Not Completely: Why It Is Right to Drop LDL-C Targets, but Wrong to Recommend Statins at a 7.5% 10-Year Risk

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The new American College of Cardiology/American Heart Association (ACC/AHA) cholesterol treatment guideline moved clinical practice in the right direction, but not far enough.1 I applaud the ACC/AHA committee for dropping low-density-lipoprotein cholesterol (LDL-C) target levels and basing recommendations on a patient’s risk of cardiovascular events. However, the committee’s recommendations should have paid more attention to the inherent uncertainties in risk estimates and the importance of individual patient circumstances and preferences.

I want to focus on the ACC/AHA recommendation that is most important for primary care physicians: to recommend a statin for primary cardiovascular prevention when a person’s 10-year risk of having a heart attack or stroke is greater than 7.5%, and to not otherwise treat LDL-C level elevations unless they are greater than 190 mg per dL (4.92 mmol per L).1

Why Drop LDL-C Target Levels?
We now have high-quality clinical trial evidence showing that the relative benefits or harms of statin use do not vary based on a person’s LDL-C level.2,3 Furthermore, multiple clinical trials have found no benefit from adding a second lipid-lowering medication to a statin, so the new guideline does not recommend using a second cholesterol medication in pursuit of LDL-C target levels.1 Indeed, the concept of treating to target levels is not supported by evidence from randomized trials.4-6 A treat-to-target approach ignores how other patient factors impact expected risks and benefits, and has the possible downside of promoting polypharmacy by not considering the amount of potential treatment benefit and harm. In short, surrogate treatment target levels distract us from the central tenet of good decision making—weighing the chances of benefits against the chances of harms.

Why Treat Based on Overall Cardiovascular Risk?
To date, the evidence suggests that a statin’s relative risk reduction is similar across lower-and higher-risk primary prevention patients younger than 70 years.7,8 This means that a person with a 10-year risk of 20% receives about the same relative reduction in heart attacks as someone with a risk of 10%, but the former patient receives about twice the absolute benefit as the latter patient.4 Therefore, the 10-year absolute benefit for any individual without known cardiovascular disease is best estimated by multiplying his or her overall cardiovascular risk by the average relative risk reduction of a particular statin dose.

A Personal Example of Patient Preferences
I am 58 years old, and my 10-year cardiovascular risk is about 7% to 8%, but I have decided to not yet take a statin. Why? The statin dose recommended by the

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ACC/AHA guideline for persons like me (40 mg of simvastatin [Zocor] or 10 to 20 mg of atorvastatin [Lipitor]) has about a 35% to 40% relative risk reduction,\(^4,7\) meaning that it would reduce my 10-year risk of having a heart attack to about 4% to 5% (roughly a three in 100 chance of preventing a heart attack over the next 10 years). To some, this is probably high enough to warrant starting a statin, but I am willing to accept a slightly higher chance of a heart attack (most of which are mild in my age group) over the next five years instead of starting a medication for which we currently lack good long-term safety data. If my 10-year cardiovascular risk were closer to 15%, a reduction to roughly 8% seems well worth the risks of taking a daily statin. However, I am happy to prescribe a statin earlier to my patients if they wish.

**When Should Physicians Prescribe a Statin for Primary Prevention?**

My biggest criticism of the new guideline is that it does not acknowledge a specific gray zone—a range in which the potential benefits and harms of a statin make the “right decision” predominantly a matter of individual patient circumstances and preferences.\(^9,10\) It may be reasonable to set 7.5% as a starting point for discussion (e.g., for every 33 patients treated for 10 years, roughly one heart attack will be prevented [i.e., number needed to treat = 33]). But these risks and benefits are estimates with a nontrivial margin of error (different risk calculator estimates can vary by 20% to 30%). The guideline does note that shared decision making should be used, but it provides no clear direction on when statins should be recommended rather than just discussed. Specifying a gray zone, such as a 10-year risk of 7.5% to 12.5%, could be a solution. In this range, treatment is more appropriate for those who worry more about heart attacks and less appropriate for those who worry more about adverse events from medication use. To avoid polypharmacy, one might be more likely to recommend a statin in the latter group when a patient is taking two medications vs. 15 medications.

I have heard many suggest that such nuances are beyond the abilities of primary care physicians, but I strongly disagree. Those who make guidelines and performance measures need to stop behaving as if primary care physicians need rigid rules for every decision, even those that are close calls.\(^9,10\) They need to recognize that for virtually every decision in life, there is a gray range in which the right decision is purely one of personal preference, a range in which they should defer to the primary care physicians who actually know the patient. The ACC/AHA committee did a great job of moving us to a measure that better estimates the chance that our patients benefit from a statin (overall cardiovascular risk), but they should now revise their guideline to specify a range in which the decision to start a statin should be tailored to the individual and not recommended by a central committee.

The opinions above are the author’s and do not represent those of the U.S. Department of Veterans Affairs or the University of Michigan.

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**EDITOR’S NOTE**

The AAFP endorsed the ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults with “qualifications” in June 2014. The qualifications include a concern that the cardiovascular disease risk assessment tool has not been validated and may overestimate risk with a cutoff of 7.5% leading to greater statin use; a note that many of the recommendations were based on expert opinion; and mention of conflict of interest in nearly one-half of the panel members.—SUMI Sexton, MD, Associate Medical Editor, American Family Physician

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**REFERENCES**