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New Study Confirms What We've Known About Statins for 15 Years

Analysis by Dr. Joseph Mercola | August 10, 2024

STORY AT-A-GLANCE

- A 2024 Lancet study confirms that statins increase diabetes risk, with high-intensity statins raising the risk by 36%. This validates concerns first raised by the 2008 JUPITER trial
- Statins may also increase risks of cancer, cataracts and neurological issues. Long-term use is associated with higher pancreatic cancer risk, particularly after five years of use
- Updated guidelines could lead to a 40% reduction in statin prescriptions, as new risk assessment tools suggest fewer adults need statins for primary prevention
- Insulin resistance, not high LDL cholesterol, may be the primary driver of atherosclerosis. Gut health and metabolic function play significant roles in cardiovascular health
- A holistic approach to heart health is recommended, considering factors beyond cholesterol. Additional tests like fasting insulin levels can provide a more comprehensive risk assessment

For over a decade and a half, the medical community has grappled with a paradox in cardiovascular health management: statins, the widely prescribed cholesterol-lowering drugs, while undeniably effective in lowering cholesterol, do little to reduce heart disease risk and cause significant side effects, including an increased risk of Type 2 diabetes.

A groundbreaking study published in 2024 in The Lancet[1] has now provided the most comprehensive evidence to date on this connection, confirming and expanding upon findings first hinted at in earlier research, including the landmark JUPITER trial from 2008.[2]

This new meta-analysis, conducted by the Cholesterol Treatment Trialists' (CTT) Collaboration, delves deep into individual patient data from multiple large-scale, long-term randomized controlled trials. Its findings not only solidify our understanding of the statin-diabetes link but also offer crucial insights into the magnitude, timing and risk factors associated with this side effect.

To fully appreciate the significance of this new research, it's essential to look back at how our knowledge has evolved since the JUPITER trial first raised concerns about statins and diabetes risk.

The JUPITER Trial — A Pivotal Moment in Statin Research

In 2008, the JUPITER (Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin) trial marked a significant milestone in our understanding of statin therapy.[3]

This study, involving 17,802 participants, was designed to evaluate the efficacy of the statin drug rosuvastatin in preventing cardiovascular events in individuals with normal low-density lipoprotein (LDL) cholesterol levels but elevated high-sensitivity C-reactive protein (hsCRP), a marker of inflammation.

The trial's primary focus was on cardiovascular outcomes. However, buried within the cardiovascular data was an observation that would spark years of debate and further research: the rosuvastatin group showed a higher incidence of physician-reported diabetes. This finding raised important questions about the long-term metabolic effects of statin therapy.

The diabetes finding in JUPITER was particularly intriguing because it emerged in a study population that was not initially at high risk for diabetes. Participants had normal

LDL cholesterol levels, and the study excluded individuals with diagnosed diabetes at baseline. This suggested that the diabetes risk associated with statin use extends beyond those with pre-existing metabolic risk factors.

When the U.S. Food and Drug Administration (FDA) reviewed JUPITER's results, it "reported a 27% increase in investigator-reported diabetes mellitus in rosuvastatin-treated patients compared to placebo-treated patients."[4] It also found that high-dose atorvastatin was associated with worsening glycemic control in a substudy.[5]

In the years following JUPITER, numerous studies and meta-analyses attempted to quantify and explain the diabetes risk associated with statin therapy. These efforts produced a growing consensus that statins do indeed increase diabetes risk,[6] but the magnitude of this risk and its clinical significance remained subjects of debate.

2024 Lancet Study — A New Level of Understanding

Fast forward to 2024, and the landscape of statin research has been transformed by a landmark meta-analysis published in The Lancet.[7] This study, leveraging the vast resources of the CTT Collaboration, represents the most comprehensive examination of the statin-diabetes connection to date.

By analyzing individual participant data from 23 large, long-term, randomized, double-blind trials, the researchers were able to provide unprecedented clarity on several key questions:

1. **The dose-dependent nature of diabetes risk —** The study definitively showed that the risk of new-onset diabetes increases with statin intensity. Low to moderate-intensity statin therapy was associated with a 10% increased risk of new-onset diabetes, while high-intensity statin therapy raised the risk by 36%. This dose-dependent relationship provides crucial information for clinicians weighing the benefits and risks of different statin regimens.

2. **Quantifying glycemic changes —** The researchers found that statin therapy led to small but significant increases in blood glucose and HbA1c levels. HbA1c, or

glycated hemoglobin, is a measure of a person's average blood sugar levels over the past two to three months.

In participants without baseline diabetes, mean glucose increased by 0.04 mmol/L with both low/moderate-intensity and high-intensity statins. HbA1c increased by 0.06% with low/moderate-intensity statins and 0.08% with high-intensity statins. These findings help explain the mechanism behind the increased diabetes risk.

3. **Identifying high-risk individuals —** Importantly, the study revealed that approximately 62% of new-onset diabetes cases occurred among participants who were already in the top quarter of baseline glycemic measures. This suggests that individuals with pre-existing impaired glucose tolerance are at highest risk for statin-induced diabetes.

4. **Effects on existing diabetes —** The study also examined the impact of statins on individuals with pre-existing diabetes. It found that statins were associated with a modest worsening of glycemic control in these patients, with relative risks of 1.10 for low/moderate-intensity therapy and 1.24 for high-intensity therapy. In other words, statins had a small negative effect on blood sugar control in diabetics, and this effect was stronger with higher doses.

5. **Consistency across populations —** The relative effects of statin therapy on new-onset diabetes were similar across different types of participants and over time, suggesting a broad applicability of these findings.

   These results provide a much more nuanced understanding of the statin-diabetes relationship than was available from the JUPITER trial or subsequent studies, but ultimately confirm what we've known all along — that statins increase diabetes risk.

Statin Drugs Linked to Cancer, Cataracts and Neurological Adverse Effects

Statin cholesterol-lowering medications are among the most-prescribed drugs in the U.S., but they can cause serious adverse effects, even beyond diabetes.[8] The most common and well-documented adverse event is muscle-related symptoms, ranging from mild myopathy to severe rhabdomyolysis. These muscular issues are thought to stem from mitochondrial dysfunction and alterations in muscle protein metabolism.

While severe cases are rare, the impact on quality of life and treatment adherence is significant for those affected. Neurological effects of statins have also been examined, revealing a possible link to an increased risk of hemorrhagic stroke.[9]

Research published in Scientific Reports also found a significant association between long-term use of anticholesterol drugs (primarily statins) and an increased risk of pancreatic cancer.[10] This effect was particularly pronounced in individuals who had been using these drugs for more than five years.

The increased pancreatic cancer risk was observed in the total population as well as when looking at men and women separately. This suggests the effect is not limited to a specific gender. While the study doesn't definitively explain the mechanism behind this increased risk, it references an animal study that suggested statins might have carcinogenic properties at doses equivalent to those commonly prescribed to humans.[11]

There's also concern that statins increase cataract risk by interfering with cholesterol biosynthesis in the lens epithelium. One study found that 1.9% of patients underwent cataract surgery during a three-year follow-up period.[12]

Notably, rosuvastatin was associated with a 1% higher incidence of cataract surgery compared to atorvastatin, likely due to its greater LDL cholesterol-lowering capacity. This suggests that more potent statins like rosuvastatin carry an increased risk of cataract formation.

Updated Guidelines May Lead to 40% Reduction in Statin Prescriptions

Recent developments in cardiovascular risk assessment could lead to a significant shift in statin prescription practices in the U.S. A new study published in JAMA Internal Medicine suggests that if U.S. health agencies adopt updated guidelines based on the American Heart Association's 2023 Predicting Risk of Cardiovascular Disease Events (PREVENT) equations,[13] the number of adults eligible for statin therapy could drop dramatically from 45.4 million to 28.3 million.[14]

This 40% reduction in statin prescriptions represents a major change in the conventional approach to cardiovascular disease prevention. The study, which analyzed data from the National Health and Nutrition Examination Survey (2017 to March 2020), found that the PREVENT equations estimate a much lower 10-year risk of atherosclerotic cardiovascular disease (ASCVD) compared to the previously used Pooled Cohort Equations (PCEs).

On average, the PREVENT equations estimated a 4.3% 10-year ASCVD risk, nearly half of the 8% risk calculated using PCEs. This difference was particularly notable among Black adults and individuals aged 70 to 75 years. If these new guidelines are adopted, it could mean that approximately 17.3 million fewer adults would meet the criteria for primary prevention statin therapy.

Moreover, about 4.1 million individuals currently taking statins might no longer meet the eligibility criteria, which could lead to discontinuation of their medication. This shift could have far-reaching implications for patient care and public health strategies, including fewer prescriptions for statin drugs.

Metabolic Dysfunction May Drive Atherosclerosis

As far back as 1977, with the publication of the Framingham Study,[15] no correlation between heart disease and total cholesterol could be found. Further, while statins are primarily prescribed to lower LDL cholesterol, some experts argue that **insulin resistance, not high LDL**, is the primary driver of atherosclerosis, which underlies many heart diseases.

If statins worsen insulin sensitivity while lowering LDL, they're doing little to address the root cause of cardiovascular disease. This suggests that strategies focusing on improving insulin sensitivity and reducing oxidative stress may be more effective in preventing heart disease than lowering LDL cholesterol. It also raises questions about the widespread use of statins, especially in light of their ability to increase diabetes risk.

Meanwhile, research suggests that gut health plays a significant role in cardiovascular health. Certain gut bacteria, particularly Oscillibacter, have been associated with lower cholesterol levels and reduced heart disease risk.[16,17] These bacteria can break down cholesterol into smaller molecules that don't raise heart disease risk.

Maintaining a diverse and balanced gut microbiome, especially fostering oxygen-intolerant bacteria like Akkermansia, can strengthen intestinal defenses and overall health. The importance of gut health in heart disease prevention extends beyond cholesterol management.

Oxygen-intolerant bacteria produce beneficial short-chain fatty acids that support intestinal health. However, modern lifestyle factors like **seed oil consumption** and exposure to toxins like **endocrine-disrupting chemicals** in plastics can disrupt this delicate balance, leading to increased endotoxin production and systemic inflammation.

A Holistic Approach to Heart Health Is Best

This highlights the need for a holistic approach to heart health that considers gut microbiome, mitochondrial function and a range of health indicators beyond traditional cholesterol measures — and therapeutic strategies beyond statin drugs.

Keep in mind, too, that as you age, your body's natural production of CoQ10 declines, and statin use further depletes this important coenzyme. Statins work by inhibiting an enzyme that's crucial for both cholesterol and CoQ10 production, leading to side effects like muscle problems. Additionally, the reduction of LDL cholesterol by statins inadvertently decrease CoQ10 transport in the bloodstream.

For individuals taking statins, supplementing with CoQ10 or its more bioavailable form, ubiquinol, is important. The recommended dosage can vary widely, from 100 to 200 milligrams (mg) daily for statin users to 30 mg to 1,200 mg for others, depending on their health status and lifestyle factors. Consult with your health care provider to determine the appropriate dosage.

It's also important to look beyond total cholesterol and LDL cholesterol in determining your heart disease risk. You can get a more accurate idea of your risk of heart disease with the following tests:

Omega-3 index	HDL/total cholesterol ratio
Fasting insulin level	Fasting blood sugar level
Triglyceride/HDL ratio	Iron level

The reduction in statin prescriptions based on updated risk assessment tools — and their continued link to health issues, including diabetes, further emphasizes the importance of personalized, comprehensive strategies for maintaining cardiovascular health.

As our understanding of the complex interplay between metabolic health and cardiovascular disease evolves, it will hopefully lead to a reevaluation of current prevention and treatment strategies, shifting away from a singular focus on LDL cholesterol reduction toward a more comprehensive approach to metabolic health.

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