New Evidence for Stroke Prevention
Clinical Applications

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CLINICAL CONTEXT
Patient 1
A 76-year-old woman was treated in the emergency department for a complaint of palpitations. On admission, she was observed to be in atrial fibrillation and had a ventricular heart rate of approximately 120/min. She was given diltiazem by the emergency physician, who then referred her to a resident on our team for assessment. When the resident assessed her condition, the patient was still experiencing atrial fibrillation, but her heart rate had slowed to 80/min. Her blood pressure was 160/100 mm Hg, and the remainder of the examination revealed no other problems. During history taking, the patient stated that she had not been examined by a physician in several years but had been told that she had an irregular heartbeat; an electrocardiogram (ECG) from 2 years before (when she presented to an emergency department with a fractured wrist) showed atrial fibrillation.

When we reviewed the patient’s condition with our team, the resident raised the question of long-term antithrombotic therapy. This issue led to some debate among our team, with the resident advocating the initiation of warfarin and one of the interns expressing concern about the risk of bleeding, given this woman’s age, blood pressure, and risk of falling. The intern advocated the use of aspirin. One of the medical students expressed concerns about bleeding with either of these agents, reminded us of the dictum primum non nocere, and championed avoiding any antithrombotic therapy in this woman.

Patient 2
We assessed a 62-year-old man in our resident’s primary care clinic for a follow-up visit regarding hypertension. His only medication was lisinopril at 20 mg/d. His blood pressure during the visit was 160/95 mm Hg. He was known to have left ventricular hypertrophy on ECG, and his fasting lipid profile showed a low-density lipoprotein (LDL) level of 151 mg/dL (3.90 mmol/L) and a high-density lipoprotein level of 39 mg/dL (1.01 mmol/L). During our discussion with the patient, we learned that his father recently died after a lengthy admission to a long-term care facility following a stroke. Our patient expressed concern that he would experience the same fate as his father, and we used this opportunity to address relevant issues regarding the primary prevention of stroke.

HOW CAN EVIDENCE BE APPLIED IN PRACTICE?
The evidence about stroke prevention cannot be broadly applied to all patients. A recent observational study1 highlighted the importance of this issue in patients who have nonrheumatic atrial fibrillation (AF) and are considering anticoagulation treatment.

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Stroke is a leading cause of morbidity and mortality in most developed nations. There is a significant body of evidence supporting strategies that target primary and secondary stroke prevention. This evidence cannot be broadly applied to all patients, and each patient’s situation and values must be considered with regard to shared evidence-based decision making. Several models can be used to apply evidence to individual patients, including formal clinical decision analysis, decision aids, or simpler tools such as the likelihood of being helped vs harmed. Various programmatic models of providing patient care in stroke prevention may also be useful; these include specialized clinics or disease-management programs, anticoagulation management services, and self-testing and management of anticoagulation by patients.

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See also p 1388.
There are several models available for applying evidence in practice.2 Formal clinical decision analysis could be used to guide this process, but performing one for each patient would be time consuming and beyond the skills of most physicians. Occasionally, an existing decision analysis could be applied, but to be able to use it, the patient must have values approximating those in the analysis or the analysis must provide information about the impact of variation in patient values on the results of the decision analysis. For example, when discussing the treatment of patient 1, the house staff expressed concern about the risk of falls in an elderly person who is considering anticoagulation (one of the most common reasons cited by physicians for not prescribing warfarin in elderly people).3 However, a recent decision analysis found that, regardless of the patients’ age or baseline risk of stroke, the risk of falling was not an important factor in determining their optimal antithrombotic therapy.4 Considering the risk of subdural hematoma from a fall (and the increased risk of bleeding for patients receiving warfarin), the authors of the decision analysis concluded that an elderly person would need to fall 295 times in 1 year for the risks of warfarin to outweigh the benefits.

Decision aids could also be used to present information about the target disorder, management options, and outcome events. A recent systematic review of randomized trials on patient decision aids revealed that they reduce decisional conflict and stimulate patients to be more involved with decision making (level 1 evidence).3 However, decision aids have little effect on satisfaction and a variable effect on decisions. We identified a recent randomized trial that assessed the use of an audiobooklet decision aid for patients who have nonrheumatic AF (similar to patient 1) and are considering antithrombotic therapy (level 1 evidence).6 For these patients, the use of the decision aid improved their understanding of the risks and benefits associated with the management options and helped them choose options. Studies are under way to test this decision aid in other settings. Several Web sites provide information on other decision aids (eg, http://www.ohri.ca/programs/clinical_epidemiology/ohdecision_aids.asp).

One of the problems faced by busy physicians is how to incorporate a patient’s unique situation and values concisely and comprehensively. One proposed method is to use the likelihood of being helped or harmed by an intervention. This concept is based on the number needed to treat for target events produced by the intervention (to express the likelihood of being helped), the number needed to harm for the adverse effects of therapy (to express the likelihood of being harmed), and their ratio.2 This result, when modified for the patient’s baseline risk and adjusted by an individual patient-centered conviction about the relative severities of these 2 events, provides a rapidly calculated measure of the likelihood of being helped or harmed by a particular therapy.

**WHAT MODELS OF PROVIDING PATIENT CARE ARE EFFECTIVE IN STROKE PREVENTION?**

There is a growing body of literature describing different models of care and their effectiveness, but the efficacy of primary or secondary stroke prevention clinics has not been examined rigorously. We can extrapolate from a systematic review of 12 trials (9803 patients) evaluating the impact of specialized clinics or disease-management programs run by specialist physicians in patients with established coronary artery disease.8 Compared with usual care by primary care physicians, these disease-management programs had positive impacts on processes of care (improving the prescription of efficacious medications by 19% to 114%) and all-cause hospitalizations (odds ratio [OR], 0.84; 95% confidence interval [CI], 0.76-0.94); however, too few events occurred for a definitive effect on mortality (OR, 0.91; 95% CI, 0.79-1.04) to be apparent.8

Although rigorous evaluations of comprehensive stroke prevention clinics are pending, there is growing evidence that better clinical outcomes may be achieved when warfarin therapy is managed by an anticoagulation management service (AMS).9 The core factors essential to any form of a coordinated AMS include dedicated and qualified health care providers; reliable patient tracking and scheduling; accessible, accurate, and frequent international normalized ratio testing; patient-specific decision support; and ongoing patient education.8,11 Usual care in North America consists of the delivery of anticoagulation therapy by individual physicians without a systematic approach to quality assurance, and control is often suboptimal.9,10 For example, usual care is associated with international normalized ratios outside of the therapeutic range about half the time (level 2 evidence)9,12 and rates of major bleeding from 2- to 5-fold greater than those reported from randomized trials of anticoagulation therapy (level 2 evidence)9,11.
to have major bleeding episodes. Some studies have suggested that an AMS may actually be cost saving.11 Until the results of large randomized trials of AMS (eg, Managing Anticoagulation Services Trial12) are available, the true benefits and costs of AMS remain unknown. Despite the absence of level 1 evidence, some authorities have concluded that the failure to use an AMS might increase a provider’s risk of medicolegal liability.14

Self-testing by patients and self-management of anticoagulation have also been studied. This topic was recently reviewed in detail,9 and it was concluded that although a few studies indicate that self-testing or self-management may be superior to usual care, there is little evidence comparing these methods to a reference standard such as AMS. In one small (n=50) randomized crossover study, Cromheecke and colleagues15 demonstrated that patient self-management was at least as effective in achieving and maintaining target international normalized ratios as an AMS.

**HOW DOES THE EVIDENCE INFLUENCE TREATMENT OF PATIENTS 1 AND 2?**

**Patient 1**
From Table 6 in the Scientific Review, we can determine that patient 1’s risk of stroke at 2 years is at least 20%. We discussed with her that warfarin can decrease her risk of stroke by two thirds, while aspirin can decrease the risk by one quarter. Indeed, we would need to treat only 8 patients like her with warfarin to prevent 1 bad outcome (stroke). However, warfarin therapy is not without complications, and it can increase her risk of bleeding. She was told that we would need to treat more than 150 patients like her with warfarin to cause 1 significant bleed and that warfarin was approximately 19 times more likely to help than harm her. Moreover, from the decision analysis described previously, we informed her that she would need to fall 295 times a year for the risk of warfarin to outweigh the benefits. We explored the patient’s circumstances and determined what values she placed on major bleeding and on a stroke. She did not mind having her international normalized ratio checked or avoiding contact sports and felt that it was more important to avoid a stroke than a bleed. Thus patient 1 was more likely to be helped than harmed by warfarin, and therapy was initiated. She was subsequently referred to our hospital’s AMS for ongoing treatment.

**Patient 2**
We discussed the patient’s risk factors for stroke, including those that are modifiable (partially treated hypertension, left ventricular hypertrophy, and elevated LDL levels) (see Table 1 in the Scientific Review) and those that are not modifiable (age >55 years, male sex, and family history of stroke). The attending physician suggested it would be useful to apply the Framingham stroke equations10 to stratify patient 2’s risk of stroke, but he could not remember the scoring system. Fortunately the resident had access to the algorithm on her personal digital assistant, and the 10-year risk of a stroke was estimated to be 20%.

With this elucidation of stroke risk, patient 2 helped us develop a comprehensive plan to reduce his risk of stroke. A low-dose thiazide diuretic was initiated with the goal of achieving a blood pressure lower than 140/90 mm Hg. Although the patient was eager to start aspirin therapy, this decision was deferred until his blood pressure was better controlled. He was referred to a dietitian for recommendations to promote cholesterol lowering and weight loss. The patient agreed that if his LDL cholesterol level was not lower than 130 mg/dL (3.36 mmol/L) within 3 months, pharmacotherapy would need to be considered. He was assured that the diet, lifestyle, and medication changes that he was undertaking would reduce his risk of stroke as well as his chances of myocardial infarction or death. A follow-up blood pressure measurement was scheduled for 6 weeks, and a follow-up visit to readdress his overall vascular health was arranged for 12 weeks.

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