FDA advises no more than 5 grams a day of EPA+DHA from supplements. Bleeding time may lengthen at 2–15 grams.

And specifically: if you take an anticoagulant or antiplatelet, whether warfarin, apixaban, rivaroxaban, clopidogrel or daily aspirin, tell your prescriber before you take fish oil at any dose, and do not go above one gram a day without them signing off. The bleeding effects add.

Muscle? Lalia and colleagues, 2017, gave 12 young and 12 older adults 3.9 grams a day for 16 weeks. That increased mitochondrial and sarcoplasmic protein synthesis in the older adults, and reduced mitochondrial oxidant emissions 20–25%.

But it was open-label with no placebo, and it didn't measure muscle mass or strength.

Smith, Mittendorfer and colleagues have work suggesting omega-3 augments the muscle protein synthesis response and, in a six-

month study, increased thigh muscle volume around 3.6% and grip strength about 2.3 kg.

Summary: omega-3 for muscle is a surrogate-endpoint literature (synthesis rates and mitochondrial markers, small samples, often no placebo). It's plausible and low-risk, but it isn't proven.

The one large trial that measured physical function directly (DO-HEALTH, 2,157 people, 1 gram a day, three years) found nothing on physical performance.

What I'd do

If your triglycerides are high, omega-3 works and that's a conversation with your doctor about dose.

At 1 gram a day for general heart health, the primary prevention trials say it doesn't do anything. It's cheap and safe at that dose, so take it if you want.

Don't take 3–4 grams a day without a reason. That's the dose range where the atrial fibrillation signal lives, and unless you're being treated for hypertriglyceridemia, you're taking on that risk for benefits that two large trials couldn't agree existed.

Eat fish. The dietary evidence has always been more consistent than the supplement evidence.

Chapter 33 — The Boring Ones That Matter

These aren't exciting. But per dollar and per risk, this chapter probably has more value than the last two.

Vitamin B12 — the one that matters most for the people it applies to

Atrophic gastritis affects 8 to 9% of adults 65 and over. It impairs the release of food-bound B12. That means you can eat plenty of B12 and not absorb it.

That's why the NIH advises adults over 50 to get B12 from fortified foods or supplements, in the crystalline form, which doesn't require the same stomach acid handling.

Prevalence in adults 60-plus: deficiency 3.7%, insufficiency 12.3%. Community estimates run from 3% to 43% depending on the cutoff used.

Two extremely common medications make it worse:

Metformin reduces B12 absorption and significantly lowers serum B12. The long-term diabetes prevention follow-up study found roughly 4.3% versus 2.3% deficiency with about thirteen years of metformin, along with higher rates of anemia and neuropathy.

Proton pump inhibitors and H2 blockers interfere with absorbing food-bound B12. A large case-control study found an odds ratio around 1.65 for deficiency with two-plus years of PPI use.

The absorption arithmetic that justifies high-dose tablets: you absorb about 50% of a dose under 1–2 mcg, but only 2% at 500 mcg and 1.3% at 1,000 mcg. A 1,000 mcg tablet still delivers about 13 mcg by passive diffusion, which is why high oral doses work even in people who can't absorb B12 the normal way.

Practical rule: if you're over 50 and on metformin or a PPI, get B12 checked (ideally with methylmalonic acid, which is more sensitive), and most people in that situation should take 500–1,000 mcg a day orally.

It's one of the few recommendations in this book I'd make to nearly everyone in that group. B12 deficiency causes neuropathy and cognitive problems that can become irreversible, and it's trivially preventable.

Magnesium

RDA: 420 mg/day for men 51+, 320 mg/day for women 51+.

48% of Americans consume less than the estimated average requirement, and older men are among the highest-risk groups.

Form matters. Absorption is 30–40% of intake, but aspartate, citrate, lactate and chloride are absorbed more completely than oxide and sulfate. Magnesium oxide is the cheapest and the worst. It's mostly a laxative.

What the evidence supports:

- Blood pressure: a Cochrane review of 12 trials in 545 hypertensive participants found diastolic BP down 2.2 mm Hg. Small but real.
- Type 2 diabetes: 7 prospective cohorts found each additional 100 mg/day associated with 15% lower risk (observational, and randomized trials conflict). The ADA says evidence is insufficient.
- Migraine: 3 of 4 small trials showed modest reductions at up to 600 mg/day. The American Academy of Neurology rates it "probably effective" for migraine prevention.
- Sleep: this is the claim you hear most, and the randomized evidence is thin and low-quality: a few small trials in older adults with insomnia. It's widely oversold.

Upper limit for supplemental magnesium: 350 mg/day. Diarrhea is the dose-limiter.

Interactions: PPIs used more than a year can cause low magnesium. Loop and thiazide diuretics increase urinary losses. Both are common after fifty.

Zinc

RDA: 11 mg/day men, 8 mg/day women. About 15% of US adults are below the requirement.

- Common cold: a 2024 Cochrane review of 34 trials and 8,526 participants found zinc may shorten symptom duration by about 2 days, and is ineffective for prevention.
- Macular degeneration: the AREDS trials found 80 mg/day of zinc with antioxidants gave 25% lower risk of advanced AMD over 5 years; AREDS2 found 25 mg performed similarly.

Upper limit: 40 mg/day. Doses of 50 mg/day or more for weeks inhibit copper absorption. Chronic high-dose zinc causes copper-deficiency anemia and a neurological syndrome. This is a real harm and it happens in the megadose "immune support" crowd.

One correction: zinc doesn't raise testosterone in men who aren't deficient. That claim comes from studies where deficient people were repleted.

Fiber supplements

Psyllium is the only fiber supplement with consistent trial-grade outcomes. It's viscous and gel-forming, which is what produces the effects.

- LDL cholesterol: roughly 6–7 mg/dL reduction at about 10 g/day.
- The FDA permits a soluble-fiber heart disease claim for psyllium at 7 g/day.
- Constipation: increases stool frequency and improves consistency; beats wheat bran head-to-head.
- Glucose: modest blunting of post-meal glucose; small effect on HbA1c.

Inulin, FOS, wheat dextrin, methylcellulose and polycarbophil don't reproduce psyllium's lipid effect. Inulin reliably produces gas and bloating in a lot of people.

Supplemental fiber isn't dietary fiber. All the cohort evidence I gave you in Chapter 23 (the 15% lower all-cause mortality, the 31% lower heart disease mortality) is about whole-food fiber. You can't transfer that to a scoop of powder.

Psyllium is a real tool for cholesterol and bowel function, but it isn't a substitute for eating plants.

Protein powder

Covered thoroughly in Part III, so just the supplement-aisle version:

Whey has the most leucine and produces the biggest acute response. Casein is slower and reasonable before bed. Plant proteins work if you blend them (rice plus pea fixes the amino acid profile, since rice is limiting in lysine and pea in methionine) and dose them about 1.25 to 1.5 times higher to match whey's leucine.

Remember Morton's two findings: the benefit of supplementation shrinks with age, and the plateau's confidence interval runs from 1.0 to 2.2 grams per kilogram. Powder is how most people close the gap between what they actually eat and at least a gram per pound of desired body weight. (Kidney disease, or a different number from your doctor? Use your doctor's.)

Powder isn't an anabolic agent. Collagen shouldn't stand in for a complete, leucine-rich protein (see Chapter 18).

Chapter 34 — The Maybe Pile

These are things with a plausible mechanism and some human data, where I'd say "reasonable to try if you'll measure something," not "you should take this."

Grape seed extract

I made a video about this one. Here's where the evidence stands.

The one endpoint with repeated randomized support is blood pressure. Meta-analyses report roughly 3 to 6 mm Hg systolic reduction in hypertensive and metabolic-syndrome subjects, with high heterogeneity and mostly small and short trials.

There's also modest evidence for chronic venous insufficiency and leg swelling.

No credible human evidence for the anti-aging, cancer or general "antioxidant" claims.

Verdict: might work, narrowly, for blood pressure. If you take it, measure your blood pressure. If it doesn't move in eight weeks, stop.

Berberine

The strongest of the "natural metabolic" compounds.

Meta-analyses of predominantly Chinese trials report HbA1c reductions of roughly 0.7 to 0.9% and fasting glucose reductions comparable to low-dose metformin, plus LDL reductions around 20–25 mg/dL, at 500 mg two to three times a day.

Those are real numbers. Now the problems.

Most trials are small, short, from a single region, at high risk of bias, with evidence of publication bias. Bioavailability is under 1%, which makes the reported systemic effects mechanistically awkward.

“Nature’s Ozempic” is a marketing invention. Berberine has no GLP-1 mechanism and there are no weight-loss trials supporting that comparison. Whoever coined it should be embarrassed.

The real risk nobody mentions: berberine is a potent CYP3A4 and P-glycoprotein inhibitor. That’s clinically meaningful with statins, calcium channel blockers, anticoagulants and cyclosporine. If you’re over fifty you’re statistically likely to be on at least one of those.

Verdict: might work for glucose and lipids. Do not take it without telling your doctor what else you’re on.

Urolithin A

The most rigorous of the longevity compounds, and still not there.

Andreux and colleagues, Nature Metabolism, 2019: a first-in-human study in healthy sedentary elderly. Four weeks at 500 or 1,000 mg modulated plasma acylcarnitines and skeletal muscle mitochondrial gene expression. Good safety profile, which was the primary outcome.

The paper reported molecular signatures, not functional improvement. It was sponsored by Amazentis, the company selling the product, with multiple authors as employees or board members.

A subsequent four-month randomized trial in about 66 middle-aged adults missed its primary endpoints but reported improvements in hand and leg muscle endurance versus placebo, plus reduced CRP.

The mechanism (mitophagy, clearing out damaged mitochondria) is interesting. Only about 40% of people convert dietary ellagitannins to urolithin A themselves, which is the commercial rationale for supplementing.

Verdict: real trials, real safety data, consistently modest and partly negative functional results, near-total dependence on one company’s funding. Might work, not proven, expensive.

Probiotics

Strain-specific and indication-specific. That's the whole story.

What works:

- Antibiotic-associated diarrhea: L. rhamnosus GG (12 trials, 1,499 people) took diarrhea down from 22.4% to 12.3%. Saccharomyces boulardii (21 trials, 4,780 people) took it from 17.4% to 8.2%.
- IBS: 23 trials, 2,575 people, a 21% reduction in persistent symptoms. Multi-strain products did better.

A finding directly relevant to this book: LGG, the most-studied probiotic strain, is ineffective in adults 65 and over.

Constipation and "healthy aging" have no established benefit in the NIH's evidence review.

Safety note: systemic infections have been documented in ICU patients. Guidance is to restrict use to proven strains and indications in the immunocompromised.

The regulatory problem: listing the live-bacteria count (CFU) on the label is voluntary. Only total weight is required. No FDA premarket review. Combined with strain-specific effects, most retail probiotics cannot be matched to any trial.

Verdict: might work for specific indications with specific strains. Buy the strain that was studied for your problem, or don't bother.

Chapter 35 — The Hype Pile (Including Some of My Own Videos)

This is the uncomfortable chapter. I've covered several of these on my channel, and some of them I got wrong.

NAD+ precursors: NMN and nicotinamide riboside

These raise NAD+ levels. That's the one consistent finding. Everything else is small, short-term and mixed.

Martens and colleagues, Nature Communications, 2018: 30 enrolled, 24 completed, ages 55–79, NR at 1,000 mg/day.

- Blood NAD+ rose about 60%. The pathway definitely engaged.
- Systolic blood pressure: −3.9 mm Hg, not significant after correcting for multiple comparisons.
- In the subgroup with elevated blood pressure, about 9 mm Hg lower, but that's a post-hoc subgroup in a 24-person crossover. Hypothesis-generating only.
- Aortic stiffness: trend, not significant after correction.

The authors call it a pilot with insufficient sample size.

Katayoshi and colleagues, 2023: NMN, 36 people aged 40 to 59 (note: mostly younger than this book's readership), 250 mg/day, 12 weeks.

- Serum nicotinamide rose. But NAD+ and NMN themselves were below the limit of quantification in blood.
- Arterial stiffness: between-group $p = 0.097$. Not significant.
- Significant only in post-hoc subgroups.
- No change in SIRT1 expression, oxidative DNA damage markers, or skin AGEs.

The negative trials get less coverage:

- Elhassan 2019 (NR 1 g/day, 21 days, aged men): raised the muscle NAD+ metabolome, no change in mitochondrial bioenergetics or muscle function.
- Dollerup 2018 (NR 2 g/day, 12 weeks, 40 obese insulin-resistant men): no effect on insulin sensitivity, glucose production, mitochondrial function, liver fat, or body composition. Arguably the most important negative trial in the field.
- Remie 2020 (NR 1 g/day, 6 weeks): raised NAD+ metabolites, no effect on insulin sensitivity, mitochondrial function or energy metabolism.
- Yoshino 2021, Science (NMN 250 mg/day, 10 weeks, 25 postmenopausal prediabetic women): improved muscle insulin sensitivity about 25%, but no change in body composition, blood pressure, liver fat, or most metabolic endpoints.

A regulatory wrinkle: the FDA concluded in 2022 that NMN was excluded from the dietary supplement definition, because it was authorized for investigation as a new drug before being marketed as a supplement. It reaffirmed that in 2023. Then, in September 2025, it reversed itself: NMN can be sold as a supplement, though it still has to meet the new-ingredient notification rules. Legal to sell doesn't mean it works, and that's the rest of this section. Check current status before you buy.

Verdict: HYPE. Every human trial is small, short, and reports surrogate biochemistry. A few small trials show changes in intermediate markers, like muscle insulin sensitivity, but nothing durable has been shown. There's no human evidence for lifespan, healthspan, muscle function or cognition.

Niacin — and this one has a safety angle

I've made two videos about niacin. Here's the correction.

The cardiovascular trials failed twice, and enormously.

AIM-HIGH, 2011: 3,414 patients with established cardiovascular disease and well-controlled LDL on a statin, given extended-

release niacin 1,500–2,000 mg/day. Stopped early for futility. Niacin raised HDL from about 35 to 42 and lowered triglycerides. Primary composite hazard ratio about 1.02, p = 0.79, plus a non-significant excess of ischemic stroke.

HPS2-THRIVE, 2014: about 25,673 patients on background statin therapy, median 3.9 years. No reduction in major vascular events (relative risk about 0.96, p = 0.29). And a significant excess of serious adverse events: new-onset diabetes, diabetic complications, GI problems, musculoskeletal problems, infections and bleeding. Roughly one extra serious adverse event per 27 people treated.

Niacin was removed from mainstream lipid guidelines as a result. It's one of the cleanest refutations of a surrogate endpoint in all of cardiology: raising HDL pharmacologically does not reduce events.

Then 2024 made it worse. Ferrell, Hazen and colleagues published in Nature Medicine on 4PY, a terminal metabolite of niacin.

Discovery cohort of 1,162 stable cardiac patients plus validation cohorts of 2,331 and 832. 4PY predicted three-year major adverse cardiac events with adjusted hazard ratios of 1.89 and 1.99. A related metabolite, 2PY, gave 1.64 and 2.02. In mice, 4PY induced VCAM-1 expression and leukocyte adherence to blood vessel walls, a plausible inflammatory mechanism.

The authors raised implications not just for supplements but for mandatory niacin fortification of flour and cereal.

The pushback is real. A correspondence in the same journal argued the mechanism is contradicted by prior work showing niacin suppresses VCAM-1, and that the finding must be weighed against decades of clinical trial experience.

What's fair to say: 4PY is an association study plus a mouse mechanism. It isn't proof that niacin causes heart attacks. But combined with AIM-HIGH and HPS2-THRIVE, there's no remaining case for taking niacin as a cardiovascular or longevity supplement, and a plausible case for avoiding megadoses.

“Flush-free” niacin is usually inositol hexanicotinate, which doesn’t release free nicotinic acid and has no lipid effect at all. It’s a widely sold, inert product.

Nicotinamide, NR and NMN all funnel into the same methylation and excretion pathway that produces 2PY and 4PY. Whether high-dose NAD precursors meaningfully raise 4PY in humans isn’t yet answered, and it’s the most important unresolved safety question about them.

Taurine — and the 2025 reversal

Singh and colleagues, Science, 2023: taurine declined with age across mice, monkeys and humans, and taurine supplementation extended median lifespan about 10–12% in mice with improved healthspan measures.

It was covered everywhere and drove a supplement boom.

Then in 2025, a follow-up in Science from the NIA’s Baltimore Longitudinal Study of Aging group directly contradicted the premise: circulating taurine does not reliably decline with age in humans, rhesus monkeys, or mice. In within-person longitudinal data, taurine was stable or increased.

If the age-related decline isn’t real, the “restore youthful taurine” rationale collapses.

There’s no human randomized trial of taurine with an aging or longevity outcome. Human taurine trials exist for heart failure and exercise performance, at 1.5–6 g/day, with small and inconsistent effects.

Verdict: HYPE, and a good lesson in waiting for replication.

Resveratrol

The sirtuin and red-wine story did not survive.

Human trials are small and inconsistent, and several found nothing. Then there’s Gliemann 2013, Journal of Physiology (27

older men), which found resveratrol blunted the cardiovascular training adaptations to eight weeks of exercise.

That's a harm signal on exactly the thing this book is about.

Semba 2014, JAMA Internal Medicine (783 people in the Chianti cohort followed nine years): urinary resveratrol metabolites were not associated with inflammation, cardiovascular disease, cancer, or all-cause mortality.

Verdict: HYPE. The science moved on, and the marketing didn't.

Spermidine

Human evidence is essentially one trial: SmartAge, about 100 older adults with subjective cognitive decline, twelve months of spermidine-rich wheat germ extract. No significant benefit on the primary memory endpoint. An earlier three-month pilot in 30 people had shown a small signal that didn't replicate.

Everything else is yeast, flies, mice, and epidemiology confounded by overall diet quality.

Verdict: HYPE. The one adequately sized human trial was negative.

TUDCA

Human randomized evidence exists almost exclusively for cholestatic liver disease and ALS, at pharmaceutical doses.

Those trials have nothing to do with "liver support," longevity, or supporting a supplement cycle. The mechanism people cite (ER stress and chaperone activity) is cell and rodent work.

There's essentially no randomized trial in healthy adults over 50 for any outcome TUDCA is sold for.

Verdict: HYPE, with a legitimate but unrelated clinical literature attached to it.

C15:0 (pentadecanoic acid)

I made a video about C15. Here's what I'd add now.

The human data is dominated by researchers at a company that holds the patents and sells the product. That's not automatically disqualifying, but it has to be disclosed every time, and it usually isn't.

The supporting work is cell-line screening, dolphin cohort observations, and epidemiological associations between odd-chain fatty acids and lower cardiometabolic risk, associations heavily confounded by dairy intake, since dairy is the dietary source.

The claim that C15:0 is an "essential fatty acid" isn't accepted by any nutrition authority. No deficiency syndrome has been demonstrated in humans.

Verdict: HYPE, and the least supported item on this whole list with the highest density of commercial conflict.

DHEA

Nair and colleagues, NEJM, 2006: 87 men and 57 women, two years of DHEA in elderly people with low DHEAS levels.

No benefit on body composition, physical performance, insulin sensitivity, or quality of life.

That remains the definitive trial. Meta-analyses since show at most trivial effects. DHEA is an androgen and estrogen precursor with unpredictable individual conversion, and it's banned by WADA.

Verdict: HYPE.

DMSO — and this one I want to actively warn you about

I've covered DMSO twice. I'd handle it differently now.

The only FDA-approved human use is instillation into the bladder for interstitial cystitis. There's no approved oral or topical use, and no modern randomized support for musculoskeletal pain.

The specific danger: topical DMSO is a powerful percutaneous carrier. It drives whatever else is on your skin into systemic circulation. Industrial-grade DMSO isn't pharmaceutical grade. It can contain impurities you're then driving into your bloodstream.

Known effects include near-universal garlic breath and body odor, skin irritation, and lens changes and cataracts in animal studies that drove the FDA to restrict it in the first place.

Verdict: HYPE, plus a real safety problem. This is the one item on this list I'd recommend against, not just decline to recommend. If I could pull one thing back off my channel, it'd probably be this.

Why I'm putting my own videos in this chapter

If I write a book full of "here's what the evidence says" and quietly leave out the places where I've said something the evidence doesn't support, the book is just a longer version of the problem.

I made those videos in good faith. I read what was available, found the mechanisms interesting, and in some cases tried the thing myself and felt something. That's how everybody in this space ends up promoting things. It's usually not dishonesty, just a mechanism plus an anecdote and nobody checking.

The checking is the part I did for this book, and some of it came back badly for me. I'd rather be corrected than consistent.

Chapter 36 — Testosterone

This is a different category from everything else in this section: a prescription drug with real trials behind it. I'm including it because it gets discussed like a supplement, and it shouldn't be.

The safety question — mostly answered

TRAVERSE, published in 2023. About 5,246 men aged 45–80 with symptomatic hypogonadism (two morning testosterone readings under 300 ng/dL) plus established cardiovascular disease or high cardiovascular risk. Testosterone gel targeting 350–750 ng/dL. Mean follow-up around 33 months. Run under an FDA mandate specifically to answer the cardiac safety question.

Major adverse cardiac events: hazard ratio 0.96 (95% CI 0.78–1.17). Testosterone met non-inferiority.

But the non-MACE signals deserve attention. All three were more common on testosterone:

- Atrial fibrillation: 3.5% versus 2.4%
- Pulmonary embolism: 0.9% versus 0.5%
- Acute kidney injury: 2.3% versus 1.5%

Testosterone can raise your hematocrit and cause erythrocytosis (too many red blood cells). If you're on it, you need regular hematocrit checks.

Here's the finding that surprised me. The TRAVERSE fracture substudy found more clinical fractures on testosterone, roughly 3.5% versus 2.5%, hazard ratio about 1.43.

That's the opposite of what bone density surrogates predicted. Testosterone reliably improves bone mineral density, and in the trial that counted fractures there were more of them in the treated group.

I include that because it shows why surrogate endpoints can mislead you, and because you won't hear it from anyone selling testosterone.

The efficacy question — modest and domain-specific

The T-Trials, Snyder and colleagues, NEJM, 2016. 790 men aged 65 and over with testosterone under 275 ng/dL, one year of testosterone gel, seven coordinated trials.

- Sexual function: clear, consistent benefit in libido, erectile function and activity. The most robust result by far.
- Physical function: missed its primary endpoint, the proportion increasing six-minute walk distance by 50 meters or more. Benefit appeared only in a pooled secondary analysis.
- Vitality: no significant effect on fatigue or energy.
- Cognition: no improvement in memory or cognition.
- Bone: increased volumetric BMD and estimated bone strength, a surrogate, and see the fracture result above.
- Anemia: corrected in a meaningful proportion, a real benefit.
- Cardiovascular: increased non-calcified coronary plaque volume on CT. That was the signal TRAVERSE was designed to adjudicate.

Where that leaves you

In men who are hypogonadal, testosterone reliably improves sexual function and anemia, modestly improves mood and bone density, and doesn't reliably improve walking, vitality, or cognition. It appears cardiovascularly non-inferior over two to three years, with a fracture signal that nobody expected.

It isn't a longevity intervention, and it isn't a performance intervention for men with normal testosterone. There's no outcome trial in men with normal levels at all.

If you're over fifty and tired and want to feel better, testosterone isn't the first thing to look at. Sleep, training, protein, body composition and getting your thyroid and iron checked all come first. If those are handled and you have documented, symptomatic hypogonadism on two morning tests, it's a legitimate

conversation with an endocrinologist, with hematocrit monitoring.

Chapter 37 — Menopausal Hormone Therapy

I gave testosterone a chapter, so I owe you this one. Half the people reading this book went through menopause, and the drug that treats it has been argued about more publicly, and more badly, than anything else in this book. I'm not a doctor and this is not a prescription. It's the evidence, laid out so you can have a better conversation with somebody who is qualified to write one.

One thing before the numbers. "Hormone therapy" here means estrogen, with a progestogen added if you still have a uterus, prescribed and monitored by a physician. It doesn't mean compounded pellets, custom "bioidentical" creams from a wellness clinic, or anything bought online. Those carry the same manufacturing and dosing problems I take apart with gray-market drugs in Part V.

The trial everybody argues about, and what it actually tested

The Women's Health Initiative, 2002. 16,608 postmenopausal women aged 50–79 with a uterus, randomized to conjugated equine estrogens 0.625 mg plus medroxyprogesterone acetate 2.5 mg or placebo. Mean follow-up 5.2 years, stopped early.

Hazard ratios: coronary heart disease 1.29 (95% CI 1.02–1.63), breast cancer 1.26 (1.00–1.59), stroke 1.41 (1.07–1.85), pulmonary embolism 2.13 (1.39–3.25), colorectal cancer 0.63 (0.43–0.92), hip fracture 0.66 (0.45–0.98). The global index came out at 1.15.

In absolute terms, per 10,000 women per year: 7 more coronary events, 8 more strokes, 8 more pulmonary emboli, 8 more breast cancers, against 6 fewer colorectal cancers and 5 fewer hip fractures.

That's a real result. But two facts about who was in the trial change how it applies to a fifty-two-year-old with hot flashes. Mean age at enrollment was 63. Most participants were more than a decade past menopause. The WHI was designed to test hormone therapy as *chronic disease prevention in older women*,

and on that question it gave a clear answer: no. It was never a test of treating symptoms at the age symptoms happen.

The estrogen-alone arm (10,739 women who'd had a hysterectomy, no progestogen) didn't read the same way. There was no increase in breast cancer, and in the 20-year cumulative follow-up of both trials (Chlebowski and colleagues, JAMA, 2020, 27,347 women) estrogen alone was associated with *lower* breast cancer incidence, hazard ratio 0.78 (0.65–0.93), and lower breast cancer mortality, 0.60 (0.37–0.97). Estrogen plus progestin ran the other way: incidence 1.28 (1.13–1.45), with no significant difference in breast cancer mortality.

Two different drugs, two different answers, one headline. That's most of why the last twenty years have been so confused.

And on the outcome that matters most: at 18 years of follow-up (Manson and colleagues, JAMA, 2017), all-cause mortality across both trials was 27.1% on hormone therapy versus 27.6% on placebo, hazard ratio 0.99 (0.94–1.03). Neither harm nor benefit for survival.

The timing hypothesis — the strongest evidence in this chapter, and still soft

Look at that mortality paper by age at randomization, during the treatment years. Women 50–59: hazard ratio 0.69 (0.51–0.94). Women 60–69: 1.04. Women 70–79: 1.13. Same drugs, opposite directions, depending on when you start.

That's the timing hypothesis, and two trials were built to test it directly.

ELITE (Hodis and colleagues, NEJM, 2016). 643 healthy women randomized within one of two strata: fewer than 6 years past menopause, or 10 or more. Oral 17β-estradiol 1 mg daily, plus vaginal micronized progesterone for women with a uterus. Median 5 years, carotid intima-media thickness measured every 6 months. In the early stratum, progression was 0.0044 mm/year on estradiol versus 0.0078 on placebo, $p = 0.008$. In the late stratum, 0.0100 versus 0.0088, $p = 0.29$.

KEEPS: 727 women, mean age 53, between 6 and 36 months past their final period, randomized to oral conjugated estrogens 0.45 mg, transdermal estradiol 50 µg, or placebo, all with cyclic micronized progesterone, for four years. Hormone therapy did not slow carotid thickening in either active arm, and did not move coronary artery calcium.

So one early-window trial found a vascular benefit on a surrogate and one didn't. And intima-media thickness is a surrogate. ELITE's own cardiac CT (calcium, stenosis, plaque) showed no difference in either stratum. Nobody has run an adequately powered randomized trial of hormone therapy started inside the window with heart attacks and deaths as the endpoint, and given what such a trial would cost, nobody is going to.

That's the state of the timing hypothesis. It's biologically plausible, it's consistent with the WHI's own age-stratified data, and it rests on surrogate endpoints and subgroup analysis. It's a reason not to apply the 2002 headline to a fifty-two-year-old. It isn't a reason to take estrogen for your heart.

Bone — the hardest endpoint in this chapter

This is the one place where hormone therapy produced a hard outcome in a large randomized trial, and it deserves more attention than it gets.

In the WHI estrogen-plus-progestin arm (Cauley and colleagues, JAMA, 2003), total osteoporotic fractures ran 8.6% versus 11.1%, hazard ratio 0.76 (0.69–0.83). Hip fracture 0.66. Total hip bone density rose 3.7% over three years versus 0.14% on placebo.

Read that against Chapter 12. Hormone therapy reduced fractures in a population that was *not* selected for osteoporosis, which is more than any bone-loading exercise trial in this book has shown. It's also the mirror image of the testosterone fracture result in Chapter 36, where bone density went up and fractures went up with it. Estrogen moved both in the same direction.

The catch is the same as everywhere else: the benefit lasts while you take it. Bone density falls back after you stop, which is why

hormone therapy isn't a substitute for the osteoporosis drugs in Chapter 12 when you have diagnosed osteoporosis, and why that decision belongs to your physician.

Systemic and vaginal are not the same drug

Low-dose vaginal estrogen (cream, ring or tablet) treats genitourinary syndrome of menopause: vaginal dryness, pain with sex, urinary urgency, recurrent urinary tract infections. Systemic absorption is very low. Observational data has not shown an increase in major adverse cardiovascular events, and the endometrial safety data on low-dose vaginal preparations is reassuring. The major society guidance treats it as a separate, much lower-risk decision from systemic therapy, usable at essentially any age and for extended duration.

If your concern is dryness or recurrent UTIs and somebody has told you that "hormones cause breast cancer" and left it there, they've handed you the systemic answer to a local question. Ask specifically about vaginal estrogen.

One more distinction worth raising with your prescriber: route. A 2015 meta-analysis of 15 observational studies found oral estrogen carried more venous thromboembolism than transdermal, risk ratio 1.63 (1.40–1.90), and deep vein thrombosis 2.09 (1.35–3.23), with no significant difference in myocardial infarction. That's observational, low-confidence evidence, but it's why current guidance leans transdermal where there's a clotting concern. If you're on an anticoagulant or have a clotting history, this is a specialist conversation, not a preference.

What the societies actually say

The Menopause Society's 2022 position statement is the reference document, and its shape is consistent: for healthy women under 60, or within 10 years of menopause, with bothersome vasomotor symptoms, the benefits generally outweigh the risks. It is not recommended as a general strategy for preventing chronic disease. There is no arbitrary stop date at 65. Women with premature or early menopause should generally be treated until at least the average age of menopause. Low-dose vaginal estrogen

is a separate, lower-risk decision. Lowest effective dose, transdermal where appropriate, periodic reassessment.

The 2024 JAMA review of the WHI by the investigators themselves lands in the same place: the trials do not support hormone therapy for chronic disease prevention, and women under 60 with low-to-average cardiovascular and breast cancer risk may see more benefit than risk when treating moderate-to-severe symptoms.

In November 2025 the FDA moved to remove the boxed warnings on cardiovascular disease, breast cancer and probable dementia from menopausal hormone therapy labels, while keeping the endometrial cancer warning on systemic estrogen-alone products. I'd read that the way I'd read any labeling decision: it changes what the box says, not what the trials found. Apply the same rule I give you at the head of Part V: check the current regulatory status before you act on any of it.

Where the evidence runs out

Cognition. In the Women's Health Initiative Memory Study (4,532 women aged 65 and over, estrogen plus progestin, 4.2 years) probable dementia roughly doubled, about 23 extra cases per 10,000 women per year. Whether starting in the window protects cognition is unresolved. Do not take hormone therapy for your brain.

Muscle. One small trial has tested the combination I'd most like to see. Dam and colleagues, 2021: 31 women within five years of menopause, 12 weeks of supervised lifting, with estrogen patches or placebo. The estrogen group gained about twice as much thigh muscle, 7.9% versus 3.9%. Leg strength and jump height improved about the same in both groups. Grip strength improved only on estrogen, the sit-to-stand test improved more on placebo, and neither group improved its six-minute walk. Small, short, and not enough to say hormones make lifting pay off where it counts. Everything in Part II applies to you whatever you decide about hormones, and it applies more, not less.

Contraindications are real and they're not subtle: a history of breast cancer, estrogen-sensitive cancer, unexplained vaginal bleeding, active liver disease, a history of venous thromboembolism or stroke, or known clotting disorders. That list is a conversation-stopper for systemic therapy, and it's exactly the kind of history a wellness clinic selling pellets is not going to take carefully.

Where that leaves you

Hormone therapy is the most effective treatment there is for menopausal symptoms, and it reduces fractures. Started in the decade after menopause in a woman without contraindications, the risk profile looks very different from the one the 2002 headlines produced, and the twenty-year data on estrogen alone is reassuring on breast cancer. Started at 65 or 70, or taken to prevent heart disease or dementia, the evidence doesn't support it.

It's a symptom treatment with a real bone benefit, not a longevity drug. That's a smaller claim than the internet is currently making and a much larger one than most women were told in 2003.

I'm not a doctor and I can't tell you what to do about this. What I can tell you is that "hormones are dangerous" isn't what the evidence says, and neither is "every woman should be on them." Take this chapter to a physician who treats menopause (a certified menopause practitioner if you can find one) and ask about your own history, risk and symptoms, and the route and dose that fit them.

PART V — PEPTIDES AND GLP-1s

The regulatory status described in this part was checked as of August 2026, with the muscle-drug approvals in Chapter 41 updated in October 2026. Check the current status before acting on any of it.

Chapter 38 — Let's Be Honest About This Whole Category

This is the part of the book I thought hardest about.

I talk about peptides publicly. I've used them. My channel has videos about retatrutide, LL-37, MOTS-c, SLU-PP-332, BPC-157, peptide stacks. Those videos have done well, because there's enormous interest and not much honest information.

I could write a chapter that gives people what they want, or the one they need. I'm going to try for the second, and some of it is going to annoy people who came here looking for permission.

The single distinction that matters

Everything in this category falls into one of three tiers, and almost all the confusion in this space comes from treating them as the same thing.

Tier A: FDA-approved drugs with phase 3 trials. Semaglutide. Tirzepatide. Tesamorelin, for one narrow indication. Tens of thousands of people, randomized, adverse events counted, labels with warnings, manufactured under pharmaceutical quality control.

Tier B: late-stage but not approved. Retatrutide. Real phase 3 data now exists. It is not approved, cannot legally be prescribed or compounded, and everything in circulation is gray market.

Tier C: research chemicals. BPC-157. TB-500. LL-37 injected. MOTS-c. GHK-Cu injected. KPV. SLU-PP-332. The "GLOW" and "KLOW" stacks. These have no controlled human efficacy trials for the uses they're sold for. Most have none at all.

When somebody in a comment section says "peptides changed my life," they might be talking about a phase 3 drug with a cardiovascular outcomes trial behind it, or about a powder from a website with no human data whatsoever. Same word, completely different universes.

Why I'm being careful

Because people will make decisions based on what I write, and if I present tier C like tier A, somebody gets hurt.

I monitor myself at a level most people don't, and I told you what that looks like in Chapter 6. Most people trying these things aren't doing any of it.

When I've talked about my own experience with these compounds, I'm reporting what happened to me, not making a recommendation. That distinction gets lost the moment a video gets shared. It won't get lost here, because I'm going to keep saying it.

The grading system for this section

For every compound I'll give an evidence grade, and I'm not going to soften it:

- PHASE 3 HUMAN: large randomized trials with clinical endpoints
- EARLY HUMAN: phase 1 or 2, or uncontrolled human case series
- ANIMAL ONLY: rodent or other animal work, no human efficacy data
- IN VITRO ONLY: cells in a dish
- NO DATA: none

You're going to notice that a lot of the most popular compounds land in the bottom three.

Chapter 39 — The Approved Drugs

Start with what's real, because it's remarkable.

Semaglutide — PHASE 3 HUMAN

STEP 1, Wilding and colleagues, NEJM, 2021. 1,961 people, semaglutide 2.4 mg weekly versus placebo, 68 weeks, both arms with lifestyle counseling.

- Weight: −14.9% versus −2.4%. Treatment difference −12.4 percentage points.
- 86.4% lost at least 5%. 69.1% lost at least 10%. 50.5% lost at least 15%.
- Waist: −13.5 cm versus −4.1 cm
- Systolic BP: −6.2 versus −1.1 mm Hg

Adverse events: GI problems in 74.2% versus 47.9%. Gallbladder disorders 2.6% versus 1.2%. Serious adverse events 9.8% versus 6.4%.

SELECT, Lincoff and colleagues, NEJM, 2023. This is the one that matters most. 17,604 people aged 45+, BMI 27+, with established cardiovascular disease but no diabetes. Mean age 62. Mean follow-up about 40 months.

- Major adverse cardiovascular events: 6.5% versus 8.0%. Hazard ratio 0.80. A 20% relative reduction.
- All-cause mortality: hazard ratio 0.81
- Nonfatal heart attack: hazard ratio 0.72

That's a drug reducing heart attacks and strokes in people without diabetes. Those are actual events, not a surrogate.

Note the weight loss in SELECT was −9.4%, less than STEP 1's −14.9%: real-world adherence in a cardiovascular population.

Discontinuation for adverse events: 16.6% versus 8.2%.

The label warnings, which matter after fifty: boxed warning for rodent thyroid C-cell tumors (contraindicated with personal or

family history of medullary thyroid carcinoma or MEN2). Warnings for pancreatitis, gallbladder disease, acute kidney injury, retinopathy progression, aspiration under anesthesia. Older labels also carried a suicidal-thoughts warning; in January 2026 the FDA asked for it to be removed from Wegovy, Zepbound and Saxenda after its review found no increased risk. Check the current label. Nausea 44%, diarrhea 30%, vomiting 24%, constipation 24%.

One safety signal worth flagging specifically: SUSTAIN-6 found retinopathy complications 3.0% versus 1.8%, hazard ratio 1.76. That's attributed largely to rapid glucose lowering rather than the drug itself, but if you're diabetic with existing retinopathy, that's a conversation to have before starting.

Tirzepatide — PHASE 3 HUMAN

SURMOUNT-1, Jastreboff and colleagues, NEJM, 2022. 2,539 adults without diabetes, 72 weeks, three doses versus placebo.

- Weight: −16.0% / −21.4% / −22.5% versus −2.4%
- At the top dose: 90% lost at least 10%. 63% lost at least 20%. 39.7% lost at least 25%.

SURMOUNT-5, published in 2025: head-to-head against semaglutide in obesity. 751 people, 72 weeks, open-label.

- Tirzepatide −20.2% versus semaglutide −13.7%. About a 6.5 percentage point difference.
- GI-related discontinuations were lower on tirzepatide (2.7% versus 5.6%)

Caveat: open-label design, and the semaglutide arm didn't reach the roughly 15% seen in STEP 1.

What this means

These drugs work, and the effect size is enormous. Weight loss of up to 20% in one set of trials and a 20% cut in cardiovascular events in another isn't something diet and exercise advice has

ever produced at a population level. Pretending otherwise because it feels like cheating isn't a serious position.

At the same time, they don't build muscle, bone or fitness, and the next three chapters are about the problems they create.

Chapter 40 — Retatrutide: My Four Months On

Now the one people ask me about most.

What it is, and its exact status

Retatrutide is a triple agonist: it hits GLP-1, GIP, and the glucagon receptor. That third one is what makes it different, and I'll come back to why.

Let me state its regulatory status as precisely as I can, because this matters more than anything else in this chapter.

Retatrutide is not FDA-approved for any indication. As of this writing, the manufacturer has stated it plans to submit to the FDA in the first quarter of 2027. It cannot legally be prescribed, purchased, or compounded. Outside the clinical trials, any retatrutide sold to consumers today is gray market.

That's not a technicality. Every vial being sold right now comes from a supply chain with no regulatory oversight, and I'll show you in Chapter 44 what analytical testing of that kind of supply chain finds.

The trial data

Phase 2, Jastreboff and colleagues, NEJM, 2023. 338 adults without diabetes, 48 weeks.

Weight at 48 weeks: −8.7% / −17.1% / −22.8% / −24.2% across dose arms, versus −2.1% on placebo.

At the top dose: 93% lost at least 10%, 83% lost at least 15%, about half lost at least 25%, and roughly a quarter lost more than 30%.

Adverse events were dose-related GI problems, mostly mild to moderate, plus a dose-dependent heart rate increase that peaked around 24 weeks and then declined.

Two things about that heart rate signal. First, it's in a drug that hits the glucagon receptor, which raises energy expenditure, so an elevated resting heart rate is doing something, not just drifting.

Second, the readership of this book is over fifty, which means a meaningful share of you have cardiac history, arrhythmia, or blood pressure being managed. A sustained heart rate elevation is a different proposition at sixty-five than at thirty-five, and it's the one signal from these trials I'd want a cardiologist looking at before I did anything.

And here's the asymmetry I want you to notice. In the last chapter I gave you a full page of warnings for semaglutide: the boxed warning for rodent thyroid tumors, the contraindication with medullary thyroid carcinoma and MEN2, pancreatitis, gallbladder disease, kidney injury, retinopathy, aspiration under anesthesia.

Retatrutide is in the same drug class. There is every reason to expect class warnings would apply. But there is no approved label and no manufacturer safety tracking for what's sold outside the trials. You can still report a bad reaction to the FDA through MedWatch, but there's no label for it to land on. If something goes wrong on an approved drug, it gets counted and eventually it shows up on the label. If something goes wrong on a gray-market vial, it may never get reported, and if it does, it's hard to trace back to what was actually in the vial.

You get more documented warning about the legal, monitored drug than about the illegal one, and that's not because the illegal one is safer.

Phase 3 (the TRIUMPH program), reported through 2026:

TRIUMPH-1: 2,339 people, 80 weeks. −19.0% / −25.9% / −28.3% versus −2.2% on placebo. A prespecified extension out to 104 weeks in people with BMI 35+ reached −30.3% at the top dose.

At 80 weeks on the top dose: 62.5% lost at least 25%, 45.3% lost at least 30%, 27.2% lost at least 35%.

Adverse events: nausea 42.4% versus 14.8%, vomiting 25.3% versus 4.8%. Discontinuation for adverse events climbed to 11.3% at the top dose versus 4.9% on placebo. That dropout number is the real-world limiter, and it doesn't get quoted alongside the weight loss figures.

TRIUMPH-2 in type 2 diabetes with obesity: −12.7% / −19.1% / −20.8%. TRIUMPH-3 in severe obesity with established cardiovascular disease: −21.6% / −22.6%.

Those are the biggest weight loss numbers anybody has produced with a drug.

Here's what happened to me

I did it for about four months, and I've been off it for a while now. Here's what I observed, with the caveat I'll repeat as many times as it takes: this is one person, I'm not a doctor, and this is not a recommendation of anything, including whether to do it at all.

Before I started, my baseline was well established because I'd been tracking for years. It took 2,200 calories to maintain my weight. Carbs were around 50 grams, because I'd been running keto for years and my body was well adapted to using fat for fuel. Protein was at a gram per pound or more, which at my weight is 175 grams a day and up. I've eaten that way for decades.

On it, I pushed my protein higher, past 200 grams most days. That was deliberate and I'll explain why in the next chapter. Today I'm still around 200.

What surprised me most was my baseline calories. They went from 2,200 to about 2,700. That put my maintenance up by roughly 500 calories a day.

After I came off it, my baseline stayed up around 2,700 for a while. It didn't last. Today I'm back around 2,200.

I want to be careful about what I claim there. My baseline was still up more than a month after I stopped, and retatrutide's half-life is around six days, so by then most of it was gone. I can't explain that shift by saying there was still drug in me. I don't have an explanation for it, or for why it then faded. It's an observation from one person with good records, and I'd rather say "I don't know why" than invent a mechanism.

The carbohydrate thing was the biggest change. I went from about 50 grams of carbs a day to around 400 while I was on it.

Today I'm around 200. None of these numbers are the same every day. On it, I hit a wall twenty minutes into a workout unless I ate 120 to 150 grams of carbs beforehand. My body had run on fat for years, and it couldn't on this. I craved pasta, rice, potatoes, oatmeal.

Why? My guess, and it's only a guess, is that it's the glucagon receptor, which affects how the body uses and burns fuel. Some people report more energy on it. Some report less, possibly because they're burning more and not eating enough to keep up, and their glucose drops. The mechanism is a question for a specialist, not me.

Both make sense and both are real, which is the point I make in Chapter 1.

Other things I noticed: sensitive skin (long sleeves felt uncomfortable). I've heard from others about diarrhea, and from others about constipation, in the same conversation.

What it did for my body composition: I increased lean tissue. At sixty-four I run between 12 and 14% body fat at about 175 pounds. I was already lean and not carrying much fat, and it still changed my composition.

Now let me undercut that immediately, because it's the most encouraging sentence in this chapter and the weakest evidence in it. It's one person, self-measured, with no control group and no idea what would have happened if I'd changed nothing. And a 3D body scan cannot distinguish real lean tissue gain from water and glycogen, which is exactly the criticism I'm going to make of the DXA data in the next chapter, so I'd be a hypocrite not to apply it to myself.

The dangerous part, stated plainly

My maintenance went to about 2,700 calories, and at first the drug made it harder to eat, because appetite drops. So somebody in that position might easily be eating 1,800 or 1,900 calories.

That's almost a 1,000-calorie daily deficit without adding any cardio, and that's too much. It isn't a weight loss plan, it's wasting.

This stuff is powerful. I'm telling you, this is no joke. People lose a lot of weight fast on it. Eating less is clearly part of that, and the trial authors think energy expenditure may play a part too. My own calorie records can't tell you which matters more.

Which brings me to the two things I'd call non-negotiable on any of these drugs: you have to lift weights and you have to eat a lot of protein.

They're the same two non-negotiables as the rest of this book, but here the consequence of ignoring them is faster and more severe. If you don't, there's a very good chance you lose muscle along with the fat and end up smaller, softer and weaker at the same time.

And one more thing about appetite

I found that once it got in my system, my appetite dropped at first and then it came back.

What I'd take from that is a point about mechanism, not about dosing: appetite coming back doesn't, on its own, show the drug has stopped working. People who read a returning appetite as automatic failure may be misreading it.

I'm deliberately not going to tell you what to do with that, because I don't know what you're taking, where it came from, or what's actually in it. And the phase 3 data shows discontinuation for adverse events climbing to 11.3% at the top dose. The top of the range is where people fall out of the trials, not where the results live.

What I'd say to anyone considering it

You're going to hear a lot of people tell you exactly how to do it: you have to eat carbs, you don't have to eat carbs, keto works fine, you have to stack it with three other things.

Most of them are telling you the truth about themselves.

Some people don't have to eat carbs and some do. I did. I was certain I didn't, and I was wrong about my own body within a matter of weeks.

Nobody knows how it's going to affect you, not me, not the person in the comments and not the person selling it to you.

And the bottom line: it's not approved. Whatever else I've told you in this chapter, that's the fact that should drive your decision. If you want a GLP-1 drug, there are two approved ones with cardiovascular outcome trials behind them, available legally with a prescription and pharmaceutical manufacturing. That's an available option. This isn't, yet.

Chapter 41 — The Muscle Problem

Nobody wants to talk about this, and it's the single most important issue in this entire category for anyone over fifty.

How much of that weight is muscle?

STEP 1 DXA substudy, a subset of 140 people from the semaglutide trial.

- Total fat mass: −19.3%
- Total lean body mass: −9.7%
- Visceral fat: −27.4%

Do the arithmetic: roughly 8.2 kg of fat plus roughly 5.2 kg of lean mass, out of about 13.4 kg total.

Roughly 39% of the weight lost was fat-free mass.

SURMOUNT-1 body composition substudy, tirzepatide: fat mass −33.9%, lean mass −10.9%. About a 3-to-1 ratio, so roughly 25% of the weight lost was lean mass. Better than semaglutide, but still substantial.

Now let me be fair about that number

Two important qualifications, and they cut in the drug's favor.

One: 20–30% fat-free mass loss is typical of any substantial caloric restriction. Diet somebody down 15% of their body weight by any method and you'll see something in that range. The drugs aren't uniquely catabolic. Large deficits are.

Two: DXA "lean mass" includes water and glycogen. When you deplete glycogen, the water bound to it goes too. So the DXA number overstates actual contractile muscle loss.

But here's why it matters more after fifty than at thirty. You're heading toward a position where, by your seventies, you're losing about 1% of leg lean mass per year and 2.6 to 4.1% of strength per

year (Chapter 4). A 5 kg lean mass loss on top of that trajectory is a different event at sixty-five than at thirty-five.

And the STEP 1 substudy was an exploratory secondary analysis in 140 people with no multiplicity correction. So even the number itself is softer than it looks.

Does lifting and eating protein fix it?

This is the question everyone asks, and the answer is uncomfortable.

There is no completed randomized controlled trial testing resistance training plus protein specifically during semaglutide or tirzepatide therapy with lean mass as the outcome.

Grade: NO DATA for that specific question.

There's a trial underway, LEAN-PREP, a four-arm randomized trial of 232 people with home-based resistance exercise three times a week plus protein at 1.6 g/kg, all on semaglutide or tirzepatide, with MRI quadriceps cross-sectional area as the primary outcome. Results are not available yet.

The closest existing evidence is S-LiTE, published in NEJM in 2021: 195 people after an 8-week low-calorie diet, randomized for 52 weeks to exercise, liraglutide, both, or placebo. The combination held weight off best (−3.4 kg from randomization versus +6.1 kg on placebo) with the best body fat percentage change. But the per-arm lean mass results aren't something I could verify well enough to quote you numbers on.

So combining resistance training and adequate protein with a GLP-1 is biologically sensible, universally recommended by expert consensus, and not yet demonstrated in a completed randomized trial in GLP-1 users.

I'm telling you to do it. I'm also telling you that the evidence for it is inference, not proof. Those are different things and you should know which one you're getting.

The drugs being built to solve this

There's an entire pharmaceutical race happening around muscle preservation, and the early data is striking.

Bimagrumab, an antibody against the activin receptor. Phase 2 in 75 people with type 2 diabetes and obesity, 48 weeks: fat mass −7.49 kg while lean mass went UP 1.70 kg, versus −0.44 kg on placebo. Weight down 5.9 kg. Side effects: diarrhea 41%, muscle spasms 41%.

BELIEVE (bimagrumab plus semaglutide, 507 people, 48 weeks), published in Nature Medicine in 2026:

Arm	Weight change	Lean mass change
Placebo	−3.3 kg	—
Bimagrumab alone	−9.3 kg	—
Semaglutide alone	−14.2 kg	−4.7 to −6.9%
Combination (high dose)	−17.8 kg	−0.8 to −2.3%

COURAGE: trevogrumab, an anti-myostatin antibody, given with semaglutide, and in one arm also with garetosmab, an anti-activin-A antibody. 599 people at 26 weeks. Semaglutide alone: −10.6% weight, of which 33% was lean mass. The three-drug combination: −13.4% weight, of which only 7.4% was lean mass. Ninety-three percent fat.

Note: the three-drug arm had higher discontinuation and two deaths.

EMBRAZE: apitegromab with tirzepatide, 87 people, 24 weeks. Weight loss similar between arms. Lean mass −1.6 kg versus −3.5 kg. Lean fraction of weight lost: 14.6% versus 30.2%. About 55% relative lean mass preservation, p = 0.001. No treatment-related serious adverse events.

As of October 2026, two of these have FDA approvals for rare diseases: garetosmab for fibrodysplasia ossificans progressiva (August 2026) and apitegromab for spinal muscular atrophy

(September 2026). None of the four is approved for obesity or for preserving muscle during weight loss, and none has phase 3 obesity data.

The endpoint gap is the headline: none of them has demonstrated that preserved DXA lean mass translates into strength, function, falls, or mortality benefit.

Which takes us right back to Chapter 4. Newman's data showed muscle mass did not predict mortality, and muscle strength did. Preserving a DXA number isn't the same as preserving function. Nobody has shown these drugs preserve function, because nobody has measured it.

The clearest statement of this problem I've heard

Josh Holyfield laid this out in a video better than most clinicians do, and I want to give him the credit because it's the practical version of everything in this chapter.

His framing: these drugs create aggressive calorie deficits, but none of them change your protein requirement. If anything, faster weight loss raises it. And appetite suppression doesn't distinguish between the calories you need and the calories you don't. So somebody goes from eating 2,500 calories to 1,200 without trying, and inside that 1,200, if they're not deliberately prioritizing protein, they might be getting 40 or 50 grams. That's nowhere near enough when the body needs 120, 150, or more.

Then the body goes into triage. From a survival standpoint you don't need all that lean tissue, so it gets broken down to supply amino acids elsewhere. The scale drops and it looks like progress. Less muscle means a lower metabolic rate, so the same deficit produces less weight loss, and that's the plateau people blame on the drug. Less muscle also means less glucose uptake, so insulin sensitivity goes the wrong way. Then the symptoms show up: brain fog, mood changes, hair thinning, skin looking worse. By the time you can see it, it's been compounding for months.

His numbers on lean mass loss run a bit higher than mine. He cites roughly 40–45% for semaglutide and 34% for tirzepatide,

where the substudies I read give 39% and 25%. Those are different analyses of overlapping data. The range is somewhere between a quarter and nearly half of the weight lost, and the exact figure matters less than the fact that it's enormous.

His advice matches mine: treat protein as non-negotiable and track it every day. My number is at least 1 gram of protein per pound of desired body weight. (Kidney disease, or a different number from your doctor? Use your doctor's.) Lift two to three times a week minimum. Walk daily. Protect sleep.

And he names the marker to watch if you're not lifting hard enough to notice performance changes: resting heart rate, taken before you get out of bed. Elevated 5 to 10 beats above your baseline for three or more days running means your body is under systemic stress. That's a free, sensitive early warning and I think it's a good call.

I'll be clear that I'm citing him here for his cautions, which I think are excellent. He and I are both in a corner of the internet that talks about compounds a lot, and I'd apply the same skepticism to his enthusiasm, and mine, that I've applied to everything else in this section.

What I actually did about it

I pushed my protein from my usual 175-plus grams a day to over 200 grams. I kept lifting an hour and a half, five days a week, which is what I was doing anyway. And I ate enough. That was the hard part, because my appetite dropped and my maintenance requirement went up at the same time.

I increased lean tissue over that period, with every caveat I put on that sentence in Chapter 40.

But the logic behind it (lift, eat protein, don't run a massive deficit) is the same logic as the rest of this book, and it's what every expert consensus group recommends. A joint advisory from four major nutrition and obesity organizations in 2025 listed "adequate protein intake and strength training to preserve lean

mass" among its eight nutritional priorities for people on these drugs.

Consensus isn't evidence. But when the consensus lines up with the mechanism and with everything else we know about muscle after fifty, I'll act on it.

Chapter 42 — What Happens When You Stop

Short chapter, important chapter.

The regain data

STEP 1 extension, published in 2022. 327 people from the original trial, followed 52 weeks off the drug.

- During the trial, these 327 on semaglutide: −17.3%
- After 52 weeks off: regained +11.6 percentage points
- Net at the end: −5.6%

Roughly two-thirds of the weight lost came back within a year of stopping.

And blood pressure, HbA1c, lipids and CRP all reverted toward baseline, retaining only a modest advantage.

The claim I have to correct

You will hear this constantly, including from people I respect: "When you stop a GLP-1, you regain the fat but not the muscle."

I've probably implied it myself.

The STEP 1 extension collected no body composition data at all. The claim that you regain fat preferentially isn't a finding from that trial. It's an inference. Grade for that specific claim: NO DATA.

It's a plausible inference. Weight regain after dieting does typically favor fat, and there's a body of literature on that in other contexts. But plausible isn't the same as demonstrated, and the specific claim about these drugs has never been tested.

I'm flagging it because if it's true, it means each cycle on and off leaves you with a worse body composition than before, and that would be a serious problem for anyone over fifty considering intermittent use. If it's false, it doesn't. Nobody knows, and people are making decisions as if somebody does.

What this means practically

If two-thirds of the weight comes back within a year of stopping, then these drugs are being used for a chronic condition and stopping is the same as stopping any chronic medication.

Nobody expects blood pressure to stay down after you stop your lisinopril.

Framing obesity pharmacotherapy as indefinite, like antihypertensives, is the position most of the field has landed on.

That means you plan for the discontinuation problem before you start, not after.

That includes cost, whether you can maintain the training and protein habits you built while on it, and whether you'd rather build those habits first and see how far they get you.

I'll say what I think. The people who do best are the ones who used the drug as a window to build training and eating habits that survive it. The drug bought them appetite control while they learned to lift and learned to eat protein. If you come off and you're still lifting three times a week and still hitting at least a gram of protein per pound of desired body weight, your outcome looks very different from somebody who just stopped eating for a year. (Kidney disease, or a different number from your doctor? Use your doctor's.)

That's not a finding from a trial. That's thirty years of watching people in gyms.

Chapter 43 — The Research Chemical Tier

Now the part where I'm going to disappoint people.

I've made videos about several of these. When I went and looked at what exists in the human literature, it was thinner than I expected, in some cases dramatically thinner. Here they are with the grades.

BPC-157 — ANIMAL ONLY

What it is: a synthetic 15-amino-acid partial sequence attributed to a protein found in human gastric juice. Isolated by a research group in Zagreb, Croatia. First appears in the literature in 1992.

The animal evidence is voluminous: hundreds of rodent papers on tendon, ligament and muscle healing, ulcer healing, and angiogenesis. It's real work and there's a lot of it.

Two things you should know about it. First, the great bulk of it comes from one research group, whose lead investigator holds financial interests in related patents and companies. Second, it is rodent.

The entire published human evidence base is three papers. All in the same lower-tier journal, all from the same author group, none randomized, none controlled, none blinded:

1. n = 2 healthy adults, open-label single IV infusions, two-day observation
2. n = 16 with chronic knee pain, retrospective, 14 reported subjective improvement, with no control, no blinding, no objective endpoint
3. n = 12 women with interstitial cystitis, single injection, retrospective

That's thirty people total, uncontrolled and retrospective.

A phase 1 trial registered in 2015 was withdrawn with no results published. A phase 2 trial for hamstring strain was registered in early 2026 with no results yet.

The quotable version: there is no published, peer-reviewed, randomized human trial with accessible results showing BPC-157 is effective or safe for any indication.

And here's a detail that should give everyone pause. In July 2026, FDA scientists stated that there is no universally accepted chemical formula for some of these compounds. One FDA official's line was, in substance: we've never before faced the problem of "what is it?"

Grade: ANIMAL ONLY. Human efficacy: effectively NO DATA.

LL-37 — EARLY HUMAN (topical wound healing only)

I made a video called "Why LL-37 Is the Peptide Everyone's Talking About Now." Here's what I'd add.

What LL-37 is: the sole human cathelicidin antimicrobial peptide. A 37-residue innate immunity molecule expressed by neutrophils and epithelial cells. It's a host-defense protein.

It is not an anabolic agent and it is not an anti-aging agent. That's not its biology.

And here's the context that essentially never gets mentioned by anyone selling it: LL-37 is pro-inflammatory and is implicated in the pathogenesis of rosacea, psoriasis and lupus. It's a molecule your body uses as a weapon, and weapons have collateral damage.

Real human trials do exist, but they're topical, for hard-to-heal venous leg ulcers. Randomized, placebo-controlled, dose-finding work published in 2014 and a multicenter trial in 2021. That's legitimate research into a legitimate wound-healing application.

Injectable or systemic LL-37 for immune support, chronic infection, Lyme, biofilms, or longevity: NO DATA.

Grade: EARLY HUMAN for topical wound care. NO DATA for everything it's actually sold for.

MOTS-c — ANIMAL ONLY

What it is: a 16-amino-acid peptide encoded in mitochondrial DNA, specifically the 12S rRNA region. Interesting biology.

The foundational work (Lee, Cohen and colleagues, Cell Metabolism, 2015) was in mice and cell lines. MOTS-c targets the folate-methionine cycle and activates AMPK, and treated mice showed improved insulin sensitivity and resisted diet-induced obesity. No human administration.

A 2021 Nature Communications paper gave MOTS-c to mice: old mice ran about twice as long and 2.16 times as far. Impressive.

The human component of that paper was purely observational. Young men cycling showed skeletal muscle MOTS-c up 11.9-fold after exercise and circulating MOTS-c up about 1.5-fold.

Read that carefully, because it's the crux: exercise raises your own MOTS-c. That is not evidence that injecting MOTS-c does anything in a human.

The first human interventional trial (phase 2a, 120 people with prediabetes, daily subcutaneous MOTS-c for 12 weeks) started in February 2026 with primary completion expected in 2027. No results.

Grade: ANIMAL ONLY.

SLU-PP-332 — ANIMAL ONLY, and it isn't a peptide

I need to correct something I said in a video title.

SLU-PP-332 is not a peptide. It's a synthetic small molecule, a pan-ERR agonist. It gets routinely mis-sold and mis-described as a peptide, including by me.

It came out of Thomas Burris's lab (Saint Louis University, hence "SLU"). The published work (2023 in ACS Chemical Biology, 2024 in Journal of Pharmacology and Experimental Therapeutics) describes a compound that produces an "exercise-like" transcriptional response and weight and fat loss in mice.

All published work is mouse and cell-based. It has never been administered to humans in a registered trial. There is no human safety data, no human pharmacokinetics, no toxicology package supporting human dosing.

It is a laboratory research tool compound. Vendors selling it are selling a reagent.

Grade: ANIMAL ONLY / NO HUMAN DATA.

GLOW and KLOW stacks — NO DATA

GLOW is BPC-157 plus TB-500 plus GHK-Cu. KLOW adds KPV.

I made a video breaking these down. Then I went looking for the literature.

A literature search returns zero peer-reviewed studies of either blend. Every result is a vendor product page, a dosing calculator, or an affiliate review.

These are marketing constructs. They originated with compounding pharmacies and gray-market vendors, not research entities. There are no controlled human trials of the combinations, no pharmacokinetic studies of the combinations, no interaction studies and no dosing rationale derived from any human data.

The components individually:

- BPC-157: covered above. Animal only.
- TB-500: a synthetic fragment of thymosin β-4. A company pursued thymosin β-4 itself in eye and skin indications, but TB-500 as sold has no human efficacy trials. Animal only.
- GHK-Cu: decades of topical cosmetic human skin studies, small and mostly industry-linked, with cosmetic endpoints. No human trials of injectable GHK-Cu.
- KPV: an α-MSH tripeptide fragment. Preclinical colitis and wound models. No human trials.

Grade: NO DATA. That doesn't mean "thin data." It means none.

Growth hormone secretagogues

Tesamorelin is the one approved agent, and it's worth understanding exactly what it's approved for.

FDA approved in November 2010, for one indication: reducing excess abdominal fat in HIV-infected patients with lipodystrophy. Two phase 3 trials, 816 people total, both showing meaningful visceral fat reduction, on the order of 12 to 18% reductions against increases or no change on placebo, depending on the trial and the analysis you read. Benefits sustained to 52 weeks only with continued therapy.

The FDA explicitly noted that long-term cardiovascular benefit and safety have not been studied.

It is not approved for general fat loss, bodybuilding, or anti-aging.

Ipamorelin, CJC-1295, sermorelin: these have human pharmacology data. They do raise growth hormone and IGF-1 pulses. They have no phase 3 efficacy trials for body composition, strength, recovery, sleep, or longevity in healthy adults. None is FDA-approved.

A six-month sermorelin study showed increased lean body mass and reduced visceral fat but no improvement in strength or aerobic fitness.

MK-677 / ibutamoren, in the same commercial category: a one-year trial raised GH and IGF-1 to young-adult levels and increased fat-free mass, and the increased fat-free mass did not translate into any change in strength or function. Side effects included edema, muscle pain, increased appetite, and a rise in fasting glucose.

There it is again: more lean mass on the scan and no more function.

Chapter 44 — What's Actually In the Vial

I want to spend a whole chapter on this because it might be the most practically useful thing in this section.

The analytical study

Ashraf and colleagues published work in 2024 (appearing across the Journal of Medical Internet Research and JAMA Network Open) on what people are actually buying online.

The setup: they screened 1,080 search-result links, identified 317 online pharmacies, and narrowed to 59 unique illegal online pharmacies. The top 30 of those domains drew 4.7 million visits in a single quarter.

They selected six vendors and made test purchases of semaglutide.

Three of the six products never arrived. They were non-delivery scams, and the vendors then demanded a further $650 to $1,200.

Of the three vials that did arrive and were analyzed by mass spectrometry:

- Identity: all three did contain semaglutide. That's the good news.
- Purity: 7.7% to 14.37%, against an advertised 99%.
- Semaglutide content 28.56% to 38.69% ABOVE the labeled amount.
- An unintended overdose built into the vial.
- Endotoxin: one of the three samples had a clearly measurable amount, about 9 EU/mg. The other two came back only as "below the test's limit" (under roughly 2 to 3 EU/mg), which isn't a confirmed positive. There were no live organisms, so any endotoxin is what's left of dead bacteria. Filtering doesn't remove it, and it can cause fever and inflammation.

- Packaging: 59–63% non-conformant. Visual inspection score 8–9 out of 22, versus 22 out of 22 for genuine product.

They classified them as probable substandard and falsified products.

On the face of it, most of what was in those vials wasn't the drug. Some of that may be fillers or salts the test doesn't count, and the study doesn't let you say exactly what. Either way, people were injecting a product that wasn't what the label said.

And here's the part that should really land

That study was of semaglutide, a drug with an approved reference standard, a known chemical identity, and a legitimate manufacturing process that gray-market suppliers are trying to copy.

There is no equivalent published analytical study for BPC-157, TB-500, GHK-Cu, KPV, MOTS-c, or SLU-PP-332 sold as research chemicals.

The purity of those is, empirically, unknown. That doesn't mean "probably fine." It means nobody has checked.

And remember: FDA scientists said in 2026 that there is no universally accepted chemical formula for some of these compounds. If the agency can't say definitively what the substance is supposed to be, no test can tell you whether what you received matches it.

"Research use only" is a legal fiction

You'll see it on every vial. It's meaningless.

The FDA issued warning letters to peptide sellers in December 2024 and February 2025 establishing the principle: "research use only / not for human consumption" disclaimers are overridden by objective intent as evidenced by the seller's own marketing copy. When a website says a product "significantly reduces HbA1c, body

weight and systolic blood pressure," that establishes intended therapeutic use regardless of what the label says.

The charges were unapproved new drugs and misbranding.

State authorities are acting too. The Ohio Board of Pharmacy has issued summary suspensions and settlements against clinics and distributors handling these compounds.

And the compounding door has mostly closed

A lot of people got compounded semaglutide or tirzepatide legally during the shortages. That window is mostly shut.

	Shortage resolved	Compounding discretion ended
Tirzepatide	Dec 2024	Feb–Mar 2025
Semaglutide	Feb 2025	Apr–May 2025

Once a drug comes off the shortage list, federal law bars compounding "essentially copies" of the approved product. There are narrow exceptions, for example when a prescriber documents that an individual patient needs a version that's meaningfully different from the approved drug. A mass-market copy isn't that. Outside those exceptions it's generally unlawful, not a legal loophole.

The peptide regulatory situation, as of now

This is in flux, so here's the state of play.

In September 2023, the FDA placed about 19 peptides into Category 2 ("may present significant safety risks"), including BPC-157, ipamorelin, CJC-1295, TB-500, epitalon, kisspeptin-10, MOTS-c, LL-37, GHK-Cu injectable and KPV.

In April 2026, the FDA announced removal of 12 peptides from Category 2.

Removal is not legalization. Under federal law, a bulk substance is eligible for compounding only if it has a USP monograph, is a

component of an approved drug, or appears on the Category 1 Bulks List. None of these peptides meets any of those. They remain ineligible for lawful compounding, prescribing and dispensing.

Then in July 2026, the FDA's Pharmacy Compounding Advisory Committee met. The FDA's own review scientists formally proposed that all seven substances under consideration NOT be added to the Bulks List, citing the absence of large controlled randomized human trials and the inability to chemically characterize the substances.

The advisory committee voted against its own agency's scientists. BPC-157 passed 8–6 with one abstention. KPV and TB-500 also 8–6. MOTS-c 7–5 with two abstentions.

Advisory committee votes are non-binding. Formal rulemaking, estimated at 8 to 24 months, would be required before any pharmacy could legally compound these.

Reporting also noted that the reconstituted panel included members with financial interests in peptide sales. Make of that what you will.

Bottom line: as of now these remain in legal limbo, and nothing about that vote makes buying them from a website lawful.

The risks nobody itemizes

Sterility and injection. The risks are reconstituting lyophilized powder yourself, multi-dose vials without preservative, storage abuse and non-sterile technique. And in that semaglutide study, one of the three vials had measurable endotoxin, which isn't removed by filtration and doesn't require live bacteria to cause fever and inflammation.

Dosing errors. The FDA issued a MedWatch alert in July 2024 about compounded semaglutide dosing errors: patients drawing from vials and clinicians miscalculating, with confusion between milligrams, "units" and milliliters. In most reported cases patients received 5 to 20 times the intended dose. Reported harms

included severe vomiting, syncope, dehydration, acute pancreatitis and gallstones, some requiring hospitalization.

Immunogenicity. FDA guidance establishes that synthetic peptides, and especially their synthesis-related impurities and aggregates, can provoke antibody responses. In the semaglutide study, measured purity was only about 8% to 14%. The researchers found no other peptide-like impurities and couldn't say what the rest was. That doesn't prove the rest is harmful. It means you don't know exactly what you're injecting.

Cancer signaling, and I want to be careful in both directions. BPC-157's principal claimed mechanism is VEGFR2-mediated angiogenesis. Angiogenesis is also how tumors grow. There is no human carcinogenicity data either way. Both "it causes cancer" and "it's proven safe" are unsupported. Same for TB-500, where thymosin β-4 is upregulated in several malignancies in preclinical work. These are genuine unknowns, not established harms.

Chapter 45 — Growth Hormone and the Most Misused Study in Fitness

One study deserves its own chapter, because it's the single most misused citation in this entire field and you will encounter it.

Rudman 1990

Rudman and colleagues, New England Journal of Medicine, 1990. Twelve treated men and nine untreated controls, ages 61 to 81, selected for low IGF-1. Growth hormone three times a week for six months after a six-month baseline.

Results:

- Lean body mass +8.8%
- Adipose tissue −14.4%
- Lumbar vertebral bone density +1.6%
- Skin thickness +7.1% ($p = 0.07$)
- No change at the radius or proximal femur

That study launched an entire industry. It's cited constantly as proof that growth hormone reverses aging.

Why it's misused

Twelve men.

No strength, power, endurance or functional measures were made at all. The study measured tissue compartments and nothing about what the men could actually do.

It ran six months. It wasn't a longevity study and never claimed to be.

Attempts to replicate Rudman's doses in older adults produced high rates of adverse effects, so subsequent research deliberately used lower doses. The original protocol is not clinically recommended by anyone.

And the New England Journal of Medicine later published an editorial rebuking the commercial misappropriation of the paper, titled, and I appreciate the bluntness, “Can Growth Hormone Prevent Aging?”

The definitive corrective

Liu and colleagues, Annals of Internal Medicine, 2007. A systematic review of 18 randomized trials, 508 participants, mean age 68, mean duration about 26 weeks.

- Lean body mass: +2.13 kg
- Fat mass: −2.08 kg
- Strength: no statistically significant difference
- Functional capacity: no statistically significant difference
- Total cholesterol: no change

And significantly higher rates of soft tissue edema, carpal tunnel syndrome, joint pain and gynecomastia.

Their conclusion: growth hormone cannot be recommended as an anti-aging therapy.

Adverse event frequencies from the broader GH-in-aging literature: soft tissue edema around 50%, joint pain around 21%, carpal tunnel around 19%, and new-onset diabetes or impaired glucose tolerance around 22%.

That’s one in five developing a glucose problem.

The pattern you should now recognize

Growth hormone: more lean mass on the scan, no more strength, no more function.

MK-677: more fat-free mass, no change in strength or function.

Sermorelin: more lean mass, less visceral fat, no improvement in strength or aerobic fitness.

Bimagrumab and the myostatin drugs: preserved lean mass, function never measured.

Over and over, in compound after compound, the body composition number moves and the functional number doesn't.

Now go back to Chapter 4. Newman's Health ABC data: quadriceps strength predicted mortality. Muscle size did not. The European sarcopenia group formally demoted mass and made strength the primary criterion.

The entire pharmaceutical approach to muscle in aging has been optimizing the metric that doesn't predict outcomes.

I find that striking, and I don't think it's discussed nearly enough.

The legal note

Distribution of growth hormone for anti-aging purposes is prohibited under US federal law, 21 U.S.C. §333(e). That means prohibited, not discouraged.

The American Association of Clinical Endocrinologists and the Endocrine Society both state that growth hormone should be used only in confirmed adult GH deficiency.

Chapter 46 — If You're Going To Do This Anyway

I've written four chapters explaining why most of this category is unsupported. Some of you are going to do it anyway. I've been in this industry long enough to know that.

So here's what responsible looks like, as best I can construct it.

The tier that has an answer

For approved GLP-1 drugs (semaglutide, tirzepatide) there's a real framework:

1. Prescription drug, real prescriber, real diagnosis. Approved product from a licensed pharmacy, not a website and not a mass-market compounded copy, which is now generally unlawful anyway.
2. Baseline screening. Personal or family history of medullary thyroid carcinoma or MEN2 (that's an absolute contraindication). Pancreatitis history. Gallbladder status. Diabetic retinopathy screening if you're diabetic. Kidney function. Mental health history.
3. Protein and resistance training from day one, not as a rescue. The consensus targets run 1.2 to 1.6 grams of protein per kilogram, strength training at least three times a week, plus 150 minutes a week of aerobic work. On these drugs I'd hold my rule, at least 1 gram of protein per pound of desired body weight, not the floor, because a drug-sized deficit is exactly where the floor fails (Chapter 41). (Kidney disease, or a different number from your doctor? Use your doctor's.) I'll say again: this is consensus and protocol, not yet proven by a randomized trial in GLP-1 users.
4. Measure function, not just mass. Serial body composition, yes, but also grip strength, chair stands, gait speed. Everything in Chapter 45 tells you that mass and function come apart, and function is the one that predicts your outcomes.

5. Escalate dose slowly, and treat GI side effects as dose signals. Especially over sixty, where dehydration leading to kidney injury is a real pathway.
6. Plan for discontinuation before you start. Two-thirds regained in twelve months. Know what your plan is.
7. If you're older: monitor bone density and falls, not just the scale. You're already fighting a bone and balance decline. A large weight loss is an additional stressor on both.

The tier that doesn't have an answer

For tier C research chemicals, the answer is uncomfortable:

No monitoring protocol can substitute for absent safety data.

For BPC-157, TB-500, injectable GHK-Cu, KPV, MOTS-c and SLU-PP-332 in humans, there is no validated biomarker to watch, no known therapeutic window and no toxicology package.

So when somebody tells you they're doing it "under medical supervision," ask what exactly is being supervised. A doctor watching your labs on a compound with no known toxicity profile is watching for something nobody has defined.

That's not a reason nobody should ever try anything. It's a reason to be honest that you're the experiment, not the beneficiary of one.

What I do, and the distinction I'd ask you to hold

I experiment on myself, and I've said so throughout this book.

But look at what surrounds it: glucose twice a day, blood pressure and pulse multiple times a day, full blood work every month, every gram of food logged against every result, and fifty years of training history with a very stable baseline to compare against.

That's not a protocol I'm recommending. It's a description of the conditions under which I'm willing to take a risk on myself, and most people asking me about peptides aren't doing any of it.

And I'll say the thing I say in every video, because it's the most important sentence in this section:

Do your own research. Talk to your medical practitioner. And not just any doctor. Find someone who actually specializes in this, because most physicians have never been trained on any of it.

I'd add one more thing. There's a version of "do your own research" that means reading vendor websites and watching influencers until you find someone who confirms what you already wanted to do. That's not research. That's shopping for permission.

Real research means looking for the trial, checking whether it was randomized, checking how many people were in it, checking who paid for it, and being willing to come away with an answer you didn't want. I did that for this book and it cost me several positions I'd held publicly.

PART VI — THE SYSTEMS UNDERNEATH

Chapter 47 — Stress, Cortisol, and the Adrenal Fatigue Question

I'm going to handle this one carefully, because a real thing and a fake thing sit right next to each other here.

The fake thing first

"Adrenal fatigue" is not a medical condition.

Cadegiani and Kater published a systematic review in BMC Endocrine Disorders in 2016. They screened 3,470 articles and found 58 that met inclusion criteria: studies using direct awakening cortisol, cortisol awakening response, salivary cortisol rhythms, dexamethasone suppression, ACTH measurement, and stimulation testing.

Their finding was an almost systematic pattern of conflicting results across every method used, and the insulin tolerance test, the gold standard for assessing the HPA axis, was never performed in a single included study.

Their conclusion, close to verbatim: this review proves there is no substantiation that adrenal fatigue is an actual medical condition.

The Endocrine Society, the Society for Endocrinology, and the Australian and New Zealand endocrine bodies have all issued statements against the diagnosis.

There's also a clinical danger, which is why I won't soften this. If you're fifty-eight and exhausted and somebody calls it adrenal fatigue, that label can delay the diagnosis of things that are common in your age group and treatable: genuine adrenal insufficiency, hypothyroidism, anemia, sleep apnea, depression, heart failure, occult cancer.

And treating "adrenal fatigue" with glandular extracts or low-dose hydrocortisone can cause iatrogenic adrenal suppression. You can shut down the real thing by treating the fake thing.

Commercial four-point salivary cortisol panels are sold as the test for this, but insurers won't pay for them. They classify salivary cortisol for adrenal insufficiency as experimental and investigational, along with salivary DHEA, estrogen, progesterone and testosterone for anything to do with aging. Insurers aren't a moral authority, but they're extremely good at working out what has evidence behind it, because they're the ones writing the check.

Now the real thing

What makes this chapter hard is that the underlying intuition is right. Chronic stress does physiologically damage people over decades, and it is badly under-addressed in a fifteen-minute visit.

Your cortisol has a daily shape. It peaks in the morning, with a 50 to 75% rise in the thirty to forty-five minutes after you wake up (the cortisol awakening response, a real, replicable phenomenon), and then declines across the day.

How steeply it declines predicts your health. Adam and colleagues, Psychoneuroendocrinology, 2017: 80 studies, 36,823 participants, 179 separate associations.

Flatter cortisol slopes were associated with worse health overall, and in 10 of 12 outcome categories:

Outcome	Strength of association (r)
Immune and inflammatory markers	0.288 — strongest
Cancer	0.231
Fatigue	0.167
Depression	0.106
Obesity	0.093
Cardiovascular disease	not significant
Anxiety	not significant
Mortality	hazard ratio 2.40, p = .049

Why you still shouldn't buy the panel

The effect sizes are group-level. An r of about 0.15 tells you something about 36,000 people, but it's nowhere near strong enough to diagnose you from your curve.

The measurement is also fragile. The expert consensus guidelines on the cortisol awakening response establish that a delay of even 5 to 15 minutes between waking up and taking the first sample materially distorts the result. Without electronically verified wake and sample times, the data is unreliable.

Home-collected, unsupervised, unverified saliva kits, which is what a commercial adrenal stress panel is, don't meet that standard. You're paying for a number the researchers who study this say can't be trusted without lab-grade timing control.

No trial has ever randomized people to cortisol-curve-guided management versus ordinary care, so nobody has shown that acting on the curve improves anything.

What I actually do instead

I've owned health clubs for more than thirty years, and there have been stretches (a build-out going sideways, a bad year, a partner problem) where I was sleeping five hours, training on fumes and running on cortisol and coffee. I didn't need a saliva kit to tell me. My resting heart rate was up, my recovery between sessions was worse, my glucose readings drifted, and I was short with people I love. All of that is free information and it all told me the same thing.

What fixed it was never a supplement. It was sleeping, training, getting outside, and dealing with the thing that was going wrong.

What makes the diagnostic debate a bit beside the point is that everything you'd do about a bad cortisol curve is worth doing anyway: sleep, resistance training, aerobic exercise, social connection, getting outside in the morning, reducing alcohol, time off, and addressing the sources of chronic stress in your life. Every

one of those has independent evidence behind it, and none requires a cortisol panel to justify.

So my position is to skip the test and do the interventions.

If you're exhausted in a way that doesn't respond to sleeping better, get a real workup: a thyroid panel including free T4, a CBC, ferritin and iron studies, B12 with methylmalonic acid, a sleep apnea evaluation if you snore or your partner says you stop breathing, and morning cortisol if there's real clinical suspicion of adrenal insufficiency, done properly, in blood, by an endocrinologist.

Those are the things that find the treatable causes. That's root-cause medicine, and a four-point saliva kit with a colorful graph isn't.

The part of stress physiology that matters most after fifty

Chronically elevated cortisol is catabolic to muscle. It's a stress hormone whose job includes mobilizing energy, and one of the places it mobilizes energy from is your lean tissue. Combine that with poor sleep (which suppresses muscle protein synthesis and testosterone in young men, and which I flagged in Chapter 15 as evidence we've borrowed rather than earned) and with the anabolic resistance you already have from being over fifty, and you have three forces pushing the same direction.

I can't hand you a trial that quantifies that stack in older adults, because nobody has run it. But the direction isn't controversial and the interventions are the same ones I'd recommend regardless.

Chapter 48 — Light, Dark, and the Clock

This is the chapter where my side of the argument and mainstream science agree completely, where the evidence is strongest, and where the interventions cost nothing. It's also the one almost nobody acts on.

The study that should be famous

Windred and colleagues, PNAS, 2024. 88,905 people in the UK Biobank, average age 62, right in this book's range.

They wore wrist light sensors for a week, about 13 million hours of personal light exposure data. Researchers then followed them for an average of eight years and counted deaths: 3,750 from all causes, 798 from cardiometabolic disease.

Compared to people in the bottom half of exposure:

Night light exposure:

Percentile of night light	Mortality hazard
70th–90th	1.15–1.18
90th–100th	1.21–1.34

Daytime light exposure:

Percentile of day light	Mortality hazard
50th–70th	0.84–0.90
70th–90th	0.74–0.84
90th–100th	0.66–0.83

For cardiometabolic death the effects were larger: the brightest-night group ran a hazard of 1.33 to 1.46, and the brightest-day group 0.61 to 0.76.

Separately, lower circadian amplitude, meaning a flatter difference between your day and your night, predicted higher mortality.

Bright days and dark nights is the whole message, and it tracked with how long people lived.

The authors flag the caveats themselves. This is one week of light data, the cohort is about 97% white, and it's correlational: sick people go outside less, so reverse causation is a genuine concern.

I should run my own Chapter 2 test on it too. UK Biobank volunteers are healthier and wealthier than the general population and they signed themselves up, so ask whether people like you were in this cohort. Partly, for most of you.

But the dose-response is clean, the day/night contrast is specific, the circadian amplitude finding fits, and the mechanism is well characterized. I'd act on it, and I'd call it a strong association rather than a proven cause.

The actual numbers to hit

An international expert group published consensus recommendations in PLOS Biology in 2022. They're measured at eye level in melanopic EDI, which is essentially light weighted for how your circadian system responds to it.

- Daytime: at least 250 lux melanopic EDI. Daylight is the preferred source.
- Evening, for the three-plus hours before bed: no more than 10 lux.
- Sleeping environment: under 1 lux. Up to 10 if you need to see.

For scale: an overcast day outdoors runs a few thousand lux, and full daylight is tens of thousands. A well-lit indoor office is often under 500 lux by the raw measure, and considerably less by the melanopic one. Indoor light is not daylight, and your body knows the difference.

What I actually do

I live in Northern Nevada, which hands you about three hundred sunny days a year, and for most of my life I treated that as

scenery rather than as an input, which was a mistake. Now I'm outside in the first hour I'm awake most days, my wake time doesn't move, and my bedroom is dark, with the little blue LEDs covered. Here's the whole list.

Get outside within an hour of waking, for ten to thirty minutes, with no sunglasses. Overcast counts, because an overcast morning still massively outperforms your kitchen. This is the single highest-value free intervention in this book.

Morning bright light reliably advances your circadian phase and improves sleep timing, and that's established. Its effects on insomnia severity are more modest and mixed, so I won't oversell it as a cure for bad sleep.

Get more light during the day, generally. Work near a window, take calls outside, walk at lunch. The mortality gradient in that study ran across the whole day, not just the morning.

Dim the evening, starting three hours before bed. Lower the overhead lights, use lamps, drop the screen brightness. You don't need to buy glasses, only fewer lumens hitting your eyes.

Make the bedroom dark. Under 1 lux means darker than most people's bedrooms. Cover the LEDs, and put up blackout curtains if streetlight comes in.

Keep your wake time fixed. It's the one sleep habit I'd defend against all comers (Chapter 15), because it's what anchors the clock.

Shift work, and why I'm mentioning it

The International Agency for Research on Cancer classifies night shift work as Group 2A, probably carcinogenic to humans, based on limited human evidence, sufficient animal evidence, and strong mechanistic evidence for circadian disruption.

Meta-analyses associate shift work with increased cardiovascular disease, metabolic syndrome, type 2 diabetes and probably breast cancer, with a dose-response by years of exposure.

The caveat is real: residual confounding by income, smoking, sleep and diet is hard to eliminate.

I'm raising it because a lot of people reading this spent twenty or thirty years on shifts, and nobody told them it counted as an exposure. If that's you, you're not doomed, but light and sleep deserve more attention from you than from somebody who's always worked days.

Meal timing, in its proper place

I covered fasting in Chapter 22, so here's only the version that fits a circadian chapter.

If you take insulin, a sulfonylurea such as glipizide, glyburide or glimepiride, or any other glucose-lowering drug, talk to your prescriber before you start a fasting protocol or a calorie deficit. Insulin and sulfonylureas are the big ones: fasting or eating less on those can cause hypoglycemia (low blood sugar) at doses that were safe the week before, and the dose may need to come down first.

TREAT (116 people, 12 weeks) found that time-restricted eating did not beat normal eating for weight loss, and the fasting group lost proportionally more lean mass.

A 2024 trial by Manoogian and colleagues in Annals of Internal Medicine is the better-designed one for this audience: 108 adults averaging about 59, with metabolic syndrome and prediabetes, who moved from roughly a 14-hour eating window down to 8 to 10 hours, plus nutrition counseling.

Results: a modest but statistically significant HbA1c improvement, and weight down 3 to 4%, primarily fat, not muscle. The authors called the results modest and said larger, longer trials are needed, which is fair.

That trial makes me want to soften what I said in Chapter 22, where I told you to keep the eating window at ten hours or more. Manoogian's group ran eight to ten and kept their muscle. But they came down from a fourteen-hour baseline, they had

nutrition counseling, and they had metabolic syndrome to begin with. If you're going to run eight hours, run it the way they did, deliberately and with the protein planned, not by skipping breakfast and hoping.

My synthesis: a moderate eating window (say, finishing dinner earlier rather than compressing everything into six hours), combined with adequate protein and resistance training, is defensible and fits your circadian biology. Aggressive fasting after fifty without resistance training risks the thing you can least afford to lose.

Eat earlier. Don't eat less often than you can hit your protein.

Why this chapter matters more than the supplement chapters

Everything here is free. You can't buy your way into a bright morning or a dark bedroom, which is probably why it gets a fraction of the attention a new peptide gets. I'd rather you fixed your light and your sleep before you spent a dollar on anything else in this book.

Chapter 49 — The Load You're Carrying

This is the part of the holistic argument that gets mocked the most, and some of the mockery is earned. So I'll sort it into what has hard human outcome data and what doesn't.

I'll be strict about one thing throughout: naming a chemical is not evidence of harm at the dose you're exposed to. The vague "toxin" language is where my side of the argument loses thoughtful people, and it isn't necessary, because the real evidence is better than the hand-waving.

The strongest evidence in this whole chapter: air

Di and colleagues, New England Journal of Medicine, 2017. This is one of the largest studies of anything, ever.

60,925,443 Medicare beneficiaries, 460 million person-years, 22.5 million deaths.

- Fine particulate pollution, per 10 $\mu g/m^3$: 7.3% higher mortality.
- Ozone, per 10 ppb: 1.1% higher.

The finding that matters most: when they restricted the analysis to exposures BELOW the national air quality standard, the association got steeper, to 13.6% higher mortality per 10 $\mu g/m^3$.

The dose-response is steeper at low concentrations, which implies there is no safe threshold, and that the regulatory limit is not a health-based line.

The effect estimate for Black participants was roughly three times that of the overall population. Low-income participants were also at substantially elevated risk.

There's intervention evidence too: a randomized crossover trial published in JACC in 2025 gave 154 adults living near highways either a real HEPA air purifier or an identical unit with the filter removed, one month each.

In participants whose baseline systolic blood pressure was above 120: −2.8 mm Hg with the real filter versus +0.2 with the sham. A net difference of 3 mm Hg. No effect in people with normal blood pressure.

That's a small effect from a cheap, safe intervention with a randomized design behind it, and I'll take it.

What I do, and what I'd suggest you do: run a HEPA filter in the bedroom, check the air quality index before an outdoor session and skip it on bad days (in Nevada in late summer that means checking for wildfire smoke, and some years that's most of August), and don't run or cycle along a busy road if you have an alternative, because you're breathing hardest exactly where the exposure is highest.

Lead — still, in 2026

Lanphear and colleagues, Lancet Public Health, 2018. 14,289 US adults followed a median of 19.3 years, 4,422 deaths.

Comparing a blood lead of 6.7 µg/dL to 1.0 µg/dL, both within what's considered "low level":

- All-cause mortality: 37% higher
- Cardiovascular mortality: 70% higher
- Ischemic heart disease mortality: 108% higher

The authors estimated population attributable fractions of 18% of all deaths in adults over 44, and 28.7% of cardiovascular deaths, roughly 256,000 a year in the US.

That's a very large claim from an observational study and it should be held with appropriate caution. But lead's toxicity is not in dispute, and this is a real cohort with a long follow-up.

Who this matters for: if you grew up before the phase-out of leaded gasoline and lead paint, which is everyone reading this book, you accumulated some. If you've worked in construction, renovation, shooting ranges, radiator repair, or with old

plumbing, you accumulated more. If you live in a house built before 1978 that's been renovated, likewise.

A blood lead level is a cheap, standard test. If any of that describes you, it's reasonable to ask for it once.

What I will not do is recommend chelation. Outside genuine acute poisoning, chelation therapy is dangerous and has killed people. If your lead is elevated, that's a conversation with an occupational medicine physician, not a protocol from a website.

Endocrine disruptors — real, and usually overstated

BPA and phthalates are biologically active and detectable in nearly everyone. There's real mechanistic work and real animal data, and there's regulatory movement on them for reasons.

What there isn't much of is human outcome data at typical exposure levels. Most of what you'll read is mechanistic, animal, or associational epidemiology at high exposure.

My position: the reasonable steps here cost nothing and I take them. Don't microwave food in plastic or leave water bottles in a hot car. Use glass or stainless where it's convenient. Skip the receipts if you're handed one you don't need.

On "detox"

A critical review in the Journal of Human Nutrition and Dietetics found essentially no rigorous clinical evidence that commercial detox diets eliminate toxins or produce sustained weight management. The few relevant studies were small and methodologically weak.

Your liver and kidneys perform biotransformation continuously. No commercial protocol has been shown to enhance the elimination of any specific named toxicant in a human being.

If you want to reduce your chemical load, the interventions with evidence are boring: filter your air, filter your water if your municipal report warrants it, eat less ultra-processed food, don't

smoke, drink less, and don't heat food in plastic. There's no juice for it.

Organic food — where I'll separate my preference from the evidence

I eat organic where I can, including grass-fed, grass-finished beef.

I don't have evidence that this improves my health outcomes. What I have is conflicting. The largest cohort, 623,000 UK women followed over nine years, found no reduction in overall cancer. A smaller French study found about 25% less. Both found a signal for one specific lymphoma, which is interesting and unreplicated.

What is measurable is the composition difference: a review of 343 studies found pesticide residues roughly four times more frequent in conventional produce, and about 48% less cadmium in organic. Whether that buys you anything in health outcomes is not established.

There are legitimate arguments for organic and pasture-raised food (environmental impact, soil, animal welfare, taste, supporting a food system I'd rather exist), and I hold them. The human health claim is a different claim, and the case for it hasn't been made.

I'm careful about it because whatever the residue difference is worth, the health benefit of eating produce at all is enormous and well established. If organic pricing means somebody buys fewer vegetables, that trade is bad. Eat the conventional broccoli. It's one of the best things you can do for yourself, and worrying about it is worse for you than the broccoli is.

The underrated one: what's in your supplements

I covered this in Chapter 29, but it belongs here too, because it's an environmental exposure and nobody frames it that way. Half the herbal products tested didn't contain what the label said, 88 percent of melatonin gummies were mislabeled, and plant-based protein powders consistently test higher for lead, cadmium and arsenic than whey, because plants take up what's in the soil.

If you're worried about your chemical exposure and you're taking eight uncertified supplements a day, you have your priorities inverted. The bottle is a more likely source than the produce aisle.

What I actually think about all this

The functional emphasis on environment is, on balance, more right than conventional practice, and the air pollution evidence is the proof. Almost no physician asks what your air is like, or about occupational exposure. The best data in this chapter is underused.

The defensible list is short and cheap: filter your air, know your water, get a lead level once if your history warrants it, don't heat plastic, buy certified supplements or none, and eat mostly food you'd recognize as food.

PART VII — PUTTING IT TOGETHER

Chapter 50 — The Blood Work I Run

People ask me what I test. Here it is, with the reasoning.

This is my panel, built around the fact that I'm actively experimenting on myself. Most people don't need monthly labs. Twice a year is plenty for most, more often if you're changing something significant.

But the list is worth having, because a standard annual panel misses several things that matter a lot after fifty.

The standard stuff, and what I actually watch

Comprehensive metabolic panel: glucose, electrolytes, kidney and liver markers.

The two I watch hardest:

- eGFR, creatinine and urine albumin (uACR), Chapter 19. Know these before you push protein.
- And tell them you take creatine, or your eGFR will read falsely low (Chapter 30).
- Sodium (Chapter 28). There's an association between consistently high-normal serum sodium and worse aging outcomes. It's not proven causal, but it's free information on a panel you're already running.

Complete blood count: hemoglobin, hematocrit, white cells.

Hematocrit is the one to watch if you're on testosterone, because testosterone can push it up.

Lipid panel: total, LDL, HDL, triglycerides.

Ask for ApoB if you can get it. It counts the number of atherogenic particles rather than the cholesterol they carry, and it's a better risk marker than LDL alone. Most standard panels don't include it.

HbA1c and fasting insulin. HbA1c gives you a three-month glucose average. Fasting insulin catches insulin resistance years before glucose starts drifting, and it's routinely left off, so ask for it.

Thyroid: TSH, free T4, and free T3 if you can. Thyroid problems are common after fifty, they're often missed, and they present as the symptoms people blame on aging: fatigue, weight change, cold intolerance, low mood.

Vitamin D (25-OH), Chapter 31. Test before you supplement, because the trials say supplementing when you're already sufficient does nothing.

Vitamin B12, and methylmalonic acid if you're on metformin or a PPI (Chapter 33). This is one of the highest-yield items on the list for a lot of people.

Ferritin and iron panel. Iron problems go both directions after fifty and both matter.

Testosterone (total and free) plus SHBG, if you're a man with symptoms. Get two morning draws, not one, because it swings. Symptoms come first, because a number without symptoms is not a diagnosis.

hs-CRP, a general inflammation marker that's useful as a trend line.

PSA for men, on whatever schedule you and your doctor decide. That's a nuanced screening conversation, and it doesn't belong in a fitness book.

The stuff that isn't blood work

Blood pressure at home. A cuff is fifty dollars and I think it's the best-value health purchase most people over fifty can make. One reading in a doctor's office once a year tells you almost nothing, but a pattern over weeks tells you a lot.

I check mine multiple times a day, which is more than anyone needs. A few times a week at the same time of day will give you something real.

Body composition, monthly (Chapter 6).

Grip strength, five-times sit-to-stand and gait speed, every six months (Chapter 7). These cost nothing and they're the functional markers that predict outcomes.

Your working weights on your main lifts, written down every session. This is your fastest feedback loop and most people don't keep it.

How to actually use the numbers

Trends beat single readings. Every marker on that list moves around. One small change on its own usually needs context or a repeat. But a markedly abnormal result, or one that comes with symptoms, needs your doctor now. Don't wait for a trend. Three draws trending the same direction means something.

Change one thing. Same rule as Chapter 1. If you started three supplements and changed your diet and your ApoB moved, you've learned nothing.

Write down what you changed and when. It's the habit that turns a pile of lab results into information.

Take the results to your doctor. Don't interpret a full panel yourself off the internet. I don't, and I've been doing this a long time.

Chapter 51 — Normal Isn't Optimal (And Optimal Isn't Always Known)

"Everything came back normal."

If you're over fifty, you've probably heard that while feeling terrible. It's one of the most common complaints people bring to functional practitioners, and it's why a lot of people go looking outside conventional care.

The argument for narrower ranges

A conventional reference range is usually the middle 95% of a "reference population." For a marker with a normal bell-curve spread, that's about two standard deviations either side of the mean.

Four criticisms of that, and they're all legitimate:

One: the reference population is supposed to be healthy, but screening is imperfect and methods vary from lab to lab, so it can include people with undiagnosed disease. If enough of the population has a subclinical problem, the "normal range" absorbs it.

Two: statistically normal is not physiologically optimal. Being inside a lab's reference range tells you that you look like its reference population. It doesn't, by itself, tell you what level is best for you.

Three: risk is usually continuous, and a cutoff throws information away. There's no biological switch at 5.7% HbA1c. The risk curve is smooth, and drawing a line converts useful gradient information into a yes/no.

Four: your own variation is much narrower than the population's. A result can be well inside the population range and represent a large change for you. If your ferritin has always run 90 and it's now 35, "normal" is the wrong word for what just happened.

That conceptual critique is sound, and it's partly shared by mainstream laboratory medicine. Where it goes wrong is the leap from "population reference intervals are imperfect" to "therefore this specific narrower number is the right target and you should treat toward it." That leap requires outcome evidence, and for most markers it doesn't exist.

Where the functional position is winning

Ferritin. This is the clearest case.

The conventional lower limit for iron deficiency has often been 15 ng/mL, a threshold derived from old bone marrow studies in populations that included a lot of already-iron-deficient women.

A Swiss cohort of 255,351 primary care patients showed how much the cutoff matters. Iron deficiency incidence per 1,000 patient-years: 10.9 at a 15 ng/mL cutoff, 29.9 at 30, and 48.3 at 45. The cutoff you pick more than quadruples the diagnosis rate.

The American Society of Hematology has been moving. Their draft recommendations raise the general adult threshold to 30 ng/mL and explicitly recommend against the old 15 for menstruating people. So the functional complaint that 15 is too low is correct, and mainstream hematology is coming around to it.

But the higher functional targets (50, 70, 100) are not supported by outcome evidence. There are signals that repletion helps fatigue in non-anemic women with ferritin below 50, and that's worth knowing. There's nothing supporting 70 to 100 as a goal.

And pushing ferritin up is not benign after fifty. The main hemochromatosis variant, C282Y in the HFE gene, is common, people with two copies of the C282Y variant can overload on iron, and in older men and postmenopausal women a rising ferritin can be a sign of inflammation or iron overload rather than something to celebrate. A low or falling ferritin points the other way: it can be the first sign of blood loss, including from the gut. Either way, that's your doctor's call. Iron is one place where more is not better.

Fasting insulin and HOMA-IR. Of everything in this chapter, this has the strongest case and the lowest downside. The functional position is that fasting insulin moves years before glucose does, and that's correct.

The Whitehall II study followed people with repeated measurements and caught 505 incident cases of diabetes. Insulin sensitivity declined and fasting glucose rose in an accelerating pattern beginning roughly three to six years before diagnosis, with the pancreas compensating by pumping out more insulin for three to four years and then failing. By the time your glucose is abnormal, the process has been running for years, and that isn't controversial.

A meta-analysis of 7 prospective studies in 26,976 non-diabetic adults found HOMA-IR associated with 34% higher all-cause mortality. Fasting insulin alone was borderline (13%, p = .058).

The boundary: no trial has randomized anyone to insulin-guided versus glucose-guided management, so "measure it and treat toward a number" is untested. And fasting insulin assays are not standardized between labs, so absolute cutoffs travel poorly. Compare yourself to yourself, at the same lab.

That's why fasting insulin is on my panel in Chapter 50: it's cheap, it catches a real process years early, and what it prompts is a lifestyle change rather than a drug.

hs-CRP. Ridker and colleagues, Lancet, 2023, pooled 31,245 statin-treated patients from three trials. Comparing highest to lowest quartile:

Marker	Cardiovascular death	All-cause death
hs-CRP	HR 2.68	HR 2.42
LDL-C	HR 1.27	HR 1.16

In statin-treated patients, residual inflammation predicted death better than residual cholesterol did.

The boundary: no trial has shown that targeting hs-CRP with diet or supplements reduces events. The only anti-inflammatory interventions with hard outcome benefit are drugs, canakinumab and colchicine. And hs-CRP is nonspecific: it rises with any infection, injury, obesity, or a hard workout two days ago. A single reading tells you very little, so trend it.

Where the functional position is losing

Vitamin D. I covered this in detail in Chapter 31, so briefly: the functional target of 50 to 80 ng/mL is not supported. VITAL (25,871 people) was null for cancer, cardiovascular events and fractures, with no significant benefit by starting level, though it wasn't built to test treating real deficiency.

And in 2024 the Endocrine Society reversed its own 2011 guidance. It now suggests against vitamin D beyond the RDA in healthy adults under 75. It does allow that adults over 75 may benefit, on a mortality signal, which matters for some of you. And it recommends against routine 25(OH)D testing in any population studied, because outcome-specific benefits based on those levels have not been identified. They couldn't establish a target blood level at all, because the evidence was insufficient.

That puts me in tension with what I told you in Chapter 31, so I'll resolve it. What the Society is recommending against is population screening, meaning testing everybody, routinely, forever. I still think a one-off level is worth having if you're in one of the risk groups I listed in Chapter 31, or if you're about to start supplementing and you'd like to know whether you're buying a benefit or buying insurance. What I'd no longer do is retest it every year in a healthy person whose first result was fine.

The one positive finding worth knowing: in VITAL, vitamin D reduced incident autoimmune disease, 123 versus 155 cases, and a 39% reduction when the first two years were excluded. That's one trial with borderline significance, and it needs replication. It's the strongest remaining case and I'd present it as exactly that.

Reverse T3. I'm naming this one because if I only include one "we got this wrong," it should be this.

A practice-variation analysis in Thyroid looked at 91,767 reverse T3 orders. One hundred providers, 0.1% of orderers, accounted for 29.5% of all orders. Of the 60 highest-volume orderers, all 60 were functional medicine practitioners. A systematic review found little evidence supporting those volumes.

Physiologically, reverse T3 rises in non-thyroidal illness, fasting, starvation, critical illness, trauma, and with several common drugs. The mainstream reading is that it's a conserved adaptive response, your body deliberately down-regulating metabolic demand, and treating it with T3 hasn't been shown to help.

It has no established outpatient clinical utility, and its use is concentrated in a tiny number of practitioners in my own camp. That's not a good look and I'd rather say so.

MTHFR genotyping. The American College of Medical Genetics practice guideline is direct: MTHFR polymorphism testing has minimal clinical utility and should not be part of routine evaluation.

The Cleveland Clinic's own genomics department, at the same institution that hosts the Center for Functional Medicine, publicly recommends against it. Their position is to measure homocysteine instead. It's cheaper and more accurate, and the homocysteine level determines what you do, not the genotype.

The one narrow true claim: C677T homozygosity plus low folate does elevate homocysteine. That's real, but it's largely neutralized by folic acid fortification, which the US and Canada have had since 1998.

And there's a specific harm for this book's readers. High-dose folate can mask B12 deficiency. B12 deficiency from atrophic gastritis, metformin and PPIs is common after fifty, and the neurological damage it causes can become irreversible. Enthusiastic methylfolate supplementation in an older adult with undiagnosed low B12 is not a neutral act.

TSH. The functional "optimal" range is usually 0.5 to 2.0. The conventional range runs to about 4.5.

There's a real basis for the argument: in the NHANES reference population of 13,344 people without known thyroid disease or antibodies, 85% had a TSH below 2.5. So the upper part of the conventional range is populated by relatively few healthy people.

But the leap to treating a TSH of 3.2 in somebody without symptoms or antibodies is not supported, and treating mildly high TSH has been directly tested, which is more than most of the markers in this chapter can say. TRUST randomized 737 older adults, average age 74, with a TSH between 4.6 and 20, to levothyroxine or placebo for a year: no difference in symptoms or tiredness. A 2018 JAMA meta-analysis of 21 trials and 2,192 adults found nothing on quality of life, symptoms, mood, blood pressure, BMI or cognition.

That isn't an absence of evidence. That's evidence of absence, and it's the clearest case in this chapter of a functional lab range that got tested and failed. Meanwhile thyroid hormone is not a benign drug in an older adult. Over-replacement carries atrial fibrillation and bone density risk.

My read: a TSH of 3.5 with symptoms and positive antibodies is worth a conversation with an endocrinologist. A TSH of 3.5 with no symptoms is worth watching, not treating.

The tests I'd tell you to skip

Covered elsewhere, collected here in one place:

- IgG food sensitivity panels: opposed unanimously by every major allergy society
- Commercial four-point salivary cortisol / "adrenal stress panels": the measurement fails without verified timing
- Serum zonulin: the commercial assay doesn't detect zonulin
- Hair mineral analysis: one hair sample split between six labs produced results differing by an order of magnitude or more for over ten elements, and no two labs flagged the same element as elevated

- Direct-to-consumer microbiome kits: identical samples came back classified as both “healthy” and “unhealthy”
- Routine MTHFR genotyping: measure homocysteine instead
- Reverse T3: no established outpatient utility
- Whole-body MRI screening in healthy people: no outcome data, and a high false-positive burden that leads to biopsies of things that were never going to hurt you

The rule I’d apply to any test

Before you pay for it, ask three questions:

One: would the result change what I do? If the answer is “I’d take a supplement I was going to take anyway,” don’t buy the test.

Two: has anyone shown that acting on this result improves anything? For most functional panels the answer is no, and the seller should tell you that.

Three: does the person selling the test also sell the treatment? The international microbiome consensus made this an explicit recommendation and I’d generalize it to everything. The lab that sells you the test should not also sell you the protocol. That’s not a moral judgment. It’s what happens to interpretation when there’s a product on the other end.

Where I land

The functional instinct here is right: reference ranges are population statistics, not health targets. The failure is believing we know the optimal number when usually we don’t.

So measure more than your doctor probably orders, compare yourself to yourself over time, and be humble about what the numbers mean. Trend beats threshold, and your own baseline beats a population range. Any specific “optimal” figure you’ve been given, including the ones I’ve quoted approvingly in this chapter, should be held loosely until somebody randomizes people to it and counts what happens.

Chapter 52 — A Week of Training

I'll give you three versions: what I do, what I'd give a beginner, and what I'd give someone in the middle. Take whichever fits.

What I actually do

Five days a week, about ninety minutes, on a body-part split with high volume and fifty years of accumulated tolerance behind it.

I'm putting this first so I can tell you not to copy it. If you've been out of the gym for a decade, this program will hurt you inside a month. That tolerance isn't transferable.

The beginner week — two days

Before you start: if you have known cardiovascular disease, uncontrolled hypertension, a recent surgery or joint replacement, osteoporosis, or you have been sedentary for more than a year, get cleared by your physician first. This is not a formality.

This is the floor and it's a good floor. Everything in Chapter 8 says two full-body sessions a week works.

Day A

- Leg press or machine squat: 3 × 8–12
- Chest press machine: 3 × 8–12
- Seated row: 3 × 8–12
- Leg curl: 2 × 10–12
- Farmer's carry: 3 × 30 seconds
- Balance work: 10 minutes (Chapter 13)

Day B

- Machine or trap-bar deadlift: 3 × 6–10
- Lat pulldown: 3 × 8–12
- Overhead press machine: 3 × 8–12
- Leg extension: 2 × 10–12
- Suitcase carry: 3 × 30 seconds

- Balance work: 10 minutes

Rest 90 seconds to 2 minutes. Leave 2–3 reps in the tank. Start on machines, which the NSCA recommends for beginners, not because they're better but because the failure mode is safer and the learning curve is shorter.

Add weight when you hit the top of the rep range on every set with clean form, and not before.

Do this for twelve weeks before you change anything.

The intermediate week — three or four days

Once you've got a base, this is where most people over fifty should live.

Space them out: Monday, Wednesday, Friday, with Saturday for Day 4 if you do it. If you only do three days, upper body gets one session a week, which is below the twice-a-week target. Fix that by adding a press and a row to Day 3, or by rotating which half gets the extra day each week.

Day 1: Lower

- Squat pattern (goblet, hack, or barbell): 3 × 6–10
- Romanian deadlift or hip thrust: 3 × 8–10
- Leg press: 2 × 10–12
- Calf work: 3 × 12–15
- Power set: 3 × 5 explosive at 40–60% (leg press or box step-up)

Day 2: Upper

- Bench or chest press: 3 × 6–10
- Row: 3 × 8–10
- Overhead press: 3 × 8–10
- Pulldown: 2 × 10–12
- Arms: 2–3 sets each

Day 3: Lower + conditioning

- Deadlift variation: 3 × 5–8
- Split squat or lunge: 3 × 8 each leg
- Leg curl: 3 × 10–12
- Intervals: 6–8 × 1 minute hard, 2 minutes easy
- Balance work: 10 minutes

Day 4 (optional): Upper + carries

- Incline press: 3 × 8–10
- Chest-supported row: 3 × 8–10
- Lateral raise: 3 × 12–15
- Face pull: 3 × 15
- Loaded carries: 4 × 40 m

Plus, across the week:

- Easy aerobic work on non-lifting days. Walk, bike, whatever you'll do. Volume matters (Chapter 11).
- Balance work at least 3 times a week, ten minutes each. Proactive and reactive, not standing on one leg.
- Heavy isometrics for a tendon that needs strengthening, but have a physical therapist or other qualified professional set the loading for you. The direct evidence is in healthy older Achilles tendons (Chapter 14). Painful tendon? Get it assessed first.

The rules that matter more than the template

Twelve weeks minimum before you judge anything. Neural adaptations come fast, and tissue adaptations don't.

Progress the load, not the workout. Most people over fifty who plateau do it because they keep changing exercises instead of adding weight to the ones they have.

Never train through sharp pain. Achy is normal. Pain that's sharp, localized and worse the next day is not.

Take an easy week every 8 to 10 weeks. Same movements, lighter loads, no attempt to progress. I have no trial for this, only fifty years of noticing that skipping it costs me eventually.

Two lower-body sessions, never on consecutive days. Give the same muscles a day or two between hard sessions, and let your performance and soreness tell you if you need more (Chapter 15).

If you miss three months, you did not lose everything. Small detraining studies didn't find a significant loss at 12–24 weeks. Come back.

Chapter 53 — A Day of Eating

Same structure: what I do, then what I'd suggest.

What I eat

- About 2,200 calories on a typical day. (On retatrutide it ran closer to 2,700; see Chapter 40.)
- At least 175 grams of protein (at least 1 gram per pound of desired body weight) and usually about 200. (Kidney disease, or a different number from your doctor? Use your doctor's.)
- Around 200 grams of carbohydrate, and the rest from fat, roughly a third of my calories from each. These numbers aren't the same every day. I was a 50-gram keto guy for years. My body changed.
- Everything logged, every gram.
- Organic where I can, including grass-fed, grass-finished beef. Homemade burgers on a good bun, maybe once a week.
- I can eat some pizza. I don't eat it every day and I don't need it once a week. But I can, because I've built a body that handles it.

The reason I can eat bread without a problem is that my body isn't wading through everything else. For some people, eating bread is closer to eating spoonfuls of sugar, because of what else is going on in their metabolism, their gut, their thyroid. That's a physiological difference, not a moral one, and it's why I won't tell you bread is fine.

Pre-workout: about 75 grams of protein plus carbs, in the late morning before I train. That's one of my three or four feedings, not an addition to them. On retatrutide that meal needed 120 to 150 grams of carbs, or I hit a wall twenty minutes in (Chapter 40).

A template you could actually use

For a 175-pound person, or a heavier person who wants to weigh 175. The rule says at least 175 grams, and the template below adds

up to about 175. (Kidney disease, or a different number from your doctor? Use your doctor's.) If your goal weight is 200, scale every line up by about fifteen percent. Meat weights are cooked. Protein counts are typical USDA values. Scoops and jerky vary a lot, so check your labels.

Breakfast: ~45 g protein

- 4 large eggs (about 25 g) plus a 7-oz tub of plain nonfat Greek yogurt (about 20 g), or
- 1.5 scoops whey (about 35 g) in a cup of oats, measured dry before cooking (about 10 g), with berries

Lunch: ~50 g protein

- 6 oz chicken breast (about 50 g) with rice and a big salad, or
- 8 oz salmon (about 50 g) with potatoes and vegetables

Dinner: ~50 g protein

- 7 oz lean beef (about 50 g) or 8 oz cod (about 50 g), with vegetables and a starch
- Add beans or lentils for fiber (a few extra grams of protein on top)

Anywhere it fits: ~30 g protein

- A scoop of whey (about 25 g) and a string cheese (about 6 g), or 1¼ cups of cottage cheese (about 30 g), or 3 oz of jerky (about 28 g)

Every day, alongside that:

- 25–30+ grams of fiber from whole plant foods (Chapter 23)
- Water regularly through the day. Don't wait for thirst, and don't force liters (Chapter 28). If you have heart failure or kidney disease, or you've been told to limit fluids, follow your doctor's number
- Potassium-based salt substitute if your kidneys are fine and your blood pressure isn't (Chapter 28). Ask your

doctor first if you're on an ACE inhibitor, ARB, or potassium-sparing diuretic.

The rules that survive whatever diet you pick

Hit the protein number: at least 1 gram per pound of desired body weight. This is the one thing that's diet-agnostic, whether you eat keto, Mediterranean, plant-based or anything else. (Kidney disease, or a different number from your doctor? Use your doctor's.)

At least one meal with 0.4 g/kg of protein. That's about 32 grams for an 80 kg person. The distribution research says total matters more than the split, but at least one meal should clear the threshold that maximally triggers synthesis (Chapter 17).

Don't count collagen. It scores zero on the protein-quality scale (DIAAS), so it does nothing for your target (Chapter 18).

Most of it should be food you'd recognize as food (Chapter 25).

Run the diet properly or don't run it. Dirty keto isn't keto, and junk-food vegan isn't a plant-based diet. If you're going to test something, test it.

On tracking

I log everything and I like it. That's a personality trait, not a prescription.

If detailed tracking makes you miserable or weird about food, that's a real cost and you should count it. Alternatives that work:

- Track protein only. It's the number that matters most and it's the easiest to count.
- Two-week audits, twice a year. Log everything for two weeks, learn what your habits are, then stop.
- Fixed meals. Build 4–5 meals you know the numbers for and rotate them.

The goal is information, not control. If it stops giving you information and starts giving you anxiety, change the method.

Chapter 54 — The First 90 Days

If you're starting from nothing, here's the order I'd do it in. The sequencing matters, since most people fail because they change eight things at once, feel overwhelmed, and quit by week five.

Days 1–14: Measure and start lifting

Before you start: if you have known cardiovascular disease, uncontrolled hypertension, a recent surgery or joint replacement, osteoporosis, or you have been sedentary for more than a year, get cleared by your physician first. This is not a formality.

Get baseline data.

- Blood work (Chapter 50). Get it before you change anything.
- Blood pressure, a few readings across a week.
- Body composition, however you can access it.
- Grip strength, five-times sit-to-stand, gait speed.
- Bodyweight, same time of day.

Start the two-day beginner program. Don't add anything else yet. Just show up twice a week.

Change nothing about your diet. You're establishing a baseline, and you have plenty to think about.

Days 15–45: Add protein

Now add the protein target: at least 1 gram of protein per pound of your desired body weight. (Kidney disease, or a different number from your doctor? Use your doctor's.) For most people that means adding 60 to 100 grams a day, which is real work and deserves its own phase. Do it in two steps if you need to: 1.2 grams per kilogram in the first two weeks of this phase, then the full rule by day 45.

Easiest ways to add it: a protein shake, Greek yogurt, cottage cheese, eggs, or making the portion of meat at dinner bigger.

Keep lifting twice a week, and keep logging your weights.

Add creatine. 5 grams a day, monohydrate, no loading needed. This is the one supplement with the evidence to justify starting early (Chapter 30). Yes, that's two changes in one phase. This plan is built for results, not for proving which change did what. If you want to know, start creatine two weeks later.

Still don't change anything else about your diet. Add protein, and don't subtract anything yet.

Days 46–75: Add movement and more balance

Add easy aerobic work on non-lifting days, twenty to forty minutes. Walking counts. Volume is what you're building.

You've been doing 10 minutes of balance at the end of each lifting session since day one. Now add one more short session, so it's three times a week. Proactive and reactive (Chapter 13).

Consider a third lifting day if the first two feel manageable.

Now, if fat loss is a goal, start a modest deficit of 300 to 500 calories, and not before now. You want the training and protein established first, because those are what protect your lean mass while you're in a deficit (Chapter 27).

Days 76–90: Assess

Retest your strength, function, body composition and blood pressure from days 1–14. For blood work, ask your doctor which markers are worth repeating. Not everything needs a redo at 90 days.

Then ask the questions:

- Are my working weights up? If yes, this is working, and that's the primary signal.
- Did body composition move in the right direction? Remember it's slow, and remember lighter isn't automatically better.
- What did blood work do? Take it to your doctor.

- Am I actually doing this, or did I do it for three weeks and drift?
- Adherence is the variable that determines everything else.

Then decide on one thing to change.

What I'd tell you to expect

Weeks 1–4: You'll be sore. Your weights will go up fast, and that's neural, not muscle (Chapter 5). Don't get excited and add volume. You'll feel like you can do more than you should.

Weeks 4–8: Progress slows. This is where most people quit or start program-hopping. Don't, and keep adding weight to the same movements.

Weeks 8–12: Things start feeling different: stairs, groceries, getting off the floor. This is when it becomes real, and it's usually function before appearance.

Body composition changes show up around 8–12 weeks and they're slower than you want. Especially size, especially after fifty (Chapter 9). Strength is the number that will keep you motivated, so watch that one.

The single most important thing in this chapter

Do not start with the supplements or the drugs.

I've watched this a thousand times over thirty years. Somebody wants to change their body, and the first thing they do is buy something, which is the easiest thing to do and the least effective.

The order is train, then eat, then sleep, then supplements, and the last item is last for a reason.

If you do the first three and nothing else, you'll get 90% of what's available to you. If you do the fourth and skip the first three, you'll get nothing and you'll have spent more money.

Chapter 55 — What I Got Wrong

Here's what I believed, said publicly, or implied, and what the evidence says.

I said resistance training prevents falls. The Cochrane review of 108 trials found resistance training alone had a rate ratio of 1.14, which is no clear benefit, from very low-certainty evidence. Balance and functional training is what works, with high-certainty evidence. Strength training is necessary but not sufficient (Chapter 13).

I believed older adults need more recovery time. In four of five studies, older men showed smaller damage responses than younger men. The signal for slower recovery exists only in older women, from a small literature. The researchers explicitly declined to make recommendations (Chapter 15).

I repeated "you lose 3–8% of muscle per decade after 30." I can't find a primary source for that figure and neither can the researchers who went looking. The longitudinal data says about 1% of leg lean mass per year in adults over 70, with the onset contested (Chapter 4).

I promoted Zone 2 as uniquely valuable. A 2025 review found Zone 2 doesn't raise AMPK in trained men, produces no acute PGC-1α increase, and failed to increase mitochondrial markers after four weeks or five months. Their central point was that almost no study has tested Zone 2 as such, so the whole popular case is inference (Chapter 11).

I've made videos about NAD+ precursors. Every human trial is a small, short, surrogate-endpoint pilot. NAD+ goes up and intermediate markers sometimes move a little, but nothing durable has been shown. The most important negative trial (40 men, 12 weeks, NR at 2 g/day) found no effect on insulin sensitivity, mitochondrial function, liver fat or body composition (Chapter 35).

I made two videos about niacin. Two mega-trials failed, and HPS2-THRIVE showed net harm, roughly one extra serious adverse event per 27 people treated. Niacin was removed from lipid guidelines, and "no-flush" niacin is pharmacologically inert (Chapter 35).

I covered DMSO twice. No approved oral or topical use, industrial-grade purity problems, and it carries whatever else is on your skin into your bloodstream. Of everything on my channel, that's the one I'd most want back (Chapter 35).

I made a video about C15:0. The human data is dominated by the patent holders who sell the product, the "essential fatty acid" claim isn't accepted by any nutrition authority, and the epidemiology is confounded by dairy intake (Chapter 35).

I titled a video "SLU-PP-332 Peptide." It's a synthetic small molecule, not a peptide, and it's mouse-only with no human safety data at all (Chapter 43).

I've implied that when you stop a GLP-1 you regain fat but not muscle. The STEP 1 extension collected no body composition data, so that claim has no evidence behind it in either direction (Chapter 42).

And now the harder list — what my own side gets wrong

It would be cowardly to list only the places where conventional advice fails. Here's where my own camp fails, and I've believed or repeated some of these too.

"Adrenal fatigue." A systematic review screened 3,470 articles, found 58 usable studies, and concluded there is no substantiation that it's an actual medical condition. The gold-standard test for the HPA axis was never performed in a single one of those studies. The symptoms are real, but the diagnosis and the four-point saliva panel are not, and the label can delay finding a treatable cause (Chapter 47).

IgG food sensitivity panels: every major allergy society on three continents opposes them. IgG to a food is a marker that you eat

that food, and it's the same antibody that shows up when allergy treatment succeeds. There's a real danger too: someone with a genuine IgE allergy can have low IgG and be told to reintroduce something that could kill them (Chapter 24).

Serum zonulin as a leaky-gut test. The commercial assay was analyzed properly in 2018 and it doesn't detect zonulin. It captures complement proteins instead. When researchers spiked known amounts of actual zonulin into the test, the kit didn't see it (Chapter 24).

Reverse T3: of 91,767 orders analyzed, 0.1% of providers accounted for nearly 30% of them, and of the sixty highest-volume orderers, all sixty were functional medicine practitioners. It has no established outpatient utility. If I only conceded one thing in this book, it'd be this one (Chapter 51).

MTHFR genotyping: the American College of Medical Genetics says it has minimal clinical utility. The Cleveland Clinic's own genomics department (the same institution that hosts its functional medicine center) says measure homocysteine instead. And high-dose folate can mask a B12 deficiency, which is common after fifty and can cause irreversible nerve damage (Chapter 51).

Hair mineral analysis: one hair sample split between six commercial labs produced results differing by an order of magnitude or more for over ten elements, and no two labs flagged the same element as high. The labs gave different supplement recommendations for the same hair (Chapter 51).

Direct-to-consumer microbiome kits: identical samples sent in triplicate to seven services came back classified as both "healthy" and "unhealthy," with different recommendations. For 17 of 18 common bacterial genera, the noise from the method matched or exceeded the actual biological signal (Chapter 24).

"Detox" protocols: a critical review found essentially no rigorous evidence that commercial detox diets eliminate toxins or produce lasting weight management. Your liver and kidneys do this continuously and no protocol has been shown to help them (Chapter 49).

I buy organic and grass-fed. I don't have evidence that it improves my health outcomes, and independent review says it isn't expected to. I have environmental and taste reasons and I'll defend those, but I won't defend the health claim (Chapter 49).

Almost every item in that list is a test, something with a price tag, sold by someone who also sells the thing you're supposed to do about the result. That's the failure mode on my side of the fence, the same way over-reliance on a fifteen-minute visit and a prescription pad is the failure mode on the other side.

If the mechanism is interesting but nobody has measured whether acting on it helps, say so out loud. I've tried to hold to that in this book and I've probably failed somewhere.

And the biggest one

I gave people advice through the lens of my own body. Early in my training career I told people not to eat avocados, told people to avoid fats, handed out protocols that worked for a twenty-something to people forty years older. I was confident and I was wrong, and some of those people probably still remember what I told them.

Why I'm putting this in the book

There are two reasons. The first is that it's the most useful chapter for you. If you take nothing else from this book, take the habit of asking "how would I know if I was wrong about this?" Everybody in this field, including me and the people with more credentials than me, is working from incomplete evidence, mechanisms that sound better than they are, and personal experience that doesn't generalize.

The second is that a book that never corrects anything is just a longer version of the problem. I did the research for this book to find out what held up, and if everything I'd said had held up, I'd have been suspicious of the research, not proud of myself.

I'll be wrong about things in this book too. Some of the studies I've cited will fail to replicate, and some of the confident negatives will

turn out to have been underpowered. The retatrutide chapter will look dated within two years, probably by the time you read it. That isn't a defect. It's what a live field looks like.

What I'd ask is that you hold what I've told you the same way I try to hold it: firmly enough to act on, loosely enough to drop.

Chapter 56 — The Whole Book in Two Pages

If you skip everything else, read this.

The tier-one facts

- Strength declines 2–5× faster than muscle size. The longitudinal data is mostly in adults over 70, so don't over-extend the age range.
- In the big cohorts, strength predicts mortality and size doesn't.
- Resistance training works at every age tested, including 87-year-old nursing home residents who more than doubled their strength in ten weeks.
- You can still get strong, but you won't get as big. Relative strength gains are equal across age groups, while hypertrophy is strongly age-dependent and the decline starts in your forties.
- Cardiorespiratory fitness is one of the strongest mortality predictors in large cohorts. In one of the biggest, low fitness carried a bigger adjusted hazard within the same statistical model than smoking, diabetes or coronary disease. That's not the same as saying unfitness causes more death than smoking, but it's still remarkable. And no ceiling was observed.
- Protein: at least 1 gram of protein per pound of desired body weight, with resistance training. The research floor is 1.2 to 1.6 grams per kilogram; the rule sits at the top of the range the biggest analysis called prudent. Protein without training hasn't been shown to do much. (Kidney disease, or a different number from your doctor? Use your doctor's.)
- Balance training prevents falls. Strength training alone hasn't been shown to.
- Creatine is the supplement with the strongest evidence in this population: about 1.2 kg extra lean mass on top of training, for around fifteen dollars a month at the time of

writing. B12 if you're on metformin or a PPI runs a close second and matters more for the people it applies to.

The things almost everyone gets wrong

- In the Health ABC cohort, muscle mass didn't predict how long people lived, but muscle strength did.
- The trials probably didn't include you. Median exclusion rate across 305 trials: 77% of real-world patients. In a separate review, 72% of trials excluded on age. Comorbidity excludes you from 68%.
- Genetics explains under 10% of how you respond to a meal. Diet gene-tests failed their best test.
- "Adrenal fatigue" isn't a condition, and the saliva panel can't measure what it claims to.
- IgG food sensitivity testing, serum zonulin, hair mineral analysis, MTHFR genotyping and consumer microbiome kits all fail on the evidence, and several of them fail as measurements.
- Collagen scores zero on protein quality (DIAAS). Never count it toward your target.
- Protein doesn't damage healthy kidneys. Know your eGFR and urine albumin, and have your doctor read them. (Kidney disease, or a different number from your doctor? Use your doctor's.)
- Zone 2 has no demonstrated unique properties, and volume matters.
- Intensity is more time-efficient. The mechanism story was never tested.
- You can absorb more than 30 grams of protein at a time. What plateaus is a specific synthesis measurement, not absorption.
- Fasting has no magic beyond making you eat less, and after fifty it fights against your protein needs.
- Moderate drinking doesn't protect your heart. That was confounding, and genetic studies show harm at every level tested.

- Vitamin D supplementation does nothing for fractures in people who aren't deficient, and bolus megadoses cause more falls and fractures.
- Most of the peptide category has no human efficacy data at all.

The order of operations

1. Lift, twice a week minimum. Everything else is downstream of this.
2. Eat at least 1 gram of protein per pound of desired body weight, tracked, every day. (Kidney disease, or a different number from your doctor? Use your doctor's.)
3. Move a lot, and go hard sometimes.
4. Train balance for ten minutes, three times a week.
5. Sleep seven to eight hours on a fixed wake time, and get outside in the first hour you're awake. Bright days, dark nights. It's free and the mortality data behind it is better than most supplements.
6. Then, and only then, consider supplements: creatine, vitamin D if you're deficient, and B12 if you're on metformin or a PPI. That's most of the useful list.

And underneath all of it

You are not the average of a trial you'd have been excluded from. Start where the evidence points, measure what happens in you, and when the two disagree, trust the body you're standing in, as long as you're actually measuring it. That last clause is what separates this from an excuse. This goes for everyday habits. It's never a reason to override your doctor on a medical contraindication.

The two rules for everything else

Everyone is different, so test it on yourself, one change at a time, long enough to matter, with something measured.

Lift weights and eat protein. Those two you don't get to personalize. The exceptions are kidney disease, or another

medical reason your doctor has for a different target: then your doctor sets the protein number.

And the last thing

I'm sixty-four. I weigh about 175 pounds, I've been lifting since I was twelve, I run between 12 and 14% body fat, and I get my blood work done every month because I'm still curious about what happens if I change something.

None of that is because I found a secret. There isn't one. There's a very short list of things that work, a very long list of things that don't, and about fifty years of showing up. The showing up is the part nobody can sell you, and it's the part that does it.

Go lift something heavy.

Appendix A — Quick Reference

Protein targets

Situation	Target
Minimum (RDA — probably too low)	0.8 g/kg
PROT-AGE, healthy older adults	1.0–1.2 g/kg
Research floor, training for muscle	1.2–1.6 g/kg
The rule in this book	At least 1 g of protein per lb of desired body weight (≈2.2 g/kg), unless kidney disease or your doctor sets a different target
Per meal, to trigger synthesis	~0.4 g/kg (≈32 g at 80 kg)
Kidney disease (as diagnosed by your doctor)	Set with your doctor (KDIGO: ~0.8 g/kg; avoid >1.3 g/kg if at risk of progression)
On dialysis	1.2–1.5 g/kg

Training minimums

Variable	Target
Frequency	2–3×/week per muscle group
Intensity	70–85% 1RM (roughly 6–12 reps)
Sets	2–3 per exercise
Proximity to failure	Leave 2–3 reps in reserve
Rest	1.5–3 minutes on heavy work
Balance training	3×/week, 10+ min, proactive and reactive
Aerobic	150 min/week, plus 1–2 harder sessions

Functional test thresholds

Test	Concern threshold
Grip strength	Men <27 kg, women <16 kg
Five-times sit-to-stand	>15 seconds
Gait speed	<0.8 m/s
Timed Up and Go	>20 seconds

Supplements, sorted honestly

WORKS	MIGHT WORK	HYPE
Creatine monohydrate (muscle/strength)	Omega-3 for muscle (for high triglycerides it works: Ch. 32)	NMN / NR
Protein powder (as a vehicle to hit your number)	Magnesium (BP, migraine)	Niacin for heart or longevity
Vitamin D if deficient	Zinc (cold duration)	Collagen for muscle
B12 if on metformin/PPI/atrophic gastritis	Probiotics (strain-specific)	Taurine, resveratrol, spermidine
Psyllium (LDL, constipation)	Urolithin A	TUDCA, C15:0, DMSO
Testosterone if truly hypogonadal	Berberine (glucose — check interactions)	DHEA, creatine for bone/cognition >60

Peptides, graded

Compound	Grade	Approved?
Semaglutide	PHASE 3 HUMAN	Yes
Tirzepatide	PHASE 3 HUMAN	Yes
Tesamorelin	PHASE 3 HUMAN	Yes — HIV lipodystrophy only
Retatrutide	PHASE 3 HUMAN	No — submission

Compound	Grade	Approved?
		planned Q1 2027
Bimagrumab, myostatin drugs	EARLY HUMAN (phase 2 for obesity)	Not for obesity or muscle (garetosmab: FOP; apitegromab: SMA, 2026)
Ipamorelin, CJC-1295, sermorelin	EARLY HUMAN pharmacology	No
LL-37	EARLY HUMAN (topical wounds only)	No
BPC-157	ANIMAL ONLY	No
TB-500	ANIMAL ONLY	No
MOTS-c	ANIMAL ONLY	No
SLU-PP-332 (not a peptide)	ANIMAL ONLY	No
GHK-Cu injectable, KPV	ANIMAL / topical only	No
GLOW / KLOW stacks	NO DATA	No

Appendix B — A Note on the Sources

Everything in this book is built on published research. I've named the lead author, the journal and the year in the text so you can go find it yourself, which I'd encourage — particularly for anything you plan to act on.

A few notes on how I've handled the evidence:

I've given you sample sizes. A finding from 25,871 people and a finding from 8 people are not the same kind of thing, and you can't tell them apart unless somebody tells you the number. So I've told you the number, every time it mattered.

I've flagged when evidence is weak, mixed, or extrapolated. There's a lot of that. In several places the answer was "nobody has tested this in people over fifty," and I've said so rather than borrowing a result from young men and hoping you wouldn't notice.

I've included the studies that disagree with me. The volume controversy in Chapter 8, the REDUCE-IT versus STRENGTH argument in Chapter 32, the fasting evidence in both directions in Chapter 22. Where a field is unsettled, I've shown you the disagreement instead of picking the side I liked.

Where a claim is my opinion or my personal experience, I've labeled it. Sometimes repeatedly, because those are the parts most likely to get quoted out of context.

Some of this will age badly. The retatrutide and peptide regulation chapters describe a situation moving month to month. Check the current status before acting on any of it.

If you find an error in here, I'd genuinely like to know. That's how the next version gets better.

Appendix C — Plain-English Glossary

Shorthand you'll run into in this book, in plain English.

1RM: the most weight you can lift once with good form.

CI (confidence interval): the range of results the data fit reasonably well. Technically, if the study were repeated many times, 95% of ranges built this way would contain the true value. A wide range means a shaky answer.

DIAAS: a protein-quality score: how well a protein covers your essential amino acids. Around 1.0 or above is excellent. Collagen scores zero.

DXA: a low-dose X-ray scan that measures bone density, fat and lean mass.

eGFR: estimated glomerular filtration rate, a blood-test estimate of how well your kidneys filter. Under 60 for three months or more means chronic kidney disease.

uACR: urine albumin-to-creatinine ratio, a urine test for protein leaking through the kidneys. It can flag kidney disease even when eGFR looks normal.

HOMA-IR: an insulin-resistance estimate calculated from fasting glucose and fasting insulin. Higher means more resistant.

HR (hazard ratio): how fast something is happening in one group compared with another during follow-up. Above 1 means faster, below 1 slower. 1.5 means about 50% faster, which is not the same as a 50% higher chance over the whole study.

RR (risk ratio or rate ratio): a risk ratio compares the chance of something happening over a stated period in two groups. A rate ratio compares events per unit of person-time, such as per 1,000 person-years. Both are related to a hazard ratio, but the three aren't interchangeable.

MACE: major adverse cardiovascular events: heart attack, stroke and cardiovascular death, counted together.

Melanopic EDI: a measure of how strongly light acts on your body clock, rather than how bright it looks.

Mendelian randomization: a method that uses the genes people are born with as a natural experiment to estimate cause and effect.

Meta-analysis: a study that pools the results of many studies.

Non-inferiority trial: a trial designed to show a treatment is not meaningfully worse than the comparison.

Observational study: researchers watch what people do and what happens to them. It can show links, not proof of cause.

p-value: the probability of getting a result at least this extreme if there were really no effect. It is not the chance that the finding is true. Under 0.05 is the usual bar for "statistically significant." It's a convention, not a cliff.

Randomized controlled trial (RCT): people are assigned to a treatment or a comparison by chance. It's the best way to show cause and effect.

SMD (standardized mean difference): an effect size that lets studies using different measurements be pooled. Roughly 0.2 is small, 0.5 moderate, 0.8 large.

Surrogate endpoint: a lab or scan number, like bone density, used as a stand-in for an outcome that matters, like fractures.

VO2max: the most oxygen your body can use during all-out exercise. It's the standard measure of cardiorespiratory fitness.

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