New Cholesterol Guidelines: Has Godot Finally Arrived?

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In Samuel Beckett’s tragicomedy, 2 friends, Estragon and Vladimir, are waiting for their friend Godot, who never arrives. Similarly, primary care providers have been waiting for updated guidance from the Adult Treatment Panel III since 2001 (1). In November 2013, the American College of Cardiology and the American Heart Association (ACC/AHA) published an update to the guideline on the treatment of blood cholesterol (2) that was first developed by the National Heart, Lung, and Blood Institute in 2008. Has Godot finally arrived?

For more than a decade, primary care providers have struggled with performance metrics focused on meeting threshold goals for low-density lipoprotein cholesterol (LDL-C) levels that are based on expert consensus (3). These LDL-C goals led to frequent adjustments of medications with steadily increasing doses of statins, clinically unproven but theoretically attractive combinations of lipid therapy, and repeated laboratory testing—but to what end? Enter the long-awaited and updated 2013 ACC/AHA guideline, which has garnered the attention of the media, special interest groups, physicians, and patients. Why all of the excitement and controversy?

The updated guideline differs significantly from any prior Adult Treatment Panel document in that it is narrower in scope; is focused more on randomized, controlled trial (RCT) evidence than expert opinion; more closely follows the tenets of the Institute of Medicine guidelines (4); and is more transparent about conflicts of interest. Several of the recommendations from the expert panel represent a paradigm shift with tremendous implications. As such, we applaud the panel for having the courage to make these changes, especially the decision to jettison the consensus-based “treat-to-target” method in favor of an evidence-based strategy focused on fixed-dose statins. We are less enthusiastic about several other recommendations.

The decision to discontinue the treat-to-target approach to lipid management makes sense for many reasons. First, a strategy using fixed-dose statins is consistent with RCTs as opposed to a focus on LDL-C targets, which was never supported by RCT evidence (3). As such, this evidence-based approach greatly simplifies treatment for clinicians and is clearly more patient-centered. Fewer dose adjustments and fewer laboratory studies should be a welcome change for patients and primary care providers. Of note, a fixed-dose strategy should remove the impetus for unwieldy lipid-lowering combinations, which expose patients to unnecessary harm (5) and expense. Finally, some high-risk patients who meet LDL-C goals with no or low-dose statin use could benefit from an evidence-based, fixed-dose statin strategy (6).

What is more controversial in the new guidelines but less important in our view is the lowering of statin treatment thresholds to a 10-year risk of 7.5% or greater and the adoption of a new risk calculator, which others have reported overestimates the risk for atherosclerotic cardiovascular disease by 70% to 150% (7). Like others, we believe that these changes will lead to overtreatment of some patients, especially in primary prevention. For example, a 65-year-old man without hypertension, diabetes, or a history of smoking would be considered to have a 10-year risk greater than 7.5%, and treatment would be recommended despite evidence from AFCAPS [Air Force Atherosclerosis Prevention Study] (8) showing that this patient would not benefit (relative to placebo) from receiving 40 mg of lovastatin.

However, we are less concerned about the calculator (which can be modified to improve performance) than we are about the lowering of risk thresholds for primary prevention. Given the uncertainty of any calculator in accurately predicting 10-year risk, we believe that the decision to recommend pharmacotherapy for primary prevention should be based on a risk of 10% or 15% (the latter being the 10-year event rate in the AFCAPS placebo group). The expert panel based its recommendation on a risk–benefit analysis, which underestimates the adverse events of statins. If rare adverse events, such as rhabdomyolysis, are focused on, common adverse events that lead to treatment discontinuation (such as muscle pain) are undervalued. Once a decision is made to treat lower-risk patients, we are concerned that those who cannot tolerate a statin might then be transitioned to nonstatin medications, such as ezetimibe, which have not been shown to improve any clinical outcomes.

The guidelines offer support for shared decision making in treatment decisions, primary prevention, and patients whose age or other clinical features fall outside of the recommendations. However, treatment recommendations for primary prevention in a patient with a 10-year risk greater than 7.5% are definitive (Figure 2 of guidelines), and shared decision making seems to have been considered almost as an afterthought (2). Because data on primary prevention are less robust than those on secondary prevention, we believe that shared decision making should dictate.
whether lower-risk patients (perhaps with a 10-year risk >10% or >15%) are treated with a statin. Information about the number needed to treat to prevent a clinically relevant cardiac event, balanced by the number needed to harm for serious adverse events (such as rhabdomyolysis and new-onset diabetes) and bother symptoms (such as muscle pain and weakness), would be inherent to this decision.

High-intensity statins are recommended for all patients for secondary prevention and for many patients for other reasons, such as diabetes. Moderate-dose statins have a better safety record, are better tolerated, and reduce clinical and patient-centered outcomes (including overall mortality) (9). Conversely, higher-intensity statins are not as well-tolerated and are not associated with overall mortality benefit compared with moderate-dose statins. Perhaps a more patient-centered strategy would be to start with moderate-dose statins in most patients and use a shared-decision approach to increase to a high dose as tolerated.

So, has Godot arrived? In the play, Estragon and Vladimir yearn for Godot to arrive in the hope that he will save them, but they also worry that if Godot is angered, he might punish them. Yes, Godot has arrived—but with mixed reviews. The change to a fixed-dose statin approach is simpler, is more patient-centered, will save clinicians time, and should improve the care of high-risk patients. We hope that the planned 2014 update will include improvements to the risk calculator and provisions for informed patient preference for lower-risk primary prevention. Finally, we implore organizations to drop performance metrics based on LDL-C targets and focus on statin-based therapy in at-risk patients.

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