



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 [cardiorespiratory 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:

Purified Rodent Diet AIN-93G

for Rats and Mice Diets



AIN-93G was the first of two open formulations published by the American Institute of Nutrition (AIN) committee in 1993 improving the laboratory standard, AIN-76A diet. AIN-93G is designed to accommodate the increased nutritional demands of rat or mouse growth as well as females who are pregnant or lactating, hence the "G" designation.

Dietary Ingredient Composition (% by Weight)

Corn Sugar	39.75	Solka Floc-40	5.00	L-Cystine	0.30
Casein Lactic	20.00	AIN-93 Mineral Mix	3.50	Choline Bitartrate	0.25
Granular Sugar	10.00	AIN-93 Vitamin Mix	1.00	Soy Oil	7.00
Dextrin	13.20				

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.

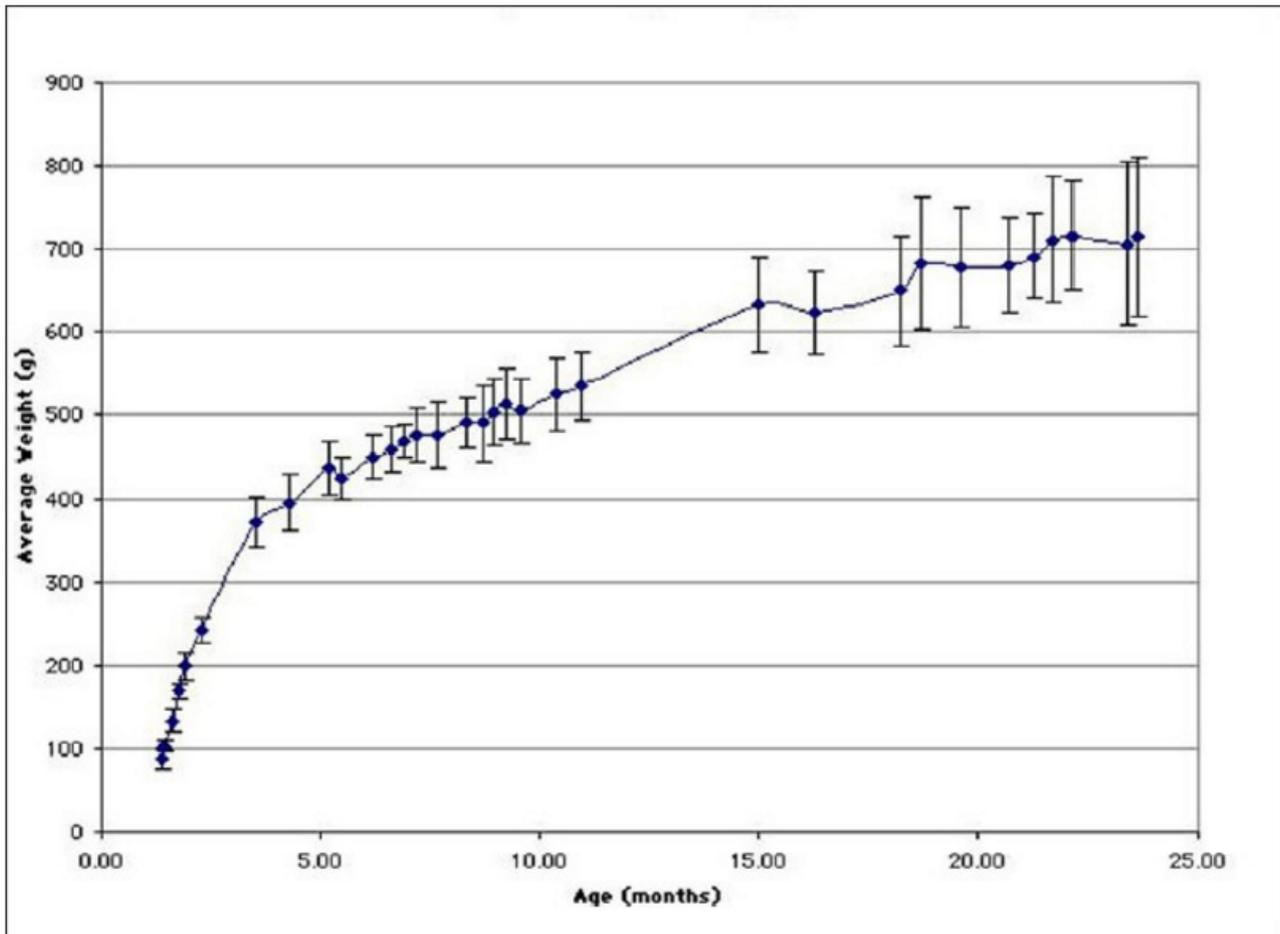
But is that aging, or is it something else.

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.](#))



Variations in body weight of male rats throughout the lifespan

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:



The Rodent NTP-2000 open formula diet is formulated specifically to meet the nutrient requirements of rats and mice involved in long-term toxicology studies supported by the National Toxicology Program.

Dietary Ingredient Composition (% by Weight)

Ground Whole Wheat	23.00	Soy Protein Concentrate	4.00	Dicalcium Phosphate	0.40
Ground No. 2 Yellow Corn	22.44	Fish Meal (60%)	4.00	Salt	0.30
Wheat Middlings	15.00	Soybean Oil	3.00	DL Methionine	0.20
Oat Hulls	8.50	Corn Oil	3.00	Premixes	1.26
Alfalfa Meal	7.50	Brewers Dried Yeast	1.00		
Solka Floc-40	5.50	Calcium Carbonate	0.90		

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.

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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.](#)

