ACC/AHA Pooled Cohort Risk Equations predicted 5-y risk for CV events in adults considered for statin initiation

Muntner P, Colantonio LD, Cushman M, et al. ***Validation of the atherosclerotic cardiovascular disease Pooled Cohort risk equations.*** *JAMA. 2014;311:1406-15.*

Clinical impact ratings: GM ★★★★★★☆ C ★★★★★☆☆ En ★★★★★★☆

Question

In community-dwelling adults without atherosclerotic cardiovascular disease (ASCVD) who are being considered for statin therapy, do American College of Cardiology/American Heart Association (ACC/AHA) Pooled Cohort Equations predict risk for ASCVD events?

Methods

Design: Population-based cohort study (Reasons for Geographic and Racial Differences in Stoke [REGARDS] study) with ≤ 5 years of follow-up for validation of existing prediction equations.

Setting: USA.

Participants: 18 498 adults 45 to 79 years of age (mean age 63 y, 58% women, 18% with diabetes, 25% using statins) who did not have atrial fibrillation, coronary heart disease (CHD), or stroke. Exclusion criteria included use of digoxin and missing data for any risk equation components. This abstract focuses on the subgroup of participants without diabetes, who were not using statins, and with low-density lipoprotein cholesterol levels of 70 to 189 mg/dL (1.81 to 4.89 mmol/L), who might be considered for statin therapy (statin-decision group, n = 10 997).

Description of prediction guide: The ACC/AHA Pooled Cohort Risk Equations are based on 9 variables: sex, race, age, smoking status, diabetes, total cholesterol level, high-density lipoprotein cholesterol level, systolic blood pressure, and use of antihypertensive drugs. Calibration of the equations was defined as poor if a modified Hosmer-Lemeshow chi-square statistic was > 20 or $P < 0.05$; discrimination was defined as moderate to good if the C index was 0.70 to 0.80.

Outcomes: Composite of ASCVD events (CHD death, nonfatal myocardial infarction, or fatal or nonfatal stroke) identified by self-report, confirmed by medical records, and adjudicated.

Main results

5-year observed and predicted event rates for the statin-decision group are shown in the Table. The Pooled Cohort Equations overestimated risk in higher-risk groups (Hosmer-Lemeshow chi-square = 20, P = 0.01, indicating poor calibration) and had moderate discrimination of risk for ASCVD events (Table). In a subgroup of 3333 participants in the statin-decision group who had Medicare claims data available to identify additional events, the Pooled Cohort Equations had a Hosmer-Lemeshow chi-square of 5.4 (P = 0.71) and C index of 0.67 (95% CI 0.64 to 0.71).

Pooled Cohort Risk Equations for predicting atherosclerotic cardiovascular disease events in adults considered for initiation of statin therapy*

Estimated 10-y risk (n)†	Event rates‡ at 5-y follow-up		C index (95% CI)
	Observed	Predicted	
< 5% (3453)	0.93%	0.95%	0.72 (0.70 to 0.75)
5% to < 7.5% (1578)	2.38%	2.40%	
7.5% to < 10% (1332)	3.06%	3.43%	
≥ 10% (4634)	5.99%	7.56%	

**CI defined in Glossary. Atherosclerotic cardiovascular disease events were coronary heart disease death, nonfatal myocardial infarction, and fatal or nonfatal stroke. Participants considered for initiation of statin therapy did not have diabetes, were not currently using statins, and had a low-density lipoprotein cholesterol level of 70 to 189 mg/dL.*

†Based on Pooled Cohort Risk Equations.

‡Calculated using number of events at 5 years estimated from the Kaplan-Meier curve (observed events) and Pooled Cohort Risk Equations (predicted events) and the number of participants in the 10-y risk groups.

Conclusion

In community-dwelling adults considered for initiation of statin therapy, the ACC/AHA Pooled Cohort Risk Equations predicted 5-year risk for cardiovascular events with poor calibration overall and moderate discrimination.

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Commentary

Updated ACC/AHA cholesterol guidelines recommend calculating 10-year CVD risk using the new Pooled Cohort Equations (1). Adults with 10-year risk ≥ 7.5% are candidates for use of statins for primary prevention (2). Thus, performance of this new risk estimator in persons for whom statins are not otherwise indicated is of particular importance. In the large, contemporary cohort studied by Muntner and colleagues, the Pooled Cohort Equations overestimated risk among adults with the highest absolute risk, although in the more relevant subgroup potentially eligible for statins based on estimated CVD risk alone, observed and predicted event rates were more similar. Guidelines (1, 2) use a 10-year risk horizon; however, the 5-year estimates validated in this study are clinically relevant because guidelines recommend updated risk assessment every 4 to 6 years to determine statin eligibility (1). Further, most clinical trials of statins have evaluated treatment effects over ≤ 5 years (3).

Muntner and colleagues showed that the Pooled Cohort Equations can fairly accurately predict CVD risk to identify adults who may benefit from statin therapy in the next 5 years, but may overestimate risk among the highest-risk subgroups. Although the C index of 0.72 is similar to that seen in the Framingham 10-year risk model used in the Adult Treatment Panel III guidelines, there may be room for improvement in model discrimination. Thus, clinicians should use caution in relying solely on 10-year predicted risk to identify statin candidates. How inclusion of other risk factors, such as C-reactive protein, family history, or apolipoprotein B, might improve discrimination remains to be seen.

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