Letter by Stone et al Regarding Article, “Perspective on the 2013 American Heart Association/American College of Cardiology Guideline for the Use of Statins in Primary Prevention of Low-Risk Individuals”

To the Editor:

We read with significant concern the perspective by Dr Breslow on the 2013 American Heart Association/American Heart Association Cholesterol and Risk Assessment guidelines. He chose to focus his perspective on the guidelines’ primary prevention recommendations for those aged 40 to 75 years with an estimated 10-year atherosclerotic cardiovascular disease risk ≥7.5% and a low-density lipoprotein cholesterol 70 to 189 mg/dL. He stated that “the guideline recommends such individuals receive moderate intensity statin therapy to reduce LDL-C between 30% and 49%.” In fact, the guidelines state that these individuals are in a group with clear net clinical benefit from statin use, and in both the original guidelines and follow-up publications by the panel, we specifically call for a clinician–patient discussion before a statin is prescribed, rather than mandated statin therapy. This is a critical distinction.

We envisioned that this clinician–patient discussion would allow for a consideration of lifestyle changes, focus on other modifiable risk factors, and initiate a discussion of the potential for benefit and the potential for adverse effects and drug–drug interactions along with elicitation of patient preference. We agree that there is a paucity of clinical trial data demonstrating the magnitude of atherosclerotic cardiovascular disease risk reduction that statins can deliver when a 10-year atherosclerotic cardiovascular disease risk ≥7.5% has been attained solely on the basis of age, whereas other risk factors are truly optimal. However, such individuals represent a small and declining proportion of the population. Nonetheless, in patients whose risk seems to derive entirely from age, it is reasonable to consider avoiding statin therapy as it would be in other patients whom the clinician thinks would not derive a significant net benefit or might have increased risk of harms.

Regarding Dr Breslow’s concerns about the risk estimator, it should be noted that the guidelines underwent 5 layers of scientific peer review, by dozens of external scientific reviewers, before their release. The Risk Assessment guideline full document provides far more extensive internal and external evaluation of the Pooled Cohort Equations (and assessment of potential overestimation of risks) than has ever been provided for any other risk equations at the time of their publication. Dr Breslow noted the “severe” (and, we note, nonpeer-reviewed) criticism of the risk estimator published by Ridker and Cook in the New York Times and Lancet, without acknowledging the detailed response of the guideline panel chairs refuting these concerns published alongside Ridker and Cook’s opinion piece. The cohorts selected by Ridker and Cook were considered and specifically rejected by the Risk Assessment panel given that they are not representative of the broad US population, did not directly measure risk factor levels, did not ascertain all clinical events during follow-up, and were subject to substantial levels of downstream therapy (including statins, aspirin, antihypertensive therapy, and elective revascularizations), rendering them inappropriate for evaluating the validity of the Pooled Cohort Equations. The Pooled Cohort Equations have subsequently been examined in a large and representative US cohort and found to calibrate extremely well in the relevant population of primary prevention-eligible individuals.

In his Perspective piece, Dr Breslow used the Pooled Cohort Equations to estimate treatment effects from a statin. This is a misuse of the risk score. Risk scores derived from natural history data cannot be used to estimate treatment effects; treatment effects should only be estimated from clinical trial results. Therefore, the numbers needed to treat based on his calculations are incorrect. The correct numbers needed to treat for statins are presented in detail in the cholesterol guideline documents, and they are lower than the numbers needed to treat seen for other widely used but more toxic therapies.

We reviewed potential side effects thoroughly and quantitatively in the guideline but agree with Dr Breslow’s point that patients who consume significant amounts of alcohol, who have multiple comorbidities, and who are on several medications are generally excluded from randomized controlled trials. This is another example of why the clinician–patient risk discussion was deemed necessary before a statin prescription is given so that the patient’s individual situation and the physician’s judgment could weigh on both the potential for benefit and the potential for adverse effects.

As noted above, we do agree with Dr Breslow that the decision to initiate statin therapy for primary prevention of atherosclerotic cardiovascular disease “…requires carefully weighing the benefits and risks of statin therapy.” Clinicians who read the guidelines, rather than misleading headlines, will find that these recent guidelines provide powerful tools that will assist patients and clinicians to do just that. Because one third of Americans will die of preventable or postponable cardiovascular diseases and >50% will have a major vascular event before they die, it is time that we promote discussion of the powerful evidence base provided by these guidelines. The guidelines advocate serious, individualized, and focused discussions with our patients. We hope that this will lead to appropriate and informed shared decision making to curb this epidemic.

Disclosures

None.

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