

The underestimation of CVD risk in SAs may be due to a high prevalence of non-traditional risk factors, notably high levels of Lp(a) and visceral adiposity with insulin resistance, despite comparatively low BMI.^{543,560,567} Observed CHD morbidity and mortality rates among SAs have been substantially higher than those predicted by Framingham Risk Score and European System for Cardiac Operative Risk Evaluation, which led to the development of QRISK2 in the United Kingdom, a calculator that incorporates social deprivation and ethnicity.⁵⁶⁸ The Joint British Societies Guideline uses QRISK2 lifetime risk, which uses a multiplier of 1.5 for Asian Indian men and 1.42 for Asian Indian women.⁵⁶⁸ The calibration factors are even higher for Pakistanis (2.05 for men and 2.04 for women) and Bangladeshis (2.14 for men and 1.6 for women). Additional research is needed to establish appropriate risk scoring methods for Asians/SAs living in the United States. Therefore, the panel does not endorse a specific risk multiplier, but instead advises that clinicians should be aware of the increased risk in SAs, which may warrant classifying SAs into a higher risk category for a given number of major ASCVD risk factors, as a matter of clinical judgment.

ASCVD risk reduction with statins in Asians/SAs

In a Canadian study from British Columbia, investigators explored the associations between statin prescriptions and outcomes in a multiethnic population with diabetes using administrative data from 1993 to 2006.⁵⁶⁹ Subjects had newly diagnosed diabetes and included 143,630 white persons, 9529 SAs, and 14,084 Chinese. White patients were older and had more comorbidity than the other groups. A statin prescription was associated with lower mortality compared with no prescription within each ethnic group, and to a similar degree: SA (HR 0.69; 95% CI 0.55–0.86; $P = .001$), Chinese (HR 0.60; 95% CI 0.49–0.72; $P < .0001$), and white (HR 0.65; 95% CI 0.63–0.67; $P < .0001$). These findings suggest that statin use is associated with lower mortality in white, Chinese, and SA patients with newly diagnosed diabetes, consistent with benefits of statins observed in other ethnic groups.

Side effects of statins in Asians/SAs

Statins are generally considered to be safe for use among Asians/SAs. Although not placebo-controlled, the Investigation of Rosuvastatin in South Asians, described previously, which was a large randomized trial of rosuvastatin 10 and 20 mg and atorvastatin 10 and 20 mg in patients of SA origin, showed that both statins were generally well tolerated.⁵⁶² There were no clinically relevant differences between statins in adverse events or the incidence of creatine kinase >10 times the upper limit of normal, alanine aminotransferase >3 times the upper limit of normal on 2 consecutive occasions, proteinuria, or hematuria. However, genetic variability in drug metabolism and increased prevalence of certain risk factors suggest the need for caution when prescribing statins to patients with Asian/SA ethnicity.

HPS2-THRIVE examined the cardiovascular outcomes of treatment with extended-release niacin/laropirant or

placebo added to simvastatin (with or without ezetimibe) in $>25,000$ patients with pre-existing CVD from the United Kingdom, several Scandinavian countries, and China (40% of patients).⁵⁷⁰ Safety data indicated significantly greater incidence of myopathy in patients receiving the combination of niacin/laropirant plus simvastatin compared to simvastatin alone (0.34%/year vs 0.08%/year of any myopathy, $P < .0001$). This appeared to be driven primarily by an increase in myopathy among Chinese patients (0.66%/year vs 0.13%/year for niacin/laropirant plus simvastatin compared to simvastatin alone). Among patients in Europe, the incidence was 0.07%/year vs 0.04%/year, respectively. Therefore, the incidence of myopathy was elevated in Chinese patients in both treatment arms compared to Europeans. Although Chinese patients were the only Asians in HPS2-THRIVE, these results have led to a warning advising caution when prescribing simvastatin to Asian patients and instructions to use the lowest dose possible.

To date, the specific cause of the increased susceptibility of Chinese patients to myopathy has not been identified. Genetic variability in drug metabolism, especially with statins, among Asians through the CYP450 pathway and P-glycoprotein, as well as uptake via organic anion transporting polypeptides may play a role. Even if pharmacokinetics is not the explanation, a potential pharmacodynamic sensitivity justifies utilization of lower doses of statins during initiation in Asian patients with titration to goal as tolerated.⁵⁷¹

Clinical trial data suggest a modest, but statistically significant, increase in the incidence of new-onset type 2 diabetes mellitus with statin use. In their review of the published evidence relating statin use to the hazard for diabetes mellitus or worsening glycemia, the Diabetes Subpanel of the NLA Expert Panel on Statin Safety concluded that the well-established benefits of statin therapy in primary and secondary prevention of cardiovascular events outweigh the risk of new-onset diabetes.³³⁶ The Panel therefore did not recommend changes to clinical practice other than measuring glycated hemoglobin or fasting glucose prior to and within one year of statin initiation in those with diabetes risk factors. The risk for diabetes with statin use seems to be greater for intensive-dosage statin therapy, and to be most evident in those with major risk factors for diabetes.⁵⁷² Because SAs have increased risk for developing diabetes at a younger age, statin therapy and new-onset diabetes is a particular concern for this population, and clinicians should be vigilant in screening and monitoring for worsening glycemia in SA patients given statin therapy.

Conclusions

Heterogeneity of risk factors such as dyslipidemia, hypertension, obesity and diabetes, as well as disparities of ASCVD and cerebrovascular disease risks, among persons of Asian ethnicity make it important to address specific prevention and treatment strategies for this portion of the US population.⁵⁶³ Among Asian subgroups, Chinese seem to have a higher prevalence of hypertension and stroke,^{565,566}