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Should people at low risk of cardiovascular disease take a statin?

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Re: Should people at low risk of cardiovascular disease take a statin?

Dear Dr. Godlee,

The BMJ Analysis of statins in low risk people stated, “the evidence does not show that the benefits of statins in low risk patients outweigh the harms and that the advice for treatment of this group should not be changed.”(1) Our Cochrane systematic review on statins for the primary prevention of cardiovascular disease (CVD) is criticized for not coming to the same conclusion.(2) Readers of the BMJ may be interested in our views on their arguments.

The timing of this Analysis predated by three weeks the publication of the 2013 American College of Cardiology/American Heart Association cholesterol treatment guidelines (November 12, 2013), but statements were made about “proposed standards” without full knowledge of these guidelines. Notably, none of the authors were acknowledged reviewers of the ACC/AHA guidelines.(3)

Abramson et al. state: "Under the proposed 2013 standards, however, no level of risk would preclude statin therapy, raising the question whether all people over the age of 50 should be treated.” Neither the Cochrane review nor the ACC/AHA cholesterol guidelines proposed treatment for everyone over the age of 50 years. The ACC/AHA guidelines recommends that initiation of moderate-intensity statin therapy be considered for patients with predicted 10-year “hard” ASCVD risk of 5.0% to <7.5%.” The Cochrane review questioned the feasibility and desirability of having to treat the majority of people over the age of 50 years with a statin.

These authors comment that the inclusion of four additional trials“ did not substantially alter the previously documented effect of statin therapy”. The updating of the evidence base resulted in an expected narrowing of confidence intervals and the addition of JUPITER trial added important evidence on diabetes risk.

The authors consider that statins should reduce total mortality if they are to have a place in primary prevention in people in lower CVD risk strata and estimate a relative risk of 0.95, 95% confidence interval 0.86 to 1.04. However, the authors included both individuals with and without prior vascular disease in this estimate. In our Table we have conducted the appropriate analysis using only low-risk individuals (<5%, 5-10%) without prior vascular disease. In the lowest risk category (<5%), the number of total deaths was small (1% of control group participants dying over 4 years) and non-CVD causes of death exceeded CVD deaths by more than 2:1. However, the risk of suffering a major vascular event (fatal and non-fatal) was 0.6% per year, which was reduced by statins (RR 0.62 [95%CI 0.47, 4.81]; 167 events on statin vs. 254 events on control; similar effect

size across major coronary event, stroke, and revascularization) in this low risk group (Figure 1, Cholesterol Treatment Trialists' 2012 Lancet paper(4)). No strong evidence of benefit for total mortality was seen because other causes of death make up a greater proportion of total deaths, and it is unlikely that taking statins influences these non-CVD deaths.

We disagree with their statement that the "best indication of the net effect of a treatment on overall health is the total number of serious adverse events — which include deaths from all causes, hospital admissions, prolongations of admission, cancer, or permanent disability." Weighting each of these events similarly is incorrect. Deaths, disability, and prolongation of admission are quite different outcomes that would not be weighted similarly by most patients.(5)

While criticizing the RCTs, they use low quality evidence from observational studies to support their statements about the hazards associated with statins despite likely high risk of bias. The authors also conflate muscle pain (mylagias), an important side effect of statins, with myopathy, a rare and more serious problem, both of which warrant ongoing study. The authors cite studies demonstrating adverse events associated with statin therapy but fail to cite systematic reviews which show no increased risk of psychological outcomes, fractures, acute renal failure, arthritis, or venous thromboembolism.(6-9) The incidence of diabetes appears to be real but is linked to the underlying risk of developing diabetes among participants and is also associated with the intensity of statin dose.

Finally, Abramson et al. set up a false dichotomy, stating: "Rather than being compelled by guidelines to prescribe statin therapy for people at low risk of cardiovascular disease, doctors would provide a far greater service by explaining the magnitude of the benefits and uncertainty about the harms of statins together with discussion of the epidemiological evidence showing that behavioural risk factors—including tobacco use, lack of physical exercise, and unhealthy diet—are responsible for 80% of cardiovascular disease." If they (and the BMJ editors) had awaited the publication of the 2013 ACC/AHA cholesterol guidelines, they would have been directed to the companion lifestyle guidelines, which aim to address these topics. Salient comment on the importance of considering benefits, harms, alternative non-pharmacological treatments are embedded in the relevant section of the report. Strong evidence to support the benefits of the type of health promotion proposed by Abramson et al. in CVD primary prevention is sadly lacking.

We have outlined several flaws in the Abramson and colleagues "Analysis", which we believe threaten its validity. The decision for patients at low risk for CVD to initiate or continue statin therapy for primary prevention remains under the purview of patients and their physicians. We hope that our Cochrane review, which will continue to be updated as further evidence accrues, will help inform those conversations for better decision-making and better health.

Regards,

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