After heart disease, stroke is the second leading cause of death worldwide in persons ≥15 years of age.1 Stroke was responsible for an estimated 5.7 million deaths in 2005, with ≈87% of the deaths occurring in low- and middle-income countries. It is the fourth leading cause of disease burden as determined by disability-adjusted life-years. In the United States, stroke caused an estimated 1 in 16 deaths in 2004; ≈780,000 new or recurrent strokes occurred; and 15% to 30% of stroke survivors were permanently disabled.2 In the United States in 2008, the direct and indirect cost of stroke is estimated to be $65.5 billion. Globally, stroke death is anticipated to rise to 6.5 million in 2015 and 7.8 million in 2030.1 Although stroke poses a major public health challenge, it is preventable.3 Observational epidemiological studies and clinical trials have laid the groundwork for well-developed evidence-based stroke prevention guidelines.

Primary Prevention of Stroke by Healthy Lifestyle: Study Design and Results

In this issue of Circulation, Chiuve et al6 report on the impact of a combination of healthy lifestyle factors on the risk of stroke and estimate the burden of stroke attributed to unhealthy lifestyle choices. Information on lifestyle habits and medical history was obtained primarily from white subjects enrolled in the Nurses’ Health Study (NHS) and Health Professionals Follow-up Study (HPFS). These studies included 71,243 women and 43,685 men free of cardiovascular disease and cancer at baseline. The following healthy lifestyle factors were the main focus of the analysis: not smoking, diet, exercise, optimal body weight as defined by body mass index, and alcohol consumption. Standard epidemiological questionnaires were used to ascertain risk. Dietary information was obtained primarily from an expanded food-frequency questionnaire and a summary diet score according to the Alternate Healthy Eating Index. “Low risk” for lifestyle variables of interest is defined in Table 1. Strokes were categorized according to National Survey of Stroke criteria and were classified as ischemic, hemorrhagic, or unknown type.

Overall, there were 1,559 cases of stroke in women, of which 853 were ischemic, 278 were hemorrhagic, and 428 were of unknown type, in NHS and 994 cases of stroke in men, of which 600 were ischemic, 161 were hemorrhagic, and 233 were of unknown type, in HPFS.6 Twenty-five percent and 23% of total strokes requiring hospitalization but for which medical records were not available were designated as probable in NHS and HPFS, respectively. For both women and men who had all 5 low-risk factors, there was a dramatic reduction in total and ischemic stroke risk (Table 2). The associations between low-risk lifestyle factors and hemorrhagic stroke followed a pattern similar to that of ischemic stroke but were not as strong because the number of incident hemorrhagic strokes was low and the population-attributable risk percent estimates were unstable and had relatively wide confidence limits. Finally, for both women and men, total and ischemic strokes were significantly associated with adherence to a low-risk lifestyle (Table 2). The authors estimated that more than half of the ischemic strokes in either group could have been prevented if all had been in the low-risk healthy lifestyle group.

Commentary and Interpretation of Study Results

Interest in health, healthy living, and healthy environment has been fueled over time by rising prosperity and other factors.7 A major aim of health promotion and prevention is to maximize health (“compress” morbidity) during life rather than necessarily preventing the inevitable.8 Many now have come to expect successful prevention of stroke, coronary heart disease, and other cardiovascular diseases if proper lifestyle habits are followed and modifiable cardiovascular risk factors are controlled. Furthermore, we are reminded of

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the importance of lifestyle factors such as smoking and alcohol use that may explain inequalities in mortality in some regions of the world.

Lifestyle management may be an effective way to reduce or delay stroke and cardiovascular disease risk. A recently published study, for example, the Nurse-Coordinated Multidisciplinary, Family-Based Cardiovascular Disease Prevention Programme (EuroAction), has shown that multidisciplinary programs are a means to achieve potential for cardiovascular prevention in coronary heart disease and other high-risk patients. This may be accomplished through lifestyle management, management of blood pressure, maintenance of lipids and blood glucose at target levels, and prescription of cardioprotective drugs. In addition, group-management of blood pressure, management of blood pressure, maintenance of lipids and blood glucose at target levels, and prescription of cardioprotective drugs. Furthermore, when population-attributable risk percent was calculated using alternate definitions of low risk (eg, most recent rather than baseline body mass index, 0.1 g/d alcohol as the lower limit of low risk, Dietary Approaches to Stop Hypertension dietary scores, or 6-nutrient diet scores), results were consistent or comparable. Overall, the findings of benefit for low-risk lifestyle in this study were similar to those of other studies.

Healthy aging may be predicated at least in part on a low-risk cardiovascular disease profile. In the Honolulu Asia Aging Study (HAAS), exceptional survival, defined as survival to a specified age without incidence of 6 major chronic diseases and without physical and cognitive impairment, was associated with avoidance of overweight, hyperglycemia, hypertension, smoking, excessive alcohol consumption, and other factors in 85-year-old subjects. How common, however, is a low-risk profile in the community? In the present study, among the NHS subjects (women), 2% were at low risk for all 5 factors, and 4% were at low risk for none of the factors. In the HPFS (men), 2% were at low risk for all 5 factors, and 2% were at low risk for none of the factors.

A key message of the study by Chiuve et al is that those with all 5 low-risk lifestyle factors had a substantial reduction (80% for women and 70% to 80% for men) of total or ischemic stroke compared with those who had none of the factors. In addition, as the number of low-risk factors increased from 3 (not smoking, top 40% of Alternate Healthy Eating Index diet score, exercise ≥30 min/d) to 4 (addition of body mass index <25 kg/m²) to 5 (addition of alcohol 5 to 15 g/d), there was a stepwise increase in population-attributable risk percent from 34% to 41% to 54% in women and from 16% to 42% to 52% in men, respectively, for ischemic stroke. Similarly, in women and men, there was a stepwise increase in population-attributable risk percent as the number of low-risk factors increased for total stroke. Furthermore, when population-attributable risk percent was calculated using alternate definitions of low risk (eg, most recent rather than baseline body mass index, 0.1 g/d alcohol as the lower limit of low risk, Dietary Approaches to Stop Hypertension dietary scores, or 6-nutrient diet scores), results were consistent or comparable. Overall, the findings of benefit for low-risk lifestyle in this study were similar to those of other studies.

### Table 1. Operational Definition of Low Risk for Lifestyle Study Factors

<table>
<thead>
<tr>
<th>Factor and definition</th>
<th>Total Stroke</th>
<th>Ischemic Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking: not currently smoking (former smokers included)</td>
<td>0.21 (0.12–0.36)</td>
<td>0.19 (0.09–0.40)</td>
</tr>
<tr>
<td>Physical activity: ≥30 min/d of moderate or vigorous activity</td>
<td>0.31 (0.19–0.53)</td>
<td>0.20 (0.10–0.42)</td>
</tr>
<tr>
<td>Moderate alcohol consumption: at least 5 g/d with an upper limit of 15 g/d for women and 30 g/d for men</td>
<td>47 (18–69)</td>
<td>54 (15–78)</td>
</tr>
<tr>
<td>Optimal weight: BMI &lt;25 kg/m² during midlife (at baseline)*</td>
<td>35 (7–58)</td>
<td>52 (19–75)</td>
</tr>
</tbody>
</table>

BMI indicates body mass index. Data derived from Chiuve et al.

*In secondary analyses, most recent BMI before stroke diagnosis was used. When low-risk BMI was defined as 18.5 to <25 kg/m², the study results did not differ.

### Table 2. Relative Risk, Population-Attributable Risk Percent, and 95% CI for Lifestyle Study Factors

<table>
<thead>
<tr>
<th>RR by all 5 low-risk factors (95% CI)*</th>
<th>Total Stroke</th>
<th>Ischemic Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>0.21 (0.12–0.36)</td>
<td>0.19 (0.09–0.40)</td>
</tr>
<tr>
<td>Men</td>
<td>0.31 (0.19–0.53)</td>
<td>0.20 (0.10–0.42)</td>
</tr>
</tbody>
</table>

PAR% by low-risk lifestyle, % (95% CI)

<table>
<thead>
<tr>
<th>PAR%</th>
<th>Total Stroke</th>
<th>Ischemic Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>47 (18–69)</td>
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</tr>
<tr>
<td>Men</td>
<td>35 (7–58)</td>
<td>52 (19–75)</td>
</tr>
</tbody>
</table>

RR indicates relative risk; PAR%, population-attributable risk percent. RR estimates are from Figure 1A and 1B and PAR% is from Table 3 of Chiuve et al.

*Compared with those who had none of the factors.
and communities to change their behavior to a health-conscious one.²⁰ Optimism exists for this strategy, especially as it applies to low- and middle-income countries, although additional integrated, stepwise surveillance and health outcomes research are needed to solidify the approach.

This carefully done, insightful, and highly relevant analysis by Chiuve et al has potential limitations, as pointed out by the authors, in areas such as measurement error in self-reported variables; nondifferential misclassification, which could underestimate true relative risk; residual confounding; and underestimation of the burden of unhealthy behavior.⁶ However, the data remain consistent with other studies,¹⁴,¹⁵ and these potential study limitations should not deter us from concluding, as the authors have, that a low-risk lifestyle profile is associated with a substantial reduction in stroke risk. Furthermore, one wonders what may have led to adherence to an overall low-risk lifestyle in the Chiuve et al study subjects and if this information can be applied to the community at large.

Because the combined health benefits may be considerable for not smoking, consuming alcohol in moderation (if one chooses to), maintaining a proper diet, exercising regularly, and keeping weight down, a more challenging matter is to shift the risk profile of the community at large in this direction in a sustainable manner. It seems that only a relatively small percentage of us are able to maintain such a healthy lifestyle profile. There are many temptations for unhealthy lifestyle choices before us and counterforces that detract from health-promotion efforts. Therefore, we have a significant challenge in our midst before we can claim victory of achieving a remarkable record for healthy lifestyle factors in individuals and the population.

**Disclosures**

Dr Gorelick serves on and receives honoraria for participation on a safety committee for Norvartis (Alikesien); on steering committees for Bayer for the ARRIVE trial; for Boehringer Ingelheim for the PReFOSS trial; for Braingate (sphenopalatine ganglion stimulator for acute ischemic stroke); for Pharm-D (neuroprotectant in acute ischemic stroke); for adjudication committees for Myriad, TAP, and Pfizer; for a data monitoring board for Statistical Collaborative; and as a consultant for Daiichi Sankyo (olmesartan). He has lectured for AstraZeneca for acute ischemic stroke); for Pharm-D (neuroprotectant in acute ischemic stroke); for Bayer for the ARRIVE trial; for Boehringer Ingelheim for the safety committee for Norvartis (Aliskiren); on steering committees for Norvartis (Aliskiren); and received honoraria from diaDexus and Boehringer Ingelheim. He has served as a consultant for Daiichyi Sankyo (olmesartan). He has lectured for Ansell, Gilead Sciences, AbbVie, and AstraZeneca for acute ischemic stroke); for Pharm-D (neuroprotectant in acute ischemic stroke); for Bayer for the ARRIVE trial; for Boehringer Ingelheim for the safety committee for Norvartis (Aliskiren); on steering committees for Norvartis (Aliskiren); and received honoraria from diaDexus and Boehringer Ingelheim. He has served as a consultant for Daiichyi Sankyo (olmesartan). He has lectured for Ansell, Gilead Sciences, AbbVie, and AstraZeneca.

**References**


**Key Words:** Editorials • lifestyle • stroke prevention • risk
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