

## More statin guidance muddies primary prevention picture

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The U.S. Preventive Services Task Force has weighed in on the debate over how and when to recommend lipid-lowering statin therapy to prevent heart attacks and strokes in at-risk patients who lack a history of cardiovascular disease (CVD). The recommendations are stirring debate over how aggressively to use statins as a primary prevention tool.

About 375,000 American adults died of coronary heart disease and 130,000 died of cerebrovascular disease in 2011, and coronary heart disease is responsible for about one in five deaths among patients 45 to 64 years old and one-quarter of deaths among patients 65 and older.

The USPSTF recommendations, published in the *Journal of the American Medical Association*, are based on two systematic reviews of the available evidence. The task force of preventive health experts concluded that low- to moderate-dose statins should be recommended for patients between 40 and 75 years old without a CVD history if they have one or more cardiovascular disease risk factors and a 10 percent chance of having a CVD event within 10 years, according to the ASCVD Risk Estimator. This recommendation got a “B” grade, meaning “there is high certainty that the net benefit is moderate, or there is moderate certainty that the net benefit is moderate to substantial.”

The task force found 19 randomized controlled trials (RCT) examining the effectiveness of statins in patients between 40 and 75 years old. Using low- or moderate-dose statins was linked to 14 percent lower relative risk of death from any cause, 31 percent lower relative risk of cardiovascular-related death, 29 percent reduced relative risk of ischemic stroke and a 36 percent smaller relative risk of a heart attack.

However, the task force said physicians should “selectively offer” low- to moderate-dose statins for similar patients in that age group whose 10-year CVD-event risk is between 7.5 and 10 percent. The USPSTF gave this recommendation a “C” grade, meaning “there is at least moderate certainty that the net benefit is small.”

“The decision to initiate therapy in this population,” the task force said in *JAMA*, “should reflect an

assessment of patients' specific circumstances and their preference for a potential small benefit relative to the potential harms and inconvenience of taking a lifelong daily medication.”

This judgment stands in contrast with the 2013 guideline on CVD risk assessment developed jointly by the American Heart Association (AHA) and the American College of Cardiology (ACC). The ACC/AHA guideline says physicians should use moderate- to high-dose statin therapy for patients between 40 and 75 without a CVD history if they have a low-density lipoprotein cholesterol level of 70 – 189 mg/dL and also have diabetes or a 7.5 percent, 10-year risk of a CVD event according to the risk estimator.

The USPSTF said there is not enough evidence to make primary-prevention recommendations on statin use for adults 20 to 39 years old and patients older than 75.

## Objections raised

In an editorial published in *JAMA* and *JAMA Internal Medicine*, Rita F. Redberg, MD, and Mitchell H. Katz, MD, argued that the data supporting statin use for primary prevention “are weak.” They questioned the reliability of the evidence base that informed the task force’s recommendations, noting that all but one of the RCTs analyzed were sponsored by industry and that the USPSTF did not have access to “clinical study reports and anonymized patient-level data” from the trials.

Drs. Redberg and Katz, editor and deputy editor, respectively, of *JAMA Internal Medicine*, added that “many of the trials did not ask about commonly reported statin effects, such as muscle pain and weakness” and pointed to other research estimating that one in five statin users experiences muscle problems. The clinical benefit of prescribing statins for primary prevention is “relatively small,” they argued, noting that 244 patients would need to take a statin daily to prevent one death from any cause over a five-year period. They recommended that physicians and patients consult a decision aid on statins available from Mayo Clinic.

The task force’s recommendations join what has become a crowded field of somewhat contradictory advice on statin use for primary prevention. In addition to the ACC/AHA guideline, there are recommendations from the Canadian Cardiovascular Society, the UK National Institute for Health and Care Excellence and a joint guideline from the European Society of Cardiology and European Atherosclerosis Society.

Despite disagreements, there is some consensus among the expert recommendations, Philip Greenland, MD, and Robert O. Bonow, MD, wrote in a *JAMA Cardiology* editorial. Both physicians are affiliated with Northwestern University Feinberg School of Medicine, and Dr. Bonow is editor of *JAMA Cardiology*.

“There is agreement on strong evidence for statin effectiveness and broad treatment indications, especially among the highest-risk segments of the adult population, including individuals with familial hypercholesterolemia or diabetes and patients with established atherosclerotic CVD. There is also consistent agreement that statins are generally safe, especially among individuals younger than 76 years. This is supported by a vast body of evidence,” they wrote.

“Despite rather substantial trial evidence on the use of statins for primary prevention of CVD, uncertainties remain, and all five of the guidelines uniformly advise that clinical judgment along with thoughtful patient-clinician discussions is indicated, regardless of level of patient risk,” the editorial said. “All guidelines also emphasize the importance of lifestyle interventions to reduce risk in all patients, regardless of lipid-lowering drug use.”

The CVD risk-estimation tool cited in the USPSTF statement uses the Pooled Cohort Equations from the 2013 guideline on CVD risk assessment developed jointly by the AHA and ACC. The risk estimator takes into account multiple risk factors including patients’ systolic blood pressure and whether they are receiving treatment for hypertension.

## Previous prevention advice

The task force's recommendations on statin use come on the heels of other recent USPSTF statements on cardiovascular disease screening and prevention. In two articles published in 2015, the task force recommended that all adults be screened for high blood pressure and that overweight or obese patients between 40 and 70 years old be screened for abnormal blood glucose as part of a cardiovascular risk assessment. The task force also recommended that patients with abnormal blood glucose be referred for “intensive behavioral counseling interventions” to promote healthy eating and physical activity.

Measuring patients’ blood pressure properly, tracking the share of patients whose hypertension is controlled and following evidence-based treatment algorithms are part of Target: BP™, the AMA’s joint initiative with the AHA to address the estimated 37 million Americans with uncontrolled hypertension. The two organizations recently announced that clinics achieving top rates of BP control in their hypertensive patients can gain national recognition for their efforts.

Type 2 diabetes also is the focus a major initiative undertaken by the AMA and the Centers for



Disease Control and Prevention. That effort, Prevent Diabetes STAT, aims to help patients, physicians, health care organizations, employers and insurers do their part to improve rates of prediabetes screening and involvement in evidence-based diabetes prevention programs.