Stroke remains the third leading cause of death in the US and other Western countries, and at least 1 population-based study found that the incidence of stroke was greater than that of acute coronary syndromes. Although there have been substantial falls in stroke incidence in some countries over the last 2 decades, a large US study found that the advances in stroke prevention during the 1990s were not associated with decreases in the rate of stroke hospitalizations or in case-fatality rates between 1993 and 1999. Moreover, based solely on demographic changes in the population of selected countries within the European Union, the World Health Organization predicts a 27% increase in stroke events between the years 2000 and 2025. The proportion of deaths attributed to stroke is even higher in Asian countries. Although much of stroke risk may be related to socioeconomic factors, more effective prevention strategies are critical. Several studies have contributed to the body of knowledge related to primary stroke prevention over the last year.

Numerous studies support an association between elevated homocysteine levels and atherosclerotic disease. The B vitamins (folic acid, B12, and B6) reduce homocysteine serum levels raising the hope that treatment would be associated with reduced risk. That hope was diminished with publication of results of the Vitamin Intervention for Stroke Prevention (VISP) trial in 2004. Although a secondary rather than a primary stroke prevention trial, VISP had compared high- and low-dose B-vitamin supplementation and found no treatment effect on the risk of recurrent stroke (risk ratio [RR] 1.0; 95% CI, 0.8 to 1.3), or in the combined risk of any stroke, coronary heart event, or death (RR, 1.0; 95% CI, 0.8 to 1.1). The difference in homocysteine levels between treatment groups, however, was small (2 μmol/L). The results of 2 additional randomized trials of homocysteine-lowering are now available. The Norwegian Vitamin (NORVIT) trial evaluated the efficacy of B-vitamin supplementation on the prevention of recurrent myocardial infarction, stroke and sudden death (primary end point) in patients who had an acute myocardial infarction. Despite a 27% reduction in homocysteine levels among patients given folic acid plus vitamin B12, there was no reduction in these combined risks (RR, 1.08; 95% CI, 0.93 to 1.25) and no reduction in stroke (10.2/1000 observation-years with treatment versus 9.7 with placebo; RR, 1.02; 95% CI, 0.68 to 1.51). Based on the primary end point, there was a suggestion of a harmful effect in those given the combination of folic acid, vitamin B12, and vitamin B6 (RR, 1.22; 95% CI, 1.00 to 1.50), and no effect on stroke (RR, 0.83; 95% CI, 0.47 to 1.47). The study, however, was not powered to detect an effect on stroke outcomes (only 98 of 3749 subjects had strokes). The Heart Outcomes Prevention Evaluation (HOPE) 2 trial randomly assigned 5522 patients with vascular disorders or diabetes to a combination of folic acid, vitamin B12, and vitamin B6 or placebo. There was no effect of treatment on the combined risk of myocardial infarction, stroke or cardiovascular death (RR, 0.95; 95% CI, 0.84 to 1.07). Significantly fewer patients assigned to active treatment had a stroke (4.0% versus 5.5%; RR, 0.75; 95% CI, 0.59 to 0.97), despite there being a small number of stroke events (n = 258). As pointed out by the study’s authors, this finding is not adjusted for multiple comparisons and may have occurred as a result of chance. Another large secondary prevention trial is ongoing, and additional studies will be required to determine whether treatment of elevated homocysteine is independently associated with a reduction of stroke in high-risk primary prevention populations.

Case-control studies have generally found an association between the presence of a patent foramen ovale (PFO) and cryptogenic stroke. Two new reports, however, suggest that PFO may not be a risk factor for stroke in the general population. In 1 study, transesophageal echocardiography (TEE) was used to identify PFO among 595 randomly sampled community subjects over age 45. Over 51 years, 41 subjects had a stroke or transient ischemic attack (TIA). After adjustment for age and comorbidity, PFO was not an independent risk factor for these events (hazard ratio, 1.46; 95% CI, 0.74 to 2.88). Only 1.9% had an atrial septal aneurysm, and larger studies will be required to determine whether its presence is independently associated with stroke risk. The second study used a case-control design. Using the presence of a large PFO in randomly selected controls as a reference, after adjustment for comorbidity, the odds of having a large PFO among those with a cryptogenic stroke was 1.10 (95% CI, 0.63 to 1.90). It was suggested that the importance of PFO in cryptogenic stroke reported in previous studies might have been overestimated because of a combination of referral bias and underascertainment in controls. The rates of recurrent cryptogenic stroke are similar in those...
with and without a PFO, and a preliminary analysis of a prospective study available in abstract form indicates that recurrent stroke is not associated with massive right-to-left shunt. Randomized trials are in progress to determine whether endovascular PFO closure reduces the risk of recurrent stroke as compared with medical therapy.

Optimal application of known preventive measures remains elusive in both primary and secondary prevention settings, and acute stroke treatments continue to be underused. For acute stroke, multilevel paramedic, hospital, and community education can improve paramedic diagnostic accuracy and reduce the time to hospital arrival after symptom onset. Stroke-center designation and selective triage in an urban community improved quality of care, patient access to acute stroke units, and timely evaluations for thrombolytic therapy. Although requiring further study, demonstration projects show that telestroke is feasible and offers the possibility of extending stroke-related expertise to remote and rural hospitals. The availability of multispecialty stroke services within hospitals is associated with reduced mortality rates in both academic and community settings but also is underused. An observational study found that adherence to best practices in hospitalized patients improved with the use of standardized orders. Quality improvement systems such as the American Heart Association’s Get with the Guidelines program should also lead to improved compliance with secondary prevention recommendations and awaits further evaluation.

Optimal service provision for patients with a TIA has yet to be determined, with some healthcare systems providing emergency inpatient care for nearly all patients and others providing rapid-access outpatient clinics. There is, however, good evidence that whichever system is used, investigation and treatment must be initiated quickly. Weekly TIA clinics, for example, which are the norm in many countries, are inadequate. Among 210 consecutive patients referred with suspected TIA to a weekly TIA clinic in the UK, the median (interquartile range) time from referral to appointment was 9 (4 to 16) days, during which time 11 (5.2%) patients had a stroke, 9 of which were disabling. Similarly, there is evidence of unacceptable delays to carotid imaging and endarterectomy after TIA and stroke in many countries. In a study of consecutive patients undergoing carotid imaging for ischemic retinal or cerebral TIA or stroke in the UK, 49 of the 85 patients found to have 50% to 99% symptomatic stenosis had endarterectomy, but in only 3 (6%) patients was surgery performed within 2 weeks of their presenting event, and only 21 (43%) had surgery within 12 weeks.

Public education about the symptoms of TIA and stroke and the need to seek emergency treatment is also required. A recent nationwide telephone survey of adults in the US revealed widespread ignorance of the symptoms of TIA and a lack of understanding of the seriousness of the condition. Using randomly generated telephone numbers, 11 400 households were contacted and 10 112 interviews about TIA were conducted. Only 8.6% of people could correctly identify a symptom of a TIA. Increasing age was associated with better knowledge of the definition and symptoms as was female sex, white ethnicity, higher income and higher educational level. Of the 2.3% of people who reported having a physician diagnosed TIA, 36% did not recall seeing a physician in the first 24 hours. An additional 3.2% recalled symptoms typical of TIA that were not brought to medical attention. The situation is similar in the UK. Of 377 consecutive patients attending specialist TIA and stroke clinics, 40% with minor stroke and 50% with TIA delayed seeking medical attention for over 24 hours. Only 41% of patients with minor stroke and 37% of patients with TIA correctly identified the cause of their symptoms, and only 45% of patients thought that the event was a medical emergency.

Part of the problem with public education about TIA and minor stroke has been the difficulty in conveying a succinct message about how to recognize an event because of the wide variety and the sometimes nonspecific nature of the symptoms. Data now available on the relationship between the nature of the clinical event and the early risk of stroke should allow public education to be more effectively focused. For example, although in 1 study focal motor weakness or speech disturbance lasting ≥60 minutes occurred in only 30% of referrals for suspected TIA, 90% of the strokes that occurred within 7 days of the TIA occurred in this group. Advances in preventive therapies combined with more effective provision of preventive services should lead to reductions in the risk of a first stroke.


