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Statins and Diabetes: Wider Utilization Is Needed in Treatment and Prevention

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In this issue of ***The American Journal of Medicine***, Hennekens et al[1] address many cogent methodologic issues concerning whether there is a valid statistical association between statins and the development of diabetes. While they conclude that the current totality of evidence is insufficient to confirm a valid association, if such an association were present, the most plausible magnitude of increased risk would be about 9%-12% of treated patients. So, even if a clinician believes that statins can increase the risk for developing diabetes, these data pale in comparison with the well-described benefits of statins in both secondary and primary prevention of clinical cardiovascular disease endpoints. Thus, clinicians should more widely prescribe statins for a wide range of subjects, for the highest-risk individuals for whom secondary prevention is the goal, as well as for other patients for whom primary prevention is sought. While it seems reasonable to debate whether the absolute benefit achieved by statins in the lowest-risk primary prevention subjects warrants the cost with respect to benefit vs risk, the evidence is cogent.

Few would disagree[2] that large-scale randomized trial evidence represents the most reliable design strategy to detect even small-to-moderate benefits and potential risks of interventions. With respect to statins and side effects, there has been a tendency to over-interpret nonrandomized evidence, including both observational studies and claims data. This hyperbole results from the failure to acknowledge that inherent and uncontrollable confounding by indication can easily be as quantifiably large as the benefits and risks being sought. Clinicians are well aware that sicker patients tend to be prescribed more drugs as well as more potent drugs. Therefore, it is not surprising that such patients have a greater, but biased, quantity of side effects. These issues have been summarized by academicians[3] as well as by the US Food and Drug Administration charged with regulatory functions for drugs and devices.[4] With respect to benefits, smaller trials, meta-analyses, and subgroup analyses can be similarly misleading.[5]

Nonrandomized evidence, however, can be useful in raising hypotheses generated by population trends. In this regard, in a Danish nationwide prospective cohort study, pejorative statin-related news stories led to early statin discontinuation. Furthermore, such early statin discontinuation was temporally related to increased trends for myocardial infarction and cardiovascular mortality.[6]

Guidelines should provide direction for clinicians, and most guideline committees recommend that statins should be the first-line drug of choice in virtually all secondary prevention patients.[7] High-risk primary prevention patients should also be strongly considered for statin use. Serious scientists may disagree about whether the absolute benefit in the lowest-risk subjects exceeds the cost, but side effects should not be a major consideration in these decisions. In addition, statins should be an adjunct, not an alternative, to therapeutic lifestyle changes. Other drug therapies for those individuals at increased risk for clinical cardiovascular events should include aspirin, for which the benefits with statins are additive, as well as converting enzyme inhibition. Most importantly, the adoption of this strategy of secondary and primary prevention by clinicians can avoid many premature cardiovascular events and deaths. Conversely, the failure to prescribe statins may increase premature morbidity and mortality from cardiovascular disease in both secondary and primary prevention patients. In this regard, the Commentary by Hennekens et al[1] provides important and relevant guidance for clinicians.

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