The American Heart Association’s goal of reducing deaths from coronary heart disease and stroke in the United States by 25% between 1999 and 2010 was achieved in 2008—a remarkable accomplishment associated with advances in stroke prevention and treatment. Yet, much work remains to be done. Stroke is still the third most common cause of death in the United States and other developed nations, and is the leading cause of death in middle-income countries. From 1979 to 2005, the number of inpatient discharges from short-stay hospitals in the United States with stroke as the first listed diagnosis increased 20% to 895,000.1 Prevention remains the cornerstone of efforts to reduce the burden of stroke on populations throughout the world, with much to be gained through better adherence to proven stroke prevention measures.3

Primordial prevention refers to societal and other efforts aimed at reducing the likelihood that persons will develop the risk factors that can lead to disease. In Scotland, a ban on tobacco smoking in public indoor spaces was enacted into law in March 2006. Although data for an effect on stroke risk is not available, a study focused on hospital admissions for acute coronary syndromes demonstrated the potential impact of such legislative efforts.4 Information on smoking status and exposure to secondhand smoke was collected prospectively based on questionnaires and biochemical findings from all patients admitted with acute coronary syndromes to 9 Scottish hospitals during the 10-month period preceding the passage of the legislation and during the same period the following year. The numbers of admissions for acute coronary syndromes decreased by 17% (95% CI, 16% to 18%) as compared to a 4% reduction in England (which has no smoking ban) over the same period. Persons who had never smoked reported a decrease in the weekly duration of smoking (a variety of lifestyle and behavioral recommendations aimed at reducing stroke risk).6 People who adhere to these lifestyle recommendations have dramatically lower stroke risks as compared to those who do not. A prospective cohort study evaluated the impact on stroke risk of following a healthy lifestyle among 43,685 men from the Health Professionals Follow-up Study and 71,243 women from the Nurses’ Health Study.8 Diet and other lifestyle factors were obtained from self-reported questionnaires. A low-risk profile was defined as not smoking, having a body mass index <25 kg/m², engaging in at least 30 minutes per day of moderate physical activity, consuming modest amounts of alcohol (men, 5 to 30 g/d; women, 5 to 15 g/d), and scoring within the top 40% in a measure of a healthy diet. The diet score was based on the Alternate Health Eating Index (higher intakes of vegetables, fruit, nuts, soy, and cereal fiber; high ratio of chicken plus fish to red meat and polyunsaturated to saturated fat; low intake of trans fat; and multivitamin use for at least 5 years). Adherence to the low-sodium Dietary Approaches to Stop Hypertension (DASH) diet and a 6-nutrient diet score were also assessed. There were 1559 strokes (853 ischemic, 278 hemorrhagic) among women and 994 strokes (600 ischemic, 161 hemorrhagic) among men during follow-up. Women with all 5 low-risk factors had a 79% reduction in the risk of all strokes (relative risk, RR = 0.21; 95% CI, 0.12 to 0.36) and an 81% reduction in the risk of ischemic stroke (RR = 0.19; 95% CI, 0.09 to 0.40) with a graded reduction related to level of adherence. Among men, there was a 69% reduction in all strokes (RR = 0.31; 95% CI, 0.19 to 0.53) and an 80% reduction in ischemic strokes (RR = 0.80; 95% CI, 0.10 to 0.42). Among the women, 47% (95% CI, 18 to 69) of all strokes and 54% (95% CI, 15 to 78%) of ischemic strokes were attributable to lack of adherence to a low-risk lifestyle; among the men, the corresponding risks were 35% (95% CI, 7% to 58%) and 52% (95% CI, 19% to 75%). The data

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provide strong evidence supporting the benefits of following healthy lifestyle behaviors.

Stroke prevention strategies are often not implemented as rigorously as they should be in routine clinical practice. This is particularly true of blood pressure-lowering, especially in the elderly.

Increasing blood pressure is strongly associated with stroke risk in patients with prior transient ischemic attack or stroke, and there is good evidence that blood pressure-lowering is beneficial. The PROGRESS trial evaluated the effects of perindopril with or without indapamide starting several weeks or months after transient ischemic attack or stroke and showed that blood pressure-lowering reduced the risk of subsequent stroke by about a third. With the exception of the small proportion of patients with bilateral severe carotid stenoses or occlusion, in whom aggressive blood pressure-lowering may be harmful, it is likely that blood pressure-lowering is beneficial in the long-term in the vast majority of patients with previous transient ischemic attack or stroke, irrespective of age.

Increasing blood pressure is also strongly associated with subsequent stroke risk in the primary prevention setting. The relationship between usual systolic and diastolic blood pressures and risk of stroke is ‘log-linear’ throughout the normal range, with no evidence of a threshold below which the risk becomes stable. The relationship between blood pressure and stroke, however, attenuates substantially with increasing age, possibly because stroke is associated with low blood pressure due to cardiac failure and other comorbid conditions in the elderly. Although isolated systolic hypertension, the most common form of hypertension in older individuals, is also strongly associated with increased risk of stroke, whether treatment of patients with hypertension who are 80 years of age or older lowers the risk of a first stroke has been uncertain.

The Hypertension in the Very Elderly trial (HYVET) randomized 3845 patients aged 80 years or older who had sustained systolic hypertension (systolic pressure 160 to 200 mm Hg; diastolic pressure <110 mm Hg) to receive either indapamide (sustained release, 1.5 mg daily) or matching placebo. The target systolic blood pressure was 150 mm Hg; the target diastolic blood pressure was 80 mm Hg. Perindopril (2 or 4 mg daily) or matching placebo was added if necessary to achieve the target blood pressure. The primary end point was fatal or nonfatal stroke. The active-treatment group (1933 patients) and the placebo group (1912 patients) were well-matched at baseline (mean age, 83.6 years; mean blood pressure while sitting, 173.0/90.8 mm Hg); 11.8% had a history of cardiovascular disease. Median follow-up was 1.8 years. At 2 years, the mean blood pressure while sitting was 15.061 mm Hg lower in the active-treatment group than in the placebo group.

The trial was stopped in 2007 after it was found that treatment reduced stroke and total mortality. In an intention-to-treat analysis, active treatment was associated with a 30% reduction in the rate of fatal or nonfatal stroke (95% CI, 1% to 51%; P=0.06), a 39% (95% CI, 1% to 62%; P=0.05) reduction in the rate of fatal stroke, a 21% (95% CI, 4% to 35%; P=0.02) reduction in death from any cause, and a 64% (95% CI, 42% to 78%; P<0.001) reduction in the rate of heart failure. Fewer serious adverse events occurred in the active-treatment group than in the placebo group (358 versus 448; P=0.001).

HYVET also evaluated the effect of blood pressure-lowering on the risk of dementia. Observational epidemiological studies show a positive association between hypertension and risk of incident dementia, but the effects of antihypertensive therapy on cognitive function in previous trials and meta-analyses have been inconsistent. HYVET subjects had no clinical diagnosis of dementia at baseline, and cognitive function was assessed at baseline and annually with the Mini-Mental State Examination (MMSE). Possible cases of incident dementia (a decline in the MMSE score to <24 points or a drop of 3 points in 1 year) were assessed with standard diagnostic criteria and expert review. 3336 HYVET participants had at least 1 follow-up assessment (mean 2.2 years; 1687 participants assigned to the treatment group and 1649 to the placebo group). There were 263 incident cases of dementia (38 per 1000 patient-years in the placebo group and 33 per 1000 patient-years in the treatment group; hazard ratio 0.86; 95% CI, 0.67 to 1.09). Although the difference was not significant, the pooled result favored treatment (hazard ratio 0.87; 95% CI, 0.76 to 1.00; P=0.045) when these data were combined in a meta-analysis with other placebo-controlled trials of antihypertensive treatment. Thus, antihypertensive treatment with indapamide (sustained release) with or without perindopril in persons 80 years of age or older reduces the risk of stroke and death. Blood pressure-lowering may also reduce the risk of dementia, but larger trials with longer follow-up are likely required.

Overall, the data that have become available over the last year reinforces the importance of adhering to healthy lifestyles, including avoidance of secondhand tobacco smoke, and extends data reflecting the benefits of treatment of hypertension to those over age 80 years.

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Disclosures

None.

References


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