

# Guideline: The USPSTF recommends low- to moderate-dose statins to prevent CVD in selected adults 40 to 75 years of age

US Preventive Services Task Force, Bibbins-Domingo K, Grossman DC, et al. **Statin use for the primary prevention of cardiovascular disease in adults: US Preventive Services Task Force recommendation statement.** JAMA. 2016;316:1997-2007.

Clinical impact ratings: **GM** ★★★★★☆ **C** ★★★★★☆ **En** ★★★★★☆ **G** ★★★★★☆

## Guideline scope

This guideline focuses on the use of statins to prevent cardiovascular disease (CVD) events in adults  $\geq 40$  years of age without CVD (history or current signs or symptoms), low-density lipoprotein cholesterol level  $> 190$  mg/dL (4.9 mmol/L), or familial hypercholesterolemia. It updates the USPSTF 2008 recommendations on screening for lipid disorders in adults.

## Guideline methods

The USPSTF commissioned a systematic review, which searched MEDLINE, Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews to June 2016 for English-language, randomized, controlled trials comparing statins with placebo or no statins in adults  $\geq 40$  years of age without CVD.\* The review found 19 RCTs ( $n = 71\,344$ , median follow-up 3 y); most trials enrolled patients who had  $\geq 1$  CVD risk factor (dyslipidemia, diabetes, hypertension, or smoking), and most used low- to moderate-dose statins. Based on the results of the review\*, the USPSTF made graded recommendations for the use of statins for primary prevention of CVD.

## Recommendations

The main results of the systematic review\* are in the Table.

1. In adults 40 to 75 years of age with  $\geq 1$  risk factor for CVD and no history of CVD, the USPSTF recommended:

- Starting low- to moderate-dose statins in patients with 10-year CVD risk  $\geq 10\%$  (grade B recommendation based on high certainty of moderate net benefit or moderate certainty of moderate-to-substantial net benefit); and
- Selectively offering low- to moderate-dose statins after discussion with adults who have 10-year CVD risk 7.5% to 10% (grade C recommendation based on moderate certainty of small net benefit).

2. The USPSTF recommended use of the American College of Cardiology (ACC)/American Heart Association (AHA) Pooled Cohort Equations to estimate 10-year CVD risk (recommendation not graded).

3. In adults  $\geq 76$  years of age with no history of CVD, evidence was insufficient to make a recommendation for use of statins.

## Conclusion

The US Preventive Services Task Force recommends low- to moderate-dose statins to prevent cardiovascular disease (CVD)

in adults 40 to 75 years of age without CVD but with  $\geq 1$  risk factor and 10-year CVD risk  $\geq 10\%$ .

\*Chou R, Dana T, Blazina I, Daeges M, Jeanne TL. Statins for prevention of cardiovascular disease in adults: evidence report and systematic review for the US Preventive Services Task Force. JAMA. 2016;316:2008-24.

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## Commentary

The USPSTF recommendations for statins for primary prevention are similar to the 2013 ACC/AHA cholesterol treatment guidelines (1), with modest differences. The ACC/AHA set a treatment threshold at 10-year atherosclerotic CVD risk of 7.5% (1), whereas the USPSTF recommends that persons with  $\geq 1$  CVD risk factor (hypertension, smoking, diabetes, or elevated cholesterol) and a 10-year CVD risk  $\geq 10\%$  should receive statin therapy, with selective offering to those with a CVD risk of 7.5% to 10%.

These recommendations are based on a high-quality systematic review of a large body of evidence from major randomized trials, including the recent HOPE-3 trial (2). The primary prevention trials reviewed showed benefits with statins in patients with  $\geq 1$  risk factor, although none enrolled patients based solely on 10-year CVD risk score. Thus, these new recommendations may be more aligned with existing evidence. The absolute benefit of statins, reflected in the number needed to treat, is clear but modest (at least over a 3-year period), but the risk for adverse events is low. Because the ACC/AHA CVD risk score relies heavily on age, the higher 10% threshold will exclude some younger people despite multiple cardiac risk factors, including diabetes, who have a high lifetime CVD risk.

How should clinicians use the various guidelines? Both the ACC/AHA (1) and the USPSTF recommend treating patients at moderate or high risk for CVD with statins, regardless of cholesterol levels. The availability of generic statins with lower cost has shifted the balance of cost and benefit to favor treating patients at lower thresholds of risk. The decision whether to use statins should be part of a broader strategy of risk factor management. Future studies should directly evaluate various risk-based approaches while considering risks and benefits in older adults and long-term effects in younger adults. In the meantime, clinicians should continue to prescribe statin therapy for primary prevention for patients at high or moderate risk for CVD and to have informed discussions with those at lower risk (10-y risk 5% to 10%), who may benefit from statin therapy in the long term.

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## References

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### Key findings of systematic review underpinning the guideline: statins vs control (placebo or no statin) in adults 40 to 75 years of age without a history of CVD†

Outcomes	Number of trials (n)	Weighted event rates		At 6 mo to 6 y	
		Statins	Control	RRR (95% CI)	NNT (CI)
All-cause mortality	15 (71 131)	3.1%	3.6%	14% (7 to 20)	250 (157 to 589)
CV mortality	10 (64 235)	1.2%	1.7%	31% (12 to 46)	233 (134 to 910)
Ischemic stroke	13 (62 863)	1.1%	1.5%	29% (18 to 38)	264 (189 to 435)
Myocardial infarction	12 (68 537)	1.4%	2.2%	36% (29 to 43)	124 (85 to 233)
Composite CV outcome‡	13 (69 215)	3.2%	4.6%	30% (22 to 37)	72 (56 to 102)
Serious adverse events	7 (41 804)	12.9%	13.0%	1% (−4 to 6)	Not significant

†CVD = cardiovascular disease; other abbreviations defined in Glossary. Data obtained from Chou R, Dana T, Blazina I, Daeges M, Jeanne TL. Statins for prevention of cardiovascular disease in adults: evidence report and systematic review for the US Preventive Services Task Force. JAMA. 2016;316:2008-24. Weighted event rates, RRR, NNT, and CI calculated from control event rates, risk ratios, and absolute risk differences using a random-effects model.

‡Events included in the composite CV outcome varied across trials.

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