Stroke Prevention
An Opportunity for Efficient Utilization of Health Care Resources During the Coming Decade

Philip B. Gorelick, MD, MPH, FACP

Background Stroke is unique among neurological diseases, since it has a high prevalence and burden of illness, high economic cost, and is preventable. Epidemiological approaches to stroke prevention include the “high-risk” and “mass” approaches. In this review we discuss these preventive strategies, target host and discretionary risk factors that are amenable to these measures, and discuss potential cost savings.

Summary of Review Projected numbers of strokes prevented for specific stroke risk factors were estimated by using the population-attributable risk estimation for hypertension, cigarette smoking, atrial fibrillation, and heavy alcohol consumption. The projected numbers of strokes that could be prevented were substantial and highest for hypertension and cigarette smoking. Projected yearly cost of stroke associated with these two treatable factors was also substantial.

Conclusions The prevention of stroke can be accomplished by the high-risk or mass approach or a combination of these approaches. The high-risk approach prevents strokes but is also expensive. The mass approach may be more cost-effective, which could lead to substantial savings, but this needs to be investigated. (Stroke. 1994;25:220-224.)

Key Words • costs and cost analysis • prevention, primary • risk factors

Stroke is unique among neurological diseases because it is preventable. Stroke is ideally suited for prevention, as it has a high prevalence and burden of illness, high economic cost, and safe and effective prevention measures that have been validated by clinical trial. It is estimated that $25 billion is spent for stroke each year in the United States. This is not surprising, given the estimated 500,000 new cases of stroke, the 150,000 deaths attributable to stroke, and the approximately 3 million stroke survivors each year. As our knowledge of stroke prevention and treatment surpasses that of other neurological disease,2 a concerted international effort to prevent stroke could lead to substantial economic savings and reduction in human suffering. In this article we will review preventive approaches to reduce stroke, target host and discretionary risk factors that are amenable to these measures, and discuss potential cost savings.

Epidemiological Approaches to Stroke Prevention

Chronic disease such as stroke has a long latent period before clinical symptoms become manifest. During this latent period, stroke risk factors (determinants) effect pathophysiological changes that may lead to clinically manifest disease. The presence of multiple risk factors heightens the likelihood of stroke.4,5

The natural history of chronic disease may be schematically represented by four stages of disease with corresponding levels of prevention and intervention (Table 1).6 As noted in Table 1, the first two stages, “susceptibility” and “presymptomatic,” are amenable to early detection and prevention strategies. These two stages may be thought of as the “upstream” stages, as primary or secondary prevention is possible. Once the risk factors are targeted and identified through health promotion and screening, specific intervention to prevent or retard pathogenetic tissue damage that could lead to clinical disease and disability can be implemented. The last two stages, “clinical disease” and “disability or recovery,” are “downstream,” or at the point where the ravages of the risk factors are quite evident. In these stages, the greater part of our window of opportunity for prevention has lapsed as we attempt to treat and limit acute disease and disability. Clearly, our public health goal is prioritized to intervene in the early or upstream stages.

Public health strategies to avoid stroke by modification of risk factors amenable to medicaiton, diet, or other interventions may be grouped into two major categories:7,8 (1) the “mass” approach and (2) the “high-risk” approach. The mass approach uses lifestyle modification to achieve modest reductions in the level of the risk factor in every individual in the population and is advanced through health education, legislation, and economic measures to discourage exposure to risk factors. Mass-market economy has taught us that there is greater profit from sales at reduced rates to the masses who possess more limited financial resources than from sales to the relatively few wealthy who are able to pay higher rates.7 Similarly, the prevention of disease among those substantial numbers of persons with mild or moderate levels of a risk factor (eg, hypertension), who are not at the highest relative risk for disease, yields the greatest absolute savings or benefit from the standpoint of morbidity and mortality. Thus, the distinction be-
TABLE 1. Scheme for the Natural History of Chronic Disease and Levels of Prevention

<table>
<thead>
<tr>
<th>Stage of disease*</th>
<th>1: Susceptibility</th>
<th>2: Presymptomatic</th>
<th>3: Clinical</th>
<th>4: Disability or recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevention level</td>
<td>Health promotion</td>
<td>Early detection,</td>
<td>Acute treatment</td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>Specific</td>
<td>diagnosis, and</td>
<td>Rehabilitation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>intervention</td>
<td>preventive</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Stages 1 and 2 may be thought of as “upstream” and stages 3 and 4 as “downstream” (see text).

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between relative and absolute benefit must be kept in mind when considering the mass approach.7 Furthermore, the “prevention paradox” (ie, a measure that brings large benefits to the community may offer little to the individual) must also be considered in this context.

The high-risk approach, on the other hand, identifies individuals in the population with high levels of a risk factor, and medication is usually administered to achieve substantial reductions in that risk factor.8 This approach is typically used by practicing physicians in outpatient offices and clinics. When applied to a community or other large population, the high-risk approach can be a massive and expensive case-finding procedure that still fails to prevent a high percentage of the target disease (ie, among those in the community with lower levels of the risk factor).

Ideally, risk factor modification is most effective when the risk factor to be targeted is common in the population, there is a strong association between the risk factor and disease, and there is a favorable effect of treatment of the risk factor. Furthermore, valid, safe, and cost-effective screening procedures and treatment are necessary.9

Host and Discretionary Risk Factors to Target for Stroke Prevention

There are two well-established risk factors, hypertension and cigarette smoking, and two less well-established risk factors, alcohol consumption and blood lipids, that are amenable to the mass approach. Hypertension, whether systolic, diastolic, or combined, is a well-documented risk factor for stroke, as seen in observational and experimental epidemiological study.4,5,10-14 Cigarette smoking has emerged more recently as a risk factor for ischemic stroke and some forms of intracranial hemorrhage.15-18 Heavy alcohol consumption may elevate the risk of ischemic and hemorrhagic stroke.19,20 Among white populations, a J-shaped epidemiological curve has been proposed to explain the relation between the relative risk of ischemic stroke and customary alcohol consumption, whereas a positive direct linear association has been proposed for the relative risk of hemorrhagic stroke with customary alcohol consumption.20 There is mounting epidemiological evidence to link hypercholesterolemia or elevations in low-density lipoproteins to ischemic stroke, although blood lipids are not considered a well-established risk factor for stroke.21-25 Furthermore, these same four factors play an important role in coronary heart disease risk.26

There is substantial epidemiological evidence to advocate treatment of hypertension to reduce stroke.4,5,10-14 Although controversial, it has been estimated that up to 70% of strokes could be eliminated by treatment of hypertension.8 Furthermore, observational epidemiological study has shown that the stroke risk dramatically reverses after abstinence from cigarette smoking for 2 to 5 years4 and after discontinuation of heavy alcohol consumption.19 Treatment of blood lipids reaps substantial benefit for coronary heart disease, but there is controversy about the benefit of treatment of hypercholesterolemia and low-density lipoprotein cholesterol for stroke. However, it has been estimated that hypercholesterolemia could account for up to 20% of strokes in Caucasians with cholesterol levels >5.7 mmol/L.9

There are several other risk factors to consider for stroke prevention. Atrial fibrillation may be responsible for 75 000 strokes in the United States, and dramatic risk reductions are noted when nonvalvular atrial fibrillation is treated with antithrombotic therapy.27-30 Furthermore, clinical trials have shown that carotid endarterectomy is efficacious in the treatment of high-grade (70% to 99%) carotid stenosis when there is mild stroke or transient ischemic attack.31,32 However, while the absolute risk reduction for ipsilateral stroke is 17% in the carotid endarterectomy treatment group compared with medically treated patients,31 the absolute benefit of carotid endarterectomy in stroke prevention is substantially lower, as there are relatively few individuals who qualify for this operation based on accepted criteria. Other risk factors such as coronary heart disease and cardiac failure contribute to the attributable risk of stroke,33 but it is uncertain at the present time to what extent the treatment of these factors affects stroke prevention.

Illustrative Examples of Stroke Reduction Through Risk Factor Modification and Potential Cost Savings

Table 2 summarizes modifiable risk factors, population-attributable risk, and theoretical numbers of strokes that could be prevented by successful treatment of these risk factors. These calculations are estimates and are based on the following assumptions that may vary by population. (1) The overall population-attributable risks for hypertension and atrial fibrillation were derived by averaging relative risk and prevalence data, respectively, over age-specific categories (50 to 59, 60 to 69, 70 to 79, and 80 to 89 years) from the Framingham Study.33 (2) The population-attributable risk of smoking was calculated by averaging the given relative risks of smoking for men and women from the Framingham Study18 and using 27% as the estimate of the prevalence of cigarette smoking in the population (data from Morbidity and Mortality Weekly Report reprinted in JAMA. 1987;258:1880). (3) As the population-attribut-
able risk of heavy alcohol consumption for stroke is unknown, it was estimated by taking the ratio of "problem" drinkers in the United States (18 million persons)\(^\dagger\) to total persons in the United States (250 million) and using an estimate of relative risk of stroke of 1.68 for heavy alcohol consumption (after Gorelick et al\(^{19}\)). The population-attributable risk is an estimate of the percentage of excess stroke in a population that is attributable to a specific risk factor.

The reader should keep in mind that the population-attributable risk was calculated from the following formula: \(A/(1+A)\), where \(A=\)prevalence multiplied by (relative risk - 1). The projected number of strokes prevented was calculated by multiplying the estimated 500 000 new stroke cases per year in the United States by the population-attributable risk.

Table 2 is substantial. This is especially true for hypertension and cigarette smoking. Let us now focus on potential cost savings from prevention of these two well-established and modifiable risk factors.

As the ideal is rarely achieved, Table 3 reviews (1) cost savings at different levels of prevention success based on a total of $25 billion spent for stroke per year and (2) cost savings at different levels of prevention success based on a theoretical 26-day hospital stay for acute stroke that includes acute diagnosis, treatment, and rehabilitation at a major private teaching hospital in Chicago in fiscal year 1991 for ICD-9 diagnosis code 436. The sum of $25 billion spent for stroke each year is an estimate of direct and indirect costs, the exactness of which could vary and thus influence the calculated savings.

The estimates in Table 3 suggest that substantial economic savings could occur by successful modification of stroke risk factors. Even if the effort were only 10% efficient, the estimate of total yearly economic savings

### Table 2. Modifiable Risk Factors, Population-Attributable Risk, and Projected Numbers of Strokes Prevented in the United States\(^{*}\)

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Estimated Percentage Exposed</th>
<th>Estimated Relative Risk</th>
<th>Estimated Population-Attributable Risk, %</th>
<th>Projected No. of Strokes Prevented</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension(^\dagger)</td>
<td>56.2</td>
<td>2.73</td>
<td>49.3</td>
<td>246 500</td>
</tr>
<tr>
<td>Cigarette smoking(^\dagger)</td>
<td>27.0</td>
<td>1.52</td>
<td>12.3</td>
<td>61 500</td>
</tr>
<tr>
<td>Atrial fibrillation(^\dagger)</td>
<td>3.98</td>
<td>3.60</td>
<td>9.4</td>
<td>47 000</td>
</tr>
<tr>
<td>Heavy alcohol consumption(^\dagger)</td>
<td>7.2</td>
<td>1.68</td>
<td>4.7</td>
<td>23 500</td>
</tr>
</tbody>
</table>

\(^{*}\)Population-attributable risk was calculated from the following formula: \(A/(1+A)\), where \(A=\)prevalence multiplied by (relative risk - 1). The projected number of strokes prevented was calculated by multiplying the estimated 500 000 new stroke cases per year in the United States by the population-attributable risk.

\(^\dagger\)Relative risk and estimated percentage exposed were calculated by averaging the relative risks and prevalence rates for a risk factor across the four given age strata, respectively, according to the Framingham data.\(^{33}\)

\(^\ddagger\)Relative risk was calculated by averaging the relative risks for men and women according to the Framingham data.\(^{18}\) and the percentage exposed was estimated to be 27% according to national data sources (JAMA. 1987;258:1880).

\(^\S\)Relative risk for heavy drinkers was estimated to be 1.68 after Gorelick et al.\(^{19}\) and the percentage exposed was estimated by taking the ratio of "problem drinkers" to the total population in the United States (18 million to 250 million).

### Table 3. Projected Cost Savings at Different Levels of Stroke Prevention Success for Hypertension and Cigarette Smoking

<table>
<thead>
<tr>
<th></th>
<th>Level of Stroke Prevention Success</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>100%</td>
</tr>
<tr>
<td><strong>Total yearly economic savings</strong> (^*)</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>12.33</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>3.08</td>
</tr>
<tr>
<td><strong>Economic savings for acute stay</strong> (^\dagger)</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>11.33</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>2.83</td>
</tr>
</tbody>
</table>

\(^*\)Calculations are based on $25 billion spent per year on stroke and the prevention of a possible 246 500 strokes among hypertensives and 61 500 strokes among US cigarette smokers, respectively.

\(^\dagger\)Diagnosis, treatment, and rehabilitation of 26 days at a major teaching hospital in Chicago in 1991 for ICD-9 diagnosis code 436. Calculations are based on a total of $46 000 spent per patient.
could reach $1.23 billion for hypertension and $310 million for cigarette smoking. If medication is necessary to control selected risk factors (eg, hypertension, atrial fibrillation), these costs are then subtracted from the projected savings, as are costs that are incurred due to medication side effects or complications, to determine the overall savings. A recent assessment of the cost-effectiveness of primary stroke prevention in atrial fibrillation in Sweden showed that after the direct and indirect costs of “stroke saved,” numbers of strokes prevented, and cost of preventive treatment were calculated, primary stroke prevention with antithrombotics resulted in a net savings.35,36 Table 3 also suggests that the economic savings for acute hospitalization and rehabilitation could be substantial as well.

An alternate approach to medication would be to reduce the population’s level of stroke risk factors (eg, hypertension, cigarette smoking, heavy alcohol consumption, and hypercholesterolemia) by effecting lifestyle changes through behavioral modification using the mass approach of economic and legislative measures and education. The public needs to be educated about healthy lifestyles, risk factors for stroke and other major diseases, treatment of risk factors, and recognition of early warning signs of stroke and other major causes of mortality. Mass education to teach healthy lifestyles through behavioral modification, targeted to groups at risk for stroke and to the youth in our school systems, could be the most cost-effective of all approaches. Furthermore, even if risk-factor control were to delay onset of stroke by only 5 years in a high proportion of persons rather than eradicate stroke in those persons, for example, substantial economic and human savings could still be realized by postponing stroke onset.

**Conclusion**

Stroke is a preventable disease that has a high economic cost. As shown in this analysis, there is potential for substantial human and economic savings. The prevention of stroke can be accomplished by a high-risk or mass approach. The high-risk approach is effective in saving strokes but is also expensive and may not save money, especially in lower-risk groups.37 The mass approach, on the other hand, may be more cost-effective, although this needs to be clarified.

How our health care resources will be allocated and used in the coming decades has become a focus of major public and presidential attention. Prudent use of these resources is paramount. As concerned citizens we should support economic and legislative measures to educate the public about healthy lifestyles, at-risk behaviors, risk factors and warning signs of disease, and the importance of standard treatments that reduce the risk of disease. Now is the time to plan healthy lifestyles for example, substantial economic and human savings could still be realized by postponing stroke onset.

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