

Application of New Cholesterol Guidelines to a Population-Based SamplePencina MJ, Navar-Boggan AM, D'Agostino RB Sr, et al. *N Engl J Med* 2014;370:1422-31.

Conclusions: New American College of Cardiology-American Heart Association (ACC-AHA) guidelines for the management of cholesterol could increase the number of adults who would be eligible for statin therapy by 12.8 million. Most of the increase will be seen among older adults without known cardiovascular disease.

Summary: The ACC-AHA new guidelines for management of cholesterol were released in November of 2013. The new guidelines recommended treatment of patients with LDL cholesterol of 70 mg per deciliter if they have either diabetes or a ten-year risk of cardiovascular disease of 7.5% or more. In addition, the new guidelines expanded the treatment recommendations for statin therapy to all patients with known cardiovascular disease regardless of the LDL cholesterol level. The authors utilized National Health and Nutrition Examination Surveys (NHANES) to estimate the number of persons in the United States for whom statin therapy would be recommended on the basis of the new guidelines as compared with the previous guidelines. NHANES data from 2005 to 2010 was used. Data provided a risk-factor profile of persons for whom statin therapy would be recommended under the new ACC-AHA guidelines as compared with the Third Adult Treatment panel (ATP-III) of the National Cholesterol Education Program. Data was then extrapolated to a population of 115.4 million U.S. adults between the ages of 40 and 75 years. Compared with ATP-III guidelines, the new guidelines would increase the number of U.S. adults receiving or eligible for statin therapy from 43.2 million (37.5%) to 56.0 million (48.6%). 10.4 million of this 12.8 million increase would occur among adults without cardiovascular disease. Among adults between the ages of 60 and 75 years without cardiovascular disease not receiving statin therapy, the percentage that would be eligible for such therapy would increase from 30.4% to 87.4% among men and from 21.2% to 53.6% among women. This effect is driven largely by the increased number of adults who would be classified solely on the basis of their estimated ten-year risk of a cardiovascular event. Those eligible for statin therapy would include more men than women and persons with a higher blood pressure but a markedly lower level of LDL cholesterol.

Comment: As compared with the ATP-III guidelines, new guidelines would recommend statin therapy for more adults who would be expected to have future cardiovascular events (higher sensitivity) and would also include many adults who would not have future events (lower specificity). It is important to keep in mind that the new guidelines also call for an informed risk-benefit discussion between the patient and physician before initiation of statin therapy. Thus, even though the risk of statins are quite low, it is possible a number of patients would opt-out of taking a pill for which they don't have a specific indication or be dissuaded by the infrequent but well-reported complications of statin therapies such as myositis, potential cataract formation, etc. Thus, based on individual patient discussions, the number of patients actually receiving statin therapy in accordance to the new guidelines may be less than estimated here.

Clopidogrel Plus Aspirin Versus Warfarin in Patients With Stroke and Aortic Arch PlaquesAmarenco P, Davis S, Jones EF, et al; and the Aortic Arch Related Cerebral Hazard Trial Investigators. *Stroke* 2014;45:1248-57.

Conclusions: A combination of the primary end point of cerebral infarction, myocardial infarction, peripheral embolism, vascular death, or intracranial hemorrhage in patients with aortic plaque is no different in those treated with a combination of clopidogrel and aspirin vs those treated with warfarin.

Summary: It is known that atherosclerosis of the aortic arch can produce cerebral embolism, particularly when the plaque is ≥ 4 mm in thickness (Jones EF et al, *Stroke* 1995; 26:218-24). In patients with prior ischemic stroke, risk of recurrent stroke or other vascular events in those with aortic plaque ≥ 4 mm in thickness is three to four times higher than in individuals with plaques < 4 mm or no plaque of the aortic arch (Tunick PA et al, *J Am Coll Cardiol* 1994;23:1085-90). Optimal treatment of patients with aortic plaques is unknown. The authors hypothesized that a combination of aspirin plus clopidogrel would be 25% superior to dose-adjusted warfarin for prevention of new vascular events in patients with aortic plaques. They performed a multicenter prospective, randomized, controlled trial, with blinded end point evaluation of aspirin 75 mg/d plus clopidogrel 75 mg/d vs warfarin (international normalized ratio, 2-3) in patients with ischemic stroke, transient ischemic attack or peripheral embolism associated with thoracic aortic plaque ≥ 4 mm and no other identified source of embolism while on best medical therapy. This was an investigator-driven trial funded by the French government and the Australian National Health and Medical Research Council. The primary end point included cerebral infarction, myocardial infarction, peripheral embolism, vascular death, or intracranial hemorrhage. Follow-up visits occurred at 1 month and every 4 months following randomization. After 349 patients were entered, the trial was stopped with randomization having occurred over a period of 8 years and 3 months. After median follow-up of 3.4 years, the primary end occurred in 7.6% (13/172) and 11.3% (20/177) of patients on aspirin and clopidogrel (A+C) and warfarin, respectively (log-rank, $P = .2$). The adjusted hazard ratio was 0.76 (95% CI, 0.36-1.61; $P = .5$). Major hemorrhages, including intracranial hemorrhage, occurred in 4 and 6 patients in the A+C and warfarin groups, respectively. Vascular deaths occurred in 0 patients in the A+C group compared with 6 (3.4%) patients in the warfarin arm (log-rank, $P = .013$). Time in therapeutic range (67% of the time for international normalized ratio 2-3) analysis by tertiles showed no significant differences across groups.

Comment: The study highlights the aortic arch as a source of stroke and peripheral embolism. The study certainly has implications for those manipulating wires within the aortic arch as part of an endovascular procedure and for those treating people with occult peripheral embolism and a suspected thoracic aortic source. While relatively underpowered, the study provides the best information to date on the treatment of patients with aortic plaques and a suspected thoracic aortic source for cerebral or distal embolism. It is unlikely more definitive data is going to be available anytime soon.