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Stroke prevention – an uphill battle

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DISCLOSURES:

Dr. Beckett serves on the External Advisory Boards for the Knight Alzheimer's Disease Research Center (Washington University) and the Shiley-Marcos Alzheimer's Disease Research Center (University of California, San Diego), and Data and Safety Monitoring Committees for the CARE Ecosystem study (University of California, San Francisco) and the Helping Hand 2 smoking cessation intervention (Massachusetts General Hospital.) She is or has recently been funded by NIH grants # P30CA093373, # P30AG010129, # P30AG010129, # R01CA115483, # R01CA115483, # R01CA199725, # R01CA216879 , # R01CA211554, # R01CA211554, # RF1AG031563, # UM1OD023221, # R01CA81237, and # RF1AG061001, and National Institute of Justice #2014-R2-CX-0012 .

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In spite of considerable advances to reduce the burden of cardiovascular disease, including stroke, these remain major causes of morbidity and mortality at the population level. A number of guidelines have identified contributory causes, many of which are similar for stroke and coronary artery disease, and identified avenues for prevention (1,2). However, it is also recognized that in spite of the need to enhance preventive efforts, stroke prevention is complex with many challenges (3). Illustrating this concept, Boehme *et al.* report disappointing levels of primary and secondary stroke prevention in a large regional cohort of stroke patients in this issue of *Neurology* (4). Despite easy access to and coverage for healthcare, 80% of subjects diagnosed with ischemic stroke had at least one untreated or inadequately treated medical risk factor for stroke (e.g. hypertension, hyperlipidemia, atrial fibrillation). Fully 95% had either an inadequately addressed medical risk factor or lifestyle risk factor (smoking, overweight or obesity, excess alcohol use). It is interesting to note that a similarly high number of risk factors for stroke patients was reported based on US inpatient data (5).

Stroke risk has long been known to be increased by these potentially modifiable factors, and as reported by the INTERSTROKE study, 10 modifiable risk factors explained 90% of the risk for stroke (6,7). The prevalence of risk factors such as hypertension, dyslipidemia, smoking and diabetes have even increased in recent years (5). The authors draw on published review studies to estimate the proportion of strokes that might be prevented, were each of these factors to be adequately addressed by best current medical practice, either individually or in combination. They conclude that with full attention to all the risk factors considered, nearly half of the existing strokes might be prevented. The impact of secondary stroke prevention (once an initial stroke has occurred) might be even greater than that for primary prevention.

The most common medically treatable risk factors were hypercholesteremia and hypertension, treatable respectively by statins and anti-hypertensive medications. The greatest potential

impact of adequate treatment of risk factors would also come from adequate treatment of these two (8,9). Undertreated or untreated atrial fibrillation, atherosclerotic cardiovascular disease, and diabetes also contributed, as did carotid stenosis, unrecognized transient ischemic attacks in the previous year, and mechanical heart valves.

Lifestyle factors also contribute to stroke risk. In this cohort, 30% of people were smokers or had quit less than 10 years previously, over half were overweight or obese, and 7% were heavy drinkers. Lifestyle changes are more difficult to implement than drug, but because they are so common, even modest success rates can have a substantial public health impact. Moreover, the presence of both lifestyle and medical risk factors may lead to an interaction, increasing the effects of each separate factor. For example, hypertension has been reported to interact with both smoking and diabetes to increase their association with risk of stroke [10]. Notably, although the authors considered the additive effect of these factors, the interrelated nature of these risk factors provides potential opportunities for considerable positive preventive effects through a comprehensive risk factor treatment. In an era of precision medicine and empowerment of patients, opportunities for self-care in stroke prevention should be noted, in particular with regard to lifestyle factors (11).

The study was conducted in the Tyrol region of western Austria, in a population that is relatively homogeneous with universal access to healthcare including tertiary stroke care. Thus, the results may not be generalizable to more diverse populations or to those where access to healthcare is more limited but could offer promise with regard to patient education and self-motivation approaches (11). Risk factors were ascertained retrospectively, which might introduce uncertainty or bias in the results, although the access to medical records mitigates this concern. In particular, assessment of hypertension offers challenges, as recognized by the authors (4). Subgroup comparisons should be viewed with caution, despite the relatively large

sample size, due to uncertainty attached to both risk factor prevalence and treatment impact. A separate, very conservative sensitivity analysis suggested that the effect might also be overestimated; instead of half the strokes being preventable, the true impact of adequate treatment might be only a 25% reduction.

MESSAGE: This article offers both discouraging and encouraging news for stroke prevention. The high prevalence of untreated or inadequately treated risk factors that should be readily controlled, even with universal healthcare available, is disheartening. However, clear intervention strategies are in place for many of these factors. These strategies have contributed to reductions in stroke incidence in many places, including more than a one-third reduction in Austria between 1995 and 2015 [12]. In spite of this, we appear to have much farther to climb on the steep slope toward reduction of strokes. On the other hand, the article also offers hope, that a more systematic effort to meet available guidelines might lead to dramatic improvements.

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