

Issues in Cardiovascular Health

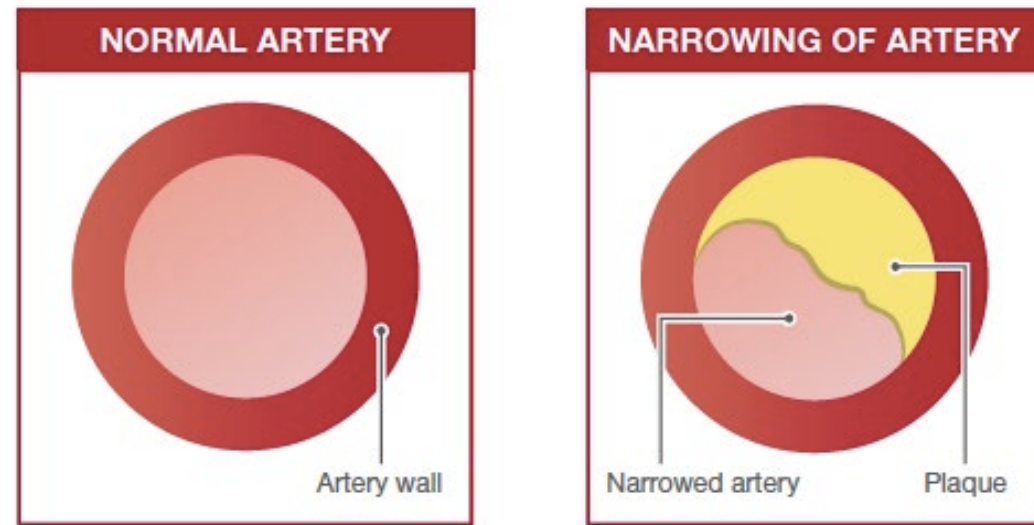
Statins and Treatment Limitations

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Atherosclerosis and hyperlipidemia

- Atherosclerosis is a chronic inflammatory disease where plaque builds up in the arteries¹
 - A primarily asymptomatic condition
- Atherosclerosis is the major cause of cardiovascular diseases and the underlying cause of almost **50% of all deaths** in westernized society²
- Hyperlipidemia is a contributor to atherosclerosis because extra circulating cholesterol forms the basis for plaque³



1. NIH/National Heart, Lung, and Blood Institute web site. Atherosclerosis. Accessed 12/10/20. <https://www.nhlbi.nih.gov/health-topics/atherosclerosis>.

2. Pahwa R. NCBI Bookshelf (NIH). StatPearls Publishing, LLC; Jan 2020. **3.** NIH/National Heart, Lung, and Blood Institute web site. Blood cholesterol. Accessed 12/10/20. <https://www.nhlbi.nih.gov/health-topics/blood-cholesterol>

Statins: An important tool in lowering risk for cardiovascular disease

- Statins are a first-line agent for decreasing cholesterol, and thereby reducing risk for CVD¹
 - Statins are associated with a reduction in the risk of heart disease or stroke²
- Evidence-based tools like the ASCVD Risk Estimator Plus (online from the American College of Cardiology) may help identify patients who could benefit from treatment¹

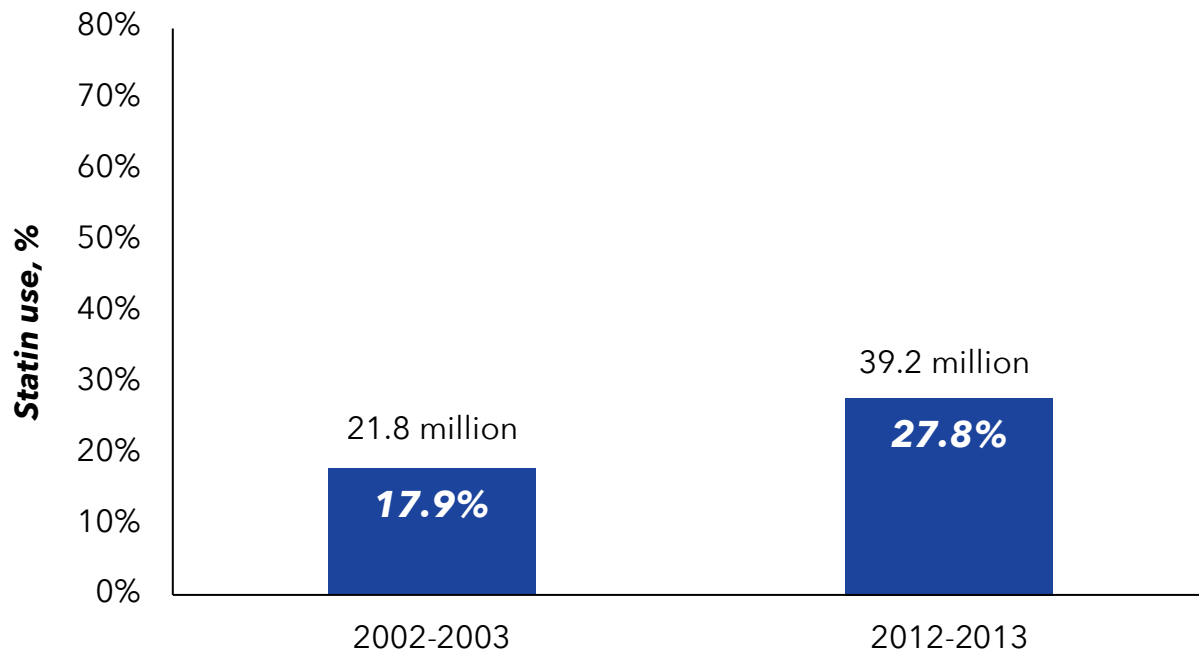
ASCVD=atherosclerotic cardiovascular disease.

1. Grundy SM, et al. *JACC*. 2019;73(24):3168-3209. **2.** American Heart Association. Cholesterol medications. Last reviewed 11/11/20. Accessed 12/10/20. <https://www.heart.org/en/health-topics/cholesterol/prevention-and-treatment-of-high-cholesterol-hyperlipidemia/cholesterol-medications>

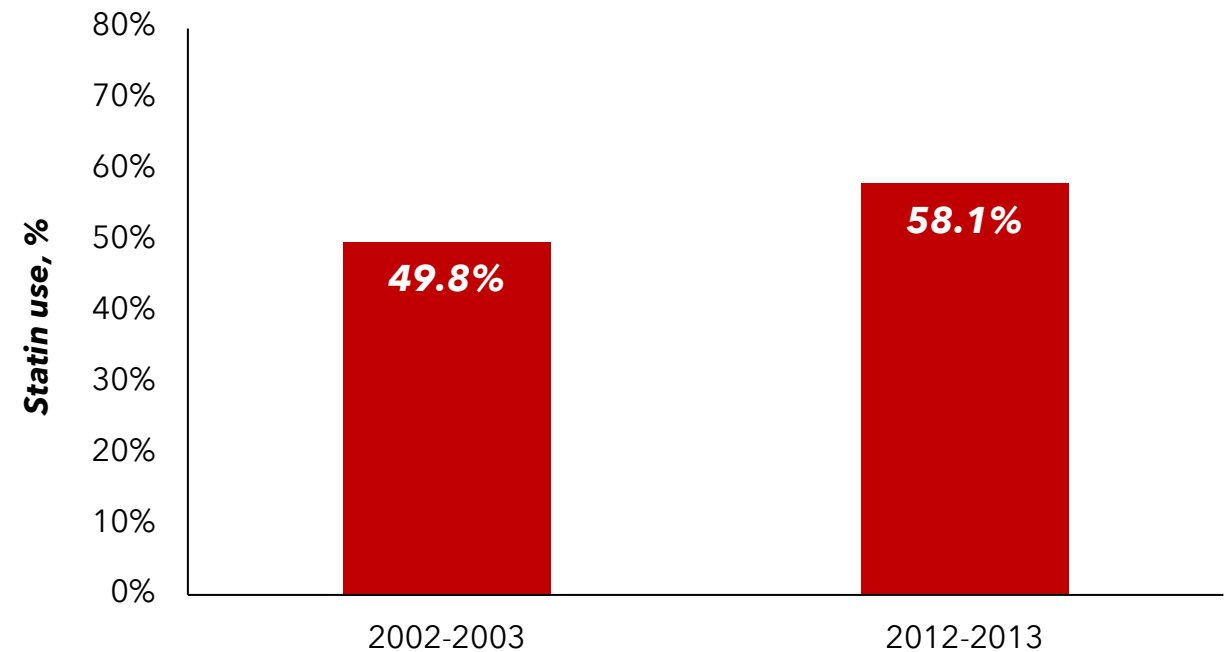
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Increase in use of statin therapy over time

Statin use in adult patients (40+) increased 79.8% over 10 years



But statin use among patients with ASCVD is suboptimal



Commonly used statins

Selected statins prescribed in the United States:

Atorvastatin (Lipitor®)

Fluvastatin (Lescol®)

Lovastatin (Mevacor®, Altoprev®)

Pravastatin (Pravachol®)

Rosuvastatin (Crestor®)

Simvastatin (Zocor®)

In combination: atorvastatin + amlodipine (Caduet®)

In combination: simvastatin + ezetimibe (Vytorin®)

Statins are generally well-tolerated

However, adverse events may include¹⁻⁷:

- Impaired liver function
- Risk of muscle damage
- Myopathic symptoms
 - Weakness, muscle pain, cramps and fatigue
- Worsening diabetic control or development of diabetes in individuals already at risk
- Rare: rhabdomyolysis and peripheral neuropathy

1. Newman C, et al. *Arterioscler Thromb Vasc Biol.* 2019;39:e38-e81. **2.** Thompson PD, et al. *JACC.* 2016;67(20):2395-2410. **3.** Feng QP, et al. *Pharmacogenomics.* 2012;13(5):579-594. **4.** Ridker PM, et al *NEJM.* 2008;359:2195-2207. **5.** Ridker PM, et al. *Lancet.* 2012;380(9841):565-571. **6.** Chang JT, et al. *Pharmacoepidemiol Drug Safety.* 2004;13(7):417-426. **7.** Backes JM, Howard PA. *Ann Pharmacother.* 2003;37(2):274-278.

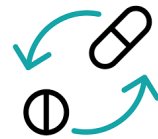
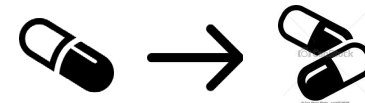
Importance of managing statin-related adverse events

Consequences of statin-related adverse events may include^{1,2}:



- Reduced quality of life

- Multiple dose alterations



- Switching statins

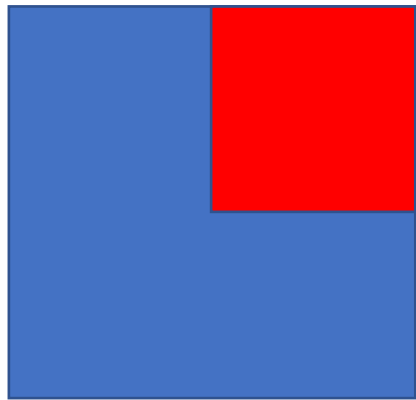
- Nonadherence



1. Thompson PD, et al. *JACC*. 2016;67(20):2395-2410. **2.** Ward NC, et al. *Circ Res*. 2019;124:328-350.

Many patients go untreated: A 2019 AHA report

Of 5693 adults recommended for statin therapy in the PALM (Patient and Provider Assessment of Lipid Management) registry:

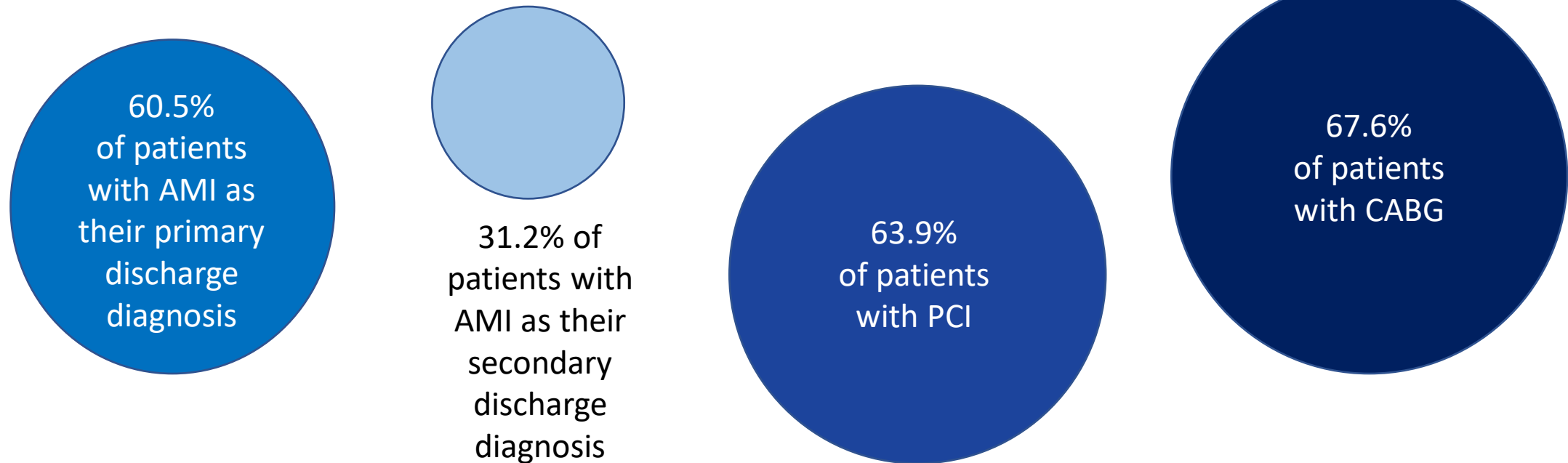


- ← 26.5% were not on treatment with a statin. Of this subset:
- 59.2% reported never being offered a statin
 - 10.1% declined
 - 30.7% discontinued

Patients reported **side effects** (55%) as the most common reason for discontinuation of treatment, followed by “felt like they no longer needed one” (18%). The most common reason for declining treatment was **fear of side effects** (37%).

Statin use is lacking, despite evidence of benefit

8,175 Medicare patients with a CHD event* who had filled a statin prescription within 90 days after discharge



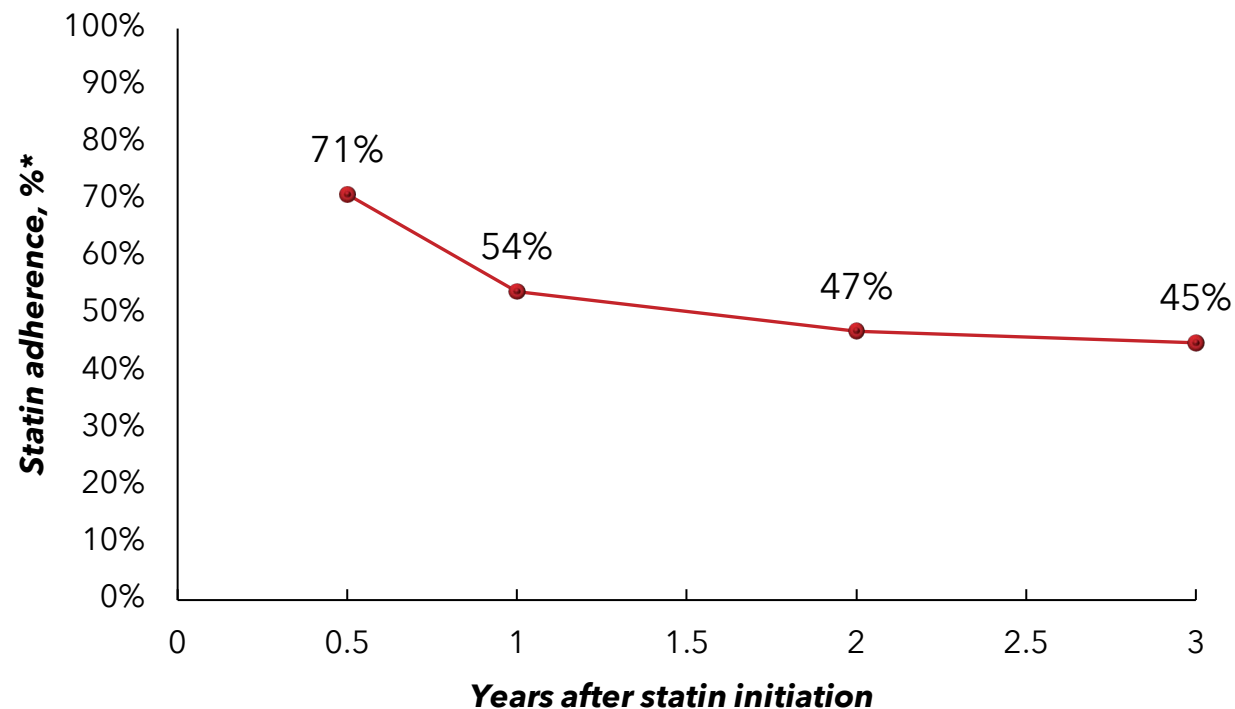
CHD=coronary heart disease; AMI=acute myocardial infarction; PCI=percutaneous coronary intervention; CABG=coronary artery bypass grafting.

*Patients who had not previously been prescribed a statin.

Yun H, et al. *J Am Heart Assoc.* 2015;4:e001208.

Drop in adherence over time

Statin use after hospital discharge for new onset of atherosclerotic CV disease identified from 169,624 patients



Study was conducted in Taiwan. *Statin adherence measured by proportion of days covered ≥ 0.8 (80% of days covered).

Chen S, et al. *BMC Cardiovasc Disord.* 2019;19:62. <https://doi.org/10.1186/s12872-019-1032-4>

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Nutrients and statins

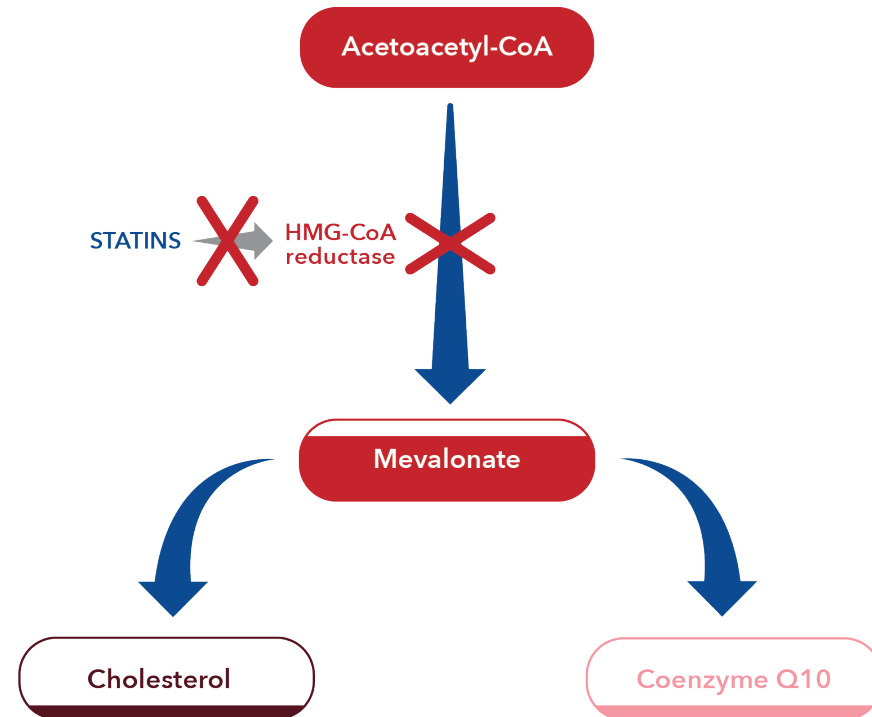
CoQ10

- Due to a shared pathway, statins reduce cholesterol in the body—but also reduce the nutrient CoQ10^{1,2}
- Statins can reduce levels of CoQ10 even when a patient has taken a standard dose for just 3 months¹

Vitamin D

- Low serum levels of Vitamin D is associated with statin intolerance³

Patient taking a statin



1. Passi S, et al. *BioFactors*. 2003;18(1-4):113-124. **2.** De Pinieux G, et al. *Br J Clin Pharmacol*. 1996;42(3):333-337. **3.** Khayznikov M, et al. *N Am J Med Sci*. 2015;7(3):86-93. doi:10.4103/1947-2714.153919

Can supplements help manage the myalgia associated with statins?

Emerging evidence suggests that restoring CoQ10 levels with ubiquinol may help to manage statin-related muscle symptoms^{1,2}

- While use of CoQ10 for statin-related myalgia is not supported for routine use in current guidelines³, more research into ubiquinol is warranted
- If a patient reports feeling a health benefit with a supplement, it's practical to continue the supplement
 - Use of CoQ10 and other nutrients are not associated with adverse events

1. Zlatohlavek L, et al. *Neuroendocrinol Lett.* 2012;33(suppl 2):98-101. **2.** Fedacko J, et al. *Can J Physiol Pharmacol.* 2013;91(2):165-170. **3.** Grundy SM, et al. *JACC.* 2019;73(24):3168-3209.

Ubiquinol vs CoQ10: What's the difference?

<i>Ubiquinol</i>	<i>CoQ10 (ubiquinone)</i>
The active, electron-rich, antioxidant form of CoQ10	The oxidized cellular state
>90% of the CoQ10 in a young, healthy adult is in the ubiquinol form ¹	CoQ10 must be converted to ubiquinol in the body in order to play a role in creating cellular energy, but conversion gets less efficient as a person ages or with certain health conditions ^{2,3}

Both are naturally made in the body and available as a nutritional supplement.
But the supplement ubiquinol is up to 70% more bioavailable than conventional CoQ10⁴

1. Tang PH, et al. *Clin Chem*. 2001;47(2):256-265. **2.** Niklowitz P, et al. *J Clin Biochem Nutr*. 2016;58(3):240-245. **3.** Wada H, et al. *JAGS*. 2007;55(7):1141-1142. **4.** Langsjoen PH, Langsjoen AM. *Clin Pharmacol Drug Dev*. 2013;3(1):13-17.

Statins play an important role in cardioprotective therapy

- While diet and exercise can lower CV risk, alone they may not be enough to effectively manage CV risk
- Statins are a key tool in maintaining CV health
- Statins are associated with adverse events, some of which may be manageable
 - Supplemental ubiquinol has been shown to effectively replenish low levels of CoQ10 depleted by statins^{1,2}
- Use shared decision-making to decide if statins are right for your patient

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