

WRITTEN BY THE AUTHOR OF THE LONGEVITY CODE

HOW TO

LIVE
LONGER

TIPS AND INSIGHTS INTO THE ART AND
SCIENCE OF LIVING HEALTHIER FOR LONGER

Dr. Kris Verburgh, MD

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Foreword

Dear Reader,

NOVOS did not come about suddenly. It has been a long road, one that took nearly a quarter of a century.

When I was 16, I was diagnosed with a brain tumor. This was a big shock to me, given that from the age of 12 I started to pay a lot of attention to my health, including working out and eating a – what I believed at the time to be healthy – high protein, low fat diet.

I was eventually cured of my brain tumor. Nonetheless, this period left a big mark on me. I began asking myself existential questions about life and mortality, and became curious about the genetic and lifestyle factors that may have contributed to my disease. This planted a critical seed in my unconscious, which has matured into my passion for longevity medicine.

I met the author of this book, Dr. Kris Verburgh, at a longevity science conference in Berlin in early 2019. We talked about how despite the promising developments being made in longevity biotech, there was still a lack of science-based interventions that people could safely use here and now.

Our conversations continued in Brussels, Belgium, then again in a serendipitous run-in in Lisbon, Portugal. By the time I returned home to New York, the decision was obvious: I had found my cofounder.

At the root of it, Kris and I decided to join forces because of a common concern and vision.

The concern wasn't simply that people are becoming increasingly sick, unhealthy and suffering from diseases of aging earlier in life. That's obviously a major motivator, but it was even more than that.

It was that a lot of health advice and products – even with the best of intentions – weren't good for long-term health span and lifespan. Antioxidants, high protein diets, high fat diets, certain herbs, etc., might be good for short-term goals (weight loss, muscle gain, energy, etc.), but aren't ideal for long-term, disease-free living.

Our common vision was to think about health from an entirely new vantage point: the common denominators of what causes us to age, get sick and not feel our best. That is, from the perspective of longevity science.

Over the past decade, we've learned more about aging than we learned in hundreds of years combined. A lot of that work has been categorized and is known in the field as the 9 mechanisms of aging.

When looked at through the lens of these mechanisms, or causes of aging, we can filter out the noise (the advice that's not good for you in the long-term), and instead focus on the signal (what is good for you both today and in the long-term).

Dr. Verburgh, is on the tip of the spear when it comes to extending lifespan and health span. He is an investor on behalf of a \$100 million biotech fund that focuses on extending lifespan. He is an advisor to the X Prize on the topic of longevity. He has sold nearly 500,000 copies of his books, including the Longevity Code, which received acclaim from scientists like Harvard University Professor David Ludwig. And he is my cofounder and Chief Scientific Officer at NOVOS, where we promise to bring you the latest formulations, tests and knowledge in longevity health, in a safe and accountable manner.

We provide this book, [knowledge](#) and age [tests](#) for free as part of NOVOS' commitment as a Public Benefit Corporation; our passion in reducing the suffering, frailty and loss incurred from aging and the diseases that develop as a result; and our desire to enable more joyful experiences derived from a long and healthy life.

Read it in good health!

Yours truly,



CHRIS MIRABILE
Founder & CEO, NOVOS

Introduction



Dear Reader,

This book will provide you with the information you need to live a long, healthy life.

Health is a complex matter. Lots of information circulates about the best ways to live longer.

A problem is that a lot of this information is contradictory, oversimplified, outdated, or simply not true. Do antioxidants slow down aging? Is a high-protein diet the best to live longer? Or is a keto diet? Do I need to take supplements if I eat healthy?

For a long time, it has been difficult to answer these questions. It was not easy to see the forest from the trees regarding health advice that is oftentimes confusing or conflicting.

However, if we approach nutrition, supplements and health from the viewpoint of aging (implementing knowledge about why and how we age), we can do a much better job at assessing the long-term impact of diets, foods and other interventions on our health and aging process.

The more we approach these complex subjects from the viewpoint of aging, the easier it is to see that most antioxidants don't extend lifespan, and that most diets, while having health benefits in the short term, are unhealthy in the long term. Further, many official government or institutional guidelines are outdated or can be much improved.

This book intends to give you a quick overview about what we can do to live a longer, healthier life, based on the best science and approaches. We will explore these topics from different angles, not just from nutrition science, but also from biogerontology (the science of aging), medicine, evolution, and biology in general, without compromise.

Enjoy!

DR. KRIS VERBURGH, MD

Longevity Researcher, Author of "The Longevity Code"

Why Do We Age?

Why are we mortal? What is it about the process of aging that prevents any single body from being able to last forever? And what causes aging in the first place?

In the last 20 years we have learned more about aging than the previous 2,000 years combined, and we're now finally making progress with products and therapies that will slow down our aging process, enabling us to live longer, healthier lives.

It was long believed that we mainly age because of DNA damage. That would make sense, because DNA contains all the instructions to build up our cells and our bodies.

There are also diseases in which DNA repair is impaired, making patients look as if they were aging at an accelerating pace. Examples of such "accelerated aging diseases" are progeria (Huntington-Gilford disease), Werner syndrome, trichothiodystrophy, Rothmund-Thompson syndrome and Cockayne syndrome.

However, these diseases do not mimic the aging process completely. For example, people with progeria do not have many of the very common diseases and symptoms of aging, like Alzheimer's, cataracts, decline in vision and deafness.

Also, animals with high DNA mutation rates do not age faster, nor do they have reduced lifespans.^[1] Interestingly, mice with defects in DNA repair do seem to age faster, but this didn't depend on the rate of DNA mutations.^[2]

But perhaps the most powerful argument against the role of DNA damage in aging

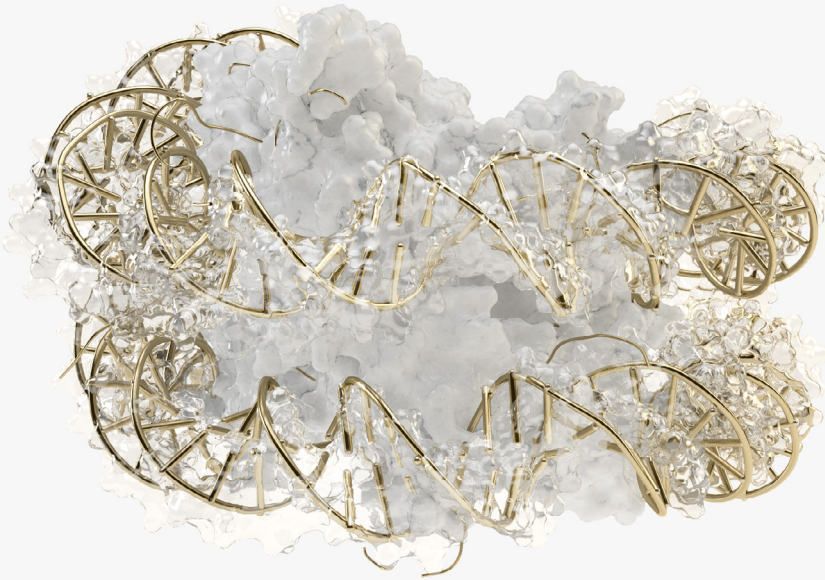


is that it's possible to clone healthy, young animals from the old cells of old animals. That seems to suggest that the cloning process can reverse damaged, aged DNA.

During cloning, the DNA-containing nucleus is extracted from an aged cell (derived from an aged animal), and put into an egg cell (of which the nucleus has been removed). From that egg cell a new, young animal is born, with in many cases a normal lifespan. So during cloning, the DNA damage that the old animal has accumulated during its lifespan and from which the nucleus is extracted to be put into an egg cell, seems to be suddenly repaired when the animal (and its successors) is born.

This does not mean that DNA damage plays no role in aging. It just means that DNA is just one part of why we age, and very likely not even the most important reason. Aging is caused by many other processes. So what are some of these other reasons why we age (and eventually die)?

Epigenetic Dysregulation



Epigenetic dysregulation could be one of the most important reasons why we age.

The epigenome determines which genes are active and which ones are not. You can look at the epigenome as an on-off switch for our genes. When we get older, the epigenome becomes dysregulated: genes that should be switched off are switched on (like cancer-promoting genes), and genes that should be turned

on are turned off (like genes that protect and repair our cells). Also, the hugely complex machinery that winds up our DNA becomes less organised, so that the DNA and eventually the entire cell becomes unstable.

Some scientists believe that we mainly age because of epigenetic dysregulation, and not because of DNA damage.

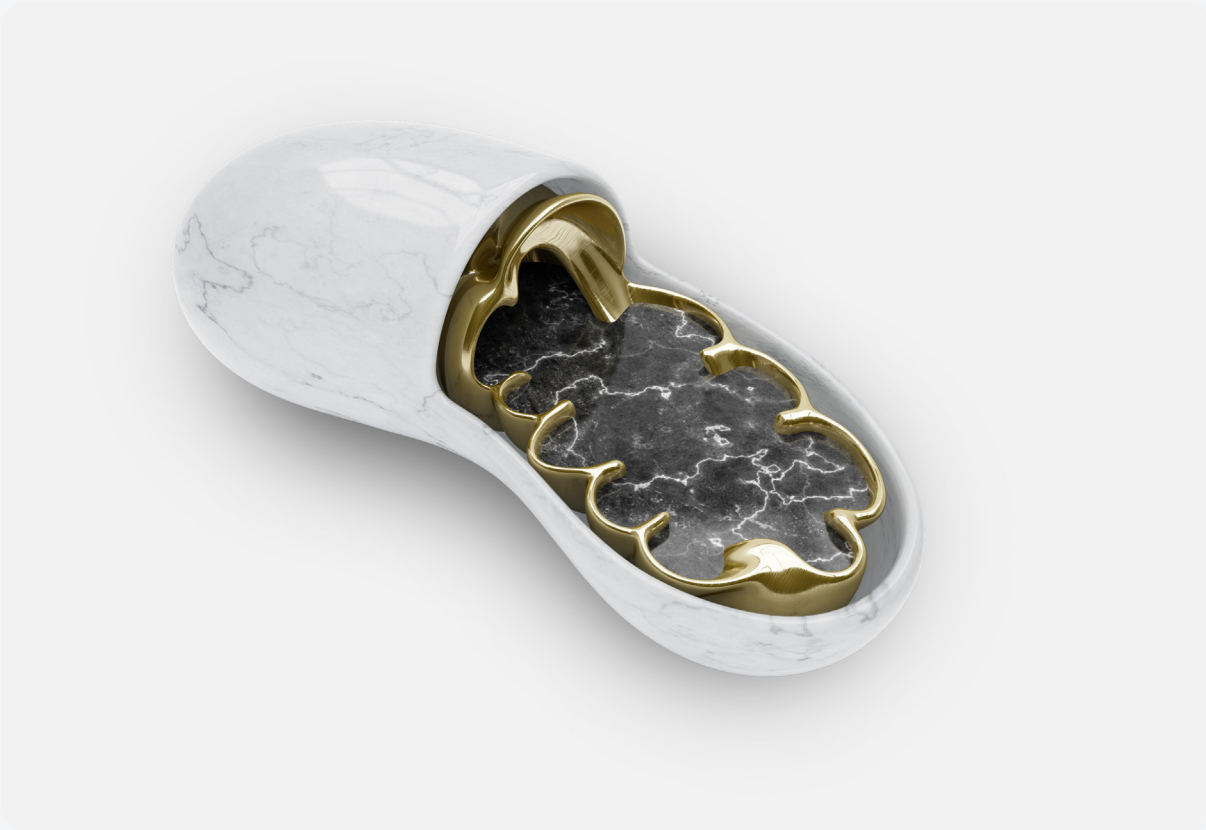
Protein Accumulation



Proteins are the building blocks and workhorses of our cells. A cell contains millions of proteins. These proteins are continuously built up and broken down in a complex and intricate recycling process. However, this process is not perfect. Here and there proteins are not broken down

and start to linger in and around the cells. They also start to clump together. These protein clumps hamper the functioning of the cells. This “protein toxicity” caused by what is also known as a “Loss of Proteostasis” (protein homeostasis), is one of the reasons why we age.

Mitochondrial Dysfunction



The mitochondria are the powerhouses of our cell. Each cell can contain hundreds to thousands of mitochondria. Mitochondria produce the energy that we need to live. In fact, the oxygen you breathe and the food you eat are transformed by the mitochondria into the energy you use to move, think and survive.

The older we get, the more the mitochondria become damaged. Without sufficiently functioning power plants, the cells decline, leading to symptoms of aging.

Telomere Shortening & Damage



The telomeres are the outer ends of our DNA strand. Telomeres are composed of repetitive DNA and protect the ends of our DNA, just like the plastic caps at the ends of our shoelaces that protect them from unraveling.

With each cell division, the telomeres become shorter, until they are so short they cannot protect the DNA well enough. In non-dividing cells (in which the telomeres do not become shorter) this is not an issue. Still, these cells can

become damaged because the dividing surrounding cells that nourish and protect these cells become damaged because of telomere shortening (e.g. telomeres in dividing glial cells become shorter, impairing the ability of glial cells to support non-dividing neurons in the brain).

Also, during aging, the telomeres become damaged, not just shortened, which further stresses our cells.

Advanced Glycation Crosslinks (& Other Crosslinks)



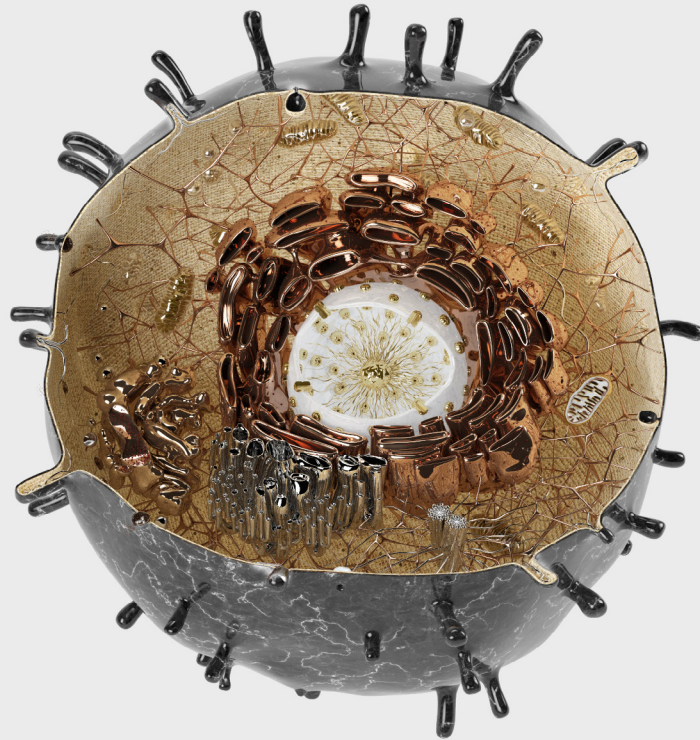
During aging, crosslinks form between the proteins that make up our tissues. These crosslinks glue proteins together, making our tissues more stiff.

Crosslinked and glued-together collagen and elastin in the skin and blood vessels contribute to stiffer blood

vessels (and thus hypertension) and wrinkles, for example.

Examples of crosslinks in our body are glucosepane and pentosidine crosslinks.

Senescent Cells

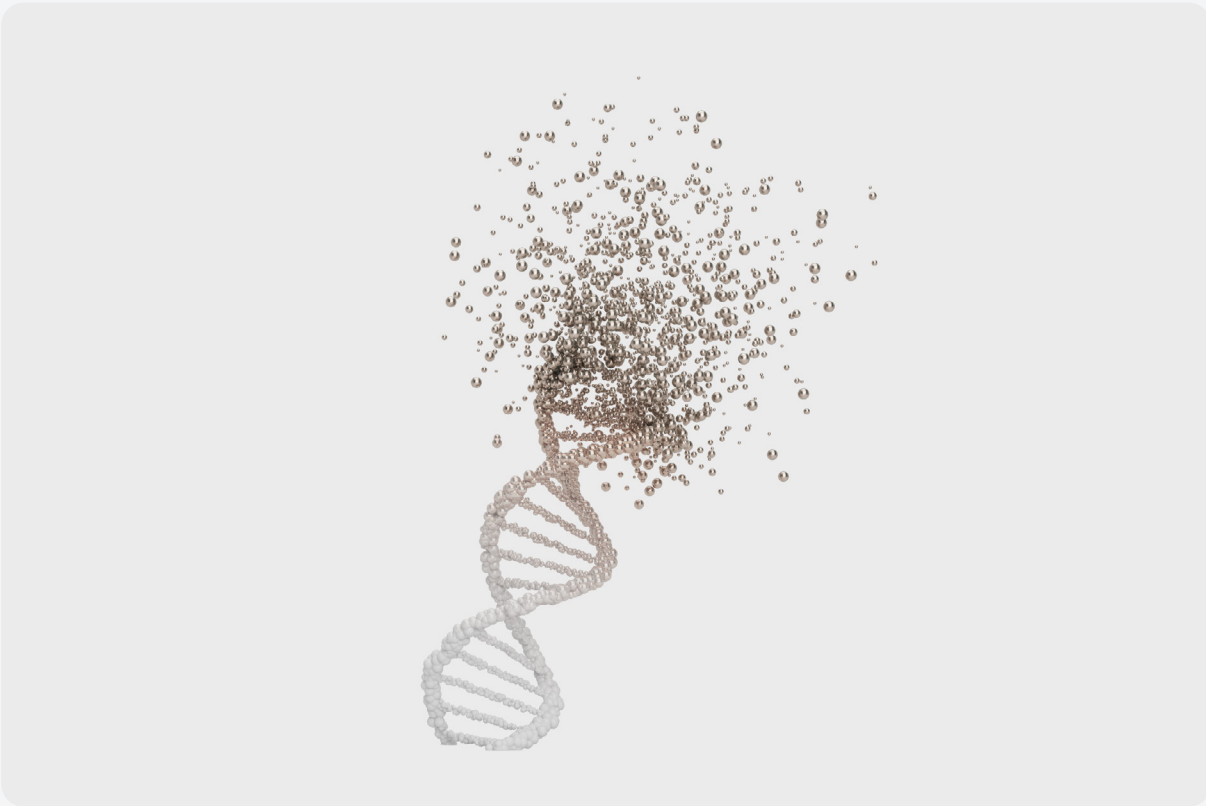


When we get older, more and more senescent cells start to appear everywhere in our tissues. Senescent cells are called “zombie cells”: these cells should normally have died but they keep sticking around. Senescent cells are previously healthy cells that have accumulated a lot of damage. Normally, they should kill themselves because of this damage, but they don’t. They keep lingering around,

secreting substances that damage the healthy surrounding cells.

Accumulation of senescent cells in the skin contributes to wrinkles, for example. Senescent cells in the blood vessels make the blood vessels more stiff and prone to atherosclerosis. Senescent cells in the brain contribute to brain inflammation and aging.

Genomic (DNA) Instability



In the beginning of this chapter we discussed that DNA damage is probably not the major driver of aging. This doesn't mean that DNA damage is not important. For example, double strand DNA breaks do seem to play a role in aging. Other forms of DNA damage can also contribute to the aging process.

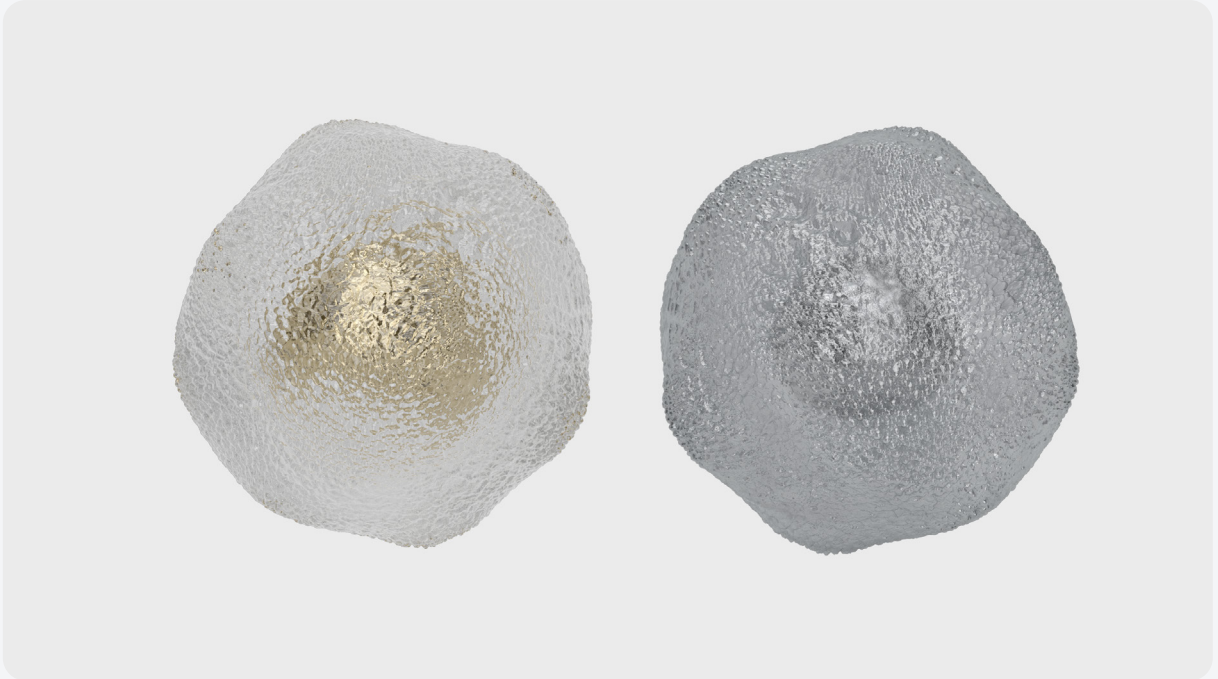
However, some scientists speculate that DNA damage can accelerate aging indirectly. To repair a DNA break, specific repair enzymes are lured away from their usual spot, where they normally help to stabilize the epigenome. When a lot of DNA breaks happen, the enzymes cannot maintain the epigenome properly because they have to repair the DNA breaks, which

could result in a dysregulated epigenome, an important driver of aging.

Also, our telomeres (the ends of DNA) become shorter in fast-dividing tissues and stem cells, a process that contributes to aging. This telomere shortening and attrition can also be considered as DNA instability or damage.

Additionally, during aging, specific rogue parts of our DNA start to jump around and insert themselves haphazardly into other DNA regions. These roaming pieces of DNA are called retrotransposons, and they also contribute to genomic instability.

A Decline In Stem Cells



Stem cells grow new cells that replenish our tissues. For example, mesenchymal stem cells generate bone, cartilage and fat cells. Neuronal stem cells create neurons. Hematopoietic stem cells produce red and white blood cells.

During aging, the amount of stem cells in our body declines. Additionally, the remaining stem cells function less properly. This leads to our tissues being less maintained, repaired and replenished, contributing to aging.

But why do stem cells decline? They do this because of the aforementioned aging mechanisms, such as epigenetic dysregulation, mitochondrial dysfunction, protein accumulation, and crosslinking, which also happen in stem cells. Furthermore, senescent cells popping up everywhere in the body secrete substances that impair the function of stem cells.

Altered Intercellular Communication & Deregulated Nutrient Sensing



When we get older, communication between cells goes awry. For example, cells, especially senescent cells, secrete substances that damage other healthy cells. These senescent cells also secrete proinflammatory substances that travel throughout the body and cause damage everywhere.

During aging, cells also become more numb to specific triggers, like insulin or other nutrients, leading to insulin resistance, a precursor of diabetes, or resulting in aging-switches (like mTOR) that are switched on for too long.

Other Reasons Why We Age

Scientists will undoubtedly discover more reasons why we age. For example, dysregulation of the transcriptome is also being found to be a contributor to aging. The transcriptome is a bit like the epigenome: it finely regulates how active genes are.

What Can We Do About Aging?

Currently, scientists all over the world are creating powerful new biotechnologies to impact each of these aging mechanisms.

They try, for example, to epigenetically rejuvenate the cells, or revive the mitochondria, or mitigate protein accumulation and DNA damage. In the coming decades we will see fascinating technologies coming about that will impact aging itself.

Why is impacting aging so important? Because one addresses the root cause of all-aging related diseases, like heart disease, Alzheimer's disease or osteoarthritis.

Slowing down and partially reversing aging will drastically improve the treatments of aging-related diseases, given these aging treatments would treat the underlying cause of these diseases: aging itself.

This is all very fascinating. But the best technology we currently have to slow down aging is... our lifestyle! The longevity biotechnologies we mentioned will take decades to be developed. In the meantime, nutrition, specific supplements, exercise, sleep, and stress reduction are the best methods we have to live longer.

References

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- 2 DOLLÉ, M. et al. *Increased genomic instability is not a prerequisite for shortened lifespan in DNA repair deficient mice. Mutation research* vol. 596,1-2 (2006). <https://pubmed.ncbi.nlm.nih.gov/16472827/>

How To Slow Down Aging

It is possible to slow down aging.

Even better, in the future aging may even be reversed. That would mean it would be possible to make old people younger again. But for that, we will need cutting-edge biotechnology.

To address aging, there are two approaches: the low-tech approach and the high-tech approach.

The low-tech approach mainly involves lifestyle. These are things like healthy nutrition, exercise, sleep, stress reduction, happiness, and supplements.

The high-tech approach involves new kinds of biotechnologies that are currently being developed. These biotechnologies, for example, aim to rejuvenate aged mitochondria, clear up protein accumulation in our cells, or epigenetically rejuvenate cells.

Currently, the best approach to live longer is our lifestyle. New biotechnologies to tackle aging will come into being in the next decades.

Let's first dive deeper into the low-tech approach. What are the best things we can do now to live longer?

The Low-Tech Approach To Living Longer

01. Follow a longevity diet



What, when, and how much we eat impacts the rate of aging. Nutrition is the most powerful lifestyle intervention to live longer. Yes, it's even more important than exercise. Some general tips:

- **Shy away from sugary foods**, like soda drinks, sweets, candy, cake, pastries, doughnuts, cookies, candy bars, and chocolates. Be also wary of seemingly healthy products which contain lots of sugar, like low-fat yogurt, vitamin waters, sport drinks, health drinks (e.g. flavored green tea), granola and health bars, ketchup, fruit juices, breakfast cereals, salad dressings, and vegetable milks (choose the low-sugar varieties).
- **Reduce your intake of starchy, empty-calorie foods** like bread, pasta, rice, and potatoes. These foods cause high and protracted glucose peaks in the blood, leading to cross-linking and the (over)stimulation of aging mechanisms (e.g. insulin and IGF receptors). This also includes whole-grain products.
- **Don't consume too much animal protein** (especially red processed meat). Too much animal protein accelerates aging. If you do eat animal protein, eat white meat (poultry) and fish. Some scientists even advise to only eat fish and vegetable protein (e.g. nuts and legumes). If you consume fish, opt for species that have low mercury content and don't eat too much high-mercury fish like tuna, swordfish, mackerel and halibut.

- **Avoid unhealthy fats such as trans fats and omega 6 fats.** In general, try to avoid fried foods, fast-food, and bakery products. More specifically, reduce your intake of crackers, cookies, cakes, and other baked foods, refrigerated dough products (e.g. cinnamon rolls, biscuits, ...), snack foods (e.g. microwave popcorn), fast-food (e.g. frozen pizza), ready-to-eat meals, various vegetable shortenings (made from partially hydrogenated vegetable oil), french fries, and omega-6 rich oils and fats, like sunflower oil, corn oil, safflower oil, margarine, sesame oil, mayonnaise and many salad dressings.
- **Don't drink milk** (milk accelerates aging in many ways, as we will explain in future blog posts).
- **Consume lots of vegetables, legumes, mushrooms,** fruits, nuts, seeds, white meat, and fatty fish.
- **Consume foods that have been processed as little as possible,** e.g. foods your great grandmother would recognize.
- **Eat specific foods that improve longevity,** like blueberries, pomegranate, broccoli, kale, salmon, chia seeds, dark chocolate, and many others.
- **Don't drink too much alcohol:** that means maximum one glass per day, ideally with alcohol-free days.
- **Drink lots of water.** Drink green tea or coffee (yes, coffee can reduce the risk of various aging-related diseases).
- **Eat less.** Try to eat two meals a day, with breakfast being the most important meal of the day. Eat within a 12-hour period, so your body can fast for

12 hours. Fast for ideally 3 days a few times per year, like at the start of every new season. If you are up to it, practice caloric restriction. We will discuss fasting and various longevity diets in upcoming blog posts.

So in a nutshell, consume lots of vegetables, legumes and mushrooms - instead of bread, pasta and potatoes. Eat little animal-based food, and if you do, try to eat white meat (poultry) and fatty fish instead of red meat. Consume healthy fats from olives, olive oil, walnuts, flaxseeds, or avocados. Don't drink soda and animal milk. Be mindful of drinking too much alcohol.

Specific longevity foods are green leafy vegetables (kale, broccoli, spinach, Brussels sprouts), fatty fish, mushrooms, dark chocolate, blueberries, pomegranate, green tea, strawberries and walnuts.

02. Take supplements

Even if you eat very healthily, it is not easy to take in adequate amounts of nutrients.

Also, the official recommended daily intakes of many nutrients are too low: they are based on the minimum amount you need to take in order to not die or become seriously ill in the short term (e.g., months). But they are therefore not always the ideal amount for optimal longevity and health.

In short, despite following a healthy, balanced diet most people don't get ideal amounts of magnesium, vitamin D or iodine (which are also higher than what most governments recommend).

Some important supplements for optimal health are vitamin D3, vitamin K2, iodine,

selenium, magnesium malate, B vitamins, and minimally-oxidized (low TOTOX) omega-3 fatty acids.

Many people are deficient in these, or do not take in sufficient amounts for optimal health. However, many of these supplements do not really seem to extend maximum lifespan. But they can be very useful to improve health span, and to solve deficiencies which can accelerate aging.

Nonetheless, there are also supplements that can extend lifespan and slow down aging in various animal models. These are supplements like fisetin, alpha-ketogluta-

rate, lithium, glycine, nicotinamide mononucleotide (NMN), and glucosamine.

Unfortunately, many supplements claim to be “anti-aging” but contain substances that have shown not to extend lifespan in animals. An example are antioxidant supplements. Most antioxidants do not extend lifespan according to well-conducted scientific studies, and some may even shorten lifespan! We will dig into specific anti-aging and longevity supplements -- those that work and those that don't, further on in this book.

03. Exercise



Engage in both anaerobic exercise (like weightlifting) and aerobic exercise (like running or swimming). High-intensity in-

terval training (HIIT) is especially good to improve metabolism, leading to increased mitochondrial biosynthesis (Mitochondri-

al Health is one of the 9 mechanisms of aging), among other things.

Even a 20-minute walk on a daily basis can reduce your risk of heart disease, Alzheimer's, and many other aging-related diseases.

04. Take care of your sleep

Sleep is very important for your health. During sleep, the body repairs itself. Sleep deficiency leads to accelerated aging, and a higher risk of aging-related diseases, like diabetes and Alzheimer's.

Get sufficient sleep (on average 8 hours per day), and make it high-quality.

Besides the amount and quality of sleep, regularity is also important. Try to get to bed always at the same time.

We will give many tips to improve your sleep in this ebook.

05. Cultivate a positive mindset

Happiness, stress reduction, and having purpose and goals in life (feeling useful) all contribute to longer lifespans. Studies show that people who are happy, meditate or have goals (even as simple as taking care of a pet) live longer.

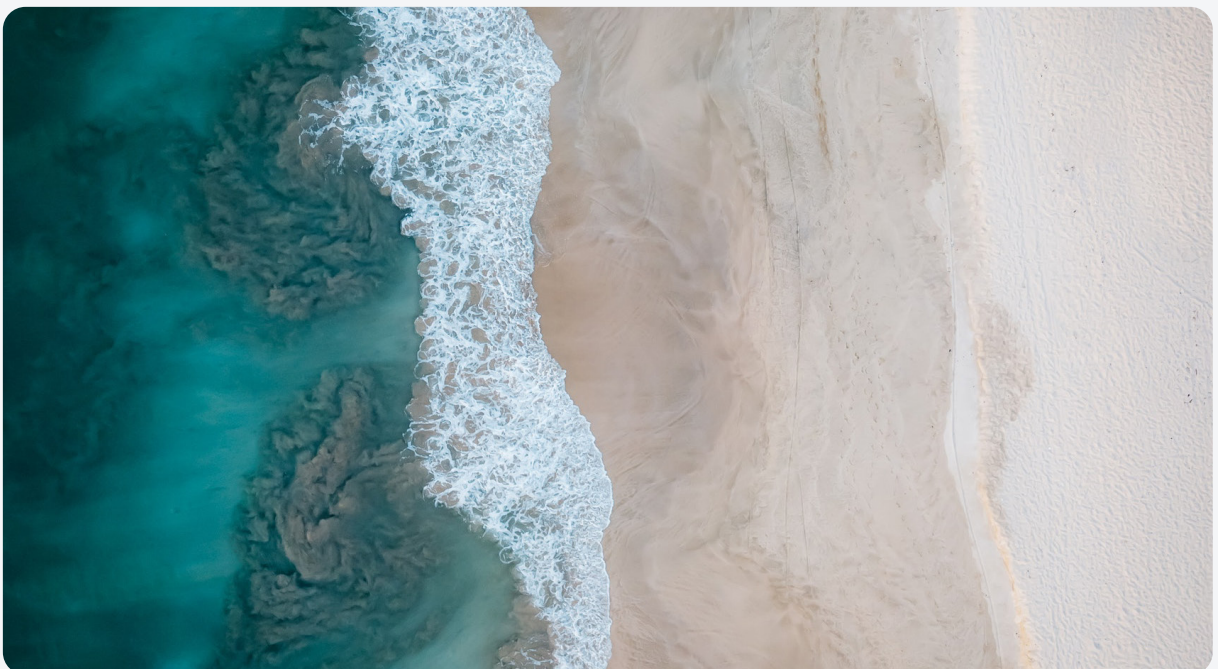
06. Be social

Humans are social animals. We need each other. When we are among friends and family, we feel good because the body produces all kinds of substances that have beneficial effects, such as endorphins and serotonin.

Loneliness induces inflammation and activates stress hormones like cortisol that damage the body.^[1] Studies show that people who are social live longer, healthier lives.

07. Don't smoke

Duh.





08. Challenge your mind every day

Your brain is like a muscle, the less you use it, the more it languishes. Train your brain daily to keep it healthy.

Explore new neighborhoods, museums, cities, or countries. Learn a new language, or follow a cooking, programming, or gardening course. Play chess, bridge, mastermind, or any other game that requires some brainpower.

Download brain training apps on your smartphone. Be open to new experiences and challenges. Take on challenging tasks, they are great learning experiences and train your brain.

09. Participate in preventive medicine

It's so much better to prevent than to cure when it's too late. Get regular health checkups so problems can be detected early, like high blood pressure, pre-diabetes, or nutrient deficiencies (however, don't over-rely on your blood check-ups: many vitamins and mineral deficiencies can appear normal in a blood work test).

Find an MD experienced in preventive medicine and lifestyle. Participate in programs screening for colon cancer, prostate cancer, or HPV-induced cancers.

10. Brush and floss your teeth

People with healthy teeth live longer.

If you do not take good care of your teeth, bacteria in your mouth and the substances they secrete get into the bloodstream and cause inflammation and other damage everywhere in the body, which increases the risk of a heart attack, dementia or type 2 diabetes.

Brush your teeth at least twice a day, and floss every day. Regarding mouthwash, opinions are divided. Mouthwash can kill off the resident bacteria in your mouth, which is also not a good thing.^[2]

11. Use medication sparingly

Many people greatly underestimate the side effects of medication.

Even medication known for its low side effect profile can be unhealthy, especially in the long term.

Gastric acid inhibitors (proton pump inhibitors/PPIs) hinder the uptake of important minerals like iron, calcium and magnesium, and disturb the gut microbiome. Painkillers such as ibuprofen and diclofenac are highly stressful for the kidneys and other organs, and even the mild painkiller acetaminophen (Tylenol) can be very toxic to the liver (4 tablets of 1 gram combined with alcohol can lead to liver failure and death).

Try to take as little medication as possible, but always consult your doctor for your individual medical decisions.

12. Be an empowered health advocate for your own body

Don't just rely on the health care system to keep you healthy.

The traditional health care system focuses primarily on treating symptoms of diseases, and not tackling the causes. Currently, our healthcare system is more of a sick care system that kicks into gear when it's already too late: when you already have cancer growing in your body, or when you are having a heart attack and being rushed in an ambulance to the hospital.

If you want to stay healthy, you have to take action yourself and be your own health advocate.

The High-Tech Approach To Live Longer



Besides the low-tech approaches we just discussed that involve healthy nutrition, exercise, and many other lifestyle changes, many researchers around the world are working on new therapies that can slow down aging considerably, and that could even partially reverse aging.

More and more the idea is gaining ground that aging is the root cause of all aging-related diseases, such as heart disease, Alzheimer's disease, osteoporosis, and macular degeneration. People increasingly realize -- and science continually demonstrates -- that by tackling aging, the root cause of all these diseases is addressed.

Trying to treat aging would enable far more effective and better treatments

to prevent, slow down, or even reverse aging-related diseases.

Take heart disease for example. Imagine we could cure all heart disease so nobody gets a heart attack anymore. How much longer do you think people would live on average? Only about 2.9 years.^[3] That is not much. People wouldn't die of heart disease anymore, but they would die a few years later from another aging-related disease. Therefore, it's so important to target aging itself, instead of individual diseases.^{[4][5]}

Heart disease is a good example to show why it is so much better to treat the causes of aging than the actual disease itself. Many physicians will say that heart disease is caused by

the accumulation of cholesterol and inflammation in the blood vessel walls. More specially, they will say that white blood cells stuffed with cholesterol accumulate in the blood vessel walls, leading to the narrowing of the arteries.

However, these processes happen because of underlying aging mechanisms. Cholesterol accumulates in the white blood cells because their lysosomes cannot break down the cholesterol properly. Lysosomal dysfunction is one of the hallmarks of aging. Atherosclerosis also

happens because of many other mechanisms, such as cells in the blood vessel walls becoming senescent, stem cells in the blood vessel walls becoming dysfunctional, and other cells incurring damage caused by mitochondrial dysfunction, protein accumulation, cross-linking, epigenetic dysregulation, and so on. And all of these are aging mechanisms, leading to atherosclerosis, and many other aging-related diseases.

So what are some technologies that aim to extend and even reverse aging?

01. Mitochondrial rejuvenation



Mitochondria are the powerplants of our cells. The older we get, the more dysfunctional they become, which contributes to the aging process.

One important driver of mitochondrial dysfunction is mitochondrial DNA becoming

more and more damaged. Which is a problem given the mitochondrial DNA contains blueprints to build and maintain the mitochondria.

There are many ways in which mitochondria can be rejuvenated. One way is to introduce new, undamaged mitochondrial DNA into the mitochondria that contains the building instructions to make mitochondrial proteins. This is possible by intravenously injecting mitochondrial DNA that is tagged so that it travels to the mitochondria automatically.

Other ways involve administering specific peptides that improve mitochondrial health,^{[6][7]} or moving mitochondrial genes from the mitochondria into the cell nu-

cleus, where they are better protected against damage,^[8] or administering new and safer mitochondrial decoupling agents,^[9] or even injecting whole young and healthy mitochondria in animals, which is called mitotherapy.^[10]

It will take a while for all these therapies to be further developed. In the meantime, there are various natural substances that can improve mitochondrial health, like fisetin, glycine, alpha-ketoglutarate, nicotinamide mononucleotide (NMN) and pterostilbene.

02. Epigenetic reprogramming



The epigenome is the complex molecular machinery that surrounds the DNA and decides which genes are switched on and which genes are switched off. You can look at the epigenome as an on-off switch for our genes.

The older we get, the more the epigenome becomes dysregulated: some genes are switched on while they should be switched off, and vice versa. For example, cancer and inflammation-promoting genes are switched on, which increase our risk of cancer and inflammatory diseases.

Scientists succeeded in partially reversing aging in mice by reprogramming their epigenome to a more youthful state. They made old mice younger again by increasing Yamanaka factors in the cells of the mice during short periods of time.^[11] Many scientists are now looking into

epigenetic reprogramming to rejuvenate cells and organisms.

There are some natural substances that can improve epigenetic health, like alpha-ketoglutarate, vitamin C, lithium, nicotinamide mononucleotide (NMN) and glycine.

03. Clearing up the protein mess



When we get older, more and more proteins accumulate inside and outside our cells.

Protein accumulation in the brain plays an important role in Alzheimer's disease. Protein accumulation in the heart is involved in aging-related heart dysfunction. Protein accumulation in the blood vessel walls makes them more prone to tearing or clogging up.

Protein accumulation can be slowed down or reversed in several ways. The

immune system can be induced to clear up specific proteins with the aid of a protein vaccine, or by infusing antibodies that latch onto and clear up specific proteins that accumulate during aging.^[12]

Another approach involves infusing lysosomal enzymes. The lysosomes are the incinerators of the cell which break down protein and other cellular waste. The older we get, the less well the lysosomes work.^[13] Lysosomal enzymes, injected into the bloodstream, can travel to the aged lysosomes and help them to break down

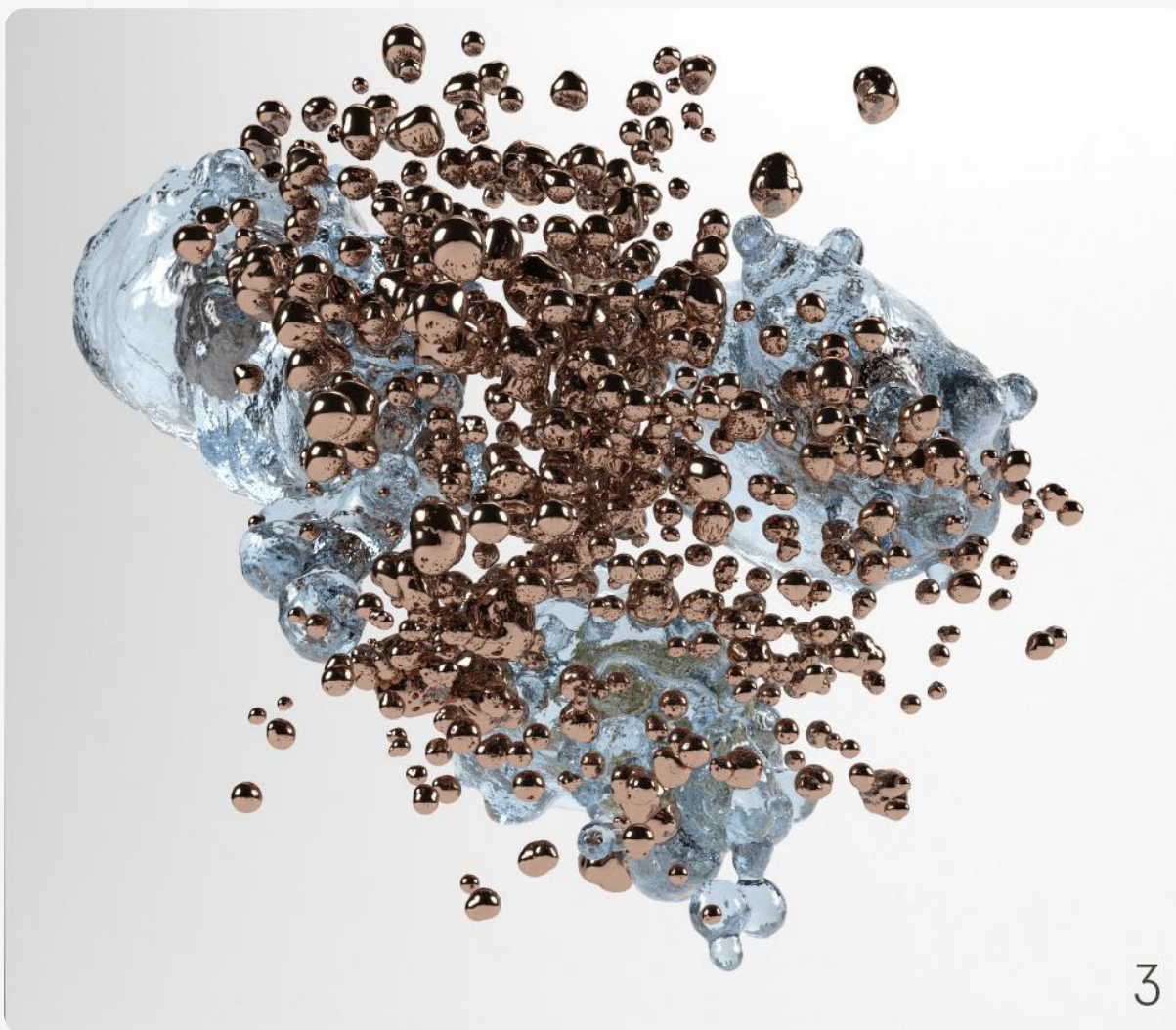
protein. This already works for successfully treating previously lethal lysosomal storage diseases.^[14] Some scientists try to improve lysosomal function by making the lysosomes more acidic so they can better “digest” cellular waste.^[15]

Another approach to tackle protein accumulation is by improving autophagy, which is the process in which the cell

digests or breaks down its own protein waste. During aging, autophagy decreases, so kickstarting this system again could prove beneficial to tackle aging.^{[16][17]}

There are natural substances that can improve protein homeostasis, like glucosamine, lithium, glycine, and acetyl-glucosamine (a building block of hyaluronic acid, which also improves skin health).

04. Stem cell therapy



3

Stem cells are cells that generate new cells and maintain our tissues and or-

gans. When we get older, stem cells in our body become dysfunctional or die off.

Stem cells can be infused in the body to replace dwindling stem cell pools, or to reboot existing stem cell populations.^[18]

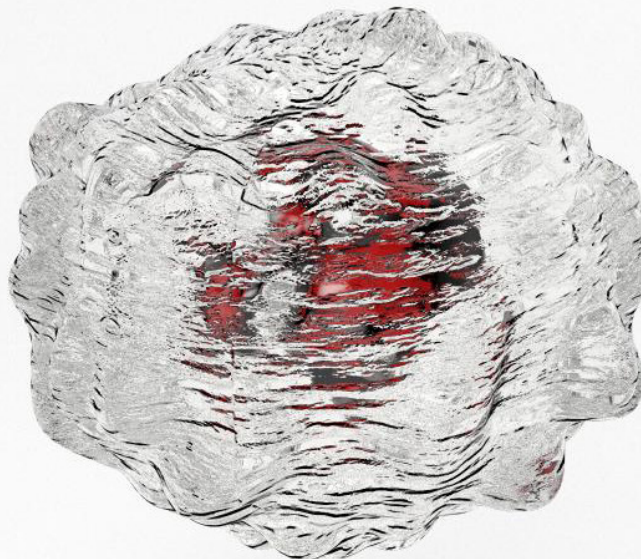
There are, however, various problems to overcome for stem cell therapy. For example, stem cells are rejected by the immune system (this is the case for “allogeneic” stem cells that come from other people), or they are already aged and damaged (this is the case for autologous stem cells, which come from your own, aged body).

Also, most stem cells, when injected in the bloodstream get trapped in the lungs, and even the ones that reach the tissues do not graft well.

There are many companies that offer stem cell therapies to treat aging and aging-related diseases, but almost all of them tout treatments that have not been approved. These stem cell therapies are not effective and can even be dangerous. For example, injected stem cells can cause clots in the lungs, or the stem cell infusion is contaminated by bacteria.

Also, more and more scientists believe that the health effects brought about by infusing stem cells are not caused by the stem cells grafting and creating new cells, but by stem cells briefly secreting substances that can rejuvenate the body, before they die off or are eliminated.

05. Young blood



Studies show that young blood administered to old mice can make them younger in some ways.^{[19][20][21]}

It seems that specific substances in young blood have rejuvenating effects in old mice. Conversely, specific substances

in old blood can accelerate or maintain the aging process.

Various biotechnology companies and research groups are trying to identify the

rejuvenating substances in young blood, with the aim to administer them to humans to improve health and slow down or even partially reverse aging.^[22]

06. Extending telomeres



Telomeres are the caps at the end of our DNA strands, preventing them from unraveling, a bit like the plastic caps on shoelaces. The more cells divide, the shorter their telomeres become, which is a bad thing.

There are a lot of misconceptions about telomeres. It's indeed true that telomere length is not strongly correlated to aging. Many people therefore think that telomeres are not important in aging. But the rate of telomere lengthening (or shortening) is correlated to lifespan.^[23]

For example, mice have very long telomeres compared to humans (while having much shorter lifespans). However, the telomeres of mice become shorter much faster compared to humans.^[24]

Scientists are exploring ways to administer the enzyme that lengthens telomeres (telomerase). Contrary to what many people think, lengthening telomeres for short periods of time does not increase cancer risk.^{[25][26][27]}

Cancer cells have active telomerase, the enzyme that lengthens their telomeres so they can keep dividing and become

immortal. Therefore, many people believe that lengthening telomeres in normal cells can make them more prone to becoming cancerous. This can indeed be the case when telomerase is continuously active since birth in organisms (these organisms get more cancer). However, studies show that now and then (“facultatively”) upregulating telomerase does not increase the risk of cancer.^[28] In fact, too short telo-

meres leads to genetic instability which can actually increase the risk of cancer.

Another misunderstanding is that some cells hardly divide (like brain cells) so their telomeres don’t become shorter, but still these cells age. However, the cells that surround the rarely-dividing brain cells still divide a lot (like glial cells or endothelial cells) and their dysfunction also contributes to the aging of the brain cells.

07. Clearing senescent cells



Senescent cells are some sort of “zombie” cells given they are damaged cells and normally should die because of this damage, but they stay alive, secreting all kinds of substances that “infect” neighboring cells and lead to more “zombified” senescent cells.^{[29][30]}

Senescent cells stem from healthy cells that became damaged by the aging process and stop dividing. Instead of dying off, they linger around in the tissues, secreting substances that damage healthy cells.

Senescent cells in the skin play a role in wrinkling, senescent cells in the blood vessel walls contribute to atherosclerosis, senescent cells in the cartilage are involved in osteoarthritis.^[31]

Studies have shown that it is possible to clear or destroy senescent cells in ani-

mals. For example, small molecules or peptides -- some of which are found in nature -- can eliminate senescent cells, leading to longer lifespans and less aging symptoms and diseases in these animals.^{[32][33]}

08. Drugs that can slow down aging



Most drugs are currently prescribed to treat diseases, not aging.

Additionally, most drugs don't even treat diseases, they just reduce the symptoms of diseases (like painkillers, anti-gastric reflux proton pump inhibitors, or corticosteroids).

However, some drugs could extend lifespan, like rapamycin or metformin. Currently, clinical trials are ongoing to see if these medications can extend lifespan in

humans (and combat many aging-related diseases at the same time).

An example is the TAME trial (Targeting Aging with METformin), which wants to find out if the anti-diabetic drug metformin can slow down aging and reduce the risk of many aging-related diseases at the same time.^[34]

Some companies are testing whether rapamycin or rapalogues (substances that function like rapamycin) might

slow down aging or reduce the risk of aging-related diseases.^[35] There is even a trial going on in dogs, which are given rapamycin.^[36]

However, specific natural substances could also have great potential to slow down aging. They are often overlooked, because these natural ingredients cannot be patented. That is unfortunate, because these substances could be at least as effective, or even better, than prescription drugs in slowing down aging.

Additionally, probably the most effective intervention to slow down aging will not be a single drug or substance, but a combination of substances: a polypill to slow down aging.

It is frustrating to see the disinterest of big pharma in natural substances that can safely extend human lifespan, and the narrow focus on using only one substance instead of many substances that work synergistically.

Conclusion

We are living in exciting times. Now, at the beginning of the 21st century, we know much more about why we age and how aging-related diseases come about than in the 10,000 years prior. Never before were humans able to access so many healthy foods, supplements, and therapies to live life to the longest and fullest.

In the coming decades, fascinating new biotechnologies will come to light to substantially slow down or extend lifespan. To maximize your chances of being able to profit from these new biotechnologies, it's important to stay healthy, and alive, as long as possible.

Eating healthily, taking longevity supplements, exercising, getting sufficient sleep and so on is the best way to stay alive long enough to profit from the first technologies that extend lifespan, enabling you hopefully to be around long enough to profit from yet another new life-extension technology, and so on, in order to reach

Longevity Escape Velocity (LEV), which would enable you to live a healthy life much longer than is currently the case.

Also, even in a future with new technologies at our disposal to slow down aging or even partially rejuvenate people, it will still be very important to eat well and take supplements, so you can postpone the use of these therapies, which will likely not be perfect and would still not address all aspects of aging.

Furthermore, if you eat healthy and take supplements (tackling deficiencies many people suffer from, even if they eat healthy - as we will discuss later), you will feel better, more energized, and more productive, compared to when you don't.

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The Problem With Most Anti-Aging Supplements



Countless companies sell “anti-aging” supplements, each one claiming that its supplements can slow down aging and increase lifespan.

How can you know if an anti-aging supplement has scientific merit? And how to find an anti-aging supplement that could actually work?

To answer these questions, we have to discuss some of the major problems of many anti-aging supplements.

01. Most Anti-Aging Supplements Are Based On Outdated Science



It's strange and sad that many supplement manufacturers still believe that antioxidants slow down aging. This is despite the fact that in the past 20 years many studies have shown that most antioxidants don't slow down aging or decrease mortality.^{[1][2][3]}

In fact, we even see that some antioxidants, such as vitamin E and vitamin A, might even increase mortality.^[4] Other research shows that antioxidants can undo the beneficial effects of exercise,^[5] or increase the risk of cancer progressing and metastasizing.^[6]

There are many reasons why most antioxidants don't slow down aging.

One reason is that antioxidants switch off the defense and repair mechanisms in our cells, so that cells do not produce their own antioxidant proteins (like catalase, superoxide dismutase or glutathione peroxidase), which are far more powerful than exogenous antioxidants (the ones you take orally from a supplement bottle, and that your body doesn't make itself).

Another reason is that antioxidants cannot reach high enough levels in specific compartments of the cells where they could exert an antioxidant effect. Furthermore, we see that aging is not just caused by oxidative damage, but by many other processes,

like epigenetic dysregulation and protein accumulation.

Of course, there are scientific studies showing that antioxidants do extend lifespan.

Often, these studies are of inferior quality. And in the cases that antioxidants do extend lifespan, it's mostly not because of the antioxidant properties of the substances tested, but because of other reasons, like their anti-inflammatory or epigenetic effects. After all, many substances have many effects in the body, not just an antioxidant effect.

The outdated idea that antioxidants slow down aging is based on Denham Harman's free-radical theory of aging, which came to light in the 1950's. It sounded good at that time, but now science has discovered that aging is far more complex than just free radicals damaging cells. We see that many other mechanisms cause aging, like protein accumulation, epigenetic dysregulation, telomere attrition, mitochondrial dysfunction (not only caused by free radical damage), transcriptional changes, inflammation, cross-links and so on.

Some notions about aging are not only outdated, but even dangerous. Many websites advocate or sell growth hormone or testosterone to slow down aging. However, if there is one common thread running through all aging research of the last decades, it is that growth hormone and male hormones accelerate aging.

Growth hormone makes your body "grow" more and thus age faster. Many canonical aging pathways impinge on growth

hormone-like pathways, like the growth hormone, insulin-like growth hormone (IGF), and mTOR pathway.

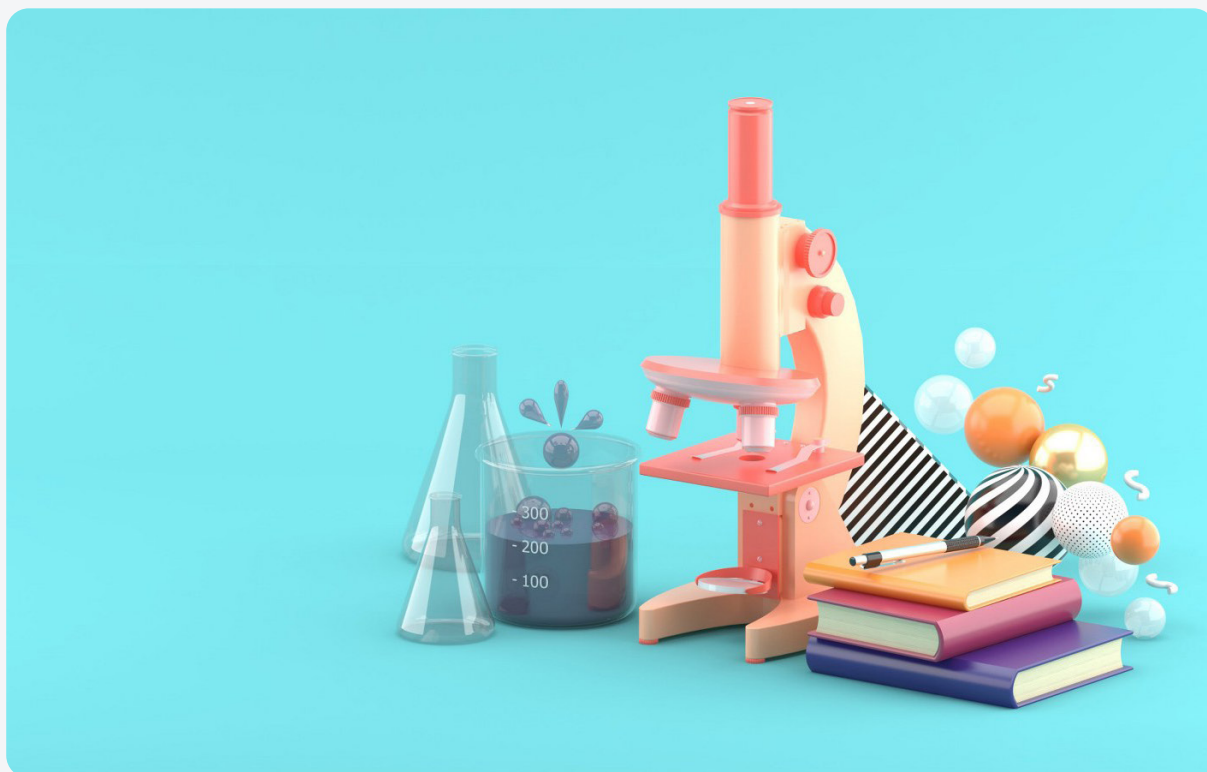
Testosterone shortens lifespan of male mice.^[7] Male hormones are one reason why men live shorter lives than women, and why neutered animals and eunuchs live considerably longer (eunuchs live up to 14 years longer compared to their GONAD-bearing counterparts).

Of course, often, taking growth hormone and testosterone will make you *feel* better and younger in the short term, and you may even gain some muscle mass and lose abdominal fat. But in the long term, growth hormone and testosterone accelerate aging. People and many studies tout the short-term effects, ignoring the long-term consequences.

Some studies show that older people with more growth hormone-like substances live longer, but higher levels of various hormones can often be found in people who are healthier anyway, compared to more frail, sick or malnourished people, which produce less of various hormones because of their condition. The correlation isn't causal.

Most (well-conducted) aging research shows that growth hormone-like substances accelerate aging, as do male hormones. People who recommend these substances to slow down aging are either not very knowledgeable about aging research, or just want to make a profit.^{[8][9][10]}

02. Most Anti-Aging Supplements Are Not Substantiated By Scientific Studies



Many sellers of anti-aging supplements claim that their supplements slow down aging, but it is rare that there are any legitimate scientific studies to corroborate this. Or almost equally bad, they quote old or ill-conducted scientific studies. Most anti-aging substances have not been rigorously tested in animals demonstrating that they can extend lifespan.

Sometimes, of course, you read about substances that do extend the lifespan in laboratory animals, but often these scientific studies have not been carried out properly or are based on bad study design.

For example, a substance is tested in an animal model that does not accurately reflect aging. Take coenzyme Q10. Some studies show it can extend

lifespan in mice. But that turned out to be only in mice that are genetically deficient in coenzyme Q10. Often such studies appear in scientific journals with a low impact factor, which means that these journals publish scientific studies with lower quality or evidence. It can also be that one study shows that a substance extends lifespan, while several other studies indicate that the same substance did not affect lifespan (and these studies are not mentioned by the seller).

Luckily, some people take aging very seriously and conduct rigorous scientific studies in animals to verify if specific substances can extend lifespan.

An example is the Interventions Testing Program (ITP), which consists of different labs that meticulously

test if specific substances can extend lifespan in mice. Unfortunately, many substances of which it is often believed they can slow down aging, such as green tea extract, curcumin, oxaloacetic acid, medium-chain triglyceride oil, and resveratrol, didn't extend lifespan.^[11] Nor did resveratrol or simvastatin, and fish oil and mitoQ.^[12] Hitherto, the ITP labs found that only rapamycin, 17 alpha-estradiol (only in males), acarbose, NDGA (nordihydroguaiaretic acid, only in males) could extend lifespan.^{[13][14][15][16]}

Other studies found that most vitamins, such as vitamin A, vitamin E, B vitamins, vitamin K, and most minerals didn't extend lifespan.^{[17][18][19]}

Of course, that doesn't mean that antioxidants, vitamins, minerals, green tea extracts, curcumin or fatty acids are useless. They are still important, given many people are deficient in these substances, or take in suboptimal amounts. Deficiencies or suboptimal amounts of these substances can shorten lifespan, or can increase your risk of all kinds of aging-related diseases.

But healthy people taking extra amounts of these substances probably won't extend lifespan.

03. Most Anti-Aging Supplements Don't Have Backing From Esteemed Scientists

Most aging scientists shy away from anti-aging supplements. Mainly because they know that most supplements don't slow down aging. In addition, many scientists do not want to be associated with a commercial product.

So if esteemed aging scientists do support a specific formulation, it is very likely there will be a lot of scientific evidence showing this formulation can have a beneficial impact on aging.

Of course, scientists vouching for a specific supplement need to be real and reputable aging scientists, being very active in the field, like having published many times in leading scientific journals and running their own research lab, preferably at a university or esteemed aging institute.

Also, be careful not to buy into doctors recommending anti-aging supplements: There are many doctors who still believe in outdated aging theories, such as that antioxidants or growth hormone slow down aging, and very few (dozens, globally) who are intimately familiar with the latest longevity research.

04. Most Anti-Aging Supplements Target Mechanisms That Are Less Relevant In Aging

Often, anti-aging supplements focus on aging mechanisms that may be less important than others. In recent years, scientists have unraveled many mechanisms that cause us to age. These are processes such as accumulation of proteins, mitochondrial dysfunction, epigenetic changes, DNA damage, telomere shortening, and so on.

However, not all of these mechanisms are equally important. The latest research seems to hint that especially dysregulation of the epigenome is a major driver of aging. The epigenome is the complex molecular machinery surrounding the DNA

that decides which genes are active and which genes are not.

In fact, when the epigenome is dysregulated, many other aging mechanisms kick into gear. A dysregulated epigenome can lead to reduced DNA repair, shortened telomeres, accumulation of proteins, and so on.

We can appreciate the power of the epigenome by looking at fascinating experiments in which old differentiated cells (like fibroblasts) can be epigenetically reprogrammed into young stem cells. These reprogrammed cells have repaired their DNA damage, mitochondrial damage, telomere shortening, and protein accumulation, demonstrating the incredible flexibility of cells and the power of the epigenome.^{[20][21]}

Similar clues are all around us in nature. Take queen bees for example, which can live up to several years compared to worker bees, which have a lifespan of only a few weeks, despite queen bees and worker bees having the same DNA. When a worker bee larva is given royal jelly, it transforms into a queen bee that can

live twenty times longer. That is because royal jelly reprograms the epigenome of the bee.

Another hint comes from cloning. It is remarkable that a young animal can be cloned from the cells of an old animal. During the cloning process, an old, aged and damaged nucleus of, for example, a skin cell can be transplanted into an oocyte without nucleus, producing a young offspring. This means when an old nucleus is introduced into an oocyte, it becomes epigenetically reprogrammed and rejuvenated, so that a young offspring can be born.

These and many other examples seem to suggest that perhaps the epigenome is the most important driver of aging. Whether this is the case or not, it is very clear that the epigenome plays a very important role in aging. That is why we added to NOVOS various ingredients that impinge on the epigenome, like glycine, lithium, calcium alpha ketoglutarate, fisetin and NMN (nicotinamide mononucleotide).

05. Most Anti-Aging Supplements Don't Contain High-Enough Doses



As a famous ancient physician already said, dosing is everything.

Unfortunately, many supplements contain ingredients that are far too low, meaning that they will not have a significant impact on your health. Take magnesium for example. Many supplements only contain 50 to 100 milligrams of magnesium, while an ideal intake of magnesium is estimated to be around 400 to 600 mg per day.

It is remarkable that most anti-aging supplements are capsules or tablets. Many ingredients that can slow down aging need to be taken in doses way too big to fit in a capsule or tablet.

Take glycine for example, which can improve mitochondrial functioning and the epigenome: ideal doses are two grams or more per day. Or take malate, which also

improves metabolism, which you would also need to take in the range of two grams. Other examples are glucosamine sulphate, of which you can take about 1 gram per day, or alpha ketoglutarate, that is ideally dosed at around 1 gram per day.

Before you know it, a proper anti-aging supplement would contain at least 6 grams of ingredients – that is, if you want to use substances at dosages that have been scientifically shown to extend lifespan in various animals.

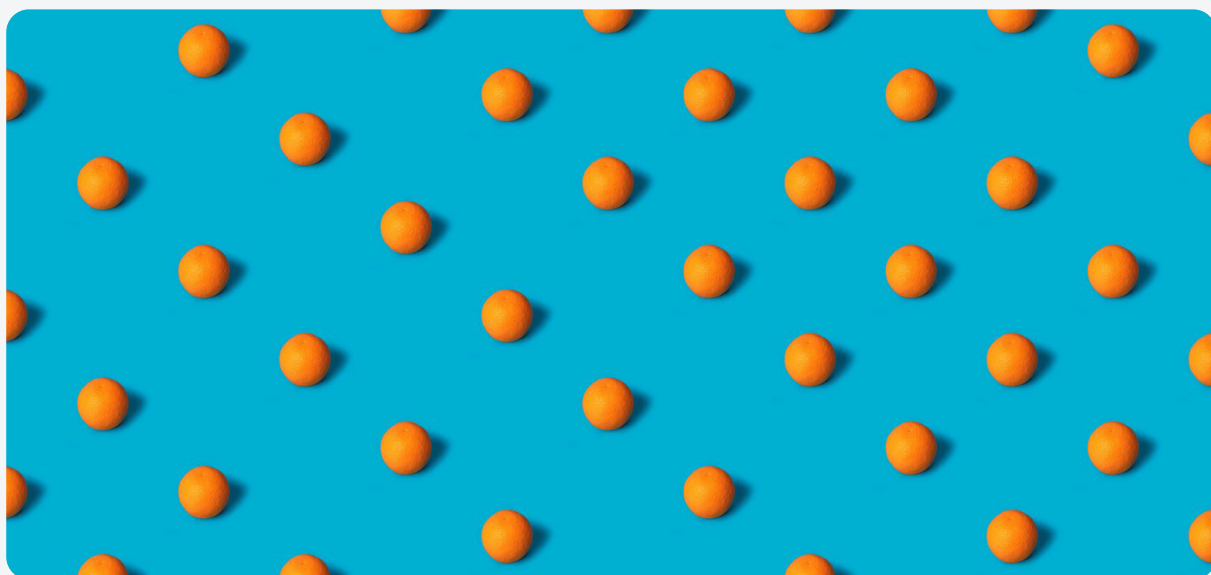
Of course, there are other substances that need to be taken in small amounts, like lithium or fisetin, but the combined ingredients are too great to fit into fewer than ~10 pills.

06. Most Anti-Aging Supplement Companies Don't Test Their Ingredients.

Most anti-aging supplement sellers don't test their supplements in animals or humans. Mostly because they don't bother, or because they know there is not a lot of scientific evidence corroborating their claims. Another reason is that testing in animals and humans is very expensive and requires a high level of expertise.

Also, it is not easy to test if a supplement can slow down aging, given you

have to follow up with the animals for a long time (until they die), which is even more difficult in long-lived humans. You can measure surrogate biomarkers of aging, like inflammatory biomarkers in the blood, or mitochondrial functioning, or physiological tests (e.g. treadmill test in old mice), but these tests are less ideal. However, this is still better than nothing.



Conclusion

There are many anti-aging supplements on the market. Most of them are based on outdated science, are not corroborated by well-conducted scientific studies, focus on aging pathways that are less relevant, contain doses that are too low, and are not verified in animals or humans.

It is time that very science-based, well-corroborated supplements come to market. We will see a new wave of anti-aging supplements that are of great quality and are based on the best and most recent scientific insights into aging.

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04

Why Antioxidants Don't Slow Down Aging



Many people still believe that antioxidants slow down aging.

Antioxidants are substances like vitamin A, vitamin E, coenzyme Q10, beta-carotene, acetyl-cysteine, and so on. Antioxidants neutralize free radicals.

Free radicals are mainly a by-product of our metabolism. Free radicals are highly reactive particles that damage our DNA, proteins and cell membranes. It has been thought for many decades that this

accumulation of cellular damage by free radicals contributes to aging. And that antioxidants, which mop up these free radicals, extend lifespan.

However, in the past two decades, many large studies found that antioxidants do not slow down aging and don't reduce mortality.^{[1][2][3]}

One large meta-analysis consisting of 230,000 people even found that some antioxidants are associated with an increased risk of dying:^[4] vitamin A, vitamin E and beta-carotene intake was associated with slightly increased mortality.

Of course, many arguments can be brought up to counter these findings: in many studies the wrong form of antioxidants are given, or too low doses, or too late.

Still, both animal and human studies have painted a disappointing picture about the role of antioxidants in longevity. Animals have been given all kinds of antioxidant cocktails, but they didn't live longer. At least according to well-conducted studies; there are many low-quality studies that sometimes do show that antioxidants slow down aging. But often, when these studies are reproduced by other research groups no longevity effects are seen.

Other studies show that antioxidants can even be dangerous, and help cancer to spread (metastasize).^{[5][6][7][8][9]}

This makes sense: cancer cells are metabolically very active, so they produce huge amounts of free radicals as a side effect of their metabolism. This means that especially cancer cells benefit from antioxidants that neutralize free radicals. So it is not always advisable for cancer patients to take antioxidants.

Other studies show that antioxidants can undo the beneficial effects of exercise.^[10] Taking antioxidants to "recuperate" faster from exercise is also not always a good idea.

Research seems to suggest that most antioxidants do not extend lifespan.

And if some antioxidants do extend lifespan, it's often not because of their antioxidant activity, but because of other mechanisms, such as their anti-inflammatory, epigenetic or mitochondrial activity.

One problem is that antioxidants, when taken orally, cannot enter the regions in the cells where they are most needed, and this in high enough concentrations. But even then, studies in which animals are genetically modified to produce much more antioxidant enzymes (like catalase), do not live longer. Such antioxidant enzymes work much better than antioxidants (small-molecules) taken by mouth, but still they do not seem to have significant effects on lifespan.

Even more confusingly, mounting evidence shows that the substances antioxidants are supposed to neutralize, free radicals, can even have life extension effects.

For example, genetically modified worms that produce more free radicals live 32% longer. Giving worms a weed-controlling herbicide that creates a surge in free radical production extends lifespan in these worms by 58%.^[11]

How is this possible? Free radicals can function as a benign warning sign, revving up the cell's defense mechanisms, like detoxification enzymes and repair proteins, protecting our cells against age-related damage.

That's one reason why exercise is healthy: during exercise you produce a lot of free radicals because your cells have to work

much harder. These exercise-induced free radicals activate all kinds of repair and defense mechanisms in our cells, so that the cells can better protect themselves against the next time you exercise. In the meantime, these revved-up defense and repair mechanisms also protect you against aging and aging-related diseases.

Besides exercise, we know that foods like vegetables, fruits and green tea are

healthy. The classic, main explanation for this is that these foods contain antioxidants. But this is an oversimplification. A reason that healthy food is healthy is not because of its antioxidant activity, but because this food contains slightly toxic substances. These substances upregulate detoxification and repair enzymes in the body, so that our body is better protected against damage.



Healthy foods are also healthy due to reasons other than their oxidants. Healthy food contains substances that have epigenetic effects, that reduce inflammation, that are beneficial to the gut microbiome, that do not overstimulate aging pathways (like mTOR or insulin receptors), that improve mitochondrial functioning. And of course, healthy foods deliver vitamins

and minerals our body needs to function properly. So healthy food is much more than just oxidants.

Also, the whole notion that antioxidants can slow down aging is a huge oversimplification of the aging process. We know that we age because of many other mechanisms than accumulation of oxi-

ductive damage. We also age because of epigenetic dysregulation, protein accumulation, lysosomal dysfunction, telomere shortening, cross-linking, mitochondrial dysfunction (in which most mitochondrial damage is not caused by oxidative damage, but by mutations in the mitochondrial DNA as a consequence of mitochondrial division), and so on. Aging is much more complex than just free radicals damaging our cellular machinery.

In conclusion, taking antioxidants is not a good way to extend your lifespan. Of course, when you are deficient in specific antioxidants, such as vitamin A, vitamin

E or other vitamins, taking these antioxidants can be very useful. But taking large doses of extra antioxidants to slow down the aging process doesn't seem to work unfortunately.

To slow down aging and to extend human lifespan, we need to look beyond oxidants and their counterparts, antioxidants. We need to take in substances that act on various other aging mechanisms, like epigenetic dysregulation, protein accumulation and mitochondrial dysfunction.

In the next chapters, we will explore the most interesting substances to do this.

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Why Combinations Of Longevity Drugs Are The Future



Everywhere around the world, scientists are looking for substances that can slow down aging. They are testing thousands of ingredients in laboratory animals, hoping that one of these will make them live longer.

But that is very likely not the right approach.

Chances are small that one substance will be able to significantly slow down aging. A far better approach is to use combinations of substances. Different ingredients act on different aging mechanisms

simultaneously, enabling synergistic effects, which can at times be impressive.

Imagine that ingredient X succeeds very well in slowing down an important aging mechanism. You then would expect that this ingredient will significantly extend lifespan. But this is often not the case. After all, aging is caused by many different mechanisms, each of which contributes a small part to aging. Ingredient X may impact one aging mechanism, but then there are many other mechanisms that will still slowly kill you.

Compare this to repairing a dilapidated house, and that you repair only the gutter. Fixing the gutter is a great idea in itself, but probably will do little to slow down the collapse of the house if you do not also repair the flooded basement, the broken windows, the crumbling walls, or the leaky sewerage.

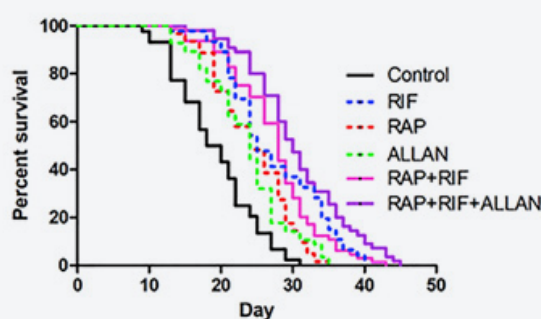
It is not that repairing the gutter does not work. It is that if you solve one thing, there are many other things that will cause the house to eventually collapse. Repairing the gutter will only postpone the collapse a little bit longer, at best, because other mechanisms contribute their part to the inexorable decline.

The same for our aging bodies. If you slow down one aging mechanism, usually, you will not significantly increase lifespan. However, if you tackle several aging mechanisms at the same time, you will see a much larger effect on lifespan.

An increasing amount of scientific studies show that combining different longevity substances works much better than just administering each one separately. Strong synergistic effects can be achieved by combining different ingredients.

In one study, three longevity drugs were examined to see if they could extend lifespan in fruit flies. These drugs were lithium (a mood-stabilizing drug), trametinib (a MEK inhibiting anti-cancer drug) and rapamycin (a mTOR inhibitor). Each substance in itself extended its life by about 11 percent. Combining two drugs extended lifespan by about 30 percent. Combining all three drugs prolonged lifespan by 48 percent compared to the untreated fruit flies.^[1]

Another study looked into combinations of rifampicin (an antibiotic), rapamycin (an mTOR inhibitor), psora – 4 (a potassium channel blocker), metformin (an anti-diabetic drug) and allantoin (an uric acid metabolite) in the little worm *C. elegans*. A combination of rapamycin, rifampicin and allantoin resulted in an impressive 89 percent lifespan extension. A combination of psora-4, rifampicin and allantoin even resulted in a 96 percent lifespan extension, far more than each ingredient separately.^[2]

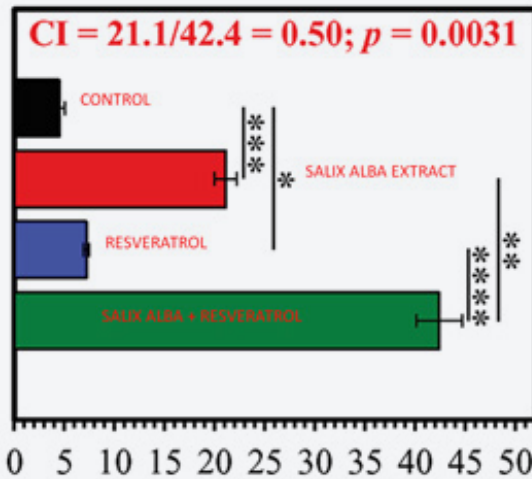


Source: Drug Synergy Slows Aging and Improves Healthspan through IGF and SREBP Lipid Signaling. *Developmental Cell*. T. Admasu et al.

In another study, combining valproic acid with trimethadione resulted in a considerably synergistic effect compared to using valproic acid or trimethadione alone.^[3]

Another study compared various ingredients like resveratrol and plant extracts to see if they could extend lifespan in yeast cells. The plant extracts were made from valerian root, *Passiflora incarnata*, ginkgo biloba, *Salix alba*, *Apium graveolens*, and *Cimifuga racemosa*. Using valerian extract or *Cimifuga racemosa* extract alone each extended yeast lifespan by about 5 days, while a combination of the two extracts extended lifespan by about 12 days. Interestingly, resveratrol alone only had a relatively small effect on lifespan (achieving an increase of about 3

days), compared to *Salix alba* alone which increased lifespan by about 10 days. However, a combination of resveratrol with *Salix alba* increased lifespan by no less than 20 days, a considerable synergistic effect:^[4]



Source: Pairwise combinations of chemical compounds that delay yeast chronological aging through different signaling pathways display synergistic effects on the extent of aging delay. *Oncotarget*, P. Dakik et al.

This important principle applies not only to drugs, but also to genes. In one study, several genes were introduced into mice. Each of these genes could theoretically slow down aging. These genes were FGF21 (fibroblast growth factor 21), *klotho* and TGFb-R2 (transforming growth factor-b receptor 2). The combination of TGFb-R2 and FGF21, or the combination of TGFb-R2 and *Klotho*, resulted in a synergistic effect: they significantly improved or even abrogated heart failure, renal failure, type 2 diabetes and obesity. Combination of two genes lead to an almost 60 percent increase in heart functioning in a heart failure model, a 75 percent reduction in kidney atrophy in a kidney failure model, and complete reversal of obesity and diabetes in mice that were fed a continuous high-fat diet.^[5]

In another study, scientists genetically modified aging-related pathways in *C. elegans* worms, such as the TOR and insulin pathway. Only modifying the TOR pathway resulted in a lifespan increase of 30 percent. Tweaking the insulin pathway led to a 100 percent longer lifespan. However, when both the TOR and insulin pathway were modified simultaneously, lifespan was increased by 500 percent, an impressive fivefold difference.^[6] Dr. Jarod Rollins, co-author of the study, said the following about this:

“The synergistic extension is wild. The effect isn’t one plus one equals two, it’s one plus one equals five. Our findings demonstrate that nothing in nature exists in a vacuum; to develop the most effective anti-aging treatments, we have to look at longevity networks rather than individual pathways.”

The longevity drug of the future will not be one drug, but a combination of drugs. Far better results can be achieved when different substances or different genetic modifications are combined.

This important insight guides the development of NOVOS. NOVOS contains various ingredients that target different aging pathways, enabling synergistic effects. This not just to repair the gutter, but also to repair as much of the house to keep it in an excellent condition for as long as possible.

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The Best Anti-Aging Supplements



There are so many supplements claiming that they are “anti-aging”. But unfortunately, they aren’t.

Most anti-aging supplements contain ingredients that have not shown to extend lifespan in scientific studies.

And for the few ingredients that did lengthen lifespan in organisms, often these studies have not been well-conducted, or have not been confirmed by other research groups, or use experimental set-ups that are not good models of the

real aging process (like accelerated-aging mice with very debilitating mutations in their mitochondria, that then receive a mitochondrial antioxidant).

Most supplements are based on outdated notions about aging, such as the idea that aging is mainly driven by oxidative damage, caused by free radicals which antioxidants can neutralize.

Unfortunately, large studies, sometimes even with hundreds of thousands of participants, have shown that antioxidants do not extend lifespan.^{[1][2][3]} Sometimes, antioxidants may even accelerate aging or increase the risk of cancer.^[4]

We know now that aging is a far more complex process than just oxidative damage. There are many other and more important reasons why we age, like epigenetic dysregulation, protein accumulation, mitochondrial dysfunction, and so on.

Which are some examples of these popular “anti-aging supplements” that in fact will do little to slow down aging? Examples are most vitamins, minerals, and herbs. Vitamin A, vitamin E, co-enzyme Q10, copper, and potassium are not going to extend your lifespan. They can be useful if you have deficiencies in these vitamins or minerals, but taking extra of these substances is not going to extend lifespan.

However, there are real anti-aging ingredients that can extend lifespan, because:

- They have good scientific studies supporting them, preferably in different organisms

- Intake is associated with reduced mortality in humans
- Intake is associated with reduced-risk or mitigation of typical aging diseases, like cardiovascular disease or Alzheimer’s
- They have shown to impact aging mechanisms, like epigenetic dysregulation, mitochondrial dysfunction or protein accumulation (e.g. autophagy, unfolded protein response, chaperone functionalities, etc)

Ideally, these ingredients also act on specific aging mechanisms, often in ways different than being an antioxidant. For example, they improve the stability of the epigenome (like alpha ketoglutarate) or reduce the accumulation of proteins (like glycine and glucosamine).

Here is our list of the best anti-aging, longevity supplements.

01. Fisetin

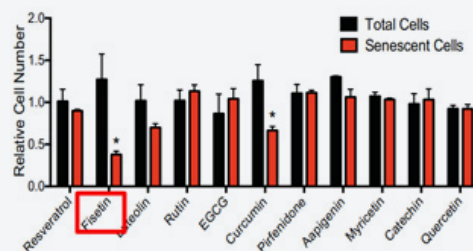


Fisetin is a natural ingredient found in vegetables and fruits, especially in strawberries. Fisetin is mostly known for its senolytic activity, meaning it can clear away senescent cells, and increasing lifespan in various organisms.^{[5][6][7][8]}

Senescent cells accumulate everywhere in our body during aging. Senescent cells were previously normal cells that turned into “zombie cells”: senescent cells are cells that cannot divide anymore but refuse to die, and secrete all kinds of substances that damage healthy surrounding cells.

Senescent cells in the skin contribute to wrinkles, senescent cells in the blood vessels make them more stiff and senescent cells in the liver impair its proper functioning.

There are various natural substances that can have senolytic activity. One of them is quercetin. In fact, quercetin and fisetin look very similar. However, fisetin seems to be the most potent natural senolytic:^[9]



Fisetin is far better in destroying senescent cells (red bar) than other substances, such as quercetin or curcumin or EGCG.

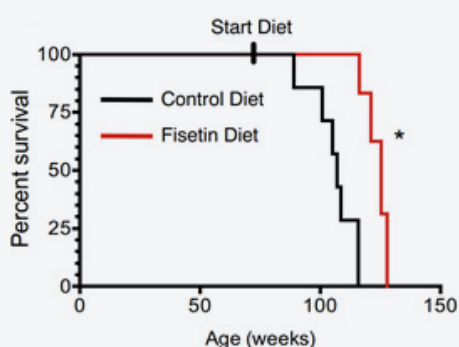
Source image: Fisetin is a senotherapeutic that extends health and lifespan. EBioMedicine, 2018

Researchers concluded that “fisetin had the most potent senotherapeutic effects in several cell types in vitro

and showed strong anti-geronic effects in vivo.”

Besides clearing senescent cells, fisetin reduces inflammation,^{[10][11]} inhibits mTOR (an important aging switch),^[12] reduces glycation (which also contributes to aging),^[13] increases the production of cell protective substances, and has many more beneficial effects.

Various studies show the lifespan extending effects of fisetin.^{[14][15][16]} For example, one study found that fisetin extends median and maximum lifespan in mice, even when taken late in a mouse’s life (equivalent to 50 or 60 years old for a human):^[17]



Fisetin extends lifespan (red graph) versus control group (black graph) in mice.

Source image: Fisetin is a senotherapeutic that extends health and lifespan. EBioMedicine, 2018

02. Alpha-Ketoglutarate

Alpha-ketoglutarate (AKG) is a substance that naturally occurs in our bodies. When we get older, the levels of AKG decline.

Various studies show that AKG extends lifespan.^{[18][19][20][21][22]} In one study, mice that received AKG lived on average 14 percent longer.^[23] But even more interestingly, the mice stayed healthy for much longer: the mice that received AKG had less aging-related diseases and symptoms, including a fur that became grey

less fast. This probably has to do with AKG improving the stem cell function of the stem cells surrounding the hair shaft.

How can AKG extend healthspan and lifespan?

AKG has many functions in the body. For example, it is involved in mitochondrial health. Mitochondria are the power plants of our cells, which create energy so cells can go about their daily business. When we get older, our mitochondria function less and less well. AKG provides energy for the mitochondria, among many other functions.^[24]

AKG also helps to maintain the epigenome.^[25] The epigenome determines which genes are active or not. The older we get, the more the epigenome gets dysregulated. Substances like AKG can slow down this decline. AKG is also involved in stem cell maintenance.^[26] Interestingly, AKG also improves synthesis of collagen,^[27] which could improve skin appearance.^[28]

AKG needs vitamin C to function properly, especially for its epigenetic functioning.^[29] So ideally, a good anti-aging supplement would contain both AKG and vitamin C to enable synergistic effects. Interestingly, vitamin C also has epigenetic effects.^[30]

03. Microdosed Lithium



Lithium is a mineral found in nature. It seeps from rocks into water, including drinking water. Various studies showed links between the amount of lithium in the drinking water and mortality rates,^{[31][32]} while other studies showed that people living in regions with more lithium in the drinking water had less neurodegenerative diseases like Alzheimer's^[33] and have lower suicide rates.

Of course, correlation is not causation. However, many studies in animals show that lithium can reduce the risk of Alzheimer's disease and various other neurodegenerative diseases.^{[34][35][36]}

A systematic review and meta-analysis demonstrated that lithium may have beneficial effects on cognitive performance in people with mild cognitive impairment (often the precursor to Alzheimer's disease) and Alzheimer's disease.^[37]

Also, many studies show that lithium can extend lifespan in organisms.^{[38][39][40]}

Lithium has also been used for many decades as a medicine to treat psychiatric diseases, especially to stabilize mood disorders, such as bipolar disorder.

However, the amounts of lithium given to psychiatric patients are hundreds to thousands of times higher compared to the amounts of lithium in drinking water, and given in trials to reduce dementia, and in longevity food supplements like NOVOS. We see that very low or microdoses of lithium (in the range of 0.3 milligram to a few milligram) can have lifespan effects and protect the brain against neurodegenerative diseases like Alzheimer's.^{[41][42][43]}

There are many ways by which lithium can impact the aging process. Lithium has been shown to increase autophagy (the digestion of proteins that would otherwise accumulate in the cells, a process that contributes to aging),^{[44][45]} enhance the generation of pluripotent stem cells demonstrating its epigenetic effects,^[46] and improve neurogenesis,^[47] the formation of new neurons.

04. Glycine

Glycine is an amino acid that occurs naturally in our body. When we age, glycine levels decline.

Low glycine levels also have been associated with various aging-related diseases like cardiovascular disease and with type 2 diabetes.

Glycine extends lifespan in different species.^{[48][49][50][51]}

Glycine has many functions in the body. It improves the epigenome (the machinery that determines which genes are switched on or off, a process that gets more and more awry when we get older). Glycine especially improves the epigenome of mitochondria, the power plants of our cells.^[52]

Glycine also functions as a chaperone. Chaperones are small molecules that gently stick to proteins and protect the

proteins. That is important, because one of the reasons why we age is due to proteins accumulating everywhere inside and outside our cells, eventually hampering the proper functioning of our cells.

Glycine also reduces inflammation^[53] and has many other beneficial effects, especially for the cardiovascular system. People with higher glycine levels in the blood had less risk of a heart attack,^[54] and glycine can protect the blood vessels.^[55]

05. Pterostilbene



Pterostilbene is the better brother of the famous anti-aging substance resveratrol.

Resveratrol has long been hyped as a longevity substance. However, it could not live up to that hype unfortunately. Studies showed disappointing results regarding resveratrol extending lifespan.

One reason for this is that resveratrol has a very short half-life: most of it is broken down in less than an hour. Also, resveratrol, when taken orally, is not very well absorbed.

Pterostilbene, on the other hand, has a far longer half-life and better absorption,

so that higher levels reach the blood stream and stay around for longer in the body.

Pterostilbene has been associated with longer lifespans,^{[56][57]} and could reduce various aging symptoms and mitigate aging-related diseases, including Alzheimer's disease.^{[58][59][60]}

06. Malate



Malate is found in apples, and in our own bodies.

Malate is an important substance in the mitochondria. In fact, malate is a component of the Krebs cycle, which consists of various substances that are chemically modified to provide the energy that keeps all cells going.

Studies show that malate can extend lifespan in *C. elegans*.^[61]

In humans, malate is given to provide energy, especially in combination with magnesium.^[62] That's why the best

form of magnesium is magnesium malate (and not magnesium oxide, magnesium citrate and other forms of magnesium).

07. Magnesium

Magnesium is an indispensable mineral for the body to function properly.

Magnesium helps innumerable enzymes in our body to function properly. Cells shuttle magnesium in and out to propagate nerve signals and to

generate muscle impulses, including the beatings of our heart.

Magnesium also sticks to our DNA, stabilizing our DNA, protecting it against damage.^[63] Increasing DNA damage is one of the reasons why we get older.

Low intakes of magnesium are associated with increased inflammation, increased blood pressure, increased risk of heart disease, neurodegenerative diseases, insulin resistance, osteoporosis and even development of cancers.^[64]

Magnesium also provides energy, and can help people to deal with stress. Magnesium especially teams up well with malate, another substance that can provide energy.

08. Glucosamine Sulphate

Most people know glucosamine as a substance to reduce wear and tear of cartilage and to improve joint health.

Few people know that glucosamine can also extend lifespan in different organisms, including mice.^{[65][66]}

Interestingly, studies show that glucosamine is one of the few supplements associated with reduced mortality in humans,^{[67][68]} and also reduced risk of cardiovascular disease in humans.^[69] There are also associations between people taking glucosamine and reduced inflammation.^[70]

Various animal studies showed that glucosamine reduces atherosclerosis^{[71][72]} and inhibits platelet aggregation,^[73] making the blood less clotty.

This should not be surprising, given the many effects glucosamine has on the body. It does much more than protecting cartilage.

Glucosamine can improve mitochondrial health, thus enabling the mitochondria (the power plants of our cells) to function better. One way of doing this is by increasing “mitochondrial biogenesis”, which means that glucosamine induces the formation (genesis) of extra mitochondria.

Glucosamine also reduces inflammation,^{[74][75][76]} which is a good thing given inflammation increases during aging. This low-grade inflammation is called “inflammaging”.

09. Hyaluronic Acid



Hyaluronic acid is an important component of the skin. But hyaluronic acid surrounds and embeds many other cells in the body than just the skin cells.

The older we get, the less glucosamine there is in the body. A 70 year old has only about 19 percent of the HA as a young person.

Studies show that hyaluronic acid, taken orally, can improve skin appearance by reducing wrinkles, improving moisturization of the skin and increases skin radiance.^{[77][78]} It can also improve osteoarthritis,^{[79][80][81]} which makes sense given joints and cartilage contain a lot of hyaluronic acid.

Interestingly, hyaluronic acid is made up of acetyl-glucosamine (do not confuse with glucosamine).

Acetyl-glucosamine has been shown to extend lifespan in mice.^[82]

Acetyl-glucosamine could do this by inducing the “unfolded protein response”, which is a defense mechanism that kicks into action when the cell senses that there are too many improperly folded proteins accumulating in the cell.^[83]

Protein accumulation is one of the reasons why we age. When you consume hyaluronic acid, parts of the molecule are broken down in the gut into acetyl-glucosamine, which can be absorbed by the gut cells and end up in the bloodstream.

10. Ginger



Ginger is a well-known spice. But it's not just any spice.

Many scientific studies demonstrated many beneficial health effects of ginger, like reducing inflammation^[84] and protecting cells against damage.^[85]

Ginger can also extend lifespan in simple organisms, like fruit flies.^[86]

Ginger can improve type 2 diabetes^{[87][88]} and inflammation in humans.^{[89][90]}

Studies show that ginger can protect mice against lethal doses of radiation, which is quite impressive.^[91] The mice that received ginger before they got exposed to a high dose of radiation lived considerably longer. High-energy radiation is very damaging to cells, the radiation oxidizes (damages) many

components of the cells, rips molecules, including DNA apart, and induces strong inflammation.

However, ginger seems to be able to mitigate this molecular onslaught.

11. Rhodiola Rosea

Rhodiola rosea is a very interesting plant that grows in the northern regions of Europa and Asia.

Rhodiola rosea has been used for centuries as an adaptogen, a substance that can improve resilience against both physiological stress and mental stress.

Rhodiola rosea extends lifespan in various organisms, for reasons that

scientists have not completely understood yet.^{[92][93][94][95]}

Interestingly, Rhodiola can also improve nerve regeneration; specific substances in Rhodiola, like salidroside could be responsible for this very interesting effect.^{[96][97]} This could be one of the several reasons

demonstrating neuroprotective effects of Rhodiola rosea.^{[98][99][100]}

Studies in humans show that Rhodiola rosea can improve memory, concentration and can reduce fatigue.^[101] Students and people with demanding jobs take Rhodiola rosea to improve their productivity and energy levels.^{[102][103][104]}

12. L-Theanine



Theanine is a substance found in green tea, and is one of the reasons why green tea is healthy.

Theanine has been shown to extend lifespan in simple organisms.^{[105][106][107]}

Theanine has been associated with healthier blood vessels, and could reduce blood pressure and even obesity.^[108]

Theanine has shown to reduce neurodegeneration and protect neurons.^[109]

It could also perhaps improve neuronal stem cell health and neurogenesis (the creation of new neurons in the brain).^{[110][111][112]}

In humans, theanine can improve concentration, while also improving relaxation.

13. Nicotinamide Mononucleotide (NMN)



NMN is needed to make NAD⁺.

NAD⁺ is a very important substance in the cells. It provides energy for cells and also is a cofactor for proteins that repair and maintain our epigenome and our DNA.

The epigenome is the intricate machinery that surrounds the DNA and that determines which genes are active. During aging, the epigenome becomes more and more dysregulated.

NMN also improves the functioning of our mitochondria, the power plants of our cells.

NMN improves metabolism and reduces inflammation.

The older we get, the less NAD⁺ there is present in our cells. Taking in NMN can increase NAD⁺ levels.

Various studies show that NMN has beneficial effects on aging diseases and symptoms.^{[113][114][115][116]} For example, long term administration of NMN mitigated age-associated decline in mice: NMN reduced the typical age-associated increase in body weight, improved energy metabolism, improved lipids in the blood and insulin sensitivity and ameliorated eye function.^[117] NMN can also improve aging-related decline in fertility,^[118] improve bone health^[119] and vascular health.^{[120][121][122]}

For more information on NMN and aging, and for a comparison between NMN and NR (nicotinamide riboside), visit our website www.NovosLabs.com.

The Importance Of Synergy In Anti-Aging Supplements



In conclusion, many anti-aging supplements are based on outdated insights and don't have any or just very little science backing up their claims. They do not contain substances that have been shown to act on aging mechanisms (the "hallmarks of aging").

A good anti-aging supplement is one that contains substances that are based on science and that act on aging mechanisms. This also enables these supplements to have an additional important benefit: synergy.

After all, aging is a complex process caused by various different mechanisms, such as epigenetic dysregulation, mitochondrial dysfunction, and accumulation of proteins. If you have an anti-aging supplement that only focuses on "improving mitochondrial health", then you are not addressing other important aging mechanisms, like epigenetic dysregulation or accumulation of proteins. This mitochondria-specific supplement, even if it

improves mitochondrial health, will have little impact on extending lifespan given it only tackles one facet of the aging process.

Therefore, it's very important for a good anti-aging supplement to contain substances that act on different aging mechanisms and this in a synergistic way.

For example, alpha-ketoglutarate (AKG) can maintain the epigenome and improve mitochondrial health. AKG can work nicely together with other substances that improve mitochondrial health, like fisetin and malate, or that improve the epigenome, like NMN and glycine.

But addressing the aging epigenome and mitochondria is not enough. You also need to tackle many other aging mechanisms, like protein accumulation and DNA damage. For this, other anti-aging substances need to be added, like lithium (which can reduce ac-

cumulation of proteins by stimulating autophagy - the digestion of proteins) or acetyl-glucosamine which can also reduce protein accumulation, or magnesium that can help stabilize the DNA.

The ideal anti-aging supplement contains not just one or two substances that focus on one aging mechanism (like mitochondrial health or the NAD+ metabolism), but contains many substances that act on many aging pathways, and this in a synergistic way.

It's no coincidence that all ingredients described in this chapter are part of NOVOS Core, a novel nutraceutical containing 12 science-based, synergistic ingredients to slow down aging, and NOVOS Boost, which contains NMN. That is because our research, experimentation and consultation with our Scientific Advisory Board indicated that these ingredients are among the most promising to address aging, and can act in synergistic ways.

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Some Other Important Food Supplements To Take, Even When You “Eat Healthy”

Earlier, we discussed some of the best, most science-based substances to slow down aging, like alpha ketoglutarate, fisetin, pterostilbene, and so on. We call these “longevity supplements”.

There are also “health supplements”. Health supplements are micronutrients like vitamins, minerals, or omega-3 fatty acids, which in most cases when given in high doses to healthy animals, don’t extend lifespan. However, these health supplements are still very important for a long, healthy life, given deficiencies of these substances can shorten lifespan, while also substantially reducing quality of life.

For example, if you are deficient in iodine, iron or calcium, you can suffer from fatigue, sleep problems and brain fog (and many other problems). If you are deficient in zinc this can increase the risk of Alzheimer’s disease, and negatively impact the immune system, skin and gastrointestinal system. Deficiencies in omega-3 fatty acids can impair proper brain functioning, and increase the risk of heart disease and macular degeneration, a debilitating eye disease many elderly people suffer from.

And so on.

In other words, if you are deficient in important “health supplements”, you can shorten your average lifespan. But to increase your maximum lifespan, longevity supplements are needed.



Unfortunately, many people are deficient in many nutrients. So it’s important to fix this. The next section is about important vitamins, minerals and other micronutrients almost everyone should take.

However, there are a lot of misconceptions about health supplements.

Perhaps the biggest misconception is that you don’t need supplements “when you eat healthy”.

Unfortunately, that’s not true.

Even if you eat healthy, it’s very difficult to consume sufficient levels of important nutrients to achieve your optimal lifespan potential.

Let us explain why.

Even A Healthy Diet Is Often Not Sufficient



Take magnesium for example. Even if you eat a healthy diet, it's very difficult to get sufficient amounts of magnesium, which would ideally come down to around 400-500 mg per day. You would really have to eat A LOT of vegetables, nuts and legumes to reach that high amount of magnesium.

The same for potassium, an important mineral of which you ideally need several grams per day.

Or take iodine, which is found in very, very small quantities in most foods. Unless you eat seaweed regularly (seaweed contains lots of iodine). Yes, iodized salt also contains iodine,

but most packaged foods don't use iodized salt, and iodine begins evaporating from iodized salt after the package has been opened. If you use sea salt, it does not contain any iodine.

Vitamin D is another example. Even if you eat a healthy diet it's almost impossible to get enough vitamin D via your food. Vitamin D is found in only very low amounts in foods (mushrooms or salmon contain a tiny bit of vitamin D).

But can't you get your vitamin D from the sun? Most people in Western countries reside too far from the equator, making the sunlight too weak

to form enough vitamin D, even in the summer. Also, when the skin is covered by clothing, or as a result of aging, the skin is unable to use sunlight to produce sufficient amounts of vitamin D.

As you can see, in most cases even a healthy diet does not provide sufficient levels of vitamins, minerals and other micronutrients.

But wait, what levels?

Most Officially Recommended Daily Doses Are Too Low

You should know that the official recommended dietary allowances of vitamins and minerals, as defined by governments, are often just the bare minimum you need to take in to not become sick. They do not tell you what are the best amounts for a long, optimal, healthy life.

Most of these official recommendations are also based on old studies in which volunteers were deprived of a specific vitamin or mineral. Scientists then waited a while until people became sick, and then determined the minimum dose you would need to prevent this.

So these recommended daily intakes are what you need to take on a daily basis in order not to become sick after a number of months (the duration of the study). They do not tell you the ideal amounts you need to stay healthy and slow down aging for decades to come.

Take for example vitamin B12. The recommended dietary allowance is around 2.4 mcg in many countries. But that's in fact the "minimum" amount you need to not become sick after a few months or years, getting serious complications, like anemia, fatigue or cognitive problems.

This doesn't mean this is the optimal amount for a long, healthy life.

For example, we see in studies that you need at least 20 mcg of vitamin B12 to optimally protect the DNA against DNA strand breaks – more than 8 times greater than the recommendation!

Also, many people do not take up vitamin B12 well, especially as we get older. For example, atrophic gastritis affects at least 10 to 30 percent of people older than 60, leading to malabsorption of vitamin B12. So, they would need far more vitamin B12 than advised by governments.

In fact, The Linus Pauling Institute at Oregon State University recommends that all people older than 50 take at least 100 to 400 ug/day of supplemental vitamin B12.^[1] That's considerably more than the 2.4 mcg many governments advise.

It's interesting to see that many foods rich in vitamin B12 (clams, mussels, crab, and fish like mackerel and salmon) are water-borne foods. Scientists speculate that people evolved for tens of thousands of years living close to shorelines and rivers and lakes and consumed high amounts of sea food and thus vitamin B12,^[2] probably

reaching daily intake levels far more than a meagre 2.4 mcg per day.

These are just a few examples demonstrating that yes, we need to take supplements for optimal aging, and often in higher doses than officially recommended. And this for the rest of our lives, and

even more when we are older and suffer from age-related malabsorption issues and changes that hinder us to properly use these important vitamins and minerals.

So what are some vitamins, minerals and micronutrients everyone should take?

1. A Sufficiently High Dosed Vitamin B Complex

B vitamins play a very important role in metabolism, brain health, nerve health, and immune system health.

In fact, B vitamins are involved in most of the important cellular processes, like making sure the Krebs cycle runs smoothly, which fuels all life, or creating DNA or maintaining the epigenome.

A vitamin B complex contains all B vitamins, like vitamin B1, B2, B3, B4, B5, B6, B7, B9, and B12.

Make sure the amount of B vitamins is at least a few times the daily recommended dose. Note that you can oftentimes find these B vitamins in a high quality vitamin B complex multivitamin.

2. Magnesium – Not Capsules, But Powder



Magnesium is a very important mineral involved in hundreds of different enzymes and chemical reactions, is paramount for proper muscle contractions (including your beating heart), nerve conduction and stabilizes DNA.

Sufficient magnesium intake is associated with a reduced risk of heart disease, dementia and type 2 diabetes.

Ideally, people need to take at least 400 to 500 mg of magnesium per day.

Unfortunately, most magnesium supplements contain magnesium oxide. A far superior form of magnesium is magnesium malate, for several reasons, one being that malate is also an important substrate for the Krebs cycle and can extend lifespan.

One would need to take magnesium malate in powder form because capsules are just too little to contain sufficiently high daily doses. So one can take magnesium malate powder, adding about one fourth of a teaspoon (about 2-2.5 grams of magnesium malate accounting for at least 300 mg of pure magnesium) into a glass of water.

Or you can just take NOVOS Core, which contains this amount of magnesium malate.

3. Vitamin D3 – Sufficiently Highly Dosed

Vitamin D can extend lifespan. Higher levels of vitamin D are associated with less risk of heart disease, auto-immune diseases, improved brain health and a better functioning immune system.

Many governments advise 400 to 800 IU of vitamin D per day, while many vitamin

D researchers claim you need at least 2000 to 4000 units per day.

We would recommend to take at least 2000 units per day. The risk of excess accumulation of vitamin D is negligible with this amount. Make sure it's vitamin D3, and not vitamin D2 – the vitamin D3 variant works better.

4. Vitamin K – As A Vitamin K2 Complex

If you take vitamin D, you also need vitamin K.

Vitamin K is an important vitamin for bone health, but also for skin and metabolism in general.

Vitamin K can even reduce wrinkles. Often, people with vitamin K deficiency have a wrinklier skin (and greater risk of osteoporosis).

You need to take vitamin K together with vitamin D. Vitamin D ensures proper

uptake of calcium, while vitamin K makes sure that the calcium ends up in the right place: in your bones and not in your arteries, which would contribute to vascular calcification.

A recommended vitamin K dose is at least 180 ug per day, ideally vitamin K2 (not vitamin K1), and as different vitamin K2 variants, like vitamin K2-M7, vitamin K2-M6, vitamin K2-M9, etc.

5. Calcium – Without The Milk

We are not big fans of animal milk. Milk accelerates aging in a myriad of ways.

Put very simply: nature made milk for calves to grow fast, and thus milk contains many substances that induce growth pathways, which are also strong aging pathways (like insulin, IGF and mTOR pathways).

But if you don't drink milk, and also don't consume that much cheese (after all, cheese is still an animal product, and many people cannot tolerate cheese, knowingly or unknowingly), you are at an increased risk of not taking in enough calcium.

Calcium is not only important for your bones but also for nerve conduction, brain

health and innumerable other processes in the body.

Therefore, one can take calcium supplements, around 1,000 mg per day, divided

over two doses, given taking too much calcium in one time can create a high calcium peak in the blood that might accelerate calcification of the blood vessels.

6. Iodine – Ideally Together With Selenium, In The Proper Form

Many people consume too little iodine. That's not good given iodine plays an important role in metabolism, immune system health and brain health. Too little iodine increases the risk of thyroid problems, metabolic problems and even the risk of breast cancer.

That's why governments make it mandatory to put iodine in bread. However, even this measure is not enough to get optimal iodine levels. Also, more and more people eat less bread (rightfully so) because it causes high sugar peaks, contributing to aging and aging-related diseases. So these people are especially vulnerable to iodine deficiency.

Therefore, you can supplement with around 150 ug (microgram) of iodine per day, ideally as droplets.

Iodine works together with selenium. Selenium intake has been associated with a reduced risk of cancer and Alzheimer's disease. However, this was found in studies that used selenium yeast and not selenium methionine – the selenium yeast supplements contain different forms of selenium.

So we would advise to take selenium yeast supplements, around 100 micrograms per day, along with your iodine.

7. Omega-3 Fatty Acids – With Low Totox Values



We currently have a pandemic of omega-3 fatty acid deficiency, contributing to an increased risk of heart disease, depression and other neuropsychiatric disorders, Alzheimer's disease, and macular degeneration (a very prevalent aging-related eye disease).

Omega-3 fatty acids reduce inflammation, enable the immune system to carry out its tasks, and help the brain and eyes to function properly.

Many governments recommend eating omega-3 containing fatty fish, two times per week. But that is often not enough.

Ideally, people would need to eat fatty fish four times per week, while also supplementing with omega-3 fatty acids, at least 1,000 mg of pure omega-3 (DHA and EPA) per day.

Make sure you buy high-quality omega-3 fatty acid supplements, meaning that the omega-3 fatty acids are pure and have not oxidized much (having low "TO-TOX" value).

8. Vitamin A – The Retinoid Form

Vitamin A is important for skin health, metabolism, our eyes, our bones, and even for stem cell maintenance.

There are a lot of misconceptions about the need of supplemental vitamin A.

Let us start with explaining there are two forms of vitamin A: vegetable “vitamin A”, called carotenoids, found in vegetables like carrots, pumpkin and kale.

The other form is animal vitamin A, called retinoids, found in animal products like liver.

Carotenes are converted in our body into retinoids, which carry out the many functions of vitamin A.

Some people claim that you do not need to take retinoids (animal vitamin A) because you can just eat lots of carrots, pumpkin and kale and the carotenoids will be converted into retinoids, the active vitamin A.

It's not that simple. Studies have shown that administering very high levels of carotenoids do not easily increase levels of retinoids. Also, carotenoid supplements have been associated with an increased risk of cancer (often because they only contain one or a few versions of carotenoids, inhibiting the absorption of other carotenoids), so we don't advise you take these.

Therefore, we would recommend taking a maximum of 2,500 units of vitamin A, in the form of retinyl palmitate.

Why a maximum of 2,500 units of vitamin A? Studies have shown that too much vitamin A can increase the risk of osteoporosis. But don't fret: in these cases, we're talking about at least 10,000 units of vitamin A per day. Also, vitamin D was not provided, which is needed to balance vitamin A metabolism.

9. Choline – An Often Misunderstood, Ignored Supplement

Choline is often called the “forgotten, fat-soluble B vitamin”. There are proponents and detractors of choline. Let us explain why.

Choline is a very important nutrient for the brain: it serves as a building block for acetylcholine, a neurotransmitter, and as a building block for parts of brain cell membranes.

But choline is also very important for epigenetic maintenance. The epigenome determines which genes are active or not, and the older we get, the more the epigenome becomes dysregulated (it's one of the reasons why we age).

Choline is also needed to prevent DNA damage. In fact, deficiencies in choline increase DNA strand breaks.

The important role of choline in DNA and epigenetic maintenance explains why choline is the only nutrient that quickly causes liver cancer when animals are given choline deficient diets (while also causing fatty liver disease or NASH, something many people suffer from in modern society).

However, some studies show that a higher choline intake is associated with an increased risk of heart disease. Choline is converted by specific gut bacteria into TMAO, which is an atherosclerotic substance.

But it's not that simple. For example, not all studies show that choline intake is associated with an increased risk of heart disease. Also, given choline is found in animal products (liver and meat) it's difficult to disentangle the effects of choline from other substances in animal products that can increase heart disease risk.

To make a long and complex story short: too little choline (as many people have) is far worse for your health (e.g. for DNA and epigenetic stability and maintenance, fatty liver disease and brain function) than the potential increased risk of heart disease.

We would recommend to take in at least 550 mg of choline per day. If you are really worried about choline, you can take half of that as choline and the other half as trimethylglycine (aka "TMG" or "betaine"), which is also an important substance for epigenetic maintenance.

Most choline supplements are choline bitartrate. However, some people do not tolerate choline bitartrate supplements well; for example, they may become tired when taking them. One explanation for this can be that bitartrate can have a negative impact on the gut microbiome (e.g., fueling growth of specific unhealthy yeast). In that case, one can take choline chloride or choline citrate.

10. Zinc – Not Too Much, Not Too Little

Zinc is an important mineral for proper immune system function, brain health and skin health, among many other effects. Ideally, one takes 10 to 15 mg of zinc per day.

Be careful, too much zinc can have negative effects so it's important to stay in this range.

Also, if you take zinc supplements, make sure you take copper, given zinc inhibits the uptake of copper.

11. Copper – The Sh(In)Y Friend Of Zinc

Copper is a somewhat underestimated nutrient, relegated to the back seat in the movie theater of minerals that play an important role in health.

However, more and more studies show the importance of copper to reduce the risk of heart disease and diabetes. Copper also plays an important role in

collagen production, skin health and skin appearance.

Ideally, one takes 2 mg of copper per day. Taking sufficient copper is especially important when you also take zinc supplements, given zinc inhibits the absorption of copper. People often take zinc, but they forget about copper.

Health Supplements Versus Longevity (“Anti-Aging”) Supplements



As we mentioned before, the supplements mentioned above are “health supplements”. These nutrients are needed by our bodies to function properly, and enable us to achieve a healthy lifespan. Deficiencies in these nutrients increase the risk of various diseases and can accelerate aging. They can increase median lifespan, given deficiencies can shorten lifespan.

Then there are also “longevity supplements”. These supplements go one step further than the healthy lifespan supplements, in the sense that they can extend maximum lifespan and slow down aging at its roots. These are ingredients like fisetin, alpha ketoglutarate, pterostilbene, NMN (nicotinamide riboside) and others. We explained their role in aging elsewhere.

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Do I Need To Take Supplements? And For The Rest Of My Life?



In the previous chapters, we talked about supplements. Some people will ask themselves if they need to take supplements their whole life.

This important question can be answered in two ways, pertaining to whether we mean longevity supplements or health supplements.

For longevity supplements, the longer you take them, the better. In this way, the

ingredients can continuously protect your cells and slow down the aging process.

For health supplements (mainly vitamins and minerals and other micronutrients - see earlier chapters) you also ideally need to take them your whole life.

But is that not contrary to what governments, various MDs and health experts say? They often claim that supplements are not necessary.

Let's start by saying that supplements are a complex matter. Ignorance and oversimplification are one important reason why there is so much conflicting advice.

We believe it's necessary to take supplements, and this for the rest of our lives.

Scientifically speaking, there are strong arguments for this:

- Human bodies are not very well made by nature (evolution) to get all the nutrients they need for optimal long health. For example, compared to fish, plants and most animals, humans are very bad at absorbing iron (iron deficiency has plagued humanity since its dawn). Humans are one of the very few animals that cannot make vitamin C themselves, and need to get it from their diet. Throughout evolution, our species have been plagued by deficiencies in many nutrients and minerals. Likely, our bodies are not well made to absorb all nutrients we need. This makes sense, given evolution mostly creates suboptimal, "made-do" designs, not optimal ones.
- And it's even worse. Today, we eat in a completely different way than our ancestors, meaning our diets are that much more deficient in nutrients. Prehistoric, pre-agricultural diets were much richer in many vitamins and minerals (but not in all – often, these diets could still lead to substantial deficiencies in specific nutrients, like iron or iodine, as we discussed before), compared to a typical western diet today, consisting of grains, meat and a bit of legumes at best.
- Our current lifestyles are also considerably different compared to prehistoric times: we live much more indoors, so we don't get enough exposure to the sun to produce vitamin D, for example. Alcohol consumption depletes levels of magnesium and B vitamins, smoking depletes antioxidants, stress depletes B vitamins and vitamin C, allergies and infections deplete vitamin A and zinc, etc. This requires us to have a higher intake of critical vitamins and minerals.
- Current methods of agriculture and shipment (long-term storage) of foods leads to much lower amounts of vitamins and minerals in our food (especially magnesium, selenium, copper, vitamin E, etc).
- The recommended intakes of most governments are in many cases (way) too low. They are based on suboptimal studies that last only for a short time to "detect" detrimental health effects, and do not look at [required amounts for a long, optimal life](#).^[1]
- Even when consuming the recommended doses of their government, or consuming a "healthy diet", people do not reach the levels needed for a long, healthy life.
- When we get older, our bodies become worse in taking up sufficient amounts of ingredients. Less gastric acid, aged skin, an aged gut, etc., cause less uptake and conversion of essential nutrients.
- Nature (evolution) is not really interested in us having a long lifespan. It's interested in getting us to reproduce as quickly and much as possible. We, as humans, on the other hand, want to live as long and as healthy as possible. So we need to take matters into our

own hands and make sure we take in sufficient amounts of nutrients for an optimal lifespan.

What further complicates this discussion, is that both proponents and detractors of supplements are wrong (and right).

The detractors will claim that many studies show that supplements don't improve health. The problem, however, is that many studies do not last long enough to detect an effect (for example, many studies only last a few months or years while Alzheimer's or heart disease take decades to arise). Additionally, in many studies researchers use too low doses of nutrients (e.g. 100 mg of magnesium instead of 500 mg of magnesium per day), or the wrong form (e.g. magnesium oxide instead of [magnesium malate](#)),^[2] or the wrong combination (magnesium needs calcium, potassium, omega-3 fatty acids to function properly), etc.

They will also say that if you eat healthy, you don't need supplements, but we explain [here](#)^[3] why this is not the case. Even if you eat healthy, it's very difficult to get adequate levels of magnesium, iodine or vitamin D for example, let alone high enough levels for optimal health.

The proponents of supplements on the other hand often look at supplements in a too simplistic way: they believe that taking magnesium or B vitamins will solve a lot of health problems, but often it's not that simple: people are often deficient in many other vitamins, minerals and micronutrients (like omega-3 fatty acids or [flavonoids](#)),^[4] and taking some extra vitamins and minerals will often not really solve the problem, which also needs to be tackled via a healthy diet, improving the microbiome, etc.

Additionally, supplement science is very complex: you need to take the right form, combination, dose, etc., of each nutrient. Often, the wrong form, dose or combination is advised.

In general, we do believe that it's important to take supplements, and this for your entire life. There are good scientific reasons for this. Deficiencies in important nutrients are rampant in society, reducing quality of life, eroding people's health in the long term, and accelerating aging.

However, governments and others oversimplify nutrients, often basing themselves on suboptimal studies and short-term data, which leads to a lot of confusion and misunderstandings – all at the expense of our long-term health!

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What's The Best Diet For Longevity – And For Losing Weight?



We talked about supplements to live longer. However, a healthy diet is also a very important pillar for a long, healthy life.

What's the best diet to stay younger and live longer?

There are countless diets. Which one should you choose?

For example, some of the more popular diets are the ones that advise to substantially reduce carbs, like the paleo diet, keto

diet or Atkins diet. There are diets that shun fats, like the Ornish diet, and you have high-fat diets that advise you to eat lots of fats. Then there are the strange diets, like the ones that tell you to mainly eat fruits or drink smoothies.

How do you see the forest from the trees with all these diets, which oftentimes contradict each other?

The Problem With Most Diets

The problem is that most diets don't look at the big picture, nor do they look at the long-term effects. Rather, they mainly focus on short-term results such as weight loss.

Most diets have "great" short-term results, such as weight loss and improved metabolic biomarkers (like lower triglycerides), but are unhealthy in the long-term and can actually accelerate aging.

The First Diet To Focus On Slowing Down Aging

Therefore, here we introduce a diet that approaches nutrition from an entirely new angle: aging.

We maintain that the best diet is a diet that slows down aging, with the aim of keeping you younger and healthier for longer.

Such a diet will automatically lead to weight loss, given a diet that slows down

aging is the most healthy diet possible, not only improving metabolism but also addressing the root cause of all aging-related diseases, which is aging itself.

Furthermore, approaching a diet from the viewpoint of aging enables us to better assess the long-term effects of specific foods and diets.

Long-Term Effects Of Certain "Healthy" Foods & Diets

Let's look at some examples of how insights into aging can help us to better see if certain "healthy" foods diets are really healthy in the long-term.

Take for example milk. Whether milk is healthy or not is a fierce debate that has been raging on for decades. There are studies showing milk is healthy, given regular milk consumption could, for example, reduce the risk of colon cancer^[1] (unfortunately many studies are directly or indi-

rectly funded by the dairy industry), while there are also many studies showing that milk is unhealthy, given it can increase the risk of prostate cancer,^[2] Parkinson's disease,^[3] and even increase mortality.^[4]

However, if you approach the milk discussion from an aging perspective, you can immediately see that milk is very likely unhealthy, especially in the long term, given that milk accelerates aging in many ways.

For example, milk contains substances that activate multiple powerful aging pathways, like mTOR, IGF and insulin receptors. The more you activate these receptors, the faster you age.

Milk also contains galactose, a substance researchers use to actually accelerate aging in their lab animals to study aging. [\[5\]\[6\]\[7\]\[8\]](#)

Also, milk is made by nature to make calves grow quickly. One prominent, red thread running through all aging research is that “accelerating growth” accelerates aging, and increases the risk of multiple aging diseases, like heart disease, cancer and Alzheimer’s.

Is High Protein Good Or Bad?



Another example are high-protein diets, like the classic paleo diet, Dukan or Atkins diet. Often, these diets result in substantial weight loss, improved insulin sensitivity, lower triglycerides and so on.

However, these are all short-term effects. If you consider these diets from an aging (biogerontological) viewpoint, one can

predict that these diets are very likely to accelerate aging in the long term.

For example, one very important mechanism that causes us to age is accumulation of proteins inside and outside our cells, a process that also plays a role in various aging diseases, like in Alzheimer’s disease or aging-related heart failure.

Consuming lots of animal proteins accelerates this process.

Activation of “nutrient-sensing pathways” in the cell by amino acids (like the mTOR receptor), accelerates aging. If you eat meat, you strongly activate these nutrient-sensing pathways.

Giving various species (including humans) lots of animal protein shortens their lifespan and increases their risk of aging-related diseases.

Too much animal protein accelerates aging, as hundreds of scientific studies have shown (just as too much sugar and too many unhealthy fats also accelerate aging).

What About The Keto Diet?

Another very popular diet is the ketogenic or keto diet. Like the paleo diet is also a very low carbohydrate diet (you eat little sugars and starches), but instead of lots of protein you consume lots of fats.

However, this is also not a good thing in the long term. Our bodies have difficulty in processing fats (after all, fats and our watery bodies don't mix well together).

Fats have the annoying tendency to stick everywhere around in our body, and are difficult to process and store. Many fats, especially long-chain saturated fats, can induce inflammation, for example by directly stimulating immune cells.

Nonetheless, some fats can be healthy, including even specific saturated fats (like butyric acid and caprylic acid). But it's not that most fats are healthy and that you can eat large amounts of fats (like some diet gurus claim), or that most fats should be shunned (as many governments want you to believe). It's more complicated than that.

Both the paleo and keto diet are capable of bringing people into ketosis (because very little carbs are consumed), but they achieve this in an unhealthy way. Ketosis is healthy, as long as it is reached by not eating high amounts of animal protein or fats, like when you are fasting.

The Mediterranean Diet



Then there is the Mediterranean diet. This diet promotes the consumption of vegetables, fruits, nuts, white meat and whole grains. This diet is healthy, especially if you compare it to the classical unhealthy western diet. However, it still puts too much emphasis on grains.

The paleo diet, keto diet and Mediterranean diet are a few examples of how insights into the aging process can help us to much better assess diets, especially in the long term.

Most Diets Are Unhealthy. Here's What You Should Do

The conclusion is that most diets are unhealthy.

However, based on insights into aging and nutrition, we created the “NOVOS Longevity Diet”. This diet aims to slow down aging and provide the best possible health outcomes for its followers. The weight loss will follow automatically.

This diet consists of **7 simple rules**:

1. Eat **much less bread, potatoes, pasta, and rice**.
2. Replace potatoes, pasta, and rice with (extra) **vegetables** (mainly), **legumes, mushrooms** or **quinoa**. **Replace bread** in the morning for example with oatmeal-, chia seed-, cauliflower- or chickpea porridge made with plant-based milk (e.g. hazelnut, cashew, almond milk).
3. **Vegetables are the base** of the NOVOS longevity diet. **Fruit, legumes, mushrooms**, and **quinoa** are healthy additions.
4. **Eat little or no red meat** (beef, pork, and sheep) and more fatty fish (salmon, mackerel, herring, anchovies, and sardines), poultry (chicken, turkey), mushrooms, tofu (miso, natto, tempeh), or mushroom-based or pea-based meat substitutes.
5. **Drink lots of water**, several cups of **green or white tea** per day, and one glass of freshly pressed fiber-rich fruit or vegetable smoothie. Coffee is allowed in moderation (maximum 3 to 5 cups per day). Use alcohol very sparingly (maximum one glass per day, including alcohol free days).
6. **Replace animal milk or yogurt** with low-sugar plant-based (e.g. hazelnut, almond, soy cashew) milk or yogurt. Cheese and eggs are allowed in moderation.
7. Take **smart health supplements**, such as selenium, vitamin D3, vitamin K2, B vitamins, magnesium malate, and iodine. Take **smart longevity supplements** (that contain alpha-ketoglutarate, fisetin, glycine, NMN, etc.), like NOVOS Core and NOVOS Boost.

As you can see, this diet is not an “extreme” diet, like a high-fat diet or high-protein (paleo) diet.

Nonetheless, the NOVOS longevity diet incorporates insights from these diets (like not drinking milk and consuming much less grains).

But it does not agree with other recommendations of these diets (like loading up with animal protein or fats, which is not healthy in the long-term).

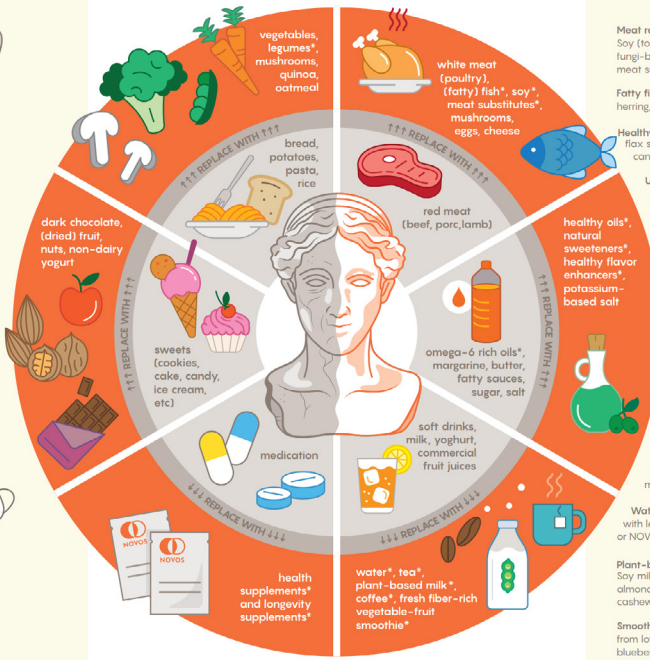
The best diet is one based on insights into aging, the fundamental causes of aging-related diseases like heart disease, Alzheimer's and cancer.

The 7 Simple Rules of a Longevity Diet

- 1** Eat much less bread, potatoes, pasta, and rice.

Replace potatoes, pasta, and rice with (extra) vegetables (mainly), legumes, mushrooms or quinoa. Replace bread in the morning for example with oatmeal / chia seed / cauliflower porridge / chickpea porridge made with plant-based milk (e.g. hazelnut, cashew, almond milk).
- 2** Vegetables are the base of the longevity diet. Fruit, legumes, mushrooms, and quinoa are healthy additions.
- 3** Eat little or no red meat (beef, pork, and sheep) and more fatty fish (salmon, mackerel), herring, anchovies, and sardines), poultry (chicken, turkey), tofu or fungi-based meat substitutes.
- 4** Drink lots of water, several cups of green or white tea per day, and one glass of freshly pressed fiber-rich fruit or a vegetable smoothie. Coffee is allowed in moderation. Use alcohol very sparingly.
- 5** Replace animal milk or yogurt with plant-based (soy, hazelnut, almond, cashew) milk or yogurt. Cheese and eggs are allowed in moderation.
- 6** Take smart health supplements, such as selenium, vitamin D3, vitamin K2, B vitamins, magnesium malate, and iodine. Take smart longevity supplements (like NOVOS Core and NOVOS Boost).

THE NOVOS LONGEVITY DIET



Legend

- Meat replacements:** Soy (tofu, miso, natto, tempeh), fungi-based or pea-based meat substitutes.
- Fatty fish:** Salmon, mackerel, herring, anchovies, sardines.
- Healthy oils:** Olive oil, flax seed oil, walnut oil, canola oil, perilla oil.
- Unhealthy omega-6 rich oils:** Corn oil, sunflower seed oil, palm oil, sesame oil.
- Healthy flavor enhancers:** Herbs and spices (turmeric, parsley, thyme, rosemary, basil, oregano mint), garlic, onion, lemon juice, vinegar (e.g. balsamic, raspberry).
- Healthy sweeteners:** Stevia, erythritol, tagatose, xylitol, applesauce, banana mash, monk fruit.
- Water:** Can be flavored with lemon, sage, thyme or NOVOS Core.
- Plant-based milk:** Soy milk, hazelnut milk, almond milk, coconut milk, cashew milk, etc.
- Smoothie:** Preferably made from low-sugar fruit like blueberries, blackberries, strawberries, as well as vegetables.
- Tea:** White tea, green tea, ginger tea, black tea, camomile tea.
- Coffee:** Maximum of 3-5 cups per day, no later than 6 hours before bed.
- Alcohol:** Maximum one drink per day; include alcohol-free days.
- Health supplements:** B vitamins, iodine, selenium, vitamin D, vitamin K2, magnesium.
- Longevity supplements:** NOVOS Core (containing folic acid, alpha-ketoglutarate, pterostilbene, glycine, etc.) and NOVOS Boost (containing NMN). Never change medication without consulting with your health-care provider.
- Calorie restriction & meal timing:** Eating 25% less extends lifespan. Try to eat 2 meals per day instead of 3 meals per day. Try to skip dinner. Attempt to go 12 - 16 hours without food each day (this includes time spent asleep).
- Exercise:** Try to exercise at least 4 times per week.
- Relaxation:** Regular meditation, yoga, prayer, self-hypnosis, or deep-breathing exercises.
- Social contact:** Spend time with family, friends, join clubs, do volunteer work.

Learn more about health, longevity and aging at NovosLabs.com. Download this brochure and send it to friends, family or anyone who could benefit from eating healthier at NovosLabs.com/longevitydiet

You can download a poster of the **novos Longevity Diet** on our website: [NOVOS-Longevity-Diet-poster](#)

You can stick this poster on your refrigerator, or email it to friends and family that you want to keep healthy!

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10

60 Top Tips To Live Longer, Doctor-Approved



How much are you doing to slow down your aging and maximize your lifespan and health span?

Lots of things contribute to the aging process, many of which will surprise you!

As the final chapter of this book, and to provide a quick snapshot of ways to slow down aging, we've put togeth-

er a list of more 60 tips to slow your aging and live longer, all backed by research.

Skim through it to see what you're already doing, and what will be easy for you to integrate into your daily routine.

I. Diet



1. Reduce your intake of animal protein, especially processed red meat such as sausages, salami, bacon, ham, hot dogs, paté, etc.
2. Replace red meat (e.g. beef, pork, mutton, veal) with white meat (poultry), fatty fish (e.g. salmon, herring, mackerel), and meat substitutes (based on tofu, pea, or mushroom protein).
3. Consume lots of vegetables, legumes, mushrooms, fruits, nuts, seeds. Vegetables should be the basis of your diet (not potatoes, pasta, rice and bread).
4. Reduce your intake of starchy, empty-calorie foods like bread, pasta, rice, and potatoes. Replace them more with vegetables, legumes, mushrooms or quinoa.
5. Avoid sugary foods and drinks as much as possible, like sodas, fruit juices, candy, cookies, sweets, cake, pastries, doughnuts, candy bars, chocolates and so on.
6. Avoid trans fats, which can be found in fried foods, fast-food, bakery products (e.g. crackers, cookies, cakes), and vegetable shortenings.

7. Significantly reduce your intake of omega-6-fat-rich foods, like corn oil, sunflower oil, safflower oil, margarine, sesame oil, mayonnaise and most salad dressings.
8. Consume more healthy fats, especially omega-3 fats, by consuming more olives, olive oil, walnuts, avocados, flax seed, chia seed, fatty fish and so on.
9. Consume foods that have come straight from nature and processed as little as possible, like foods your great-grandmother would recognize.
10. Consume a daily, freshly-made smoothie with vegetables and low-glycemic index fruits, like blueberries.
11. Eat specific foods that can slow down aging: green leafy vegetables (broccoli, spinach, kale), blueberries, dark chocolate (containing at least 70% cacao), salmon, walnuts, pomegranate, etc.
12. Don't drink milk – milk accelerates aging.
13. Don't drink too much alcohol: that means maximum one glass per day, ideally with alcohol-free days.
14. Hardly drink any sugary drinks (such as soda, commercial fruit juices, etc).
15. Hydrate a lot. Drink at least 1.5 of liters per day: that's 8 glasses per day.
16. Drink lots of water. Drink green tea, white tea, ginger tea or coffee (yes, coffee can reduce the risk of various aging-related diseases). Add spices (e.g. mint), citron or NOVOS [Core](#) to add taste to your water.
17. Don't take whey protein, testosterone or growth hormone. They all accelerate aging in the long term.
18. Don't [follow unhealthy diets](#) – most diets are unhealthy unfortunately.
19. Don't follow a paleo diet or high-protein diet: these diets accelerate aging in the long term, despite having beneficial effects in the short term (like weight loss).
20. Don't follow a keto diet (ketogenic diet) or high-fat diet: these diets accelerate aging in the long term, despite having beneficial effects in the short term (like weight loss).
21. Follow the NOVOS [Longevity Diet](#).
22. Eat less calories, less often. Try to eat two meals a day, with breakfast being the most important meal of the day.
23. Fast regularly. Eat within a 12 hour period, so your body can fast for 12 hours. Fast for ideally 3 days a few times per year, like at the start of every new season.

II. Supplements



- 24.** Take health supplements, like vitamin D3, vitamin K2, iodine, selenium, magnesium, B vitamins, and minimally-oxidized (low TOTOX) omega-3 fatty acids. You can find here the most important health supplements [here](#).
- 25.** Take longevity supplements like NOVOS [Core](#) which contain substances that scientifically have shown to slow down aging or increase lifespan, like alpha-ketoglutarate, fisetin, pterostilbene, microdosed lithium, etc.
- 26.** Don't take antioxidants beyond what you find in a healthy diet: most antioxidants don't extend lifespan and some can even shorten lifespan and increase the risk of cancer (learn more [here](#)).
- 27.** Consider taking drugs that could slow down aging, like metformin, low-dose rapamycin, low-dose (baby) aspirin, or selegiline. Always discuss with a physician experienced in this matter.

III. Exercise



- 28.** Engage in anaerobic exercise (like weightlifting)
- 29.** Do aerobic exercise (like running or swimming).
- 30.** Do high-intensity interval training (HIIT).
- 31.** Commit to stretching and posture exercises, like pilates.

IV. Sleep



- 32.** Take care of your sleep. Make sure you sleep enough and go to bed around the same time. You can find more than 50 tips to improve your sleep [here](#).
- 33.** Buy sleep aids, like an [Oura ring](#), [Dreem headband](#).
- 34.** Download sleep and relaxation apps, like Calm, Buddhify, Headspace or Insight Timer (the latter being free).
- 35.** If you are older than 50 years, use 500 ug (0.5 mg) to max 1000 ug (1 mg) of extended-release melatonin before going to sleep. Melatonin can also extend lifespan and slow down aging.^[1]

V. Tracking



- 36.** Reduce your blood sugar levels. Buy a continuous glucose sensor to track how your body processes sugars based on foods, sleep, etc. If that's out of your budget, consider a regular blood glucose monitor, available at your local drugstore.
- 37.** Measure your heart rate variability (HRV), which can be predictive of health and mortality. Improve your HRV via HRV biofeedback devices, like HeartMath and Sweetwater HRV.
- 38.** Get regular health checkups. Prevention is key!
- 39.** Track your [facial age](#).
- 40.** Assess your [overall health](#).

VI. Lifestyle



- 41.** Protect your skin very well against the sun: always wear strong sunscreen, and a hat when going outside in the sun.
- 42.** Use high-concentration retinol creams (over-the-counter) or Retin-A (aka “tretinoin”, prescription) for your face.
- 43.** Take supplements that slow skin aging and reduce wrinkles.
- 44.** Brush and floss your teeth at least twice per day.
- 45.** Always wear your seatbelt.
- 46.** Don’t smoke.
- 47.** Do yoga.
- 48.** Don’t be overweight and make sure you don’t have too much abdominal fat (a beer belly). Measure your waist circumference here and calculate your BMI (body mass index) here.
- 49.** Schedule everything.

VII. Mindset



50. Try to be positive and always see the silver lining in things. Most centenarians have a very optimistic disposition.
51. Learn how to be happy.
52. Reduce stress.
53. Practice meditation. Download meditation apps like Calm or Headless.
54. Having a purpose and goals in life (feeling useful).
55. Be social.
56. Challenge your mind every day.
57. Use medication sparingly: most drugs have significant side effects.
58. Use blue-light blocking glasses 30 minutes before going to sleep.
59. Keep a gratitude journal.
60. Be an empowered health advocate for your own body: don't just rely on the health care system to keep you healthy.

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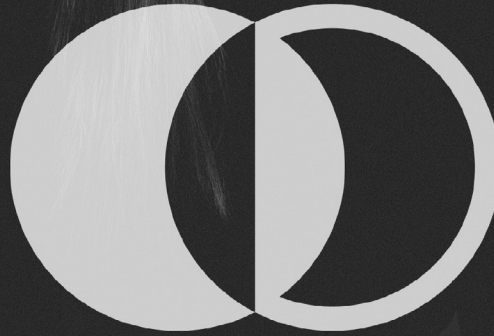
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He is a partner at a \$100 million fund that invests in new technologies to address aging.

He wrote his first science book when he was 16 years old, and by age 28 he had written four science books.

His latest two books address health, longevity and new developments in biotechnology. Since a young age, Kris has given talks on health, longevity, and new developments in medicine and biotechnology for various organizations and institutions, including the European Parliament, Google, Cambridge University, King's College, TEDx, and large international companies.