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Primary Risk Prevention in the Elderly: Use Clinician-Patient Discussions, Not Automatic Statin Prescribing

Cholesterol management in the elderly is challenging owing to competing risks for mortality, potential for interactions with more complex medical regimens, and the importance of safety issues. A recent commentary[1] suggested that the new guidelines may overtreat those in the 65-75 years age group owing its reliance on the Pooled Cohort Equations to assess atherosclerotic cardiovascular disease (ASCVD) risk.[2]

We believe the commentary is misleading because it fails to acknowledge that the guidelines expressly do not recommend automatic statin prescriptions for lower-risk primary prevention, including those in the 65-75 years age range. The cholesterol guideline specifically recommended a clinician−patient discussion (**Table**) to encourage individualization of risk reduction therapy.

The commentary suggests that statin therapy may be justified in elderly persons with 1 or more severe abnormalities of major risk factors in addition to age. However, it would leave untreated those at similar risk of ASCVD because of concurrence of moderate elevation of multiple risk factors. There are many such persons: 96%-98% of those aged 65-75 years do not have optimal risk factor status.[3] Why should the many with increased risk caused by simultaneous moderate elevation of several risk factors be denied the benefits of risk-reduction from statin therapy if clinician and patient agree? Furthermore, it is surprising that the commentary seems to recommend a return to risk factor counting despite the consensus that "multivariable risk scores tend to estimate and quantify predicted risk more accurately than schemes based solely on risk factor counting."[4]

The guidelines do not recommend automatic statin therapy for primary prevention in those older than 75 years. They noted that initiation of statins in such individuals required consideration of additional factors, such as comorbidities, safety, and priorities of care. Thus, the decision was thought best to be made according to the clinician's judgment of the individual's clinical status and the patient's preference.

The guidelines review of exclusively primary prevention trials did show net benefit and significant reduction in heart attack and stroke with statin therapy in lower-risk primary prevention individuals aged 40-75 years. Using National Health and Nutrition Examination Survey data, as many as 475,000 future cardiovascular events could be prevented if statins were given to all who exceeded the ≥7.5% cutoff in ASCVD risk.[5] Although a substantial benefit, this may be an overestimation. For purposes of analysis the authors "assumed that membership in one of the groups for whom statin therapy would provide benefit equates with treatment recommendation, whereas the new guidelines call for an informed risk-benefit discussion between the patient and physician before the initiation of statin therapy."

This risk-benefit discussion between patient and caregiver was recommended so that major risk factors such as proposed by Dr. Grundy could be considered. His arguments for coronary artery calcium score to better define risk in the elderly are reasonable, although the data must be viewed critically because the coronary artery calcium score entails expense and the potential for downstream testing whose utility must be evaluated carefully in further trials. Moreover, the new guidelines predict burden of coronary atherosclerosis as assessed by computed tomography angiography more accurately than guidelines based on arbitrary low-density lipoprotein cholesterol (LDL-C) cutoffs.[6]

The commentary asserts that the Pooled Cohort Equations recommended by the American College of Cardiology (ACC)/American Heart Association (AHA) Cholesterol Guideline "overestimate risk…where age alone and no other risk factors will trigger statin therapy." For this, it cites Ridker and Cook.[7] However, the cited article does not include an analysis of the effect of age on the predictive accuracy of the Pooled Cohort Equations, and we are not aware of any other publication that does. Furthermore, the study used a small segment of the US population with atypically low ASCVD incidence, namely, clinical trial volunteers with high socioeconomic status. Such a

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Table Elements of the Clinician-Patient Risk Discussion

Discuss before initiating statin therapy in primary prevention at any level of ASCVD risk (excludes those with primary elevation of LDL-C ≥190 mg/dL or those with diabetes aged 40-75 years with LDL-C ≥70 mg/dL):

1. Potential for ASCVD risk-reduction benefits of statin therapy*
2. Potential for adverse effects and drug-drug interactions with statin therapy†
3. Heart-healthy lifestyle
4. Management of other risk factors
5. Patient preferences
6. If decision unclear, consider primary LDL-C ≥160 mg/dL, family history of premature ASCVD, lifetime ASCVD risk, abnormal coronary artery calcium score of ≥300 Agatston units or ≥75th age, sex, race percentile, hs-CRP ≥ 2 mg/L, or ABI <0.9

ABI = ankle-brachial index; ASCVD = atherosclerotic cardiovascular disease; hs-CRP = high-sensitivity C-reactive protein; LDL-C = low-density lipoprotein cholesterol.

*The absolute reduction in ASCVD events from moderate- or high-intensity statin therapy can be approximated by multiplying the estimated 10-year ASCVD risk by the anticipated relative-risk reduction from the intensity of statin initiated (approximately 30% for moderate-intensity statin or approximately 45% for high-intensity statin therapy). The net ASCVD risk-reduction benefit is estimated from the number of potential ASCVD events prevented with a statin, compared with the number of potential excess adverse effects.

†Potential adverse effects. The excess risk of diabetes is the main consideration in approximately 1 excess case per 1000 individuals treated with a moderate-intensity statin for 1 year and approximately 3 excess cases per 1000 individuals treated with a high-intensity statin for 1 year. In randomized controlled trials both statin-treated and placebo-treated participants experienced the same rate of muscle symptoms. The actual rate of statin-related muscle symptoms in the clinical population is unclear. Muscle symptoms attributed to statin therapy should be evaluated.

Adapted with permission from Figure 2 of the 2013 ACC-AHA Cholesterol Guidelines (reference[2]).

population is expected to yield fewer events than predicted by models based on the population at large.[8-10] This phenomenon (lower than expected ASCVD incidence with higher socioeconomic status) is ripe for the clinician-patient risk discussion. Additionally, a "healthy volunteer effect" may provide additional explanation for a disproportionately low event rate in placebo groups of the drug trials analyzed by Ridker and Cook.[11,12] In fact, the magnitude of the "healthy volunteer effect" on all-cause mortality in the Physicians' Health Study (1 of the 3 studies used in the analysis) was reported to be 19%.[12] The Pooled Cohort Equations were designed to be representative of the broad population of the United States, and they do predict well in US studies that reflect that population.[13]

The 2013 ACC/AHA risk assessment guideline recommended family history of premature ASCVD, coronary artery calcium score ≥300 Agatston units or 75th age, race, and sex percentiles, ankle brachial index ≤0.9, or high-sensitivity C-reactive protein ≥2.0 mg/L as factors that could provide incremental benefit in terms of discrimination, calibration, and net reclassification. An LDL-C level ≥160 mg/dL and elevated lifetime risk were suggested as additional factors to inform risk discussions and treatment decisions. These "tie-breakers" empower clinicians to make risk evaluations and treatment decisions most appropriate for their patients. This is especially important in the elderly, for whom comorbidities, drug-drug interactions, and frailty are often considerations.

For convenience, the guidelines provided an app that not only allows estimation of 10-year ASCVD risk and lifetime risk, but also provides decision support. The number of downloads of the ACC/AHA risk estimator app has increased to nearly 121,000, and an average of more than 9500 are using the app or its Web-based counterpart on a daily basis.[14]

Application of the AHA/ACC guideline recommendations in older individuals not in a high-risk groups (secondary prevention, diabetes with LDL-C 70-189 mg/dL, or primary elevation of LDL-C ≥190 mg/dL) cannot be oversimplified to automatic statin prescribing based solely on estimation of a global risk score. The guidelines recommend using randomized clinical trial evidence, clinicians' judgment, and the preference of informed patients in risk decisions for the elderly. This strategy offers the promise of recognizing treatment-eligible elderly patients with increased ASCVD risk who can expect net clinical benefit from risk reduction therapies. It simultaneously limits the harmful effects of unnecessary medication in those least likely to benefit.

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