New Guidelines to Reduce Risk of Atherosclerotic Cardiovascular Disease
Implications for Stroke Prevention in 2014

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In November 2013, the American College of Cardiology/American Heart Association (ACC/AHA) Task Force on Practice Guidelines released 1 new statement on general cardiovascular risk assessment and 3 statements focused on reducing the risks of cardiovascular disease and stroke, including lifestyle management, treatment of blood cholesterol, and the management of overweight and obesity (the latter written in collaboration with The Obesity Society). A fifth statement on effective approaches to high blood pressure (BP) control, a collaboration among AHA, ACC, and the Centers for Disease Control and Prevention (CDC), also was published. In addition, in December 2013, separate guidance statements from the Eighth Joint National Committee (JNC 8) and the American Society of Hypertension/International Society of Hypertension for management and control of hypertension to minimize cardiovascular risk and complications were released. Each of the new statements is relevant to reducing the burden of stroke, and although they all represent a major step forward, they are not without controversy.

New Recommendations and Changes in Practice Guidelines

For the first time, risk prediction emphasizes both heart disease and stroke. The risk calculator is derived from pooled cohorts representing both whites and blacks in the US population who were followed for ≤12 years (for the atherosclerotic cardiovascular disease [ASCVD] risk calculator, see http://my.americanheart.org/cvriskcalculator). There has, however, been some concern that the ACC/AHA risk prediction algorithm overestimates risk by 75% to 150%, potentially leading to the unnecessary treatment of many patients with a statin. The prediction calculator has nonetheless been defended as a means of identifying people who might not otherwise be considered at risk, thereby prompting healthcare providers to optimize preventive behavioral strategies and other interventions.

The new guidelines simplify the approach to cholesterol lowering. Statin therapy is highlighted because there is less evidence that nonstatin drug treatment reduces the likelihood of cardiovascular events or stroke. Treatment to a target low-density lipoprotein cholesterol (LDL-C) goal or lowest is best cholesterol management is no longer advocated because of an overall lack of evidence for such approaches and concerns about adverse events that can occur with multiple drug regimens. It is now recommended that 4 primary groups of patients be considered for statin therapy, including those (1) having clinical ASCVD; (2) with elevation of LDL-C ≥190 mg/dL; (3) people ages 40 to 75 years who have an LDL-C 70 to 189 mg/dL with a history of diabetes mellitus regardless of the presence of ASCVD; and (4) otherwise having an estimated 10-year ASCVD risk ≥7.5%. High-dose or moderate-dose statin therapy is recommended according to the presence of ASCVD or the level of ASCVD risk and age (younger or older than 75 years). Other factors such as coronary calcium score, high sensitivity c-reactive protein level, and ankle-brachial index may be considered in the treatment decision for those individuals who do not fall into 1 of the 4 primary treatment groups.

This guidance differs from the prior National Cholesterol Education Program Adult Treatment Panel III statement in which, rather than overall ASCVD risk, treatment decisions were based on the 10-year coronary heart disease Framingham Heart Study prediction equation, the number of coronary heart disease risk factors or risk equivalents, and baseline LDL-C levels. Also, in contrast to the new guidelines, Adult Treatment Panel III recommendations included specific LDL-C target goals. Both Adult Treatment Panel III and the new guidelines recommend statin therapy for those with coronary heart disease or other high-risk conditions such as diabetes mellitus or symptomatic carotid atherosclerosis. In these groups, statin treatment is associated with an ≥20% reduction in the risk of a first stroke. The new recommendations expand the indication for statin treatment to people without ASCVD or diabetes mellitus who have a 10-year predicted risk of vascular events ≥7.5%. Although the efficacy of statins for stroke prevention in this latter group is less well known, there is no evidence that the risk of stroke (particularly hemorrhagic stroke) in these patients would be increased with treatment. For secondary stroke prevention, treatment with a high-potency statin has been recommended for those without another indication who have an LDL-C >100 mg/dL. The single clinical trial on which the latter recommendation is based evaluated the

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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(Stroke. 2014;45:945-947.)

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Stroke is available at http://stroke.ahajournals.org
DOI: 10.1161/STROKEAHA.114.004560

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highest approved dose of a high-potency statin, which resulted in an average 50% reduction in LDL-C levels (average LDL-C, 70 mg/dL). The new guideline supports this practice and obviates the need for follow-up assessments of lipid levels because the maximum statin dose is endorsed regardless of lipid levels.

The ACC/AHA/CDC Science Advisory, An Effective Approach to Blood Pressure Control, considers those with a systolic BP ≥140 mmHg or those with a diastolic BP ≥90 mmHg to have hypertension, stresses system-level approaches, and provides a general management algorithm to achieve a BP goal of ≤139/89 mmHg in adults regardless of age. For those requiring drug treatment, initiating therapy with a thiazide diuretic (hydrochlorothiazide) with the addition of an angiotensin-converting enzyme inhibitor (lisinopril; except in child-bearing age women) is recommended regardless of age or race/ethnicity. The authors, however, acknowledge other hypertension treatment algorithms. The JNC 8 report includes updated recommendations based on the results of individual clinical trials of BP control published between January 1, 1966, and December 31, 2009, and a systematic review of studies published between December 2009 and August 2013. Key differences between the prior JNC 7 and the new JNC 8 report, and in contrast to the aforementioned AHA/ACC/CDC Science Advisory, are 9 age-group–based primary recommendations. JNC 8 advises a BP treatment goal of <150/90 mmHg for people aged ≥60 years (grade A recommendation) and a goal of <140/90 mmHg based on expert opinion and clinical circumstance (eg, the treatment target of <140 mmHg systolic BP has already been achieved and is well tolerated). For those with chronic kidney disease or diabetes mellitus, the target BP treatment goal is <140/90 mmHg based on expert opinion. For the general non-black population including those with diabetes mellitus, a thiazide-type diuretic, calcium channel blocker, angiotensin-converting enzyme inhibitor, or angiotensin receptor blocker may be used as initial therapy (grade B recommendation). A thiazide-type diuretic or calcium channel blocker should be initial therapy in blacks, including those with diabetes mellitus (grade C recommendation if diabetic). β-Blockers are not recommended as initial therapy nor is combination therapy with an angiotensin-converting enzyme inhibitor and an angiotensin receptor blocker.

Concerns
As noted above, the ACC/AHA Writing Group acknowledged that the global prediction calculator may overestimate risk because it was not intended for the management of certain racial and ethnic populations including Hispanics, Asians, or native Americans. Concern was also raised because the overestimation of risk could greatly expand the use of statins for primary prevention with unclear consequences. This is a particularly important issue because even the presence of high risk in select patient populations (eg, those with isolated heart failure, dialysis for renal insufficiency) does not necessarily equate to benefit from statin therapy. An alternative approach of directly applying clinical trial data in specific clinical scenarios for making cholesterol-lowering treatment decisions has been advocated.

Unlike the ACC/AHA/CDC Science Advisory, JNC 8 departs from the long-standing BP target goal of <140/90 mmHg. The relationship between BP and stroke risk is continuous to levels of ≥115/75 mmHg. It is possible that the JNC 8 cut point for BP control (<150/90 mmHg) will be interpreted as less stringent and might result in an increase in stroke on a population-wide basis. The differences in the BP target goals and treatment algorithms of the ACC/AHA/CDC Science Advisory and JNC 8 recommendations also could lead to confusion for both healthcare providers, payers, and the public.

Additional Implications for Stroke Prevention
Whereas the new guidelines include stroke as a major ASCVD outcome end point, they do not specifically address the role of statin therapy or BP targets in reference to stroke prevention (primary or secondary) and stroke type (hemorrhagic or various ischemic stroke subtypes). The benefit of statins in reducing stroke in high-risk populations with established ASCVD and diabetes mellitus is established, but the role of treatment for primary stroke prevention in other populations is less definitive. Based on a recent Cochrane meta-analysis of statin therapy for primary prevention of CVD including people with risk factors and low CVD risk, stroke was statistically significantly reduced by 22% as was all-cause mortality by 14%, fatal and nonfatal CVD by 25%, and fatal and nonfatal coronary heart disease by 27%. These findings provide reassurance about statin administration in diverse populations. Statins are not currently recommended for patients with a history of cardioembolic stroke who do not meet one of the new ACC/AHA criteria for statin administration.

Hypertension is the single most important treatable stroke risk factor. It has been argued that a J-shaped relationship between BP and vascular risk does not exist for primary stroke, although low systolic and diastolic BP may lead to cardiovascular but not stroke complications in general populations. Much of the reduction in stroke related mortality in the United States during the last decades is attributed to better BP control in the population, and setting specific targets for BP lowering for primary and recurrent stroke prevention remains an important goal. The current AHA secondary stroke prevention guidelines note that the target BP level and reduction are uncertain, but that benefit has been associated with an average reduction of ≈10/5 mmHg. For such patients, it is reasonable to consider a BP target of <140/90 mmHg. The results of the Secondary Prevention of Small Subcortical Strokes (SPS3) study also indicate that a BP target of <130 mmHg is safe and may be beneficial in people with recent lacunar infarction.

Guidelines remain important sources of knowledge; however, they have inherent limitations and are not a substitute for clinical judgment and pragmatic reasoning.

Disclosures
Dr Gorelick serves as a speaker for Boehringer Ingelheim and Pfizer in relation to stroke prevention in atrial fibrillation. Dr Goldstein has been a past consultant for Pfizer and has spoken at a Pfizer sponsored meeting. The other author reports no conflicts.
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Key Words: prevention ■ preventive measures
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Stroke. 2014;45:945-947; originally published online February 20, 2014;
doi: 10.1161/STROKEAHA.114.004560

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World Wide Web at:
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