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Metformin Could Lessen Some of the Benefits People Get from Exercise

Analysis by Dr. Joseph Mercola | July 14, 2026

STORY AT-A-GLANCE

- Metformin is a widely prescribed Type 2 diabetes drug that works by lowering liver glucose production and improve insulin sensitivity
- A 16-week Rutgers trial in 72 adults found that metformin dulled exercise benefits, reducing the usual improvements in aerobic fitness
- Long-term risks for prolonged metformin use include vitamin B12 deficiency, rare lactic acidosis, and hypoglycemia
- Skipping breakfast, not getting enough sleep, consuming too much alcohol, and social isolation can greatly disturb glucose regulation and increase the risk of developing diabetes over time
- Lifestyle strategies such as consistent movement and a bioenergetic, nutrient-dense diet can support insulin sensitivity. Berberine may also help to slowly wean you off metformin medication

Type 2 diabetes affects nearly 35 million Americans and more than 450 million people worldwide,[1] and the numbers are still climbing. Behind these figures are individuals navigating the daily challenge of controlling their blood sugar.

For decades, experts believed that pairing metformin, the most widely prescribed diabetes medication, with exercise was beneficial.[2] This recommendation, reinforced by clinical guidelines since 2006, is grounded in the idea that exercise improves glucose

control and cardiovascular health, while metformin helps regulate blood sugar levels.[3]

Now, researchers are questioning whether this long-standing combination truly delivers on its promise, and emerging evidence suggests the answer may not be as straightforward as once thought.

Study Challenges Beliefs About a Popular Diabetes Drug

A 2025 study conducted by researchers from Rutgers University, published in The Journal of Clinical Endocrinology and Metabolism, examined how metformin interacts with exercise. In their clinical trial, the researchers found that metformin may actually blunt or weaken the improvements typically gained from exercise,[4] including improved blood vessel function, aerobic fitness, and blood sugar control.[5]

- **Study subjects and how they were grouped —** The research team recruited 72 adults at risk for metabolic syndrome, which is characterized by high blood pressure, increased blood sugar, and excess body fat. These factors raise the likelihood of diabetes and heart disease. The participants were randomly divided into four groups:[6]
    - **Low-Intensity Exercise + Placebo (LoEx + PL) —** Participants performed low-intensity exercise at about 55% of VO_2max, five days per week, and received a placebo.
    - **Low-Intensity Exercise + Metformin (LoEx + Met) —** Participants followed the same low-intensity exercise regimen (~55% VO_2max, 5 days/week) combined with metformin at 2,000 milligrams (mg) per day.
    - **High-Intensity Exercise + Placebo (HiEx + PL) —** Participants engaged in high-intensity exercise at about 85% of VO_2max, five days per week, and received a placebo.

    - **High-Intensity Exercise + Metformin (HiEx + Met) —** Participants followed the same high-intensity exercise regimen (~85% VO_2max, 5 days/week) combined with metformin at 2,000 mg per day.

- **Study methodology —** For 16 weeks, researchers monitored changes in vascular insulin sensitivity, a measure of how well blood vessels respond to insulin and dilate to deliver oxygen, hormones, and nutrients after meals.[7] They also tracked aerobic fitness (VO_2max), fasting glucose, and inflammation markers, including tumor necrosis factor alpha (TNF-α) and endothelin-1.[8]

- **No metformin, no problem —** Participants who exercised without metformin experienced improvements in aerobic fitness and decreases in inflammation markers, changes that indicate better metabolic health and a lower risk of disease.

  Steven K. Malin, Ph.D., a professor in the Department of Kinesiology and Health at Rutgers' School of Arts and Sciences and the study's lead author, told the Independent:[9]

  > *"Blood vessel function improved with exercise training, regardless of intensity. Metformin blunted that observation, suggesting one type of exercise intensity is not better either with the drug for blood vessel health."*

  Exercise alone enhanced vascular insulin sensitivity, meaning blood vessels became more responsive to insulin and allowed for greater blood flow to muscles. This is important because insulin's ability to dilate blood vessels is crucial for transporting glucose from the bloodstream into tissues, helping to lower blood sugar after meals.[10]

- **What happened when metformin was added —** Upon the addition of said drug, the gains in aerobic fitness disappeared, and reductions in fasting glucose and inflammation were smaller.[11]

> *"If you exercise and take metformin and your blood glucose does not go down, that's a problem. People taking metformin also didn't gain fitness. That means their physical function isn't getting better and that could have long-term health risk,"* Malin explained.

Facts About Metformin

Metformin is an oral antidiabetic medication from the biguanide class, and was approved for use by the U.S. Food and Drug Administration (FDA) in 1994. It lowers blood sugar without prompting the pancreas to produce more insulin, making it a safer alternative to older diabetes drugs that can cause hypoglycemia.[12]

- **Medicine with a botanical history —** Metformin originates from Galega officinalis (French lilac or goat's rue), a plant once used in Medieval Europe as an herbal remedy for diabetes-like symptoms. In the 1920s, researchers discovered it contained guanidine, an anti-hyperglycemic compound. Its predecessor, phenformin, was the first oral biguanide but was later withdrawn due to a high risk of fatal lactic acidosis.

  Today, metformin is available in immediate- and extended-release forms and is often combined with other medications to improve blood sugar control.[13]

- **In conventional medicine, it is the first-line treatment for Type 2 diabetes in adults and children over 10 —** In addition to diabetes management, metformin is prescribed off-label for preventing prediabetes, gestational diabetes, polycystic ovary syndrome (PCOS), and to reduce weight gain caused by antipsychotic medications.[14]

- **Despite its widespread use and safety claims, there are side effects associated with this drug —** When you start taking metformin, you might experience the following symptoms:[15]

  - Heartburn

- Stomach pain
- Nausea or vomiting
- Bloating
- Gas
- Diarrhea
- Constipation
- Weight loss
- Headache
- Metallic taste in your mouth

Metformin May Not Be as Harmless as You Think

Metformin is commonly prescribed for blood sugar management and is often compared with newer options such as **GLP-1 injections**. However, like most pharmaceutical solutions, it comes with certain risks. Long-term use can lead to adverse effects, including:

- **Vitamin B12 deficiency —** Numerous studies have found that people on long-term metformin medication may develop this deficiency because the drug interferes with calcium ions in the gut, blocking the formation of the vitamin B12-intrinsic factor complex needed for absorption in the ileum.[16]

  One notable study found that individuals with Type 2 diabetes on long-term metformin therapy have a significantly increased risk of vitamin B12 deficiency compared to those not on the medication. This deficiency can occur in up to 93% of patients over prolonged use. According to this study:[17]

"The mechanism behind it can be either directly reducing the vitamin B12 absorption or altering the motility of the small intestine. According to reports, 14% to 30% of people on long-term metformin have lower level of vitamin B12 in blood, and 30% develop vitamin B12 malabsorption."

The risk is notably higher with doses exceeding 2,000 mg daily and treatment durations of over four years, which makes older adults more susceptible. This can be problematic because vitamin B12 deficiency is associated with a range of health issues, such as:[18]

- Peripheral neuropathy
- Numbness or tingling in your feet and legs associated with diabetes
- Anemia

If you want to know more about how metformin impacts your vitamin B12 levels, check out "**Metformin Use Shown to Induce Vitamin B12 Deficiency in Diabetics**."

- **Metformin-associated lactic acidosis (MALA) —** Although rare, lactic acidosis is one of the most serious complications associated with metformin. This risk is higher in patients with kidney dysfunction, severe infection, dehydration, or heart failure.[19]

  One review estimates the incidence of MALA at 2.4 to 3.9 cases per 100,000 patient-years, but the mortality rate can reach 30% to 50% if not treated promptly. Risk rises sharply in patients with a low estimated glomerular filtration rate (eGFR), which refers to how much blood the kidneys filter per minute (low eGFR is below 30 mL/min), those with liver disease, or those experiencing acute illness. Symptoms to watch for include:[20]

  - Extreme fatigue and weakness
  - Muscle pain

- Abdominal discomfort
- Rapid breathing and shortness of breath
- Confusion or dizziness

According to the authors of the study, even if MALA is life-threatening, it is still treatable:[21]

> *"Since critically ill patients often have risk factors — such as hypoxemia, cardiac failure, and renal impairment — that combine with metformin to elevate the risk of MALA, it is prudent to stop metformin for these patients initially even in the absence of lactic acidosis.*
>
> *Once clinicians diagnose MALA, treatment needs to start immediately with the cessation of metformin. In the setting of severe metformin toxicity, supportive management of affected organ systems is necessary."*

- **Hypoglycemia —** Metformin is often compared to sulfonylureas, which can trigger hypoglycemia by stimulating insulin release. According to the American Diabetes Association (ADA), metformin itself is not typically linked to hypoglycemia. However, prolonged use may still affect blood sugar regulation in ways that warrant caution. As noted in a Diabetes Care paper:[22]

> *"[The] reported risks of hypoglycemia for metformin users varied between 0 and 21%. Since metformin does not directly stimulate insulin secretion, hypoglycemia risk may be lower than for that of other oral antidiabetes drugs. However, hypoglycemia in patients using metformin may occur in association with strenuous physical activity or fasting."*

One case report documented a 58-year-old man on standard-dose metformin monotherapy who developed symptomatic hypoglycemia, including severe weakness, confusion, sweating, dizziness, and palpitations. Continuous glucose

monitoring showed episodes occurring up to 4% of the time, mostly at night. Within two weeks of stopping metformin, all hypoglycemic episodes ceased, challenging the belief that metformin never causes hypoglycemia on its own.[23]

> *"This case report supports that there is a risk of symptomatic hypoglycemia with therapeutic doses of metformin. Although advised to be taken with meals to avoid gastrointestinal upset, patients should be educated to take metformin with meals to reduce the risk of metformin-associated hypoglycemia, especially in individuals who frequently engage in strenuous activities,"* the authors concluded.

What Increases Your Risk of Diabetes?

While obesity, genetics, and an unhealthy diet composed of ultraprocessed foods are major factors that increase your chances of developing diabetes, there's an interesting twist — Avoiding certain habits can also raise your risk. These aren't the usual suspects, but they play a surprisingly important role in how your body handles blood sugar.

- **Choosing to skip breakfast —** A 2019 review found that people who regularly skip breakfast have a significantly higher risk of Type 2 diabetes, even after accounting for weight. Why does this happen? Missing that first meal often leads to overeating later in the day, blood sugar spikes, and poor appetite control. Breakfast eaters tend to maintain a healthier BMI and better glucose balance.[24]

- **Alcohol overload —** Alcohol-related deaths in the United States are skyrocketing, with more than 54,000 lives lost in 2021 alone.[25] Despite this alarming trend, many people still believe in moderation myths fueled by glitzy marketing. Drinking outside of meals or exceeding one drink for women and two for men significantly increases health risks.

  Excess alcohol adds calories, promotes weight gain, and inflames the pancreas, impairing insulin secretion.[26] If you need practical advice on how to say no to alcohol, read "**US Alcohol-Related Deaths Are Skyrocketing, New Data Shows**."

- **Being sleep deprived —** Ongoing sleep deprivation disrupts hormone levels, increasing cortisol and decreasing insulin secretion after eating. Over time, these changes lead to higher blood sugar levels and a greater risk of diabetes. A 2023 systematic review confirmed that both short (typically less than six hours) and long (normally more than nine hours) sleep durations are associated with an increased risk of developing Type 2 diabetes.[27]

  > *"The studies showed that short sleepers had greater levels of circulating insulin during fasting, fasting glucose, and homeostatic model assessment for insulin resistance (HOMA-IR). Insufficient sleep and poor sleep hygiene were linked to increased glycated hemoglobin (HbA1c) levels in an adult Type 2 diabetes study.*
  >
  > *In a research of middle-aged Caucasian volunteers, it was discovered that there was a substantial association between poor sleep quality and metabolic syndrome, as well as between sleep condition and insulin, fasting glucose levels, and insulin resistance. Type 2 diabetes and sleep disorders are prevalent conditions that often coexist.*
  >
  > *People with Type 2 diabetes frequently experience sleep problems, which can have a detrimental effect on their general health, emotions, and quality of life."*

- **Lack of social connection —** Loneliness affects more than just your emotional well-being; it also negatively impacts your metabolic health. A follow-up study, based on a 20-year-old research piece published in Diabetologia, investigated the link between loneliness and the development of Type 2 diabetes, utilizing data from the Trøndelag Health Study (HUNT Study) in Norway. The researchers found that the risk of diabetes was two times higher in people who felt most lonely.[28]

  > *"This study suggests that loneliness may be one factor that increases the risk of Type 2 diabetes; however, there is no strong support that the effect of loneliness on Type 2 diabetes is mediated by depression or insomnia.*

> *We recommend that loneliness should be included in clinical guidelines on consultations and interventions related to Type 2 diabetes,"* the researchers concluded.

Your HOMA-IR Score Helps You Identify Insulin Resistance Early

If metformin causes side effects and might reduce exercise benefits, ask yourself, "Do I really need it?" Before choosing medication, assessing your body's response to insulin and risk of insulin resistance is helpful. One easy way to gauge this is with the HOMA-IR test, which stands for Homeostatic Model Assessment of Insulin Resistance.

- **What HOMA-IR tells you** — This test shows how hard your body works to control blood sugar. A higher score indicates your pancreas produces more insulin due to poor cell response, a sign of insulin resistance that appears before blood sugar rises. Ideally, your score should be under 1.0, but going above signals it's time to act.

- **How your score is calculated** — Unlike complex hospital procedures, HOMA-IR uses two simple fasting blood tests: glucose and insulin. These numbers are plugged into a formula:

  HOMA-IR = (Fasting Glucose in mg/dL × Fasting Insulin in μU/mL) ÷ 405

  Most labs can run these tests quickly and affordably, making HOMA-IR far more practical than invasive research methods.

- **Why it's better than waiting for your blood sugar levels to rise** — Standard blood sugar tests often miss early metabolic changes. By the time glucose levels rise, insulin resistance has been brewing for years. HOMA-IR fills that gap by detecting trouble early, giving you a chance to intervene before medication becomes necessary.

Doctors frequently prescribe metformin as the initial treatment for insulin resistance, but HOMA-IR provides a more innovative method. It assists you and your healthcare provider in determining whether medication is genuinely necessary or if lifestyle modifications can suffice.

If you want to read more about HOMA-IR and insulin resistance, check out "**Are Mood Disorders Actually Metabolic Diseases Rooted in Insulin Resistance?**"

Tips for Drug-Free Diabetes Management

Lifestyle changes such as diet and exercise have been shown to prevent Type 2 diabetes more effectively than metformin alone. Studies confirm that weight loss, regular physical activity, and balanced eating significantly improve insulin sensitivity and glycemic control.[29] Beyond the basics, here are practical strategies that can help you take charge of your blood sugar naturally:

- **Make mindful swaps and choose the healthy fats —** Highly processed seed oils — including soybean, canola, corn, sunflower, and safflower — are significant sources of **linoleic acid (LA)**. This polyunsaturated fat (PUF) can interfere with mitochondrial function and disrupt metabolic balance. Keep your LA intake below 5 grams (g) per day, ideally under 2 g, and opt for heat-stable, nutrient-rich fats like ghee or beef tallow for cooking. Use a nutrition tracker to stay on target.

- **Eat for energy, not empty calories —** Choose a balanced, bioenergetic eating style that focuses on whole carbs, lean protein, and healthy fats. This approach helps your body use glucose efficiently, reduces mitochondrial stress, and supports steady energy. I talk about this in detail in my book, "**Your Guide to Cellular Health: Unlocking the Science of Longevity and Joy**."

- **Stay active —** As the featured study highlighted, exercise is a cornerstone of diabetes management, even without the use of metformin. The ADA recommends at least 150 minutes of moderate-to-vigorous aerobic activity weekly, plus two to

three resistance sessions. But don't think of it as a chore — find an activity you enjoy, like brisk walking, cycling, or strength training.

Movement improves insulin sensitivity, aids weight control, and boosts mood, making it one of the most effective tools for long-term health.[30]

- **Explore berberine's benefits** — Berberine has earned the nickname "nature's Ozempic" because of its potential to support weight loss by improving how your body uses energy. While research on weight-loss effects is still emerging, some studies show modest reductions — about 5% to 7% of body weight — when combined with healthy eating and exercise.[31]

  Beyond weight management, berberine activates adenosine monophosphate-activated protein kinase (AMPK), an enzyme that helps regulate metabolism, and improves insulin sensitivity. These actions support better long-term blood sugar control. A 2022 review of controlled trials found that taking about 1,000 mg daily can help lower fasting blood sugar, improve cholesterol levels, and reduce systolic blood pressure.[32]

  Most berberine supplements contain 500 mg per capsule, and labels often recommend taking two to three capsules per day before meals (not with food), totaling 1,000 to 1,500 mg daily. It's best taken earlier in the day rather than at night.[33]

  Berberine is generally safe for daily use, but avoid it if you're below the age of 18, pregnant, breastfeeding, or taking medications such as blood thinners, statins, or diabetes drugs.[34]

- **Supplement with B12** — Long-term use of metformin may lead to vitamin B12 deficiency, raising the risk of anemia and nerve damage. For mild deficiencies, oral supplements of 1,000 to 2,000 micrograms (mcg) daily can be effective, while more severe cases or absorption problems might require monthly intramuscular injections.[35]

Frequently Asked Questions (FAQs) About Metformin and Diabetes Management

Q: How many people are affected by Type 2 diabetes in the U.S. and worldwide?

A: Nearly 35 million Americans and more than 450 million people worldwide are living with Type 2 diabetes, numbers that continue to rise.

Q: What is metformin?

A: Metformin, an oral biguanide approved by the FDA in 1994, is the first-line treatment for Type 2 diabetes in adults and children over a certain age. Despite its widespread use, long-term use has been associated with vitamin B12 deficiency, which can exacerbate neuropathy and cognitive issues, as well as rare but severe cases of metformin-associated lactic acidosis (MALA) and occasional hypoglycemia.

Q: What longstanding belief did the study question about metformin and exercise?

A: For many years, doctors thought that combining metformin with regular exercise improved metabolic and cardiovascular health. However, the Rutgers trial disputed this, showing that metformin may diminish the positive effects of exercise on aerobic fitness, vascular insulin sensitivity, fasting glucose, and inflammation.

Q: What is berberine, and how can it help with blood sugar management?

A: Berberine is a plant-based compound often referred to as "nature's Ozempic" due to its metabolic advantages. Studies indicate that consuming approximately 1,000 to 1,500 mg daily can help lower fasting blood sugar, enhance cholesterol levels, and

decrease systolic blood pressure.

Q: What are lifestyle strategies that can aid in diabetes management?

A: Knowing your HOMA-IR score, adopting a bioenergetic diet high in healthy carbohydrates, avoiding harmful seed oils, remaining active, and taking supplements to improve health are proactive measures to manage blood sugar without medication.

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