High Cholesterol & Statins

When managing high cholesterol, the first step is often lifestyle modifications such as diet and exercise. If these changes are not sufficient, medication becomes necessary.

Statins are the most commonly prescribed and the most effective drug class for lowering cholesterol. Introduced in the 1970s, statins have demonstrated their efficacy in reducing bad cholesterol (LDL-C) and the risk of heart attack and stroke. This makes them the first-line treatment option for managing cholesterol and preventing heart disease.

How Statins Work and Lower Your Risk of Cardiovascular Disease

- **How Statins Work** Statins lower cholesterol levels by blocking a liver enzyme (HMG-CoA reductase) that is necessary for cholesterol production. Additionally, statins help the liver reabsorb existing cholesterol from the bloodstream, further lowering blood cholesterol levels.
- **How Statins Lower Your Risk of Heart Disease**
  - » **Plaque Stabilization**: Most heart attacks and strokes are caused by unstable plaques that rupture and block blood flow to vital organs like the heart and brain. Statins help stabilize these plaques.
  - » **Reduction in Inflammation**: High levels of inflammation are linked to an increased risk of heart attack and stroke. Statins have anti-inflammatory properties that help reduce this risk
  - » **Plaque Regression**: Statins can reduce the size of existing plaques in the artery walls, helping to a lower risk of cardiovascular events

What You Need to Know Before Taking Statins

Before starting statin therapy, it's important to educate yourself to make an informed decision.

- **Benefits vs Risks of Statins:** Everyone has their own level of risk tolerance, which is a personal decision.
- **Not All Statins are The Same**: There are 7 different statins available, each with unique properties.
- **Individual Responses**: Not all patients respond to statins in the same way; effects can vary from person to person.
- **Adjustments and Alternatives**: If you experience issues with one statin, you may find relief by lowering the dose or switching to a different statin.
- **Consultation with Healthcare Provider**: Always discuss the risks and benefits of any medication, including statins, with your healthcare provider before starting therapy.

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Statin Dose & Intensity

Statin intensity refers to the expected reduction in LDL-C (bad cholesterol) levels:

- **Low Intensity: Less than 30% decrease**
- **Moderate Intensity: 30-49% decrease**
- **High Intensity: Greater than 50% decrease**

Rule of 6: Doubling the statin dose (e.g., from atorvastatin 10mg to 20mg) typically results in an additional 6% reduction in LDL-C.

Statin (Brand)	Low Intensity	Medium Intensity	High Intensity
Lovastatin (Mevacor®)	10, 20 mg	40, 80 mg	
Pravastatin (Pravachol®)	10, 20 mg	40, 80 mg	
Simvastatin (Zocor®)	5, 10 mg	20, 40 mg	
Fluvastatin (Lescol®)	20, 40 mg	80 mg	
Atorvastatin (Lipitor®)		10, 20 mg	40, 80 mg
Rosuvastatin (Crestor®)		5, 10 mg	20, 40 mg
Pitavastatin (Livalo®, Zypitamag®)		2, 4 mg	

Choosing Your Statin Intensity

The appropriate statin dose and intensity should be discussed with your healthcare provider. For instance:

- **If you have had a heart attack or stroke, starting with a high-intensity or maximally tolerated statin is recommended.**
- **For individuals with diabetes aged 40 to 75, moderate-intensity statins are advised, regardless of cholesterol levels.**
- **If you cannot tolerate high-intensity statins, moderate-intensity statins still offer significant benefits.**
- **If you are not reaching your LDL-C goal, add-on therapy like ezetimibe can help you achieve your target.**

Risk vs. Benefit of Statins

When considering statin therapy, it's crucial to balance the benefits against the potential risks of side effects. A study[1] involving over 70,000 patients provides insight into this balance

- **Number Needed to Treat (NNT): For every 27 people treated with statins, one cardiovascular event (heart attack or stroke) is prevented.**
- **Number Needed to Harm (NNH): For every 197 people treated with statins, one person experiences a adverse event.**

In simpler terms, treating 1,000 patients with statins is estimated to prevent 37 cardiovascular events while causing 5 adverse events.

How Your Body Processes Statins

Some statins have a lower potential for interactions with other medications and foods. This is an important consideration if you are taking multiple medications or enjoy grapefruit juice and grapefruit products.

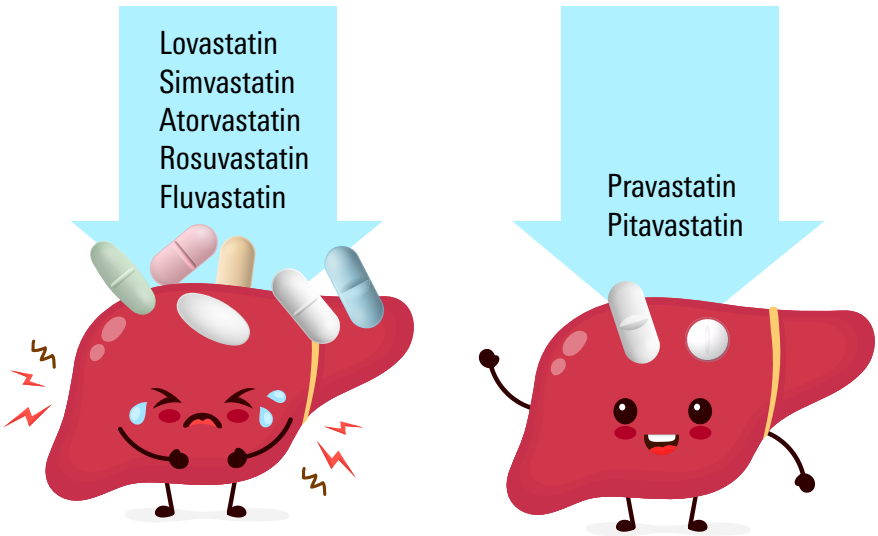
Busy Enzyme Pathways Can Create Unwanted Drug Interactions

- **CYP450 Enzymes: About 70-80% of medications are metabolized by the CYP450 family of enzymes.**
- **Interactions with Food and Other Drugs: These interactions can lead to**
  - » **Reduced Drug Effectiveness**: The interaction might cause your body to break down a drug too quickly, meaning less of it is available to do its job.
  - » **Increased Drug Levels**: Conversely, the interaction might slow down the breakdown of a drug, leading to higher-than-intended levels in your body.
  - » **Adverse Reactions**: Both too little and too much of a medication can cause unwanted side effects, some of which can be serious.

Grapefruit Juice and Statins Grapefruit juice is a classic example of a food that interacts with statins , particularly atorvastatin. Grapefruit juice can inhibit CYP450 enzymes, leading to increased levels of atorvastatin in your blood, which could increase the risk of side effects.

Statins with Reduced Interaction Potential

Pitavastatin (ZYPITAMAG®) and Pravastatin: These statins bypass the CYP450 pathways and have a lower risk of drug and food interactions. This makes them better options for people who take multiple medications or regularly consume grapefruit juice.



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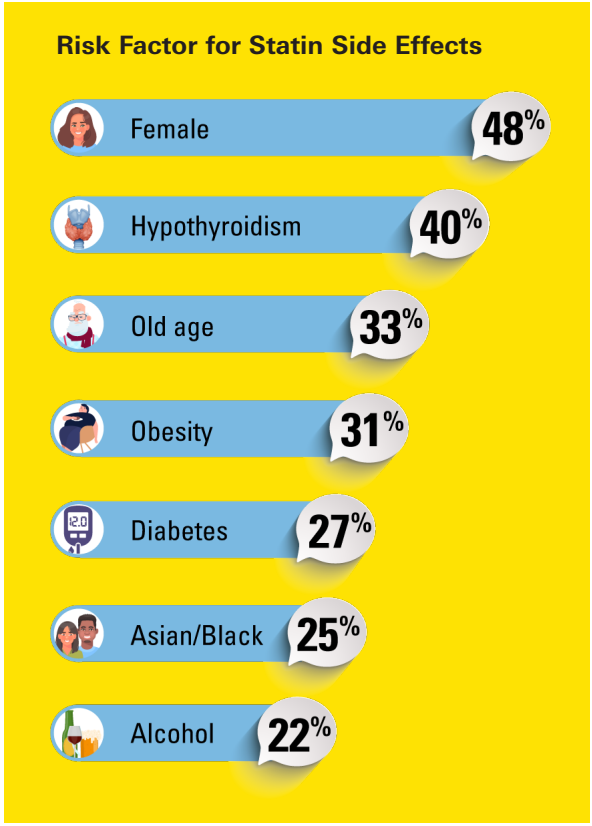
Statin Side Effects: Who is at Risk?

A 2022 analysis[2] of 176 studies involving over 4 million patients investigated the overall prevalence of statin-related issues. The analysis found that **9.1% of patients reported problems with statins**.

Who is at Risk?

Several factors can increase the risk of statin side effects. These are associations, not necessarily causal relationships. Having one or more of these factors doesn't guarantee you'll experience side effects, but it's something to discuss with your doctor.

- Female Sex: 47.9% increase
- Hypothyroidism: 37.6% increase
- High Statin Dose: 37.5% increase
- Calcium Channel Blockers: 35.5% increase
- Age 65 or Older: 31.2% increase
- Antiarrhythmics: 31.2% increase
- Obesity: 30.6% increase
- Black Race: 29.3% increase
- Diabetes Mellitus: 26.6% increase
- Asian Race: 25.4% increase
- Chronic Renal Failure: 25.2% increase
- Chronic Liver Disease: 24.3% increase
- Alcohol Consumption: 22% increase



Factors Not Associated with Higher Risk

- Smoking
- Arterial hypertension
- Duration of statin therapy
- White race
- Caucasian / **Hispanic race**
- Warfarin
- Depression: 12.2% decreased risk

References
1 Silva MA, et al. Clin Ther. 2006;28(1):26-35.
2 Adams SP et al., Cochrane Database Syst Rev. 2023 Sep 18;2023(9):CD013673

Link Between Statins and Developing Diabetes

Do Statins Increase the Risk of Diabetes?

Statins can raise blood sugar levels to varying degrees, depending on the type and dose. While all statins have this potential effect, the overall risk of developing diabetes with statin therapy is about 10% higher over five years.

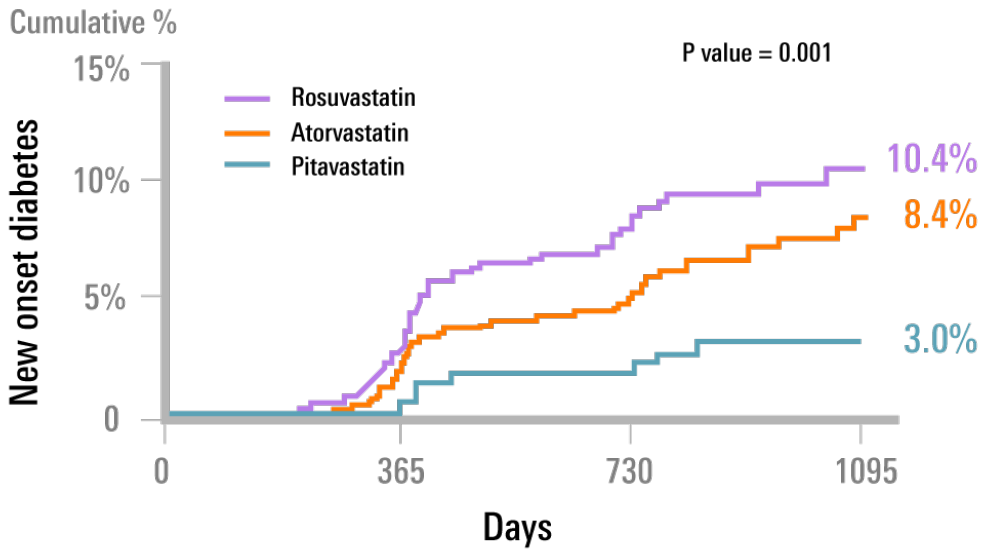
Higher-intensity statins like atorvastatin (40-80mg) and rosuvastatin (10-20mg) are associated with a greater risk of new-onset diabetes compared to moderate or low-intensity statins.

Do Certain Statins Have a Reduced Risk for Developing Diabetes?

Yes, some statins may have a smaller impact on changes to blood sugar levels and the risk of developing diabetes compared to others.

A study[3] in heart attack patients compared pitavastatin, rosuvastatin, and atorvastatin. It found that **pitavastatin was associated with a lower risk of new-onset diabetes** compared to both rosuvastatin and atorvastatin at moderate doses.

Comparing Moderate Intensity Statin Doses of Pitavastatin (ZYPITAMAG®) vs. Rosuvastatin (CRESTOR®) vs. Atorvastatin (LIPITOR®)



KEY TAKEAWAY: While statins can slightly increase blood sugar level and the risk of new on-set diabetesr, the added risk is significantly counterbalanced by the reduction in heart disease risk that statins provide.

Statins and Blood Sugar

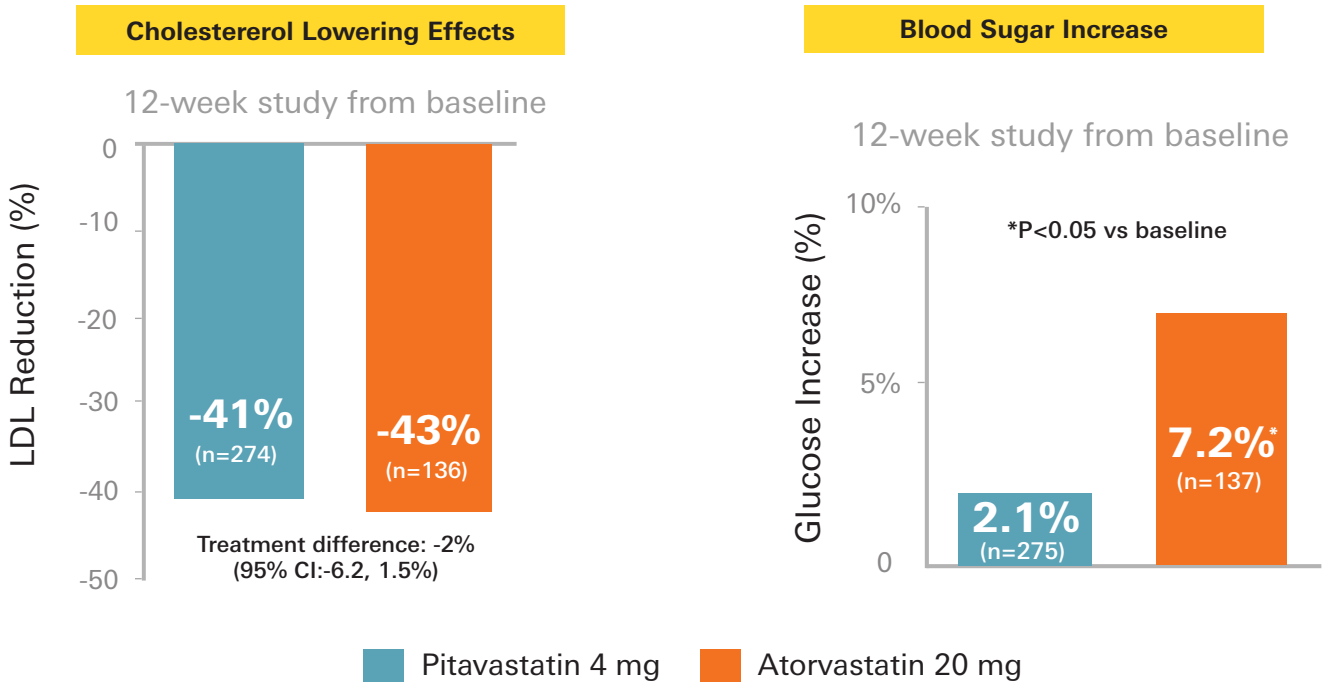
Can Statins Increase Blood Sugar?

- Yes. Statins slightly raise blood sugar levels (A1C and fasting glucose levels). This can happen in both people with and without diabetes.
- However, not all statins have the same effect on blood sugar.

Pitavastatin (ZYPITAMAG®) vs. Atorvastatin (LIPITOR®)

A study compared pitavastatin to atorvastatin in people with type 2 diabetes and high cholesterol.[4]

- **Cholesterol-lowering effects**: Both statins effectively lowered cholesterol. 4mg of pitavastatin lowered cholesterol (41%) similarly to 20mg of atorvastatin (43%).
- **Blood sugar effects**
  Pitavastatin: Had minimal impact on blood sugar levels (2.1%).
  Atorvastatin: Significantly increased blood sugar levels (7.2%).



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How Statins Affect Glucose Levels

Statins and Blood Sugar in People with Diabetes

- People with type 2 diabetes taking statins may experience a slight increase in blood sugar levels.
- Pitavastatin lowers blood sugar levels compared to other statins

A 2018 study[5] reviewed 23 clinical trials to see how different statins affect blood sugar in people with type 2 diabetes. This study found that the "moderate-intensity pitavastatin" was linked to lower blood sugar levels (A1C and fasting blood sugar) compared to statins like atorvastatin and rosuvastatin.

If you have type 2 diabetes and your cholesterol is high (above 70 mg/dL), current guidelines recommend starting you on a moderate or high-intensity statin between the ages of 40 and 75. This is because diabetes significantly increases the risk of heart disease, and statins can help lower that risk.

Statins and Blood Sugar in People without Diabetes

- Statins like **rosuvastatin and atorvastatin** may slightly increase blood sugar levels and insulin resistance in people with normal blood sugar and insulin sensitivity.
- Other statins, such as **simvastatin, pravastatin, and pitavastatin**, may have less impact on blood sugar or even improve insulin sensitivity.

A recent 2023 study[6] analyzed data from 67 studies to understand how statins affect blood sugar (A1C) and insulin resistance (HOMA-IR) in people without diabetes.

For individuals with normal A1C levels (less than 6.5%), rosuvastatin and atorvastatin significantly increased A1C levels. Simvastatin, pravastatin, and pitavastatin did not show a significant increase.

Among people with normal insulin actions, rosuvastatin, simvastatin, and atorvastatin significantly increased the HOMA-IR index, indicating increased insulin resistance. Pravastatin reduced this parameter, and pitavastatin showed a slight improvement.

KEY TAKEAWAYS

- **If you have type 2 diabetes, pitavastatin might be a suitable option for you.**
- **Statins tend to increase blood glucose and insulin resistance in individuals without diabetes. However, pitavastatin and pravastatin may have lesser of an effect than other statins.**

References
3 Choi JY et al. American Journal of Cardiology. 2018;S0002-9149(18)31257-8
4 Gumprecht J et al. Diabetes, Obesity and Metabolism. 2011;13:1047-1055
5 Cui JY et al. Journal of Clinical Pharmacy and Therapeutics. 2018;43(4):556-570.
6 Alvarez-Jimenez L. et a. European Journal of Pharmacology. 2023;947:175672.

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Get ZYPITAMAG® (pitavastatin) for $1.30 per day or less through Marley Drug

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2. Your patient is contacted to confirm the details

3. The medication is shipped via priority mail

A Different Kind of Statin

ZYPITAMAG is a third-generation statin that lowers cholesterol by up to 45%.

Statins, like most medications, are metabolized by enzymes in our body. 70–80% of medications are processed by the same family of enzymes known as CYP450. When these enzyme pathways become too busy it can lead to drug interactions.

ZYPITAMAG bypasses this enzyme family and is instead mainly processed by a less busy enzyme family. This leads to a reduced potential for certain interactions with other medications.

Key Features:

- Available in 2 mg and 4 mg
- Moderate-intensity statin
- Once daily, taken with or without food
- Compatible with grapefruit juice (unlike some other statins)

Get the Best Price for ZYPITAMAG

Marley Drug will determine the most cost-effective option for you to access ZYPITAMAG (pitavastatin)—whether it's through insurance or by cash. **No matter what, the most you will pay is $1.30/day.**

Details and Criteria to Access ZYPITAMAG For $1.30 per day through Marley Drug

This offer is valid for eligible patients purchasing ZYPITAMAG and may not be used for any other product. This offer is valid for the purchase of ZYPITAMAG manufactured for Medicure and lawfully purchased from Marley Drug located in North Carolina (5008 Peters Creek Pkwy, Winston-Salem, NC 27127, United States). This offer is valid for patients being treated with ZYPITAMAG for an FDA-approved indication who are 18 years of age or older. Patients will be charged $1.30 per day for every day listed in their prescription. For example, 30 pills over 30 days will cost $39. Patients will be charged a minimum $39 per 30 day fill because of costs incurred for shipping and handling. This offer must not be combined with any insurance coverage. Patients using insurance to pay for their Zypitamag prescription are not eligible for this offer. Patients must not apply any out-of-pocket expenses incurred using this Savings Offer toward any insurance benefit. All Program payments are for the benefit of the patient only. The patient is responsible for applicable taxes, if any. This offer is not conditioned on any past, present, or future purchase, including refills. Offer not valid where prohibited by law or restricted. This offer is non-transferable, is limited to one per person, and may not be combined with any other offer. Offer must be presented along with a valid prescription for ZYPITAMAG at the time of purchase. Marley Drug reserves the right to change or discontinue this offer at any time without notice.