

Micronutrients and Exercise Ameliorate Aging

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STORY AT-A-GLANCE

- › Vitamin D, magnesium and properly dosed exercise are factors that can delay biological aging and enhance health span and longevity
- › Acting as a steroid hormone, vitamin D significantly influences gene expression related to health and aging. Achieving optimal levels (around 60 ng/mL) through sun exposure and/or supplementation is crucial for optimal health
- › Half of the U.S. population fails to meet magnesium intake recommendations, impairing crucial processes like DNA repair and increasing cancer and mortality risks. Supplemental forms like magnesium glycinate, malate, citrate, or L-threonate, alongside a diet rich in dark leafy greens, can mitigate this deficiency
- › Vigorous exercise that reaches 75% to 80% of maximum heart rate improves VO2 max, cardiorespiratory fitness, mitochondrial biogenesis, and reduces cancer risks through mechanical blood flow forces. However, moderation is key
- › A balanced regimen that includes up to 75 minutes of HIIT per week, coupled with unlimited moderate-intensity activities and 40 minutes of strength training will maximize your health benefits without backfiring

The video above features a lecture by Rhonda Patrick Ph.D., a cell biologist and cofounder of FoundMyFitness, at the American Academy of Anti-Aging Medicine Longevity Fest in 2023. In it, she reviews key nutrients and health habits that have been shown to delay biological aging and improve health span. As noted by Patrick:

“You don't have to move mountains to make a big impact on aging. Starting with a few key areas of focus can make a big difference.”

The Importance of Vitamin D

Beyond its status as a vitamin, vitamin D also functions as a steroid hormone that interacts with DNA to regulate gene expression. This regulation impacts more than 5% of the protein-encoding human genome, which has a substantial impact on overall health and aging processes.

As noted by Patrick, vitamin D deficiency is commonplace, and that's a foundational culprit that contributes to poor public health. Approximately 70% of the population has inadequate vitamin D levels, defined as less than 30 nanograms per milliliter (ng/mL).

Factors contributing to this widespread deficiency include limited sun exposure due to modern indoor lifestyles, the use of sunscreen, melanin in darker skin tones, geographical latitudes with low UVB radiation, and decreased efficiency in vitamin D production with age.

If you live in an area where sufficient year-round sun exposure is impossible, then supplementing with oral vitamin D3, in combination with K2 and magnesium, is highly advisable.

Ideally, you'll want to measure your vitamin D level twice a year, in the middle of winter and summer, to establish your high and low points, and then supplement (or, if possible, get enough sun exposure) to maintain a level around 60 ng/mL, which is associated with the lowest all-causes mortality rates; 40 ng/mL is thought to be at the low end of sufficiency.

While Patrick recommends a daily intake of 4,000 IU's, many will need upwards of 8,000 IUs a day. Generally, 1,000 IUs of vitamin D can increase blood levels by about 5 ng/mL, Patrick says. You can optimize the bioavailability of the vitamin D by taking it with vitamin K2 and magnesium though.

Vitamin K2 and Magnesium Lower Your Vitamin D Requirement

Research¹ shows you need 146% more vitamin D to achieve a blood level of 40 ng/ml (100 nmol/L) if you do not take supplemental magnesium, compared to taking your vitamin D with at least 400 mg of magnesium per day. Your vitamin K2 intake can also affect your required vitamin D dosage.

Data² from nearly 3,000 individuals revealed 244% more oral vitamin D was required to get 50% of the population to achieve a vitamin D level of 40 ng/ml (100 nmol/L) if they weren't concurrently also taking magnesium and vitamin K2. So, a simple way to optimize your vitamin D absorption is to take it in conjunction with magnesium and K2.

As noted by Patrick, optimizing your vitamin D level has been shown to decrease epigenetic age, which suggests it has the potential to slow down the aging process. Adequate vitamin D levels are also linked to lower mortality and healthier aging, underscoring vitamin D's role in maintaining physiological functions and preventing diseases associated with aging.

Magnesium Deficiency Impairs DNA Repair

Magnesium is another common deficiency that takes a major toll on health. Approximately half of the U.S. population does not meet the recommended levels of magnesium, primarily due to insufficient consumption of magnesium-rich foods, such as dark leafy greens.

Magnesium is a cofactor for over 300 enzymatic processes, including energy production (ATP), energy utilization and DNA repair. DNA damage occurs constantly in our cells due to various internal and external factors, such as metabolic processes, exposure to harmful chemicals, and UV radiation.

Your body has a sophisticated system to repair this damage, ensuring the integrity of the genetic material is maintained, which is crucial for preventing mutations that could lead to diseases like cancer.

When magnesium levels are inadequate, the efficiency of these DNA repair enzymes is compromised. This deficiency means that the body's ability to repair DNA damage promptly and accurately is reduced, allowing the accumulation of DNA errors.

Over time, these unrepaired errors can lead to mutations, some of which may be oncogenic (cancer-causing), contributing to the initiation and progression of cancer and other diseases associated with aging.

Therefore, maintaining adequate magnesium levels is essential for your body's DNA repair mechanisms to function optimally. This alone suggests that magnesium can have a significant impact on aging and disease prevention.

Patrick cites studies showing that adequate magnesium intake is associated with a reduced risk of cancer and lower all-cause mortality rates. For example, one study noted a 24% reduction in pancreatic cancer risk with every 100 milligrams of magnesium intake, while another observed a 40% lower all-cause mortality and a 50% decrease in cancer mortality among those with the highest magnesium levels.

How Much Magnesium Do You Need?

While obtaining magnesium from dietary sources like dark leafy greens is preferred, supplemental forms of magnesium are a viable alternative to ensure adequate intake. While Patrick recommends magnesium glycinate, magnesium malate and magnesium citrate, my preferred form is magnesium L-threonate, as it's particularly good at crossing the blood-brain barrier.³

The daily magnesium requirements vary by age and gender, with adult men needing approximately 400 mg and women requiring about 300 to 350 mg. Active individuals and those who sweat significantly (e.g., through exercise or sauna use) may need 10% to 20% more than the Recommended Dietary Allowance (RDA) to compensate for magnesium loss through sweat.

How Increasing Your VO2 Max Affects Life Expectancy

Patrick also reviews the impact of exercise on life expectancy and health span. I fully understand that the bulk of the evidence points to a high VO2 max improving longevity. I did aggressive long distance running for over 40 years and ran a 2:50 marathon. But I am now unconvinced that this is true. I believe this information is inaccurate and do not recommend using it as a goal for your fitness.

So, my recommendations veer from Patrick's a bit, as I believe Dr. James O'Keefe's research, published in the March-April 2023 issue of Missouri Medicine,⁴ has nailed down the details for exercise volume and the type of exercise that provides the greatest longevity benefits.

I [interviewed O'Keefe](#) about his findings in November 2023. While Patrick highlights research showing the benefits of vigorous exercise (characterized by reaching 75% to 80% of one's maximum heart rate), O'Keefe's groundbreaking review shows that high-intensity exercise backfires if you do too much of it.

That said, before I go into my own exercise recommendations, here are some of the key points presented by Patrick:

- VO2 max, a direct measure of cardiorespiratory fitness, is tightly linked to longevity. Enhancements in VO2 max are associated with substantial increases in life expectancy, with a notable impact observed even with modest improvements in fitness levels.
- According to a 2018 JAMA study, there's no upper limit to the mortality reduction benefits of high cardiorespiratory fitness, indicating a profound 80% reduction in all-cause mortality from the lowest to the elite fitness levels. Incremental improvements in VO2 max were found to correlate with a 45-day increase in life expectancy, underscoring the linear relationship between fitness improvements and longevity.
- High-intensity interval training (HIIT) has been shown to be particularly effective for improving VO2 max, especially among individuals who do not respond to moderate-intensity exercise.

- Patrick recommends the Norwegian 4 x 4 protocol, which involves four minutes of maximum intensity exercise followed by three minutes of rest, repeated four times, for enhancing VO2 max.

Too Much Vigorous Exercise Backfires Big Time

O'Keefe's systematic review revealed that if you're sedentary and begin to exercise, you get a dose-dependent decrease in mortality, diabetes, depression, high blood pressure, coronary disease, osteoporosis, sarcopenia, falls and more. So, most definitely, you can dramatically slow aging and improve life expectancy with exercise. However, at the very high end, the people who are doing the highest volume of vigorous exercise start losing those benefits. According to O'Keefe:

"They're not as bad off as sedentary people, but virtually every study you can find, they will lose some of those benefits for longevity, and certainly for things like atrial fibrillation.

If you go from sedentary to exercise moderately, you have less atrial fibrillation. But if you're doing full distance triathlons when you're over age 40 or 45, you start seeing a 500% to 800% increase in atrial fibrillation."

O'Keefe cited a large-scale study that followed about 1 million individuals for more than 10 years. While vigorous exercise up to 75 minutes per week reduced the risk of all-cause mortality and other diseases in a dose-dependent manner, benefits plateaued after that.

So, people who were doing four to seven hours of vigorous exercise per week didn't get any additional benefit and, from a cardiovascular standpoint, lost a little.

You Cannot Overdo Moderate Exercise

In the case of moderate exercise, however – loosely defined as exercising to the point where you're slightly winded but can still carry on a conversation – it's very clear that

more is better and cannot be overdone. Examples include gardening, walking, recreational bike riding, yoga, nonintense swimming and pickleball.

Perhaps even more surprising, moderate exercise also improves all-cause survival better than vigorous exercise – about two times better. "If you look at the people who are doing the most vigorous exercise compared to the people doing the most moderate exercise, the moderate exercisers have twice as good a reduction in long-term mortality as the high volume vigorous exerciser," O'Keefe noted. What this means in practical terms is that:

- a) There's no need to engage in high-intensity strenuous exercise beyond 75 minutes per week. Doing so can be highly counterproductive. If you're an overachiever, stick to moderate exercise instead and your benefits will continue to accrue and your efforts won't eventually backfire.
- b) Once you get into your mid-40s and 50s, exercise should be fun and stress-reducing, not competitive. In his analysis, O'Keefe also stresses the importance of "social exercise" over solo exercise: playing a game of pickleball with friends, for example.

Several years ago, he conducted a study with colleagues in Copenhagen, Denmark, in which they looked at long-term granular data on physical activity and longevity.

Playing tennis conferred 9.5 years of extra life expectancy; playing badminton got seven years; running, swimming and cycling were associated with just 3.5 years of extra life expectancy. Health club activities such as weightlifting and running on a treadmill only conferred 1.5 years of additional life expectancy compared to sedentary life.

What Big Data Tell Us About the Benefits of Walking

Walking should not be underestimated either. The average American walks about 3,800 steps a day, which is just short of 2 miles. It's about 2,000 steps per mile, and every

1,000 steps you get on average per day reduces your mortality by 10% to 15%. As O'Keefe told me:

"There's been more and more studies on this all the time, using activity trackers. We're getting big data, like the UK biobank, which is a half a million people, and there's a sizable subgroup of them who have been wearing activity trackers and been followed for 10 years now.

Clearly, more is better. You get the big gains going from sedentary lifestyles – 2,000 to 3,000 steps a day – up to 7,000 or 8,000. [Here] you have this very steep reduction in mortality, improvement in survival. It continues to about 12,000 steps a day. Most of the studies show that it plateaus at 12,000."

Overdoing Strength Training Is Worse Than Doing Nothing at All

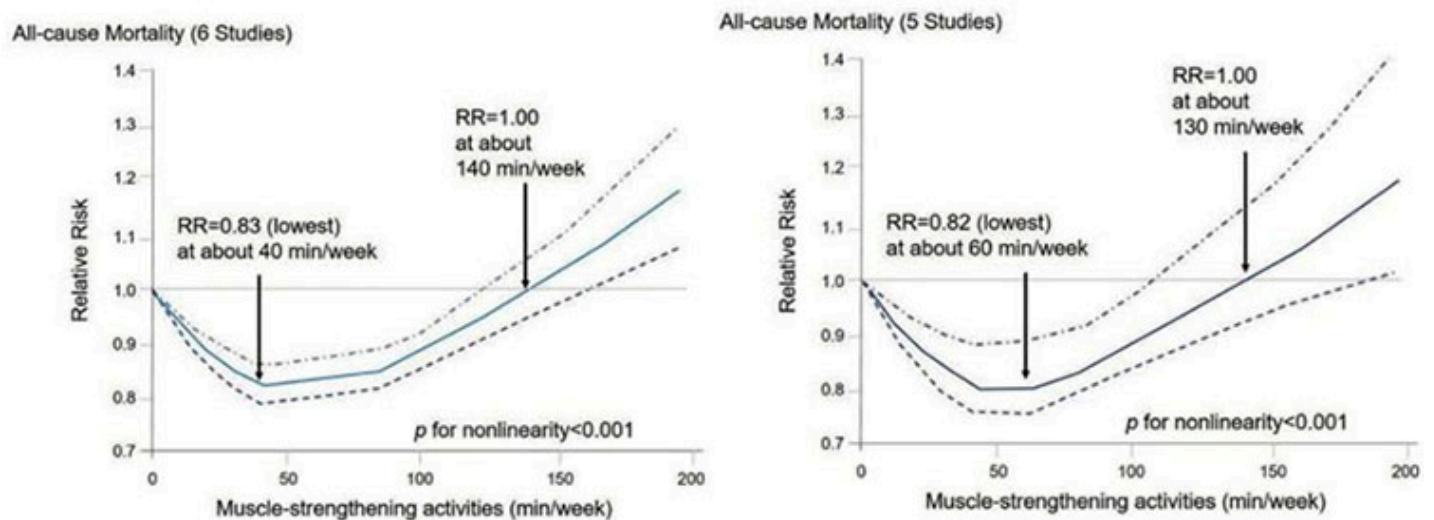
O'Keefe's meta-analysis also detailed the sweet spot for strength training, and the results truly shocked me. I radically changed my exercise program after reviewing these data.

Without question, strength training will improve muscle mass, muscle and bone strength. It can also boost your testosterone level if not overdone. It helps to improve mood and prevent falls. As you get into your 30s, you start to lose muscle mass and if you don't train to maintain muscle mass, you'll eventually end up with sarcopenia (low muscle mass) or osteoporosis (low bone density). O'Keefe commented:

"I've always been a fan of strength training ... But again, the devil is in the details about the dosing. When you look at people who do strength training, it adds another 19% reduction in all-cause mortality on top of the 45% reduction that you get from one hour of moderate exercise per day.

When I strength train, I go to the gym and spend anywhere from 20 to 40 minutes, and ... I try to use weights that I can do 10 reps with ... After that, you're feeling sort of like spent and ... it takes a couple of days to recover. If you

do that two, at the most three, times a week, that looks like the sweet spot for conferring longevity."



The graph above, from the meta-analysis, shows the J-shaped dose-response for strength training activities and all-cause mortality. As you can see, the benefit maxes out right round 40 to 60 minutes a week. Beyond that, you're losing benefit.

Once you get to 130 to 140 minutes of strength training per week, your longevity benefit becomes the same as if you weren't doing anything, which is nothing short of shocking. If you train for three to four hours a week, you actually end up with WORSE long-term survival than people who don't strength train!

Recall, when you're doing intense vigorous exercise in excess, you're still better off than people who are sedentary. But for some (yet undetermined) reason, excessive strength training leaves you worse off than being sedentary.

So, the take-home message here is that 20 minutes twice a week on non-consecutive days, or 40 minutes once a week is the sweet spot. You also don't want your exercise regimen to center around strength training. It should be an add-on, as you get far greater benefits simply from walking, or any other moderate exercise.

So, to wrap this up, each of these components – vitamin D, magnesium and optimally dosed exercise – plays a unique and pivotal role in maintaining and improving various

aspects of physiological health, which, when combined, can help slow down your aging process and help you live longer.

Sources and References

- ¹ [GrassrootsHealth](#) Is supplemental magnesium important for vitamin D levels?
- ² [GrassrootsHealth](#) Are both supplemental magnesium and vitamin K2 combined important for vitamin D levels?
- ³ [Dr. Taylor Wallace](#), February 22, 2022
- ⁴ [Missouri Medicine](#) March-April 2023; 120(2): 155–162