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Predicted vs Observed Clinical Event Risk for Cardiovascular Disease

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In Reply

Discrepancies between predicted and observed clinical event risk are a common challenge in cardiovascular medicine not limited to the ASCVD score. Typically, observed event rates are (sometimes significantly) lower than those either predicted by risk prediction instruments or derived from historical cohorts. This phenomenon has been reported in primary prevention cohorts^{1,2} as well as symptomatic patients³ and constitutes a common issue for power and sample size calculations for clinical trials.

Not surprisingly, and as suggested by Drs DeFilippis and Blaha, we observed a similar phenomenon using the ASCVD pooled cohort calculator⁴ to predict CVD risk and statin eligibility. Among participants who were newly eligible for statin therapy (n = 593), the incident CVD rate over 9.4 years of follow-up was 5.7%, whereas the calculated median ASCVD 10-year risk for this same group of participants was 10.9% (interquartile range, 8.7%–15.0%). A similar result was seen in the overall population (predicted ASCVD event risk vs observed event risk, 5.7% vs 3.0%) and for those at intermediate Framingham risk (predicted ASCVD event risk vs observed event risk, 11.1% vs 3.9%), suggesting that overestimation of risk is not only limited to participants who are newly statin eligible.

Despite these findings, an important result of our analysis was that the incident CVD rate of 5.7% among newly statin-eligible participants was comparable with the incident CVD rate of all participants that were statin eligible by the 2013 ACC/AHA guidelines and by the 2004 ATP III guidelines (6.3% and 6.9%, respectively). Moreover, the incident CVD rate among patients at intermediate Framingham risk (Framingham Risk Score, 6%–20%) was 4.8% among those eligible for statins vs 0.5% among those not eligible, yielding a hazard ratio of 9.3, suggesting that the categorization of statin eligibility by the 2013 ACC/AHA guideline provides greater accuracy than the prior 2004 ATP III classification for identification of incident CVD.

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However, it is clear that the accuracy of guideline-based statin eligibility for incident CVD could be further improved. For example, we demonstrated that among participants designated statin eligible with the 2013 ACC/AHA guideline, those with a CAC score of 0 had an incident CVD rate of 1.6%, similar to those not statin eligible by the guidelines, whereas the median ASCVD 10-year risk for this same group of participants was 10.1% (interquartile range, 8.5%–13.6%). Hence, overestimation of event risk is a common issue in cardiovascular medicine and imaging of coronary atherosclerosis provides the means for additional risk stratification.

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