**Single Dose of Rapamycin Induces Weight Loss**

I’ve talked to several people who take rapamycin for anti-aging purposes, and they’ve all reported that they lost weight when they started taking it. It appears that even a single dose of rapamycin induces weight loss, in lab animals.

**Rapamycin alleviates obesity**

A relatively low, intermittent dose of rapamycin alleviates obesity in aged rats. (Ref) Rapamycin lowers levels of leptin, the satiety hormone, by lowering body fat.

The response to rapamycin appears to be related to its peripheral inhibition of mTOR, since injecting it directly into rats’ brains had little effect. (Ref) The authors state,

“We speculate that the mechanism underlying these anorexic responses to peripheral rapamycin may be due to an initial peripheral action that communicates a signal to the hypothalamus that triggers an anorexic response to reduce food consumption.”

**Single dose of rapamycin has long-lasting effects**

Here’s where it gets really interesting, in my view: “Single Rapamycin Administration Induces Prolonged Downward Shift in Defended Body Weight in Rats”. (Ref) In this study, a single injection of rapamycin induced body weight loss that lasted at least 10 weeks, without further rapamycin administration.

The authors state it in terms of the rats defending a lower body weight set point.
The study found:

- rapamycin did not induce illness or malaise, important because if it did, that could account for weight loss
- rapamycin does not affect glucose tolerance, important because daily rapamycin does so
- rapamycin-treated animals had lower levels of body fat, although there’s no data for lean mass.

A brand new study shows that a single injection of rapamycin “blocks post–food restriction hyperphagia and body-weight regain in rats.” (Ref) When rats were food restricted and lost weight, rapamycin prevented weight regain.

These studies have obvious implications in obesity.

**Obesity and aging**

What’s perhaps more interesting is what rapamycin implies for the relation between obesity and aging.

As I’ve said many times, obesity and aging are two sides of the same coin. Obesity is aging in miniature; obesity promotes aging.

The converse is that aging promotes obesity. Older animals, including humans, are more likely to gain body fat, as well as lose muscle. The fact that rapamycin both extends lifespan and promotes lower body fat is telling, and agrees with observations on obesity and aging.

Body composition, that is, the relative proportions of lean mass to fat mass, are a solid target to slow aging.

And of course, diet, exercise, and other factors also affect body composition.

Perhaps mTOR, the mechanistic target of rapamycin, is critical to obesity. (Wouldn’t surprise me.)

Could rapamycin become a once-weekly anti-obesity drug?

A prominent scientist in this field, Matt Kaeberlein, has said that, in proper doses, rapamycin may be safer than aspirin. However, there’s no money in promoting rapamycin, since it’s off patent.

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**PS:** I’m writing less frequently here, most of my writing energy going into my email list, to which I write daily. If you want to get regular updates from me, subscribe to my email list.

**PPS:** Fight aging by losing fat. Find out the best way to lose fat
with The World’s Simplest Fat Loss Plan.

Insulin Promotes Cancer

Many people, perhaps most, think that cancer is just something that strikes. That there’s little you can do about avoiding it — other than not smoking cigarettes. That is not the case, since there’s a link between insulin and cancer, and we can control insulin levels.

Associations between insulin and cancer

People who are in the highest quintile (fifth) of insulin levels have a 62%

The above chart shows survival in terms of death from cancer in people in the top quintile (fifth) of fasting insulin, vs quintiles 1-4. You’re much more likely to die from cancer if you have high insulin. The association was even worse for GI cancer.

This doesn’t prove that high insulin causes cancer, but it’s quite suggestive. We know that obesity and diabetes are associated with higher cancer risk, and insulin may very well be why.

Diabetics have about double the risk of cancer. ([Ref](#)) That’s compared to the rest of the population, most of whom either have metabolic syndrome, are overweight or obese, are skinny fat, and in general likely to have metabolic problems. What’s the risk of cancer compared to people with healthy metabolic control?

Laron dwarfism may provide some clues.

In people with Laron dwarfism or other forms of growth hormone or IGF-1 defects, none of the IGF-1 deficient people had cancer, whereas 9-24% of their relatives had a history of cancer. ([Ref](#)) This refers to deficiency of IGF-1, or insulin-like growth factor 1, not insulin itself, but the two are closely related, with a correlation between the two of 0.58 in obese people. ([Ref](#))

Seems at least possible that if no insulin, then no cancer.

Obesity greatly increases the risk of colon cancer, and “insulin resistance and type II diabetes loom large in the theoretical framework that connects obesity and colon cancer.” ([Ref](#))

There’s a 20-fold difference in colon cancer rates between low and high
All of this evidence points in the direction of higher insulin increasing risk for cancer.

Ideally, we’d like to see an experiment in which lowering insulin, without doing anything else, means less cancer.

**Experimentally lowering insulin**

Such an experiment has now been done, in mice, for the first time. (Endogenous insulin contributes to pancreatic cancer development Anni MY Zhang, et al. bioRxiv 530097; [Link](#))

Mice were genetically engineered to have lower insulin, and they had 50% fewer precancerous lesions in the pancreas. This is highly suggestive. Makes sense too, since insulin is a growth factor and cancer is runaway growth.

“Collectively, our data indicate that endogenous insulin hypersecretion contributes causally to pancreatic cancer development. This suggests a modest reduction in fasting insulin via lifestyle interventions or therapeutics may be useful in cancer prevention.”

Cancer cells require insulin, and they have a high density of insulin receptors, so they can get all their primary fuel, glucose, from the blood.

**A high insulin and high cancer environment – ours**

We live in a high insulin environment. Food that’s loaded with sugar and refined grains is everywhere, and in abundance.

More than 70% of Americans are overweight or obese, which means many of them have high insulin.

Being sedentary also means higher insulin. Exercise lowers insulin resistance, which translates to lower insulin.

So, to lower your cancer risk overnight, lead a low insulin lifestyle.

You do that by avoiding ultra-processed foods, by exercising, and by practicing intermittent fasting.

And of course, getting or staying lean and muscular. (Although normal body fat and muscle percentage are different for women, the same applies to them too.)

Get and stay lean with [The World’s Simplest Fat Loss Plan](#).
Get and stay lean and muscular with **One-Hour Fitness: How to Get Lean, Muscular, and in Great Cardiovascular Shape in One Hour a Week or Less.**

And lower your cancer risk.
The Israeli Paradox

Probably most of you have heard of the French paradox.

The idea is that the French eat all kinds of saturated fat in their food, yet have a low rate of heart disease. Second lowest in Europe actually, after Switzerland, and the Swiss eat even more saturated fat than the French.

If you’ve been following my writing for a while, you know what I think about the French paradox: it’s B.S.

You don’t need to explain low rates of heart disease among the French because saturated fat doesn't cause heart disease.

So, the fact that the French drink wine, while probably relevant to their low heart disease rates, doesn’t counter their fat intake, because it doesn’t need countering.

The amount of resveratrol in their wine is too low to matter as well.

Anyway, there is another paradox which, well, when you look at it, is less of a paradox than you might think.

That’s the Israeli paradox.

Here it is:

1. Israel has one of the highest consumption rates of omega-6 fatty acids in the world. These fatty acids are abundant in vegetable (seed) oils, and the Israelis consume a lot of it.
2. Vegetable (seed) oils are good for you – allegedly.
3. The Israelis suffer from a high rate of heart disease, hypertension, type 2 diabetes, and cancer.
That’s a real head scratcher, according to mainstream health authorities, who tout seed oils as being uber-healthy.

But the paradox disappears when you just forget the idea that seed oils are healthy.

Of course the Israelis have high rates of chronic disease. If they used animal fats and/or olive oil in place of seed oils, they would be a whole hell of a lot healthier. (Yam, Daniel, Abraham Eliraz, and Elliot M. Berry. “Diet and disease—the Israeli paradox: possible dangers of a high omega-6 polyunsaturated fatty acid diet.” Israel Journal of Medical Sciences 32.11 (1996): 1134-1143.)

To quote the authors of the cited article, “Thus, rather than being beneficial, high omega-6 PUFA diets may have some long-term side effects, within the cluster of hyperinsulinemia, atherosclerosis and tumorigenesis.” Seed oils can give you heart disease, cancer, and diabetes.

When does anyone ever say that?

There’s only a few of us out here saying it, like voices in the wilderness.

Vegetable oils, which are better termed industrial seed oils, are made by modern manufacturing techniques from seeds that generally contain little oil.

Soybean, corn, safflower, sunflower, cottonseed, and others are all industrial seed oils.

And you should avoid them like the plague.

Seed oils like these are also implicated in obesity.

So, if you’re trying to lose some body fat, ditching seed oils is a great thing to do.

Unfortunately, the modern food supply is drenched in seed oils.

They’re in virtually all ultra-processed foods – the packaged foods in boxes and bags that you can buy in the middle aisles of the supermarket. The stuff that Big Food manufactures.

Virtually all restaurants cook with them too.

What to do about it?

Avoiding seed oils is just one of the helpful rules used in my fat loss plan. Grab a copy of The World’s Simplest Fat Loss Plan for hunger-free fat loss.
Podcast with Craig James

I recorded a podcast with Craig James of Masculine by Design. Craig is a great interviewer and came to the podcast with great questions. Head over to his site to download an audio version of this podcast. We discussed, in Craig’s words, “nutrition, training, anti-aging, supplementation and all things related to maximizing a man’s quality of life for whatever age he happens to be.”
Is Metformin Really an Anti-Aging Drug?

The anti-diabetic drug metformin is widely touted as a drug that fights aging, which would be great if true. It’s cheap and appears to be very safe, it’s been prescribed for diabetes for decades and has been studied extensively. But is metformin really an anti-aging drug? There are some reasons for skepticism.

Metformin inhibits exercise adaptations

A study just published in Aging Cell reports that metformin blunts the benefits of exercise training: Metformin inhibits mitochondrial adaptations to aerobic exercise training in older adults.

Participants, average age 62, were randomized to either metformin or placebo, and undertook aerobic exercise training for 12 weeks.

In the metformin group, there was no overall change in whole-body insulin sensitivity after AET due to positive and negative responders. Metformin also abrogated the exercise-mediated increase in skeletal muscle mitochondrial respiration. The change in whole-body insulin sensitivity was correlated to the change in mitochondrial respiration... The influence of metformin on AET-induced improvements in physiological function was highly variable and associated with the effect of metformin on the mitochondria. These data suggest that prior to prescribing metformin to slow aging, additional studies are needed to understand the mechanisms that elicit positive and negative responses to metformin with and without exercise.

In some ways, this isn’t a surprise, since it’s already known one way in which metformin works is by inhibition of Complex 1 in mitochondria. (Ref) By inhibiting mitochondria, the powerhouses of the cell, less ATP is formed, which activates AMPK, an energy sensor. In turn, AMPK activates many processes that contribute to better metabolism, including lower insulin and glucose and increased fat burning.

The blunting effect of metformin on exercise was not small either. Increase in VO2max in the metformin group was only about 50% that of the placebo group. The improvement in whole-body insulin sensitivity in the metformin group was zero, compared to a significant increase in the placebo group.

Some caveats: the metformin group took 2,000 mg daily, which is a full, anti-diabetic dose. All participants were not diabetic but had at least one risk factor for diabetes.
Since cardiopulmonary fitness is one of the strongest factors for survival into old age, and since it decreases with age, the effect of metformin on this factor is concerning.

So, what gives? Is metformin healthy and anti-aging, or not?

The relation between obesity and aging

Other studies have shown that metformin extends lifespan in lab animals (rodents), and has apparently healthy effects in humans. A clinical trial of metformin as an anti-aging drug is planned.

For example, Metformin improves healthspan and lifespan in mice. This paper’s authors include some highly regarded names in the study of aging, including David Sinclair, Rafael de Cabo, and Stephen Spindler.

The problem with this study is that the authors appear to believe that diet has no effect on the health of lab animals.

If you give animals lab chow, which has been aptly nicknamed “crap in a bag”, and you confine them to cages, they become unhealthy. That shouldn’t be a surprise, since they’re eating a highly unnatural diet of ultra-processed food, equivalent to eating pizza and drinking soda pop for every meal; the cages also ensure that they don’t get adequate physical activity.

Then there’s the psychological factor of being confined in a cage, away from a natural habitat.

Here’s the food that the scientists gave these mice, AIN-93G:

This stuff is basically sugar and seed oils, soybean oil, and a few vitamins and minerals.

Of course metformin is going to extend their lifespan.

Metformin helps diabetics too. That doesn’t mean it will help healthy people.
The scientists who performed this study seem blissfully unaware that feeding their animals garbage virtually invalidates the idea that metformin slows aging or extends lifespan.

Another study, this one with the also celebrated name of Vladimir Anisimov as the first author, found “If started early in life, metformin treatment increases life span and postpones tumors in female SHR mice”. The only mention of diet is “standard laboratory chow”, which means something similar to, if not identical with, the garbage food shown above.

In the wild, mice eat seeds, fruit, and insects, not lab chow. Metformin may not do a thing for mice in their natural habitat, and in any case, it hasn’t been tried.

The reason that scientists have been so quick to see metformin as an anti-aging drug is because (IMO) of the seemingly close relation between obesity and aging.

As people get older, they gain body fat, lose muscle, and develop insulin resistance. This is very similar to the effects of eating junk food and not exercising.

But is that aging, or is it something else.

Many humans living in natural environments, i.e. hunter-gatherers, do not gain fat with aging, or develop insulin resistance or hypertension. These health problems appear largely to be an artifact of living in the modern world.

In humans, the insulin resistance of aging is more closely associated with abdominal adiposity than with aging.(Ref.)

Likewise, lab animals also gain fat and develop insulin resistance as they age. See chart below. (Source.)
Lab rats are fully mature at 5 to 6 months of age, yet in labs they gain weight consistently with age. That seems highly unlikely in the wild.

Lab conditions make animals fat and sick.

**Calorie restriction does not extend the lifespan of wild mice.**

We see that there’s a strong resemblance between aging, or what we think of aging, to obesity and insulin resistance, but these may be merely the effects of the modern world.

if you give metformin to overweight, insulin resistant people and animals, it improves their health and increases their lifespan.

But does metformin do anything to improve the health and increase the lifespan of already healthy people? Would it enable Okinawan centenarians or Kitavans or humans doing calorie restriction to live longer? That seems doubtful to me.

One study looked at the difference between diabetics on metformin vs non-diabetics who did not take it: [Can people with type 2 diabetes live longer than those without? A comparison of mortality in people initiated with metformin or sulphonylurea monotherapy and matched, non-diabetic controls.](#) It concluded:
Patients with type 2 diabetes initiated with metformin monotherapy had longer survival than did matched, non-diabetic controls.

Case closed? No, not by a long shot. **At least 88% of the population is metabolically unhealthy.** In a group of people matched by age and other characteristics to diabetics, we could expect that they would be nearly 100% metabolically abnormal.

So the matched group could have benefited from metformin too. That does not show that metformin fights aging.

**Key to longevity: insulin**

The plausible connection of metformin to longer lifespan is due to its ability to lower **insulin, which is crucial to long life and health.**

*Insulin represents a conserved evolutionary mechanism of aging.* Keeping insulin low prolongs lifespan.

If your insulin is already low – **and mine is** – metformin very likely won’t lower it further. Plus, as we saw, metformin abrogates the benefits of exercise.

To see whether and how much diet matters to aging, let’s look at a simple organism in which quality of diet may not make a lot of difference: yeast. They feed on sugar.

*Enhancement of mitochondrial function correlates with the extension of lifespan by caloric restriction and caloric restriction mimetics in yeast.* This study showed that calorie restriction and rapamycin extended the chronological lifespan of yeast, but **metformin did not.**

Since yeast do not become obese or insulin resistant, metformin doesn’t extend their lifespan.

If you are not obese or insulin resistant, then perhaps metformin will not extend your lifespan.

**The main point**

We saw in the first study that metformin blunts the benefits of exercise. Therefore metformin has risks as well as benefits. It is not cost-free.

The close relation between obesity and aging means that it’s difficult to separate the effects of one from the other.

If you are lean, have low fasting insulin, exercise regularly and have a high VO2max, and do not eat ultra-processed foods made of refined grains, sugar, and seed oils, then it appears that any benefit of metformin would be minimal to none. Yet metformin has downsides.
In my opinion, it’s far too early to conclude that metformin fights aging.

Metformin fights the ill effects of the modern age to be sure, and probably a very high percentage, >90%, of the older population might benefit from it.

But that’s because they’re overweight, out of shape, and eat junk food, not because they’re old.

If insulin resistance does increase to some extent solely because of aging, then perhaps only very old people would benefit from it.

The rest of us should exercise and live healthy lifestyles.

The science of aging, or anyway the scientists of aging, pay little attention to healthy lifestyles and right diet. They seem to believe that feeding their animals garbage and confining them to cages is sufficient to study the process of aging.

It isn’t. They’re only studying the modern conditions that make people ill.

**Update:**

On further research I found a study from 2010, “Metformin Supplementation and Life Span in Fischer-344 Rats”, of which the abstract states:

> Calorie restriction (CR) has been known for more than 70 years to extend life span and delay disease in rodent models. Metformin administration in rodent disease models has been shown to delay cancer incidence and progression, reduce cardiovascular disease and extend life span. To more directly test the potential of metformin supplementation (300 mg/kg/day) as a CR mimetic, life-span studies were performed in Fischer-344 rats and compared with ad libitum feeding and CR (30%). The CR group had significantly reduced food intake and body weight throughout the study. Body weight was significantly reduced in the metformin group compared with control during the middle of the study, despite similar weekly food intake. Although CR significantly extended early life span (25th quantile), metformin supplementation did not significantly increase life span at any quantile (25th, 50th, 75th, or 90th), overall or maximum life span (p > .05) compared with control.

What’s different about this study? The diet they gave the rats was much better:
While this diet isn’t perfect by any means, it’s a lot better. It contains no sugar, lots of whole, fibrous grain – which mice would be expected to eat in the wild – and a slightly lower amount of seed oils. It contains no casein, which is milk protein, and mice are not likely to eat much of that in the wild either. Fish meal ensures some omega-3 fatty acids.

The study says that “the type of diet used in the current study (NTP-2000) was optimized for health and longevity benefits”.

The discussion sections contains a lengthy list of possible limitations to the study, such as too low of a dose, the particular rat strain used, and lack of a robust calorie restriction response. Nevertheless, metformin did not extend the lifespan of these rats, and that was even despite metformin-treated rats weighing less than controls at almost all time points in the experiment.

This study adds further evidence to the idea that metformin protects against a bad diet and unhealthy lifestyle, but doesn’t extend lifespan under healthy conditions.

By the way, this rodent diet contains 4 times the amount of iron necessary.

(Advertisement)

My new fitness plan is just out. Get fit in one hour a week. Go ahead and grab a copy of One-Hour Fitness: How to Get Lean, Muscular, and in Great Cardiovascular Shape in One Hour a Week or Less.
Can Ketogenic Diets Work for Bodybuilding or Athletics?

Can ketogenic diets work for bodybuilding or athletics? This is a question I’m very interested in, and one that is probably the last stumbling block for many interested in very low carbohydrate ketogenic diets. Raphael Sirtoli, a neuroscientist who works in Portugal, and the founder of Nutrita.app, wrote this article especially for Rogue Health and Fitness. When I was discussing the article with him ahead of time, I didn’t realize he’d produce such a brilliant and comprehensive account of the science behind ketogenic diets, athletics, and muscle. A real tour de force and by far the best thing I’ve
ever read on this topic.

**Intro**

When a person fuels themselves with much more fat than glucose they enter into the metabolic state known as ketosis. As an energy source, fat combusts with oxygen to make ATP in mitochondria (via oxidative phosphorylation) and glucose ferments in the absence of oxygen to make ATP in the cytoplasm (via glycolysis).

Ketosis is a normal metabolic state for humans to be in. You can be in ketosis in a variety of scenarios; when pregnant, as a breast-fed infant, or as an adult when fasting intermittently (and especially if on a low-carb high-fat diet). There’s even post-exercise ketosis that happens when you exercised hard enough to extensively deplete glycogen. And of course ketosis happens when fasting or starving. It’s physiological (normal) in the former and pathological (abnormal) in the latter.

So being in ketosis is normal. A weight-stable person eating a standard ketogenic diet consisting of something like salmon, eggs, coffee and a kale salad can pump out about 185 g of ketones a day from their liver (specifically the ketones beta-hydroxybutyrate and acetoacetate) [1].

But being out of ketosis is normal too.

Humans regularly drop out of ketosis from short bursts of explosive activity which momentarily raising their blood sugar and glucocorticoids. Most commonly though, people leave ketosis after eating a couple of baked potatoes or some fruit. The reason is that insulin rises enough in the absence of sufficient glucagon, switching you from burning fat and making ketones to metabolizing the glucose from those baked potatoes — your body hasn’t evolved to do both at the same with food.

So if both ketosis and not-ketosis are normal metabolic states to be in, which one should an athlete choose when trying to perform at their best? Should it be constant ketosis? No ketosis ever? Or ‘targeted’ ketosis, a la ‘train low (carb), compete high (carb)?’

Let’s look at data on endurance, high-intensity efforts and body composition.

**Endurance**

**Study 1**

Let’s start with mice put on an ad lib 8-week ketogenic diet (76.1% fat, 8.9% protein and 3.5% carbs) or a control diet (7% fat, 17.8% protein and 64.3% carbohydrate) [2]. Note that the control mice are getting nearly twice as much protein than the keto mice are. On the ‘time to exhaustion’ task, eyeballing the graph suggests that the keto mice lasted a just under 300
minutes whilst the control mice ~240 min. That’s a 20% difference, not bad!

We don’t know about the quality of their diet although it was probably terrible (e.g. seed oils, grain flour). But we do know that, at rest, the keto mice had 2.4 mmol/L of blood BhB and the controls had 0.29 mmol/L. However, the control mice showed post-exercise ketosis with blood BhB levels climbing to 2.8 whilst levels dropped to 0.72 mmol/L in the keto mice. Interestingly, the authors noted that the ketogenic mice appeared somewhat protected from acute liver and kidney injuries, as measured by BUN, ALT and AST right after they stopped exercising.

I can already hear the Calories In-Calories Out choir singing about how the performance difference came down to body weight. It didn’t.
Let's now jump to a human keystone study from 2015 by Volek et al. [3]. The design is simple: get 20 male endurance freaks who habitually eat a standard high-carb diet or a ketogenic one. Just before they hop on the treadmill to keep a pace of about 65% of their VO2 max, give the keto folk a keto shake (81% fat, 14% protein and 5% carbs) and the controls a standard shake (50% carbs, 14% protein and 36% fat). The first result is this beautifully crisp difference in maximal fat oxidation rates (g/min). The most fat burning carb burner can’t burn as much fat as the least fat burning fat burner.
By the way, this data required exercise physiology textbooks to update the higher maximal fat oxidation rates. It also shows that you can still burn a fair bit of fat at high intensities. Another exercise physiology dogma that falls.

What we also see is that the keto guys are burning *proportionally less* glycogen and *less absolute* amounts of glycogen overall. So is it that these keto guys *don’t need* all that glycogen or is it that they actually *can’t use* it like their counterparts can? The answer to that question is key to discerning whether or not low-carb diets are appropriate for high-intensity efforts. We’ll get to that in a bit.

Funnily enough, muscle glycogen content between the controls and keto guys was the same, both before and after exercising. I like the individual data points because they reveal the counterintuitive fact that some keto folk can have more replete glycogen stores than people eating lots of carbs.
Even back in 2004 it was known that post-exercise ‘carb-loading’ to recover faster by replenishing glycogen probably didn’t work [4]. Funny how ‘industry trends’ can give researchers amnesia...But Fournier et al. reminds us that “during recovery from exercise, it is possible for skeletal muscles to replenish their glycogen stores under conditions expected to be highly unfavourable to glycogen synthesis such as fasting or active recovery. The rates of muscle glycogen synthesis can be very high under these conditions [...] This capacity of skeletal muscles to replenish their glycogen stores under extreme conditions is clearly advantageous as it allows muscles to maintain adequate levels of glycogen stores for fight or flight responses”

If you use an evolutionary lens (or common sense), this ability to replenish glycogen without carbs isn’t surprising given the following: we evolved as apex predators subsisting on lots of animal foods without access to sugary sport gels at all times. That being said, maybe carb-loading does have a performance benefit. It’s probably not because of any supposed glycogen loading repletion effects from carb-loading but rather from the fact that carbs are ergogenic aids. Evidence this fact comes from experiments showing performance benefits in athletes whether who just tasted the sugary drink or drank it [5, 6]. This effect isn’t always reproducible however [7, 8].

### Study 3

We have talked about athletes, but what about non-athletes exercising on a keto diet? This 8-week study advised severe calorie restriction of about 30% to the 60 obese men and women that were asked to either follow a keto diet unusually high in protein (61% fat, 35% protein and 4% carbs) or a high-carb control diet (46% carbs, 30% fat and 24% protein) [9]. We don’t know what either group actually ate unfortunately. The keto group were only mildly ketotic by week 2 with 0.49 mmol/L blood BhB. After 8 weeks, during maximal exercise the keto group’s average RER stayed above 1. Clearly they’re still using carbs well. During sub-maximal exercise however their RER dropped from 0.84 to 0.77, indicating a good bit more of fat burning. The high-carb group didn’t improve their fat burning capacity with an RER of 0.81.

Both groups had their grip strength, maximal knee extensor strength, time to exhaustion on a graded treadmill, weight loss and metabolic markers taken before and after the 8 weeks. Both groups basically fared the same but for a few metrics. The keto group lost more weight, 8.4 kg vs the 6.7 kg of the high-carb control. No surprise there. Both groups gained leg strength but lost grip strength.

RERs lowered in the keto group but not in the high-carb group, and the keto group lost more weight. The keto group lost 8.1 kg (of which 6.1 kg or 75% was from fat) versus 6.7 kg in the high-carb group (of which 5.1 kg or 76% was from fat). The takeaways here are that:

- if you’re obese and wanting to lose weight, a 30% restriction of calories is unsustainable and excessive given how it worsens grip strength. Grip strength is a decent mortality predictor of all-cause mortality, with hazard ratios of 1.96 (1.30-1.52) with a 95% confidence
• if you’re obese and wanting to lose weight, a keto diet on the higher protein side of things is a good idea
• it’s a good bet that a resistance training protocol instead of treadmill walking could’ve improved their ratio of fat-to-muscle weight loss

So it’s clear that humans can perform very well in endurance events on keto. Better levels of fat adaptation that cannot be reached on high-carb diets may even turn out to be advantageous. But what about shorter-duration higher-intensity efforts?

**High-intensity**

**Study 4**

15 male and female Crossfitters with very little experience in the sport (3 months) were fed a keto or higher-carb control diet for 6 weeks [11]. There were no notable differences between both groups except for mean power output; it increased beyond significance for the controls from 8.24 to 8.7 W/kg but not for the keto folk. It’s hard to interpret this difference since both groups did equally well on all other ‘power’ tests like the 500m row, Wingate Anaerobic Test and 3-repetition maximum (3RM) deadlift). The authors, however, conclude the following:

“A 6-week ketogenic diet did not affect the performance of short-duration high-intensity exercise. Our data does not support the hypothesis that ketogenic diets induce detriments in the performance of activity that is anaerobic in nature. The current study took place over a 6 week period, allowing for keto-adaptation to occur; results may be different if a shorter time period were utilized”

Full-text wasn’t published as of 15/12/2018 so it doesn’t count for anything yet. However, it would be consistent with the majority of anecdotal reports around keto and Crossfit.

The nocebo effect (your health worsens from negative expectations) is the opposite of the placebo effect (your health improves from positive expectations). I think the nocebo effect from no longer having carbs you believe you need is significant and underappreciated. Additionally, the supposedly positive effects of glycogen loading are likely exaggerated.

**Study 5**

My friend Alessandro Ferretti and his colleagues studied the effect of ketogenic diets versus high-carb control diets on HIIT performance (high-intensity interval training) over 4 weeks [12]. The diets were considered ketogenic if subjects reported eating < 50 g of carbs a day. The HIIT sessions was a 2:1 work-to-rest ratio; 5 high-intensity repetitions consisting of 3 min at 100% vVO2max separated by 1.5 min of passive recovery.
The authors found that the ketogenic diet

- improved fat oxidation during the graded treadmill test and HIIT session
- didn’t impair performance or cardiorespiratory fitness during the HIIT session

Figure 4. Fat oxidation during the graded exercise test in the very low-carbohydrate high-fat diet (VLCHF) and habitual mixed Western diet (HD) groups. The differences over time between the VLCHF and HD groups expressed as ES ± 90% CI and its likelihood is shown (**very likely) (see also Methods). Values are expressed as mean ± standard deviation.

Table 2. HIIT results. Warm-up and cool-down excluded. Values are expressed as mean ± standard deviation.

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<td>Mean HR (% HRmax)</td>
<td>VLCHF</td>
<td>86.8 (7.3)</td>
<td>86.1 (7.3)</td>
</tr>
<tr>
<td></td>
<td>HD</td>
<td>87.4 (7.0)</td>
<td>84.3 (7.2)</td>
</tr>
<tr>
<td>Mean RER</td>
<td>VLCHF</td>
<td>0.96 (0.06)</td>
<td>0.84 (0.04)</td>
</tr>
<tr>
<td></td>
<td>HD</td>
<td>0.93 (0.06)</td>
<td>0.89 (0.05)</td>
</tr>
<tr>
<td>Mean Lactate (mmol/L)</td>
<td>VLCHF</td>
<td>5.9 (1.4)</td>
<td>6.6 (1.6)</td>
</tr>
<tr>
<td></td>
<td>HD</td>
<td>5.3 (1.2)</td>
<td>4.5 (1.6)</td>
</tr>
<tr>
<td>Mean RPE</td>
<td>VLCHF</td>
<td>13.8 (1.7)</td>
<td>13.4 (1.8)</td>
</tr>
<tr>
<td></td>
<td>HD</td>
<td>14.5 (1.3)</td>
<td>13.8 (1.4)</td>
</tr>
</tbody>
</table>

PRE – before the experiment, MID – after 2 weeks of the experiment, POST – after the experiment, VLCHF/HD – very low-carbohydrate high-fat diet/habitual mixed diet, VO₂ – oxygen consumption, HR – heart rate, RER – respiratory exchange ratio, RPE – rate of perceived exertion.

Table 3. The differences between changes in the HIIT results in the VLCHF and HD groups. Warm-up and cool-down excluded.

<table>
<thead>
<tr>
<th></th>
<th>MID vs. PRE</th>
<th>POST vs. PRE</th>
<th>POST vs. MID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak VO₂</td>
<td>0.7 ± 0.13, unclear</td>
<td>-0.2 ± 1.1, unclear</td>
<td>-0.9 ± 1.3, unclear</td>
</tr>
<tr>
<td>Mean VO₂</td>
<td>0.1 ± 0.0***, trivial</td>
<td>-0.0 ± 0.0***, trivial</td>
<td>-0.2 ± 0.0***, trivial</td>
</tr>
<tr>
<td>Mean HR</td>
<td>0.3 ± 0.0***, small</td>
<td>0.1 ± 0.1***, trivial</td>
<td>-0.3 ± 0.1**, small</td>
</tr>
<tr>
<td>Mean RER</td>
<td>-1.4 ± 0.1***, large</td>
<td>-1.5 ± 0.1***, large</td>
<td>-0.1 ± 0.1***, trivial</td>
</tr>
<tr>
<td>Mean Lactate</td>
<td>1.0 ± 0.5***, moderate</td>
<td>0.1 ± 0.6, unclear</td>
<td>-0.9 ± 0.6***, moderate</td>
</tr>
<tr>
<td>RPE</td>
<td>0.3 ± 0.8, unclear</td>
<td>-0.4 ± 0.9, unclear</td>
<td>-0.6 ± 0.8**, small</td>
</tr>
</tbody>
</table>

PRE – before the experiment, MID – after 2 weeks of the experiment, POST – after the experiment, VO₂ – oxygen consumption, HR – heart rate, RER – respiratory exchange ratio, RPE – rate of perceived exertion. The differences over time between the changes in the VLCHF and HD groups expressed as Effect Size ± 90% CI values, magnitude based inference and their likelihood are shown (*possible, **likely, ***very likely, ****most likely) (see also Methods).
These results are promising but there are limitations. My analysis arises from discussions I’ve had with Dr. Tommy Wood.

1. Blood BhB levels in the keto group increased to 0.7 mmol/L after two weeks but decreased to 0.4 mmol/L after four weeks, suggesting the athletes weren’t increasingly keto-adapting as intended. Carb-creep is the likeliest explanation.

2. The mean total energy intake was higher in the high-carb control group during the 4 weeks which could give them a potential advantage over the keto group. Indeed, the keto group lost a little weight unlike the control group.

3. Time to exhaustion tests (TTEs) aren’t sufficiently representative of real world racing. This is a fair criticism. But you can make it for any other such exercise physiology studies and it casts shade on all results (positive or negative).

4. The reporting of the effect sizes is confusing. It’s unclear if the control group had a statistically significant relative increase in TTE. If it is the case though, it would suggest an advantage from carbs and/or an increased caloric intake relative to the keto group.

**Study 6**

A bunch of Polish researchers found 8 off-road cyclists to put on a ketogenic (70% fat, 15% protein and 15% carbs) or high-carb diet (50% carbohydrates, 30% fats and 20% protein) [13]. They used a cross-over study design, where subjects serve as their own controls by being on both diets with a washout period in between (to avoid carry over effects). Bonus points to the authors for including a few meagre details about the composition of the diets.
The authors explain that blood ketone levels in the keto group elevated 4-fold compared to the high-carb controls, thus confirming dietary adherence. Problem is, 4 times 0.04 gives you 0.16 mmol/L (they measured 0.15 mmol/L). That’s not nutritional ketosis so the study can’t answer the question it’s asking. It can still be useful to learn things about a low-carb diet though.

On average, these subjects ate 3,865 kcals a day, weighed 80.3 kg and had 14.5% body fat. These off-road cyclists were expending a lot of energy! Their fitness is probably pretty good. The pseudo-keto group ended up weighing 2 kg less with 0.6% less body fat, while the control group stayed around the same weight and body fat percentage.

The authors found that “when maximal intensity was introduced, FFA metabolism was inhibited by glycolysis, which was evidenced by significant increases in LA concentration”. This occurred in both groups but more so in the pseudo-keto one. It means that the diet was indeed low-carb enough to increase the cyclist’s reliance on fat for fuel and thus down-regulate carbohydrate metabolism. This is further supported by the high-carb control group’s comparably higher RER and lactate concentrations at lower intensity levels. In comparison, the pseudo-keto group had a higher heart rate and improvements in VO2max and lactate threshold VO2 relative to their new (lower) weight.

As expected in a 4-week intervention that’s too short for full keto adaptation, “the power output during work at maximal intensity was compromised on the ketogenic diet [maybe because of] reduced activity of glycolytic enzymes due to the four-week diet intervention”. Keep in mind that there are different levels of adaptation. Some happen over a couple of days (e.g. basal fat burning), weeks (e.g. appetite) and months and months (notably, top end intensity efforts).

Study 7

The title of this last study by Caryn Zinn and colleagues from 2017 says it all [14].

Ketogenic diet benefits body composition and well-being but not performance
in a pilot case study of New Zealand endurance athletes

It studied 4 females and 1 male for 10 weeks, checking their dietary adherence by taking blood ketones levels. They always stayed above 0.5 mmol/L from week 2 onwards

- Blood ketones ranged from 0.5 – 4.2 mmol/L
- Females ranged 0.5 – 1.9 mmol/L and never exceeded 1.9 mmol/L
- The male athlete ranged between 1.0 – 3.5 mmol/L, went below 1.0 mmol/L on 2 occasions (0.8 and 0.6 mmol/L) and measured at 4.2 mmol/L on 1 occasion

Some ran, others cycled. Kudos to Zinn and colleagues who gave examples of the suggested meals. For example, the male participant’s breakfast was

- ½ cup of granola (*nuts, seeds, coconut threads and coconut oil), 150 mL of coconut cream and 100 g of mixed frozen berries and 30 mL. The daily diet had 2,450 kcals, with 24 g of net carbs, 103 g of protein (1.4 g/kg) and 215 g of fat.

His lunch and dinner had smallish amounts of salmon and other fish, respectively, which is great but still leaves his breakfast without any animal sourced food. This is not good for maintaining a nutrient dense diet, optimising exercise performance and especially body composition.

So what happened?

- Mean max oxidation improved 43% !
- The average level of exercise intensity at which VO2max occured increased 31.2% !
- Their average work rate increased 21.5% from 39.5 (± 11.9%) to 48.0 (± 8.9%) !
- 2 out of the 5 athletes showed an increase in Fatmax relative to WR max, and the remaining 3 showed no change
- All the while average fat loss was 4.0 (± 3.1%) kg !
- All participants lowered their time to exhaustion by 2 min (± 0.7 min) !

- Maximal aerobic performance was reduced !

What does this mean? Looking at the individual responses we can see

(a) big confidence limits, a statistical term representing the the upper and lower bounds of possible results you’re willing to consider. Big confidence limits represent inaccurate knowledge of risk.

(b) relatively small effect sizes in a small sample size. No surprise there and the authors are upfront about it.
Fig. 2 Individual responses and effect sizes of anthropometry and performance variables

* ES: Effect size
† CL: Confidence Limits
‡ Data overlap for two athletes
That’s why I don’t quite see the need to go into the detailed justifications for the apparent decreases in time to exhaustion. They invoked glycogen depletion, pyruvate dehydrogenase downregulation and counter-regulatory glycolytic downregulation due to increased fat burning.

I think it’s rather simpler.

The participants were in a possibly involuntary but significant caloric deficit given their weight loss. After looking over their meals, their animal food intake could have been quite a bit higher. This is all the more true given they’re consistently exercising seriously and thus placing increased demands for animal foods.

And what did they report?

General well-being improved overall. Several important subjective measures changed for the best, from improved skin to better recovery and prostate issues that resolved. Nevertheless, some felt a loss of power on the top end of their efforts, others constipation and others yet were bored by the diet. That last thing? I cannot explain for the life of me.

The takeaway is even when the diet is likely hypercaloric you can still exercise well and feel generally better, but the top end of your performance won’t be at its best. I think that all makes sense but I don’t think that being a better fat burner (i.e. more metabolically flexible) makes you a worse carb burner.

There’s the physiology of increased fat burning lowering glycolysis, which is correct. Then there’s the inference from that, that better fat burners are worse carb burners. That’s incorrect. This then leads to the assumption that low-carb or ketogenic diets must specifically disadvantage adherents when it comes to performing at high-intensity.

If it turns out that better fat burners are indeed worse carb burners, it won’t simply be because as your burn more fat you burn less glucose and vice-versa.

**Body composition**

When it comes to body composition changes on a ketogenic diet, results are more clearly are more clearly positive overall.

**Study 8**

For 3 months 12 male and female Crossfitters were either put on a high-carb control diet or a ketogenic one and changes in their performance and body composition were measured. Both groups had similar changes in their resting energy expenditure (REE), one-repetition maximum (1-RM) on the back squat
movement, 400 m run times and peak VO2 values. Knowing their sample size was small, the authors conclude that “these preliminary data suggest that adopting a ketogenic diet causes marked reductions in whole-body adiposity while not impacting performance measures in recreationally-trained CrossFit trainees” [15].
I'll take it.

The keto group seemed to actually be ketotic given the recorded blood BHB levels. As in many studies with self-reported dietary intake, we see here a decline in blood BHB levels after the first couple of weeks.

**Study 9**

Volek’s recent study is entitled “Keto-adaptation enhances exercise performance and body composition responses to training in endurance athletes” [16]. This study had 20 male endurance athletes aged 33 and weighed 80 kg. It had an interestingly intense training phase up to the last test day.

- 7+ hours a week of endurance training (moderate intensity 56 – 68% VO2max)
- 2 strength sessions per week; 6 sets of 8-10 reps on a leg press, or
free squat (70–80% of participants 1RM)

- **2 HIIT sessions every week** (10 sets of 1 minute bouts at 70% peak power with 1 minute recovery)

The authors note that during endurance training the keto group kept carbs to a minimum before training and limited food consumption during exercise. But before being tested again the subject’s breakfast was either high-carb for controls (60% carbs, 26% fat and 14% protein) or keto for the others (80% fat, 15% protein and 5% carbs). As shown in the picture above, they performed a six second (SS) sprint, then a 100 km time trial (TT) and finished on a critical power test (CPT). During the testing the controls took in 30 – 60 grams of carbs per hour (glucose, maltodextrin, sucrose and fructose) whilst the keto group only drank water and 0 calorie electrolyte drinks.

The keto group lost 5.9 kg (of which 78% was from fat and water) compared to 0.8 kg in the high-carb control group (of which 62.5 % was from fat and water). That’s a net win for keto in terms of body composition.

But it tanked their performance, right? No.

Despite the high-carb controls consuming 5.3g/kg of carbohydrate for 12 weeks – so 424 g of carbs a day for an 80 kg man – they didn’t equal the keto group’s mean time trial performance done right after the training period. Seems this study by Volek and friends really gave the high-carb group all the carbs they wanted and ensured the keto group wasn’t underfuelling either.

The keto group had very favorable body composition changes and showed that “endurance performance can be maintained [on a ketogenic diet], and in some cases improved compared to a [high-carb] diet”. Of course, this is less surprising given that the advice these athletes were given was better than in most keto-sports studies; the diet was 81% fat, protein was set at nearly a
third higher than in other studies at 1.9 g/kg of lean body mass (LBM) and carbs were kept low at 41 g per day. The keto group had ketones of 0.1 mmol/L before adapting to the diet and increased them to 0.5 by the end of it. They were mildly ketotic but with a good RER (i.e. lower), which is entirely appropriate for testing a ketogenic diet.

Study 10

In 2017, D’Agostino, Lowery and Wilson took 25 college students to see how the ketogenic diet might affect resistance training and body composition, strength and power [17]. The keto did better for losing fat mass, with 2.2 kg (± 1.2) instead of 1.5 kg (± 1.6). The high-carb group put on more lean body mass in 10 weeks, 4.4% versus 2.4% (p < 0.01). When measured again a week later, the keto group shot up higher than the high-carb group at 4.8%! Why? Because the keto group carb-loaded with 265 g of carbs. This will increase water retention which gives a false positive for increased for lean body mass, which also happens to equalize the comparison with high-carb diets. When equalized in this way we can see that the high-carb diet doesn’t fare better.

Study 11

This German study from 2017 without a control group lasted 6 weeks, had 42 subjects that were 37 years old and were asked to monitor ketosis via urine strips [18]. Their results were positive but unimpressive and their tools to measure body composition (bioimpedance analysis) were inaccurate. They reported moderate weight loss from 70.3 kg (± 11.5) to 68.4 kg (± 10.3). But 2 interesting things happened.

First, folic acid improved from 7.81 (± 3.32) ng/mL to 10.04 (± 3.92).
Dietitians are worried low-carb diets are micronutrient deficient in folic acid but they’re wrong about that.

Second, their triglyceride-to-HDL cholesterol ratio improved from 0.89 (0.43 – 4.24) to 0.76 (0.48 – 3.37). Dietitians and doctors are also worried keto diets worsen cardiovascular disease factors, which they’re also wrong about. And of course LDL cholesterol increased a little bit (12 mg/dL) which is totally uninteresting in terms of risk. Why? Because it’s not an independent risk factor for. This is clear on mechanistic grounds but unclear on epidemiological ones.

Studies 12 and 13

This 7-day study shows that carbohydrate restriction is a potentially useful tool for athletes needing to quickly cut weight for weight class competitions without the side-effects of big or small drops in performance, depending on the individual [19].

This study shows how glycogen concentrations don’t suppress the anabolic response to resistance exercise [20]. So even if your glycogen stores are sometimes lower than those of high-carb athletes, it won’t stop you from putting on muscle mass.

Conclusion

Here’s how I’d summarize the ‘keto for sports’ evidence so far:

- The longer the study...or the longer its keto-adaptation phase...or the more keto-adapted the subjects are...the more likely the study is to find favorable performance results
- Keto is worth trying for anyone in any sport (but start in the off-season!)
- It’s highly unlikely keto is better for high-intensity
- It’s unlikely that keto is bad for high-intensity
- It’s likely that keto is neutral for high-intensity
- It’s likely that keto diets are better for endurance
- It’s very likely keto diets are better for body composition
- It’s very likely keto diets are generally healthier than standard high-carb diets for athletes

About the author

Raphael Sirtoli is the co-founder of Nutrita at https://nutrita.app. He has an MSc in Molecular Biology and is a neuroscience researcher at the Behavioral n’ Molecular Lab as well as a PhD candidate in Health Sciences at the University of Minho in Braga, Portugal. His days are spent studying the
metabolic effects of antipsychotics in rodent models of schizophrenia. His understanding of metabolism, nutrition and clinical medicine forms the base from which Nutrita derives its evolving knowledge. He loves open scientific debate, Crossfit, football, hiking, psychedelic medicine, cold water immersion and cooking for loved ones.
How to Lose Weight without Hunger (Chinese version) 低碳水化合物 VS 低脂肪餐單減肥法

Note: A friend who lives in Hong Kong and who is concerned about the health of the people there had this translated into Chinese (he is not Chinese himself). He feels that much official government advice is wrong and unhelpful, and although I don’t know what official Hong Kong government advise is, one is inclined to agree with him. I don’t know how this works, like whether the article will show up in Chinese search engines, but fingers crossed. The original article is [here](https://example.com).

低碳水化合物 VS 低脂肪餐單

有讀者問我, 參照某比較低脂肪低卡路里餐單和低碳水化合物餐單的研究, 他指, 兩個餐單同樣有效, 一個在一年內讓減肥者減了11公斤, 另一個讓嘗試的人在兩年內減了7公斤。兩人餐單效果相似, 如何判斷兩者優劣?
如果細心看研究資料，就可看到答案關鍵；在低碳水化合物餐裡，每天只可攝取20克碳水化合物，是透過一些低升醣(low-glycemic)蔬菜來提供這營養。同時，他們在脂肪和蛋白質攝取是沒限制的，他們愛吃多少就多少。研究提到：「3個月後，低碳水化合物餐單的參與者，每週增加他們碳水化合物的攝取5克，直到其體重達到合理和穩定水平。這點非常值得留意，所謂穩定和令人滿意的體重，是否意味著他們之前已經減了太多體重了﹖這又看似不太可能，參加者們開始時，身高體重指數(BMI)達36，幾乎是癡肥程度。而且，低碳水化合物餐單的目的，就是為了限制碳水化合物攝取，儘管研究沒有提到這點，可是，或許到了研究末段，餐單的碳水化合物含量或已較高。另外，低脂肪攝取的餐單裡，脂肪含量一定少於30%，而卡路里攝取量每天限於1200到1500卡路里，或是1500到1800卡路里。

在這實驗裡，實驗參與者開始時，體重都屬正常，所以，或許一個癡肥的人吃同樣的餐單，不會感覺那麼肚餓；可是，這效果仍不容忽視。在著名的明尼蘇達飢餓實驗(Minnesota Starvation Experiment)裡，實驗參與者每天大概攝取1600卡路里食物，然後，他們經常覺得肚餓，常常想起食物，甚至在夢裡也夢到食物。可以說，你有兩個選擇，第一，不吃碳水化合物，可是其他範疇的食物並無限制。第二，吃低脂肪食物，但經常感到飢餓。

在這研究裡，用了低碳水化合物餐單的參加者，同時不用限制他們的卡路里攝取量，他們的血壓明顯下降，三酸甘油脂(triglyceride)也跌了不少，而且良性的高密度脂蛋白膽固醇(HDL cholesterol)明顯增多。由於三酸甘油脂和高密度脂蛋白膽固醇是血脂質(Blood Lipid)最重要的標誌，數值越低越好，可以說，低碳水化合物餐單的遵循者，他們的心血管疾病風險大大減少了。

CICO

CICO (calories in, calories out)這詞彙的意思是說攝取的卡路裡和消耗的卡路裡，簡單而言，就是指卡路里的消耗大於卡路里攝取時，就能減肥。從字面上來說，完全正確，但這資訊意義不大，這就好比說沉船的原因是因為船進了水，但知道這點，並無助於你防止船要沉掉；真正要了解的是，船為什麼不停進水。
Has All Dietary Advice Been Wrong?

Sometimes I get the feeling that those in our entrenched nutritional and health establishments don’t know what they’re talking about. Has all dietary advice been wrong? Surely not all of it, but most of the mainstream talking
points today are definitely wrong, and you’ll be healthier ignoring most of it.

Let's look at these main points.

**Saturated fat, cholesterol, and heart disease**

Mainstream health and nutrition has told us for many decades, at least since the 1960s, to avoid saturated fat, on the grounds that it blocks coronary arteries and causes heart disease. Cutting back on saturated fat has been official government policy since the late 1970s.

It’s becoming increasingly clear that saturated fat is perfectly healthy.

A meta-analysis done a few years ago, one that I’ve cited many times, found:

> **Conclusions:** A meta-analysis of prospective epidemiologic studies showed that there is no significant evidence for concluding that dietary saturated fat is associated with an increased risk of CHD or CVD. ([ref.](#))

Furthermore, carbohydrates, not saturated fat, have been found to correlate with heart disease in more recent studies. (See [here](#) and [here](#).)

Dietary cholesterol is now acknowledged even by the mainstream as being of little to no significance, after decades of telling us to avoid it.

And higher blood levels of cholesterol are associated with longer life, not shorter.

Saturated fat is clearly a case where the dietary advice has been wrong.

**Meat and cancer**

We get told a lot that meat, especially red meat and processed meat, causes cancer.

Is that really true? Was it the hamburgers and hot dogs, or was it the buns, fries, and sodas that people ate with them?

Dr. Georgia Ede has done a lot of leg work on this one: [WHO [World Health Organization] Says Meat Causes Cancer?](#)

Dr Ede finds the evidence put forth by the WHO as weak and unconvincing; “all politics and no science”. She reviews these studies in detail so please have a read at her site.

The upshot is, the evidence that meat causes cancer is exceedingly weak and in some cases non-existent.

Even the evidence against processed meat is weak. In this day and age, people
are very biased about this, wanting everything fresh and “organic”.

But bacon actually prevents colon cancer in rats. (Ref.)

**Vegetarians don’t live longer than others**

The mainstream has long held out vegetarianism or veganism as the ideal regarding diet and health.

These days they tend to call it “plant-based”, since that term may be more palatable to the public.

But, we now know that vegetarians don’t live longer than others. Previous studies that found that they did were confounded, because vegetarians are more health conscious. When you compare them to other, omnivorous, but health conscious people, the advantage disappears.

Health conscious people live longer, whether they eat meat or not.

And veganism is associated with a long list of health problems.

Any health advantage of a “plant-based” diet derives not from avoiding meat, but from avoiding ultra-processed plant foods.

**Ultra-processed plant foods, the real health scourge**

While we’ve been told to avoid meat and saturated fat, we’ve also been told to increase our intake of carbohydrates. We have to eat something, after all.

Sugar was held out as something benign.

And they told us to use seed (vegetable) oils in place of saturated fat.

So, people started eating a lot more carbohydrates and sugar, and they did cut back on saturated fat.

The result: an epidemic of obesity and diabetes.

So, the advice to eat less meat led to eating more ultra-processed junk food, which has been a disaster.

**High protein is healthy**

One of the most persistent myths that the establishment has encouraged is the idea that too much protein is harmful, and in particular, harms the kidneys.

But a recent study found that there is no evidence that high protein diets cause any harm to the kidneys.

One of the alleged disadvantages of eating a low-carbohydrate diet has been that you would ingest too much protein.
That idea needs to be laid to rest.

More protein leads to stronger bones and higher muscle mass.

**What else?**

Just off the top of my head:

- they told us that fasting was bad, and that we should eat many small meals daily, a practice known as grazing
- they told us to avoid the sun. That’s not nutritional, but is typical in that they told us not to do something that our ancestors did regularly.
- they told us to eat a lot of fiber, but fiber has been underwhelming in effect.

Even now, after all this, plans are afoot to get the world to go vegan.

There will soon be meat taxes, and the health misinformation campaign will continue.

Don’t be fooled. They got just about everything wrong so far, and they won’t be right in the future.

(Advertisement)

**PS: If you need to lose weight and you want to save yourself years of poor results with bad information, I’ve put everything in a simple guide for you. **[The World’s Simplest Fat-Loss Plan.](#)
Why Americans Are Fat and Sick

Around 80% of the American people are overweight, obese, or *skinny fat*. That leaves 20% who are of normal weight and body fat, but the fraction of these people that exercise regularly, especially resistance training, and that avoid *ultra-processed foods* may be quite low. What’s caused this situation, and why are Americans more likely to be fat and sick than healthy and lean and full of life?

The epidemic of obesity and ill health is no longer just American, either, but is spreading across the globe.

**Big Pharma**

Big Pharma, the collection of American and global drug companies, earn an enormous sum of money. See chart below. Global pharma revenue is now over $1 trillion annually.
Below are the top revenue earners by company. Johnson & Johnson is number one at nearly $80 billion in revenue.

Furthermore, the drug industry is highly profitable, with pharma companies
having among the highest profit margins of any industry.

Now, if you read this site, you know how much responsibility poor diet and lack of exercise bear for our collective health problems. Heart disease, cancer, diabetes, obesity, Alzheimer’s: lifestyle factors, mainly diet and exercise, greatly affect all of these and more.

Yet when the average person goes to the average doctor for a health problem, the doctor very often prescribes drugs.

Doctors typically offer little to no lifestyle advice. Not that they know much about what to advise anyway, and not that the patient will heed that advice.

Anyway, doctors prescribe, and patients take, drugs.

If the patient’s condition is a chronic one, these drugs must often be taken for life.

That means huge profits for drug companies.

Do you think Big Pharma will suddenly start telling people not to take drugs, or in some other way to change the current health system and with it, the health of Americans and others?

Of course not.

One can’t fault the companies for this; they’re in the business of maximizing profit for their shareholders. Nothing else. And their products are in demand.

It’s worse than that, however.

Some 60% of all doctors receive money from pharmaceutical companies.

But it gets even worse than that: medical research is corrupted by money from Big Pharma. The drug companies directly pay researchers who promote their drugs and who perform studies on them, as well as fund the studies themselves.

It’s no exaggeration to state that Big Pharma exerts huge influence on scientific research, medical education, and medical practice.

With the amount of money at stake here, don’t look to drug companies for an answer to increasing use of drugs in treating chronic disease.

**Big Food**

Big Food, a collection of large food companies, produces ultra-processed foods, which are implicated in our epidemic of obesity and chronic disease.

Ultra-processed foods, loaded with and primarily made from refined grains (flour, typically), seed oils, and sugar.
Ten companies make most of the food and drink you find in a supermarket. See graph below.

Note the foods they make. The vast majority is ultra-processed junk food, which causes obesity and chronic disease.

Ultra-processed foods are highly profitable. According to Forbes, Nestle, Coca-Cola, and Pepsi dominate the field. Nestle had revenues of $90 billion and profits of $8.6 billion in 2017.

They certainly want the gravy train to keep rolling.

Again, that’s their job: maximizing shareholder profit.

Some would argue that Big Food is only responding to demand, and while we could debate the extent of that, people are buying their foods, so the demand is there.

The foods they make using seed oils, refined grains, and sugar are highly profitable partly because the ingredients are dirt cheap and can be stored on a shelf indefinitely.

A few cents worth of these ingredients, when marketed properly with a brand name slapped on the box, sells for dollars. Pizza, soda, breakfast cereal, pastries: all made of cheap ingredients. (Allegedly the aluminum in a can of soda is the single most expensive ingredient.)

So, as with Big Pharma, Big Food is another aspect of our global diabesity
and disease epidemic which makes a huge amount of money, and therefore is not interested in changing the status quo, other than to make even more money.

No change will be coming from this quarter. The opposite, actually: they will resist change.

**Doctors and health bureaucrats**

Doctors are generally paid quite well, being among the top income earners in the professions. [The average doctor’s salary in the U.S. is about $250,000.](#) (Not saying they don’t earn it, and there’s also a large variation in their salaries. In fact, for some specialties like hospitalist, the pay strikes me as too low.)

Patients come to doctors for medical treatment obviously, so that’s what doctors give them.

Most doctors do not know the right lifestyle advice to give. (I contend.) They’re myopically focused on lowering cholesterol, for one thing. But they simply don’t know the right dietary prescriptions.

And if they do know, and tell patients about it, they can get cashiered from the profession for it, as [the cases of Drs. Timothy Noakes and Gary Fettke show](#). They got into deep, hot water for telling their patients to cut carbs.

All incentives line up for doctors to continue the status quo.

They are well paid, they can get sued or prosecuted for low-carb advice, many patients won’t change anyway. And as we’ve seen, many doctors are bribed by Big Pharma.

Many doctors do have a countervailing incentive: their patients’ welfare. But prevailing incentives seem to win out.

Dietitians associations are soundly against change. They’d look very bad if they reversed their stances on diet of the past several decades, so they won’t.

Health bureaucrats, of which there are now a huge number, are paid well enough, so they won’t be wanting to change things.

**The incentive must come from the individual**

As you can see, massive incentives, mostly in the form of money, conspire to keep the American people fat and sick.

It’s not a conspiracy (as I see it), just a large group of people and corporations acting in their own interests to keep the money flowing.

And it’s a lot of money.

Corporate food makes you fat and sick.
Corporate drugs treat the chronic disease caused by corporate food.

If you want to have any hope of being free from obesity and chronic disease, you must take up the challenge yourself.

You must learn to discern what are the correct choices to make, and you must implement them.

No one is coming to help. There are mighty forces at work to make and keep you fat and sick.

(Advertisement)

PS: If you need to lose weight and you want to save yourself years of poor results with bad information, I’ve put everything in a simple guide for you. The World’s Simplest Fat-Loss Plan.
Resistance Training Treats Depression

Depression has been called the common cold of psychiatric disorders, and at this point, huge numbers of Americans take antidepressant drugs. But there may be a better way, since resistance training treats depression.

Depression is common

Antidepressant drug use is widespread, and 11% of Americans over the age of 12 take one. When broken down by age group and sex, we find that 23% of women in their 40s and 50s take antidepressants. See graph below. (Full discussion here.)

The use of antidepressants could in theory either under- or overestimate the number of people with depression.

But either way, a large number of people, and their doctors, believe they are depressed.
However, a good deal of evidence points to the probability that antidepressants are little more, if at all, than placebos. They may also have serious side effects.

Is there a better way to treat depression, one with only benefits and no adverse effects?

**Resistance training**

Resistance training is the catch-all term for strength training or weight lifting. (Since machines or bodyweight can be used, not all cases of resistance training mean lifting weights, as in barbells or dumbbells.)

It’s long been known that exercise treats depression. A recent meta-analysis found that exercise was effective at treating depression, as much as cognitive behavioral therapy. ([Ref](#))

Given the bias in mainstream circles in favor of “aerobic” exercise, it’s reasonable to ask whether resistance training has the same effect on depression.

A meta-analysis recently published in JAMA Psychiatry found that it does, with an effect size similar to other forms of exercise. ([Ref.](#))

Of interest, resistance training improved symptoms of depression “regardless of health status, total prescribed volume of RET, or significant improvements in strength.”

That raises some questions. For example, maybe resistance training acts like a placebo, since any amount in any person seems to work. Indeed, the placebo effect may be at work in other treatments, such as antidepressant drugs (as noted above) or psychological therapy. Professional training in psychotherapy may make little difference in effectiveness, which may indicate a placebo effect. ([Ref.](#))

However, there are reasons to think that resistance training may work by decreasing inflammation. Depression is an inflammatory disease, so reducing inflammation should have a treatment effect. (Decreasing inflammation may be behind the efficacy of antidepressants, that is, the efficacy they may have beyond the placebo effect.)

**No studies needed?**

Most people who lift weights won’t need any studies to confirm the efficacy of resistance training.

The effect is that obvious.

One trip to the gym for a weightlifting session clears the mind and improves mood. It would seem to follow that frequent sessions could improve mood over the longer term.
Anxiety is closely related to depression. So resistance training, and other forms of exercise, ought to improve anxiety.

**Desire to exercise**

A common response that I hear when I discuss the fact that exercise can treat depression is that depressed people don’t want to exercise.

While that may be true, it’s an obstacle that must be overcome.

Which comes first, not wanting to exercise, or depression?

Many people defend their weaknesses and illnesses, because that relieves them of personal responsibility. If something is out of your control, it follows that doing something about it is pointless. And they get angry at anyone who suggests otherwise.

**Conclusion**

Resistance training treats depression with an approximate effect size close to therapy and antidepressants.

Virtually anyone, of any age or health status, can do resistance training. (Some people may require supervision.)

So what are you waiting for?

**PS: You can do resistance training and get great results in very little time. Find out how with One-Hour Fitness: How to Get Lean, Muscular, and in Great Cardiovascular Shape in One Hour a Week or Less.**
Senolytics, an Anti-Aging Technology

A new class of compounds known as senolytics may revolutionize anti-aging medicine. These compounds target and selectively remove senescent cells, which may be a prime cause of the aging phenotype.

Senescent cells

Cells grow and then divide, but eventually reach a limit, at which point they become senescent. Some influences from outside the cell, such as radiation or certain chemicals, can also induce senescence.

Senescent cells have been termed “zombie cells”, an apt name, as they remain alive but their presence is actively harmful to neighboring cells and tissue. They are in a permanent state of cell-cycle arrest, no longer able to grow and divide.

Senescent cells are characterized by the SASP – the senescence-associated secretory phenotype. (Ref.) They emit inflammatory chemicals – cytokines – which cause inflammation in surrounding cells, essentially poisoning the area.

Senescent cells are thought to be contributive to cardiovascular disease and diabetes (ref.) and cancer (ref.).

Among the chronic conditions successfully treated by depleting senescent cells in preclinical [animal] studies are frailty, cardiac dysfunction, vascular hyporeactivity and calcification, diabetes mellitus, liver steatosis, osteoporosis, vertebral disk degeneration, pulmonary fibrosis, and radiation-induced damage. (Ref.)
Chronic inflammation is a hallmark of aging, and since senescent cells are highly inflammatory, they may be a huge source of the inflammation of aging, which also leads to oxidative stress; they may also be a prime reason that aging increases the risk of chronic disease.

If we could get rid of senescent cells, we might be able to eliminate many of the phenotypes (outward signs) of aging. Basically, to reverse aging.

**Senolytics**

Senolytics are compounds that selectively target senescent cells, and cause them to enter apoptosis, or programmed cell suicide.

A landmark study from a few years ago showed that a combination of two drugs, quercetin (an OTC supplement and polyphenol) and dasatanib (a chemotherapeutic drug) eliminated a large fraction of senescent cells in mice. (Discussed [here](#).)

In old mice, cardiac function and carotid vascular reactivity were improved 5 days after a single dose. Following irradiation of one limb in mice, a single dose led to improved exercise capacity for at least 7 months following drug treatment.

By eliminating senescent cells, the health of the entire organism was improved.

Transient treatment with senolytic agents is enough to eliminate senescent cells, so ongoing treatment is not required.

A study published this year showed that senolytics decreased mortality rates in mice by about 35% ([ref](#)).

Moreover, intermittent oral administration of senolytics to both senescent cell–transplanted young mice and naturally aged mice alleviated physical dysfunction and increased post-treatment survival by 36% while reducing mortality hazard to 65%. Our study provides proof-of-concept evidence that senescent cells can cause physical dysfunction and decreased survival even in young mice, while senolytics can enhance remaining health- and lifespan in old mice.

If these treatments work in humans, then transient treatment, perhaps once a year, may be enough to slow or even reverse aging substantially.

**Fisetin**

Fisetin is a polyphenol found in relatively low amounts in some fruits and vegetables.
A recently published study showed that it was the most potent of 10 flavonoids tested. Fistein decreased burden of senescent cells and significantly increased lifespan and healthspan. (Ref.)

Of the 10 flavonoids tested, fisetin was the most potent senolytic. Acute or intermittent treatment of progeroid and old mice with fisetin reduced senescence markers in multiple tissues, consistent with a hit-and-run senolytic mechanism. Fisetin reduced senescence in a subset of cells in murine and human adipose tissue, demonstrating cell-type specificity. Administration of fisetin to wild-type mice late in life restored tissue homeostasis, reduced age-related pathology, and extended median and maximum lifespan.

Furthermore, fisetin reduced senescent cell burden in human adipose tissue explants in an in vitro (test tube) experiment. See chart below.

![Chart showing decrease in senescent cell burden in human adipose tissue after being exposed to 20 μM fisetin for 48 hours, as well as decrease in inflammatory cytokines.](image)

Fisetin appears to have low toxicity (ref), enough so that a clinical trial is being planned: Alleviation by Fisetin of Frailty, Inflammation, and Related Measures in Older Adults (AFFIRM-LITE). The trial will study a dose of 20 mg/kg for 2 days. That would be 1400 mg for a 70 kg person.

In the mouse trial above, mice were treated with 100 mg/kg for 5 days, which, when accounting for mouse vs human metabolism, translates into around 8 mg/kg for a human.

Fisetin is available as an OTC supplement.

Several biotechnology companies, at least 4, have formed to exploit the possibilities of senolytics. The companies are described as being in a “race”, so from that we can gather that they expect senolytic technologies to be huge.
Conclusion

Eliminating senescent cells looks like a big step forward in anti-aging. As opposed to other interventions, such as metformin or rapamycin or calorie restriction, senolytics might be said to actually reverse aging.

So far, scientists have demonstrated the power of senolytics only in lab animals, but human interventions are around the corner.

PS: I discuss many more anti-aging interventions in my course, The Anti-Aging Blueprint.
Metabolic Syndrome Promotes Chronic Disease

Metabolic syndrome is the most insidious promoter of chronic disease, such as heart disease and cancer, in the U.S. and much of the world today. If you avoid metabolic syndrome, you’ll greatly decrease your risk of ill health, even as you age. Let’s take a look at how metabolic syndrome promotes chronic disease.

What is metabolic syndrome?

Metabolic syndrome is a cluster of signs and symptoms unified by one mechanism: insulin resistance.

You have metabolic syndrome if you have any three of the following five risk factors (ref.):

- large waistline
- high triglycerides
- low HDL cholesterol
- high blood pressure
- high fasting blood sugar.

One way to look at metabolic syndrome is as a pot belly along with insulin resistance.

High prevalence of metabolic syndrome

This is where things get scary.

Metabolic syndrome is extremely prevalent, and is closely tied to the obesity epidemic.

Among American men, metabolic syndrome increase with age.

- In men from age 20-39, the rate of metabolic syndrome is 20%.
- In men from 40-59, the rate is 41%.
- In men 60 and up, the rate is 52%. (Ref.)

Among all U.S. adults, as many as 52% are diabetic or pre-diabetic. (Ref.)

These numbers may undercount the true rate, since a large fraction of the population, as much as 80%, may have some degree of insulin resistance.

If you look at the people around you, that isn’t hard to imagine, as hardly anyone is in good shape.
Metabolic syndrome greatly increases disease risk

Just insulin resistance alone may account for most increased risk of chronic disease.

In a well-known study, Reaven and colleagues measured insulin resistance in a group of healthy people, divided them into tertiles (thirds), and followed them for 6 years. They looked at how many in each group developed heart disease, stroke, hypertension, cancer, and diabetes. Results below.

No one in the lowest third group developed any of those diseases. All of those who did develop them were in the upper two thirds of insulin resistance. (Discussed here.)

Imagine adding hypertension or high triglycerides or any of the other risk factors.

Metabolic syndrome increases the risk of heart disease three times, and risk of diabetes five times. (Ref.)

Visceral (abdominal) fat, or central obesity, is highly associated with metabolic syndrome.

Men with high visceral fat have around a 5-fold increased risk for prostate cancer. (Ref.)

Women with high visceral fat have a nearly 10-fold risk of breast cancer. (Ref.)

As you can see, metabolic syndrome entails huge risks for heart disease, cancer, and diabetes.

If the Reaven study is more widely applicable, virtually all of the risk is seen in those with metabolic syndrome and/or insulin resistance.

The good news is, if you stay free of metabolic syndrome, your risk of these diseases is very low.
Metabolic syndrome: the modern condition

Why is there so much metabolic syndrome?

The conditions of modern times increase its incidence, which is highly correlated to obesity.

(Although don’t be complacent if your weight is normal. A large number of normal weight people, “skinny-fat”, have deranged glucose metabolism, if not frank metabolic syndrome.)

The processed food trifecta of refined carbohydrates, sugar, and seed oils lies behind the increase in obesity and metabolic syndrome.

Add to that 24/7 availability of garbage food, and the couch potato lifestyle so many of lead, and you’ve got the recipe for insulin resistance, metabolic syndrome, and chronic disease.

How to prevent metabolic syndrome

Only around 10% of people at age 70 are free from chronic disease and frailty. Only 1% of those 85 and up are completely healthy.

If you want to be among them, you must stay free of metabolic syndrome.

How to do this?

1. Stay lean. Avoid ultra-processed foods, with their refined carbs, seed oils, and sugar. Eat low-carb.
2. Deplete glycogen. The storage form of carbohydrates is glycogen, and depleting it regularly increases insulin sensitivity and decreases your odds of being overweight. You do this through resistance training, intermittent fasting, and avoiding refined carbohydrates and sugar.

That’s it.

If you want to live in good health and free from disease, you can’t take the path that most of our countrymen are taking.

Average people have average health and an average lifespan, which is currently a paltry 76 for men, and 81 for women.

PS: If you need to lose weight and you want to save yourself years of poor results with bad information, I’ve put everything in a simple guide for you. The World’s Simplest Fat-Loss Plan.
Ketones Protect Arteries

The health of arteries is vastly important for aging and prevention of chronic disease, most notably coronary artery disease, and it’s also important for the health of organs such as the kidney and the brain. Ketones, which are produced by fasting or the ketogenic diet, protect arteries.

You’re only as old as your arteries

Thomas Sydenham, a 17th-century English physician, famously said, “You’re only as old as your arteries.” (Ref.)

Coronary artery disease is a major killer in the U.S., and heart disease in general is the number one cause of death.
Aging is the most important risk factor for heart disease. See chart below.

**Ketones protect arteries**

Disease of the arteries is caused by inflammation in the lining, which is composed of endothelial cells.

All cells other than stem cells age, and as they age they lose function. When they've reached the end of the road, they become senescent.

Senescent cells are major contributors to chronic inflammation and are associated with SASP, the senescence associated secretory phenotype. Essentially, senescent cells produce inflammatory chemicals (cytokines) that cause an inflammatory response for any cells in the vicinity. (Ref.)

Chronic inflammation is associated with aging and plays a causative role in several age-related diseases such as cancer, atherosclerosis and osteoarthritis. The source of this chronic inflammation is often attributed to the progressive activation of immune cells over time. However, recent studies have shown that the process of cellular senescence, a tumor suppressive stress response that is also associated with aging, entails a striking increase in the secretion of pro-inflammatory proteins and might be an important additional contributor to chronic inflammation.
The new science of senolytics promises the ability to rid our bodies of senescent cells, which would negate many of the effects of aging. (Ref.)

In passing, let’s note that a single bout of resistance training (lifting weights) can also eliminate senescent endothelial cells. (Ref.)

Preventing the endothelial cells that line arteries from becoming senescent means keeping them youthful and from becoming sources of inflammatory cytokines. This in turn helps maintain youthful arteries.

A recent study showed that ketones can prevent senescence of both endothelial cells and vascular smooth muscle cells. B-Hydroxybutyrate Prevents Vascular Senescence.

Beta hydroxybutyrate is one of three ketone bodies produced during ketosis.

So, how do you produce ketones?

One way is via a very low carbohydrate ketogenic diet. The absence of carbohydrates in the diet means that glucose in the body must be spared for important uses. Ketones are produced from fat to provide energy in place of glucose.

Another way to produce ketones is through intermittent fasting. Total absence of food, and especially absence of carbohydrates, induces ketone production. Ketone supplements work too.

Calorie restriction, the most robust life-extension intervention we know of, also produces ketones.

**Ketones and autophagy**

Autophagy is the cellular self-cleansing process that rids cells of junk molecules, which are crucial in promoting aging.

Increased autophagy is essential for life extension. (Ref.) The decline in autophagy induction in aging allows the accumulation of junk molecules, and therefore cells don’t function as well, leading to the aging phenotype of increased susceptibility to damage, breakdown, and disease.

Ketones promote autophagy. (Ref.)

The promotion of autophagy by ketones may be another way that fasting and ketogenic diet protect arteries.

Increasing the ability to induce autophagy is one of the most promising anti-aging interventions. This can be done with calorie-restriction mimetics, such as resveratrol, rapamycin, and metformin, or of course by calorie restriction itself, as well as fasting and the ketogenic diet.
PS: If you need to lose weight and you want to save yourself years of poor results with bad information, I’ve put everything in a simple guide for you. *The World’s Simplest Fat-Loss Plan.*

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**Carbohydrates Increase Death Rates**

Health authorities have told us to eat more carbohydrates – “healthy whole grains” – for the past several decades, as a benign alternative to allegedly deadly saturated fat. Their story is now unraveling, as recent and divergent lines of evidence point to carbohydrates as detrimental to lifespan and
healthspan. In this article we’ll look at the evidence that dietary carbohydrates increase death rates.

**The PURE Study**

The PURE Study looked at over 135,000 people in 18 countries, and tracked what they ate and at what rate they died. The study found that dietary carbohydrates were positively associated with death and cardiovascular disease rates, and dietary fat was negatively correlated, i.e. the more dietary fat, the lower the death and disease rate. Results shown in the graph below.

![Graph showing association between energy from nutrients and total mortality and major cardiovascular disease](image)

This is an epidemiological study and therefore cannot prove causation.

Nevertheless, at least a couple other epidemiological studies have found the same: 1) carbohydrates, not saturated fat, are associated with cardiovascular disease; 2) “high carbohydrate consumption (mainly in the form of cereals and wheat, in particular) as the dietary factor most consistently associated with the risk of CVDs” (ref.)
What about evidence beyond epidemiology? If animal and other evidence supports it, then we can have better confidence in the result.

**Ketogenic diets increase lifespan**

A ketogenic diet extends longevity and healthspan in adult mice. ([Ref.](#))

In fact, ketogenic diets may be equivalent to fasting and/or calorie restriction in their effects on lifespan and health. (I wrote about that [here](#).) Since calorie restriction is the most robust lifespan-extending intervention yet found, if a ketogenic diet produces the same result, that’s great news.

You wouldn’t have to restrict calories in order to get longer life and better health, you would merely restrict carbohydrates, and [eat as much as you wanted](#).

Much interesting new research proposes that calorie restriction produces its benefits via ketones. “Ketone bodies mimic the life span extending properties of caloric restriction”.

**Benefits of fasting due to fewer carbohydrates**

Intermittent fasting duplicates many of the physiological benefits of calorie restriction.

Much of the benefit of fasting may be due to the absence of carbohydrates.

One study calculated that 100% of the changes wrought by fasting was due to eating no carbohydrates. [Carbohydrate restriction regulates the adaptive response to fasting](#). When volunteers either fasted for 3.5 days, or got an
infusion of lipid for the same time, “Changes in plasma glucose, free fatty acids, ketone bodies, insulin, and epinephrine concentrations during fasting were the same in both the control and lipid studies.”

Oncologist Rainer Klement wrote: “I propose carbohydrate restriction as probably the best way to mimic CR [calorie restriction] in humans without the need to restrict energy intake.” (Ref.)

Another study estimated that 71% of the lowered glucose seen in short-term (24-hour) fasting may be due to no carbohydrates. (Ref.)

**Acarbose and metformin**

Acarbose is an anti-diabetic drug that inhibits an enzyme responsible for uptake of glucose from the intestines, and it increased lifespan by by 22% in male mice, 7% in female. (Ref.) In humans, acarbose dramatically reduced the incidence of cardiovascular events in diabetics. (Ref.)

Since carbohydrates break down into glucose upon ingestion, and acarbose prevents that and increases lifespan and lowers the rate of CVD, then it seems that simply not eating carbohydrates would do the same.

Metformin is another anti-diabetic drug that lowers glucose and insulin by inhibiting gluconeogenesis, the production of glucose from amino acids and fats in the liver. Diabetics who take metformin may live longer than non-diabetics who do not take metformin. (Ref.)

That’s a startling fact, but must be tempered by the knowledge that even most non-diabetics in this day and age have high insulin and impaired glucose tolerance.

Metformin also increases lifespan in lab animals. (Ref.) “Treatment with metformin mimics some of the benefits of calorie restriction, such as improved physical performance, increased insulin sensitivity, and reduced low-density lipoprotein and cholesterol levels without a decrease in caloric intake.” [My emphasis.]

Metformin mimics CR, which is recapitulated by fasting, which is all (or mostly) about carbohydrate restriction.

By the way, there’s even a rapamycin connection here. Rapamycin, a drug that extends lifespan, also results in the production of ketones and better insulin sensitivity. (Ref.)

And a ketogenic diet inhibits the mechanistic target of rapamycin (mTOR). (Ref.)

**Conclusion**

Multiple lines of evidence lead to the conclusion that dietary carbohydrates, especially refined grains and starches, promote mortality and are bad for health.
Decreasing carbohydrates, either entirely via a ketogenic diet, or even somewhat, improves health and increases lifespan.

If you want to avoid these carbohydrates, then avoid the following foods:

- breakfast cereal
- bread, tortillas, naan, bagels
- pasta
- pizza
- donuts, candy
- soft drinks, fruit juice
- potatoes.

**PS:** If you need to lose weight and you want to save yourself years of poor results from bad information, I’ve put everything in a simple guide for you. *The World’s Simplest Fat-Loss Plan.*
How to Lose Weight without Hunger

There are many ways to lose weight (fat), but some entail much more difficulty than others (bariatric surgery), while others may be dangerous to health (diet pills). The greatest hurdle to losing weight, however, is hunger. If your hunger can be kept under control, then you can lose weight. Let’s see how to lose weight without hunger.

Low-carbohydrate vs low-fat, low-calorie diets

A viewer of my anti-aging course asked me about a study doing a side-by-side comparison of a low-carbohydrate vs a low-fat, calorie-restricted diet. (ref.)

He pointed out that both diets resulted in about the same weight loss, which was 11 kg (~24 lbs.) at 1 year, and 7 kg (~15 lbs.) at 2 years.

Both diets were equally effective for weight loss in this study, so why should you do one over the other?

The answer to that question can be found in looking at the study’s details.

The low-carb group was restricted to 20 grams of carbohydrates daily, consisting only of low-glycemic vegetables. Their intake of fat and protein was unrestricted – they could eat as much of those as they wanted.

“After 3 months, participants in the low-carbohydrate diet group increased their carbohydrate intake (5 g/d per wk) until a stable and desired weight was achieved.”

That’s weird right there; does “a stable and desired weight” mean they had lost too much weight? That seems doubtful, as the participants started at an average BMI of 36, which is very obese. Also the whole point of a low-carb
diet is to restrict carbs; by the end of the study, the low-carb diet may not have been very low-carb, although the study doesn’t report this.

The low-fat group ate a diet of less than 30% fat, and their calorie intake was restricted to between 1200 and 1500 calories a day for women, and 1500 to 1800 calories a day for men.

I don’t know about you, but if I had to restrict my food intake to between 1500 and 1800 calories daily, I would be hungry.

**Hungry, or not**

In the famous [Minnesota Starvation Experiment](https://en.wikipedia.org/wiki/Minnesota_Starvation_Experiment), the subjects ate about 1600 calories daily, and they were so hungry they dreamed of food and thought about it constantly. The subjects were of normal weight to start, so perhaps an obese person wouldn’t get quite so hungry. But still.

Here’s your choice between the two weight-loss diets:

1. Eat as much as you want but no carbohydrates.
2. Eat low-fat food and be hungry a lot.

Pretty simple, IMO. Stop eating bread, pasta, tortillas, rice, potatoes, etc., and if you have too much body fat, you’ll lose some or most of it.

Or you can measure all your food so you can stay within calorie limits, plus exercise a lot of willpower to keep from eating when you’re hungry.

**Biomarkers**

In this study, those who ate the low-carb diet, unrestricted in calories, had greater reductions in blood pressure and triglycerides, and greater increases in HDL cholesterol.

Since the **triglyceride/HDL ratio is the most important blood lipid marker**, and the lower the better, the low-carb group improved their cardiovascular risk more than the low-fat group.

**CICO**

CICO stands for “calories in, calories out”, and refers to the idea that all weight loss occurs because calorie expenditure is greater than calorie intake.

At face value, I think it’s correct.

But it’s not a very useful piece of information. It’s like saying that all ships sink because they take on water, which does you little good in preventing your ship from sinking when out on the water.

You need to discover why your ship is taking on water.
Hormones and other molecules in your body regulate hunger. When hunger is deranged for some reason, you eat more.

If you can control hunger, you can control calorie intake without counting calories.

A low-carbohydrate diet controls hunger. “Spontaneous reduction of calories” is commonly reported on low-carb diets. (Ref.)

Many people state that low-carb diets work only because they result in fewer calories eaten. That there’s no “magic” about them.

And? That’s a good thing, and reduction of hunger is probably the main way that low-carb diets cause weight loss.

If you can lose weight (fat) without being hungry, why wouldn’t you?

**Lifestyle, not diet**

Another commonly heard objection to low-carb diets is that when you start eating carbs again, you gain the weight back. Therefore, supposedly, low-carb diets don’t work.

That’s right: eating what made you fat in the first place makes you fat again.

As a wag on Twitter recently put it, I can rescue you from drowning, but if you go back in the water you’ll drown again.

**Weight loss without hunger**

You can lose weight with either a low-fat, calorie-restricted diet.

Or you can eat as much as you want on a carbohydrate-restricted diet, with little to no hunger.

**PS:** If you need to lose weight and you want to save yourself years of poor results from bad information, I’ve put everything in a simple guide for you. [The World’s Simplest Fat-Loss Plan](#).
I’m proud to announce the launch of my new course, The Anti-Aging Blueprint.
Are you worried about an older age filled with chronic disease?

If you follow mainstream health advice, your old age will not be a healthy one. Only 1% of the elderly have no chronic diseases.

You can see the results of conventional health advice all around you: an obesity epidemic and a massive increase in diabetes and other chronic disease. Most people take prescription drugs just to get through life.

Wouldn’t you like to know the truth?

Mainstream health care has little to offer other than drugs, which paper over problems. Or risky procedures. Or nursing homes.

Most mainstream advice on aging is DEAD WRONG.

Enroll Now

My course will show you the real way to solve problems of aging and health.

If you’re past the age of 30, aging is already catching up with you.

In the U.S., even people in early middle age suffer from the chronic illnesses of aging: obesity, diabetes, heart disease, depression, arthritis.

The current sickcare paradigm only treats you as a cog in the machine, to prescribe drugs to you and sell expensive services to, but it won’t tell you how to live a long, healthy life.

Aging is a major risk factor for virtually all chronic diseases, such as cancer, diabetes, and heart disease.

Wouldn’t it be great to avoid those? Wouldn’t you like to be strong, healthy, and mentally sharp as you get older? Not frail, weak, debilitated, ill, and overweight.

This program will tell you how to do just that.

And since aging starts by age 30, it’s never too early to put these
principles into practice.

The course consists of 12 video lectures, each accompanied by slide presentations. I've made the slides available separately in PDFs.

In this course, you'll learn:

- what aging is
- the “Big 5 of Longer Life”
why body composition can speed or slow aging
how geroprotectors lead to longer life
why healthspan is as important – or more so – than longevity
the truth about the Blue Zones
how acute stresses lead to longer life
how food – both quantity and quality – affects aging
whether ketosis is good or bad for aging
and a lot more.

The science of aging can be difficult for the average person to understand, but I’ve made it all as simple and clear as possible.

More importantly, I’ve emphasized interventions and practices that you can use to slow aging.

Anti-aging is here now. You don’t have to wait for Silicon Valley to come up with expensive, high-tech methods to slow or reverse aging.

Most of the anti-aging techniques I discuss are dirt cheap.

Click on the image below to get the course. Or click here.
Insulin Is at the Nexus of Health, Disease, and Aging

In the last two articles, we discussed the importance of a low-insulin lifestyle, and how modern foods, particularly seed oils, increase insulin resistance. In this article, we’ll discuss why insulin is at the nexus of health, disease, and aging, and why it may be the single most important factor within your control.

Insulin and aging

Insulin is strongly connected to aging. Typically, as animals and humans age, insulin resistance increases and insulin blood levels increase to compensate for it.

The first hint that insulin controls aging came when it was discovered that the worm *C. elegans* could live twice as long when it had a mutation in its equivalent of the insulin receptor.

Life-span regulation by insulin-like metabolic control is analogous to mammalian longevity enhancement induced by caloric restriction, suggesting a general link between metabolism, diapause, and longevity.

Lower insulin levels increase the lifespan of mice, and since mice are mammals, we may have reason to think that lower insulin could increase human lifespan. FIRKO, or fat-specific insulin receptor knockout mice live 18% longer than normal mice, and are protected against obesity.

In humans, insulin levels rise with age, and aging is a risk factor for
Yet centenarians have a “preserved insulin action and glucose tolerance”, probably a good reason why they got to be centenarians. (Ref.)

So, it seems clear that insulin promotes aging, and this fits with lots of other evidence on what promotes, and what counteracts, aging.

**Anti-aging interventions lower insulin**

If insulin were truly and intimately involved in aging, we’d expect to see that interventions that fight aging and increase lifespan also lower insulin levels. And we do see that.

**Calorie restriction**

Calorie restriction, the most robust life-extension intervention known, also lowers insulin, and this is likely connected to its efficacy.

Humans who practice calorie restriction had an average fasting insulin level of 1.4, compared to controls at 5.1. Fasting glucose was lower as well, indicating better insulin sensitivity. (Ref.)

Another study compared humans on calorie restriction, body-fat matched endurance runners, and Western diet sedentary controls. The CR group had the lowest insulin, although not significantly different from the runners, and both were much lower than the Western diet group. (Ref.)

<table>
<thead>
<tr>
<th>Indices of glucose tolerance and insulin action</th>
<th>CR group (n = 28)</th>
<th>EX group (n = 28)</th>
<th>WD group (n = 28)</th>
<th>Among group P</th>
</tr>
</thead>
<tbody>
<tr>
<td>HOMA-IR</td>
<td>0.29 ± 0.1*</td>
<td>0.44 ± 0.3*</td>
<td>1.6 ± 1.3</td>
<td>0.0001</td>
</tr>
<tr>
<td>ISI</td>
<td>18.5 ± 6.7*</td>
<td>20.4 ± 9.2*</td>
<td>7.0 ± 3.6</td>
<td>0.0001</td>
</tr>
<tr>
<td>Fasting glucose (mg/dL)</td>
<td>83 ± 8*,**</td>
<td>91 ± 8</td>
<td>95 ± 8</td>
<td>0.0001</td>
</tr>
<tr>
<td>Fasting insulin (µU/mL)</td>
<td>1.4 ± 0.7*</td>
<td>2.0 ± 1.3*</td>
<td>6.9 ± 5.6</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

**Intermittent fasting**

*Intermittent fasting* both acutely and chronically lowers fasting insulin levels. (Ref.) When rats are fed a high-fat diet, they develop diabetes, but when fed the same diet but within an 8-hour daily feeding window, they do not develop diabetes. (Ref.)

**Ketogenic diet**

A very low carbohydrate ketogenic diet increases lifespan and healthspan in mice (ref.), and in humans, sharply lowers fasting insulin. (Ref.)
**Metformin**

Metformin, the diabetes drug, increases lifespan in mice. (Ref.) Metformin increases insulin sensitivity and lowers insulin levels. Mice on metformin had much lower insulin levels, though not as low as calorie-restricted mice.

**Exercise**

Exercise is of course one of the best health interventions, period.

Exercise, especially high-intensity exercise, decreases fasting insulin. (Ref.) See chart below. In this study, steady-state exercise – aerobics or cardio – had no significant effect on fasting insulin.

![Chart showing effect of exercise on fasting insulin](image)

**Resveratrol**

Resveratrol, the phytochemical found in grapes and some other plants, improves health of mice on a high-fat diet, and lowers their fasting insulin by over half. (Ref.)

**Moderate alcohol**

Light to moderate alcohol consumption is associated with better health. A randomized controlled trial found that one or two daily drinks (15 to 30 grams) for eight weeks in healthy women lowered fasting insulin. (Ref.)

**What all anti-aging interventions do**

Look at the following chart, which shows the effects of aging and major longevity interventions, including gene mutations, on mouse phenotypes. (Source.)
In the first column are the effects of aging. Then follow calorie restriction, metformin, rapamycin, as well as various gene mutations.

None of the interventions increase body mass, which is closely linked to insulin.

Only one of the interventions raised IGF-1, which is also closely linked to insulin. The one intervention which raised IGF-1 was a mutation in the IGF-1 receptor, so in that case there would still be low IGF-1 activity, since the receptor can’t respond as well.

On a side note, not also that none of the interventions increased fertility, which illustrates an evolutionary trade-off between growth and reproduction, on one hand, and longevity, on the other.

**Conclusion**

While there are other factors in aging, such as protein misfolding and glycation, amyloid production, etc., for the average person, insulin is arguably the most important.
Insulin is also connected to other major factors of aging:

- mitochondrial dysfunction
- decline of autophagy
- oxidative stress
- inflammation.

The interventions that keep fasting insulin low also counteract these major aging factors.

PS: If you need to lose weight and you want to save yourself years of poor results with bad information, I’ve put everything in a simple guide for you. The World’s Simplest Fat-Loss Plan.
Why Stress and Recovery Are Essential for Long Life

Stress and recovery are essential for long life and good health. While we usually think of “stress” as something bad, that really only applies to chronic stress. Certain acute stresses lead to better health and life extension.

No stress and too much comfort shorten life.

The rhythm of stress and recovery

The graph below (which I made) shows a natural daily rhythm that the body cycles through.

This rhythm is largely driven by food and by fasting.

When we eat, insulin increases, which leads to mTOR activation and anabolism.

A feature of muscle that most don’t realize is that it constantly builds up and breaks down, and this is normal and desirable.

Eat protein and other nutrients, and muscle protein synthesis increases. When fasting, muscle breaks down to supply necessary amino acids to the rest of the body. Leucine, a BCAA, is the master regulator of synthesis.

mTOR is a nutrient-sensing cellular mechanism that promotes both growth and
A prominent theory of aging (that of Mikhail Blagosklonny) holds that over-activation of mTOR is the primary driver of aging.

Yet mTOR is also necessary for good health. What seems to be happening in aging is chronic over-activation, not sporadic activation. Although it is certainly possible that any activation of mTOR promotes aging in some manner.

When fasting, the absence of nutrients decreases insulin, de-activates mTOR, and promotes autophagy, the cellular self-cleansing process that rids our cells of junk and keeps them youthful. A build-up of cellular junk occurs in aging due to decreased autophagy as well as the accumulation of non-degradable lipofuscin, leading to the “garbage catastrophe of aging”.

### Aging flattens the wave

Besides eating and fasting, longer term processes affect the shape of the sine wave above.

Aging is perhaps the most important.

As we get older, the daily rhythm starts to look like the one below, flatter than when youthful.

![Sine Wave](source)

The peaks are lower, so muscle protein synthesis doesn’t happen at the same rate as previously, when young.

That leads to the muscle loss seen in aging.

The valleys are higher, so autophagy is not induced at as high a rate as when young. That leads to accumulation of cellular junk, which in turn leads to poor cell function and the susceptibility to illness and breakdown that virtually defines the process of aging.

Insulin becomes chronically higher in aging, which in turn activates mTOR and promotes even more aging in a vicious cycle.

The graph below (source) shows how these factors interrelate. Insulin activates mTOR, which inhibits autophagy. (This makes perfect sense, since
The importance of stress and recovery

Interventions that stress the body generally lead to deactivation of mTOR, lower insulin, catabolism, and increased autophagy.

Interventions that allow recovery generally lead to activation of mTOR, increased insulin, anabolism, and decreased autophagy.

Both are necessary.

But in the modern world, recovery and comfort dominate.

If we are always eating and resting, we never apply the necessary stress to our bodies.

Consequently, without stress, it deteriorates.

Obesity soundly represses autophagy and therefore activates mTOR and promotes...
aging. Or as I like to say, **obesity is an archetype of aging.**

It’s an open question **how much of aging is just people letting themselves go.** Certainly, animals age, and while aging is intrinsic to almost every organism, a decline in physical function leads to more aging in a cycle of reinforcement.

For example, mainstream thinking has it that insulin resistance increases with age, and that it’s closely connected to aging. Yet when abdominal fat is controlled for, **aging explains only a small fraction of the variance in insulin sensitivity.**

These results suggest that insulin resistance is more closely associated with abdominal adiposity than with age.

Therefore, you can fight aging by maintaining good insulin sensitivity. (Article coming soon on this.)

To our point here, **how much of aging is due to too much comfort and not enough stress?**

It seems to be a given that as people age, they feel they “deserve” their comfort and lack of exertion. (Not to mention lack of ambition.) Psychological feelings of entitlement (for lack of a better word) could accelerate aging in this manner.

If we stress ourselves often, allowing for full recovery, we have a means of counteracting aging.

**How to stress and recover**

The means of stress are many and have been discussed on this site many times.

- **Exercise.** Resistance training and HIIT are the most effective for both activating stress response mechanisms as well as ramping up muscle anabolism.
- **Intermittent fasting.** By going without food, we decrease insulin and mTOR activation, and increase autophagy. This stress helps keep cells in fine tune and facilitates the proper working of our physiology.
- **Other stresses include cold showers, sauna bathing, solar radiation, AMPK activators like metformin and resveratrol, other phytochemicals such as in tea and coffee.** Even occasional loss of sleep can cause a beneficial stress, relieving depression.

The means of recovery:

- **Food.** Eating puts us into recovery and anabolic mode. Quality of food is important, such as adequate protein.
- **Sleep and rest.**

In our modern world, the emphasis is on recovery. We eat constantly and never
get into a properly fasted state, then we sit on our backsides watching Netflix.

Too much stress is harmful of course, since the principle of hormesis requires a low-dose of a stress or toxin. Too much exercise, too much cold exposure, etc, can be harmful. However, those limits are reached by few.

Some form of stress should be practiced daily, in my opinion.

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