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Stroke Prevention in the Very Elderly

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Stroke remains a common cause of death and disability in the very elderly (here defined as those aged 80 years and older), with about a third of all stroke occurring in this age bracket in high-income countries.[1] There is uncertainty on the exact pattern of stroke type in extreme old age, because of potential poor ascertainment of very frail and institutionalized older people in prior studies. However, epidemiological and clinical trial data demonstrate an important increase in atrial fibrillation (AF) cardioembolic stroke in the very elderly.[2,3] Important causes of hemorrhagic stroke in the very elderly are cerebral amyloid angiopathy and anticoagulant-related hemorrhagic stroke.[4,5] Preventing, or delaying, stroke will be an important component in compressing morbidity, or increasing healthy life expectancy. For devotees of evidence-based medicine (including this author), the prevention of stroke in the very elderly is complex because of 3 main reasons: first, older people have been largely excluded by design (or by accident) from many randomized controlled trials (RCTs)[6]; second, the underlying causes of stroke change with aging; and final, there is a large body of evidence from geriatric medicine that potentially conflicts with usual stroke preventative measures, for example, data on frailty, polypharmacy, and falls.[7]

The exclusion of older people from RCTs is well known and has many causes. The age limit of 75 years in the statin trials was based on a misinterpretation of the early epidemiology,[6] the 80-year-old age limit in the ECASS thrombolysis trials (European Cooperative Acute Stroke Study) was probably related to the practical organization of German neurology units at the time, when those aged 80 years were usually admitted under general medicine, and therefore the stroke neurologists simply had no access to these patients. Exclusion criteria that include the common diseases of old age exclude the very elderly by default. Yet many of our patients are not only over 80 years of age, but have multiple comorbidities and as a result, impressive polypharmacy (often ≥10 medications). RCTs have commonly excluded such patients, and thus, our evidence base for the very elderly is inadequate.[8] Avoiding future upper age limits and these typical exclusions will help ensure a reliable future evidence base.[8]

To help understand the effects of treatments in the very elderly, it is important to consider that treatment directions in human health rarely change direction with increasing age. As relative risk reductions diminish with age, absolute risks increase, often leading to similar absolute benefits for the old and young.[9] Reasons include the increase in competing events outside the disease of interest because of increased comorbidity and increased risks of treatment. In understanding the likely change in treatment effects in the very elderly, it is useful to view the totality of evidence from epidemiology and RCTs, and whether there has been any evidence of an interaction with age for the treatment under question. A lack of any age–treatment interaction is promising evidence that treatments will retain efficacy in the very elderly, despite the paucity of direct evidence from such age groups.

It is also useful to consider the geriatric medicine perspective. In a frail older person, with multiple illnesses, and often complex and fragile social circumstances, application of Level A guideline evidence (generated from largely younger populations) for each of their multiple problems could quite possibly kill them! As medical problems accumulate and physiological systems degenerate, older people increasingly present with syndromic presentation, rather than classical symptoms of the acute medical illness. The common syndromes are delirium, falls, immobility, incontinence, pain, breathlessness, and sepsis. These syndromic presentations are sometimes referred to as atypical presentation, but in aged care, this is a misnomer, as these become typical! Myocardial infarction can present with a fall. Stroke can present with delirium. Coincidental multiple new illness is also frequently seen, such as heart failure and pneumonia. The challenge of acute geriatric medicine is to untangle the complexity, identify all the contributing illnesses (and their social context), rationalize medication (deprescribing is one of our most useful interventions), and then rehabilitate the patient back to their usual state (as the acute illness will have caused functional deterioration). This holistic approach inevitably comes with compromise and prioritization. These issues help explain why there is often a clash of evidence-based medicine between the stroke guidelines and the geriatric guidelines! Antihypertensive treatment can merely push some older people from the stroke clinic to the falls clinic! In this context, there are often good reasons why some aspects of stroke prevention are not recommended for individual patients. For the very old, it is important to do the simple things well and not make it too complicated.

With this background, I will first consider what recommendations should be made for an apparently healthy 85 years old,

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then discuss how this advice should differ if the person were frail, demented, or functionally dependent.

Primary Prevention

Epidemiological and RCT data would suggest that the top priorities for primary prevention of stroke in very elderly people would be treatment of hypertension, anticoagulation for those in AF, and stopping smoking (Table 1). There is no good reason to change our usual advice on diet, physical activity, and avoiding obesity. Although we have good evidence not to recommend low-dose aspirin, there are data to support the routine use of statins and influenza vaccination for the very elderly.

Treatment of Hypertension

High blood pressure has the highest population attributable risk for stroke[10]; randomized trials have consistently demonstrated stroke reduction with treatment of hypertension; meta-analysis has not identified a significant interaction with treatment efficacy and age[11]; and trials focused on the very elderly, such as the HYVET trial (Hypertension in the Very Elderly), have provided data on the benefits and risks for those over 80 years of age.[12] Although the HYVET trial directly addresses our idealized healthy 85 years old, the trial exclusion criteria inevitably led to a selected subpopulation of this age group, as those with accelerated and secondary hypertension, heart failure, chronic renal failure, hyper- or hypokalemia, dementia, and nursing needs were excluded. HYVET included 3845 older people with a blood pressure >160 mm Hg systolic. The antihypertensives were indapamide in a dose of 1.5 mg in a sustained release preparation, plus perindopril 2 to 4 mg as necessary. The primary outcome of the trial was fatal or nonfatal stroke. The trial was stopped early because of a statistically significant reduction in the primary outcome, and also deaths from all causes. By the end of the trial closeout, the additional events recorded led to the primary outcome not being conventionally significant (a reduction in fatal and nonfatal stroke of 30%; P=0.06), but the reduction in all deaths remained significant (21% reduction; P=0.02). There was also a significant reduction in heart failure, cardiovascular, and other adverse events. This trial is important for several reasons. First, it provides data on our population of interest; second, it demonstrates that the strategy to prevent stroke had other important benefits. This is the crux of the matter when dealing with very elderly people, as we cannot merely concentrate on stroke prevention in isolation, we need to be providing holistic care. Like many good RCTs, the results provide important data on natural history; in this case, untreated hypertension is clearly an important cause of heart failure and can be prevented in this age group. Overall, the HYVET data are consistent with the effect of antihypertensives in younger people. As these were ambulant community-dwelling older people, prepared to consent to a clinical trial (ie, a particularly robust population), this evidence may not be reliably extrapolated to those who do not fit such criteria, such as those requiring help with basic activities of daily living.

Table 1. Priorities for the Prevention of Stroke in the Very Elderly

Primary Prevention	Secondary Prevention
	Ischemic stroke
Treatment of hypertension	Blood pressure and cholesterol lowering
Anticoagulation for atrial fibrillation	Anticoagulation for atrial fibrillation
Lifestyle (especially stopping smoking)	Lifestyle (especially stopping smoking)
Statins	Antiplatelet therapy
Influenza vaccination	Influenza vaccination
	Carotid endarterectomy
	Hemorrhagic stroke
	Blood pressure lowering
	Lifestyle (especially stopping smoking)
	Avoid antithrombotics
	Influenza vaccination

The SPRINT study (Systolic Blood Pressure Intervention Trial) has provided additional support for a strategy of blood pressure lowering, with over a quarter of participants aged 75 years or older. However, similar provisos apply to this trial. There were generally robust community-dwelling people, with those requiring nursing care or with dementia excluded. Importantly, however, within both the HYVET and SPRINT trial populations, the treatment effects seemed equally efficacious among the more versus less frail participants.[13,14]

Although the data support blood pressure lowering for those with systolic blood pressure of ≥160 mm Hg, for independent ambulant older people, implementation needs careful assessment.[15] If the very elderly person does not match the above trial characteristics, then it is important to ask several questions. What is their goal of treatment? If they are very dependent and bedbound, they (and their family) may have a clear preference for comfort care and avoiding medication. Indeed, there are observational data that suggest that antihypertensive treatment together with a low systolic blood pressure (<130 mm Hg) is hazardous in nursing home patients.[16] Others in supportive care may have a particular fear of a future stroke, and thus, treatment may be justified. Assessment of potential adverse effects is important such as excluding significant postural hypotension before initiation of therapy (check standing blood pressure before any new antihypertensives are initiated), diuretics can precipitate gout, and calcium antagonists can cause troublesome constipation and leg swelling. As with younger people, nonpharmacological interventions should be discussed before medication, such as stopping smoking, regular physical activity, and salt reduction. The perils of polypharmacy also need to be considered, as the addition of yet another medication may lead to unacceptable adverse events related to the sheer number of medications, despite the supposed benefits for the antihypertensive.[7] Whether assessment of frailty will help is still a research question, as there is good evidence that increased frailty increases the risk of adverse events and may be an important treatment modifier.[17] The Fried frailty phenotype (Table 2) is probably of most use to clinicians,[18] and frailty (using a validated method) should ideally be quantified

Table 2. Fried Phenotype of Frailty[18]

Weight loss
Exhaustion
Weakness
Decreased gait speed
Diminished physical activity

at baseline in future trials designed for the very elderly.[6] The choice of medication can be individualized according to potential drug interactions and available data. An angiotensin-converting enzyme inhibitor, diuretic, or calcium antagonist is a good choice, and in geriatric medicine, it is best to start with a low dose and increase cautiously (start low and go slow).

Thromboprophylaxis of AF

As populations age, the proportion of ischemic stroke caused by AF increases. In an Australian study, the proportion of cardioembolic stroke was as high as 42%, most caused by AF.[19] There is a large evidence-practice gap with about a third of all fatal or disabling strokes being in people with known AF, who have not been treated with anticoagulation.[20] The BAFTA trial (Birmingham Atrial Fibrillation Treatment of the Aged) recruited older people (aged ≥75 years) with AF, who were eligible for anticoagulation, demonstrating that warfarin anticoagulation (international normalized ratio target, 2–3) was superior to aspirin 75 mg daily, with a 2% absolute annual reduction in stroke and arterial embolism.[21] The AVERROES trial (Apixaban Versus Acetylsalicylic Acid [ASA] to Prevent Stroke in Atrial Fibrillation Patients Who Have Failed or Are Unsuitable for Vitamin K Antagonist Treatment) recruited those considered ineligible for warfarin anticoagulation and demonstrated the benefit of anticoagulation (using apixaban) compared with aspirin (commonly thought the safer antithrombotic for older people).[22] A meta-analysis of the recent major trials of new anticoagulants versus warfarin anticoagulation included many older people (average age over 71 years, and 38% aged 75 years and older).[23] Analyses demonstrated no significant treatment interaction by age for either efficacy (stroke and systemic embolus prevention) or bleeding risk, with the newer agents superior or noninferior to warfarin.[23] There were fewer intracranial hemorrhages but more gastrointestinal hemorrhages with the newer agents. The participants had considerable comorbidity: 29% prior cerebrovascular disease, 46% heart failure, 31% diabetes mellitus, 88% hypertensive, 15% prior myocardial infarction, 19% renal impairment, and 34% were on aspirin. These data (and those from postmarketing studies) suggest that anticoagulation is likely to be generalizable to many very elderly people and support a policy of anticoagulation for the very elderly with AF.[24] In this age group, there is no need to perform the CHADS2 or CHA_2DS_2VASc scores as an age of ≥80 years put them into a high-risk population. As with antihypertensive treatment, this evidence base may not be reliably extrapolated to those with functional dependence and frailty, and treatment recommendations have to be individualized. Bleeding risks are substantially worse with concomitant antiplatelet therapy, and in general, this should be avoided in the very elderly. Falls are also a serious concern. In Australia, deaths from accidental falls have crept up the ranking of causes of death (now ranked 16th), with those dying as a result of falls being of a similar age to those dying of stroke or ischemic heart disease.[25] To put in perspective, numerically, deaths from falls represent ≈10% of those dying from ischemic heart disease and 25% of those dying from stroke. A falls risks assessment including whether they have fallen in the last year, assessment of neurological deficits or cognitive impairment, current functional ability, vision, potential for home hazards, polypharmacy, and comorbidity should be part of an anticoagulant assessment. Given the complexity of anticoagulation treatment, it is important to assess whether patients have sufficient cognitive ability to safely manage their treatment, and if not, can they be appropriately supervised?

Lifestyle Advice

The most important advice is to stop smoking as there is no evidence that this becomes inappropriate advice with advancing age, and smoking history should be established at every opportunity.[26] Given the epidemiology of stroke, and the importance of providing consistent messaging for the population at large, usual recommendations of avoiding obesity, eating a healthy diet, and remaining physically active are reasonable.[27]

Influenza Vaccination

When considering patient-centered care, influenza vaccination should not be forgotten as an additional preventative strategy. Epidemiological and trial evidence provides support that influenza vaccination can reduce the risk of vascular events, including stroke.[28,29] Influenza is a common and serious illness of old age and outbreaks in aged care facilities not only cause death and morbidity for their residents but also provide a community source of infection that prolongs circulating virus. Hence unlike the previous recommendations, influenza vaccination can be offered to all the very elderly.

Cholesterol Lowering

Lowering blood cholesterol (other than diet), in the primary prevention setting, is controversial. Although public advocacy groups recommend that you take control of your cholesterol, it is not widely accepted that this should be with medication.[27] In 2014, the UK National Institute for Health and Care Excellence published guidelines that included the statement: "the important effect of age on CVD risk suggests that all people in this group should be offered statin therapy,"[30] although acknowledging the relative lack of direct evidence for the very elderly (see later). Given that vascular disease, including stroke, remains the most important cause of death in high-income countries, interventions to lower blood cholesterol (lifestyle and possibly statins) should be discussed with the very elderly. There are a multitude of factors to consider, including consideration of risks and benefits of statins, uncertainty over interpretation of evidence, contribution to polypharmacy, perception of risk by both the doctor and the patient, and medicalizing old age, frailty, and goals of care.

There are currently no reliable data to support aspirin for primary prevention.[31] Trials in younger people provided evidence of an increased risk of hemorrhagic stroke, and it is highly likely that this risk will be more important in the

very elderly. The recently halted ASPREE trial (Aspirin in Reducing Events in the Elderly) will provide additional data for the very elderly.[32]

As current population attributable risks do not account for all stroke, it is important to consider other potential triggers.[10] Recent data have provided evidence that ambient temperature (eg, cold weather) may be an important trigger for stroke, perhaps by a blood pressure mechanism, and this could be very relevant for the very elderly.[33] Future epidemiological studies will be important in clarifying these and other new risk factors.

Secondary Prevention

Stopping smoking and blood pressure reduction remain the mainstay of secondary prevention after hemorrhagic stroke, with the addition of cholesterol-lowering, antithrombotic treatment, and carotid intervention for those with ischemic stroke.

Blood Pressure Reduction

Blood pressure reduction goals are different in secondary prevention. Whereas primary prevention for the very elderly was based on a systolic blood pressure goal of <160 mm Hg, after a stroke event we have good evidence from the PROGRESS trial (Perindopril Protection Against Recurrent Stroke Study) that blood pressure lowering, even for the conventionally normotensive, will reduce the risk of further stroke by a third. Although the average age of 64 years in the PROGRESS trial limits direct generalizability to the very elderly, subsequent individual patient meta-analysis based on cardiovascular risk has shown that the relative risk reduction with blood pressure lowering is remarkably stable over low-risk (average age, 59 years) to high-risk (average age, 75 years old) groups.[34] Given that the very elderly are at particularly high absolute risk of stroke and vascular death, these risk-based analyses are reassuring. On the basis of the HYVET and PROGRESS trials, the angiotensin-converting enzyme inhibitor perindopril and indapamide are good first-line drugs if tolerated without adverse effects. Medication can be initiated during the index hospital admission when stable or supervised early in an outpatient setting if service provision is reliable.

Cholesterol Lowering

The debate about cholesterol lowering for older people has been clarified by meta-analysis of the epidemiology and trial data. The epidemiological association of the risk of cardiovascular events with increasing age has demonstrated that a 1 mmol/L lower blood cholesterol is associated with a halving of ischemic heart disease deaths for those aged 40 to 49 years old, but attenuates with age (associated with only a reduction of a sixth for those aged 70–89 years).[35] The Cholesterol Treatment Trialists individual patient meta-analysis provided convincing data that those aged >75 years benefit from cholesterol lowering with a reduction in major coronary events (10.6% on treatment versus 12.8% control; P=0.002) and major vascular events (16.8% versus 19.7%; P=0.0001; stroke data alone were not provided, but are part of the composite outcome of major vascular events).[36] In the SPARCL trial (Stroke Prevention by Aggressive Reduction in Cholesterol Levels; n=4731 participants, average age 63 years old), cholesterol lowering with atorvastatin demonstrated a reduction in stroke (11.2% atorvastatin versus 13.1% placebo; P=0.03).[37] Differences between individual trial results are likely to be because of case mix (SPARCL participants were recruited within 6 months of their stroke) and the problems of low statistical power for older age groups given the epidemiology (patients with stroke in other cholesterol trials were often recruited many years after their stroke event when coronary events tend to predominate in vascular patients). In summary, 3 strands of evidence support cholesterol lowering after ischemic stroke in the very elderly: there is no evidence of a difference in treatment effect between older and younger people; there is direct evidence in a stroke population[37]; and there are additional benefits beyond stroke prevention, for example, prevention of other important major vascular events.[36]

A few practical points are worth discussion. Cholesterol levels tend to fall in terminal disease, so it is important to check cholesterol levels before initiation of treatment. In general, it is reasonable to consider treatment for those with ischemic stroke or transient ischemic attack (TIA) if their LDL-C (low-density lipoprotein cholesterol) levels are >100 mg/dL (2.59 mmol/L). In an inpatient setting, starting immediately on a high dose (eg, atorvastatin 80 mg) can be monitored and will avoid subsequent undertreatment. As with blood pressure secondary prevention, the strategy is one of the lowering blood cholesterol, rather than achieving a particular cholesterol level goal.

Antithrombotic Therapy

The treatment of those in AF (including paroxysmal AF) has been covered earlier. After ischemic stroke or TIA, the very elderly in AF are at even higher risk of further embolic stroke, and treatment should be considered for all eligible patients. Eligibility is determined by lack of previous major bleeding, no recent gastrointestinal hemorrhage, and no likelihood of an important future bleeding risk. Patients need to have sufficient cognitive ability to safely manage their medication (or be appropriately supervised), and risk of falls should be determined (see above). The main uncertainty is when to start anticoagulation after the initial ischemic stroke, and this is currently being addressed in RCTs.

For those in sinus rhythm, antiplatelet therapy is a proven treatment, and we have reliable evidence (mainly from aspirin trials) that treatment should be started immediately after onset of ischemic stroke.[38] For those receiving thrombolysis or thrombectomy, it is standard practice to commence aspirin after the exclusion of any hemorrhagic complications. The benefits of early secondary prevention over the first 1 to 2 weeks after TIA/ischemic stroke are approximately similar to the subsequent benefits for the subsequent 50 weeks. Meta-analysis provided no evidence of an interaction with age, with similar benefits seen for the subgroup of those aged 75 years and older, compared with younger age groups.[38]

The CHANCE trial (Clopidogrel in High-Risk Patients With Acute Nondisabling Cerebrovascular Events) has provided promising data that the combination of aspirin and clopidogrel is beneficial if used for the first 21 days after minor ischemic stroke or TIA.[39] However, the median age of the Chinese in this trial was only 62 years, and confirmatory (or otherwise) data are expected from the ongoing POINT trial (Platelet-Orientated Inhibition in New TIA and Minor

Ischemic Stroke). The combination of aspirin and clopidogrel has not been shown to be beneficial for long-term secondary prevention of stroke because of the incidence of major bleeding with this combination.[40]

There is no direct evidence of an important difference between antiplatelet regimes (aspirin alone, clopidogrel alone, or aspirin with dipyridamole) in the very elderly, and so choice of regime is an individualized decision based on patient and clinician preference, risk of polypharmacy, and side effect profile. Clopidogrel is likely to cause fewer upper gastrointestinal bleeds. Most data are from aspirin, where the benefits are clear, with evidence that as the risks of vascular events increase (eg, with age), there is also a corresponding increase in the risks of adverse events, with no clear loss of net benefit with age.[31] A recent observational study from the Oxford Vascular Study group has suggested that the risks of aspirin the very elderly might outweigh the benefits, and these authors encourage the addition of a proton-pump inhibitor to reduce the gastrointestinal hemorrhage rate.[41] However, in the absence of RCT evidence, there is uncertainty whether this would be an effective strategy and it does expose older people to the potential harms of proton-pump inhibitors,[42] and an increase in potential harmful polypharmacy.

Carotid Intervention

Carotid endarterectomy, angioplasty, and stenting have been used extensively to prevent stroke, both as primary and secondary prevention. In primary prevention, best medical care has improved so much that further trials are underway to explore whether carotid intervention has any benefit. Even if a small benefit was found for those with tight carotid stenosis, it is likely that the numbers needed to treat to prevent a stroke would be very large, and the intervention will always come with an early risk. For secondary prevention, a meta-analysis of the European Carotid Surgery Trial and the North American Symptomatic Carotid Endarterectomy Trial demonstrated that old age was not a contraindication; indeed, the large absolute risks in the very elderly led to the intervention having greater net benefit in this age group.[43] The CREST trial (Carotid Revascularization Endarterectomy vs Stenting Trial) investigators found a significant interaction with age for the comparison with stenting with endarterectomy, where endarterectomy was favored for those aged over 70 years of age.[44] As surgery within 2 weeks is associated with greatest benefit, these data would support early screening (1–2 days) for carotid stenosis in the very elderly in the select group of patients with definite TIA or minor ischemic stroke, who were previously independent, and who had a definite carotid territory event and were prepared to undergo future endarterectomy. Stenting remains an option for those unwilling or unable to have endarterectomy.

Putting It All Together

In a previously independent healthy patient 80 years or older with ischemic stroke, current evidence would support stopping smoking and antithrombotic treatment (antiplatelet therapy if in sinus rhythm, anticoagulation if in AF), blood pressure lowering (eg, an angiotensin-converting enzyme inhibitor and diuretic), and a statin, a minimum of 4 medications. Most patients of this age are willing to take this amount of medication, especially when advised that it will likely reduce their risk of future stroke by about four fifths.[45] Such idealized patients are rarely seen, and with increasing frailty and dependency, this underlying evidence base becomes less reliable. Applicability to our individual patient will depend on numerous factors, but it is unlikely that any one of these interventions suddenly becomes harmful with age. An important point to note is that some of these interventions are very time dependent (eg, immediate aspirin for ischemic stroke, and early surgery for symptomatic carotid stenosis), and older patients may present late to hospital after their stroke (or TIA) event. We need to ensure that our population are well informed about the need for speed and that those looking after older people do not unduly delay appropriate assessment. Clinicians need to use their individual judgment on how intensively to treat. For example, if a very elderly patient has recurrent anemia and is too frail for endoscopy, stopping antithrombotic therapy can restore hemoglobin levels. An approximate 1% to 2% annual absolute benefit of antithrombotic therapy is very easily overcome by the absolute risks of being anemic. Symptomatic postural hypotension should lead to reduction in culprit medications such as antihypertensives (and dipyridamole). A major bleed in a very elderly patient should lead to lifelong cessation of all antithrombotics, unless there is a compelling reason to continue (such as a mechanical heart valve). Bowman and Meyer[46] have described the concept of a social watershed that might provide an opportunity to review all prophylactic medications, such as a new admission to a nursing home, when the patient (and relative) goal of treatment may become comfort rather than survival. In this scenario, it is very reasonable to cease some or all of statins, antihypertensives, and antithrombotics. Statins, in particular, are often inappropriately used for people with life-limiting illness.[47] Rather than consider some medications for life, it is better to consider recommending starting therapy and, in a future review, consider stopping some medications if the situation has changed. Geriatricians (internists), unlike perhaps stroke neurologists, often provide care for those admitted with the serious adverse events from preventative interventions (eg, intracranial hemorrhage, trauma after falls, gastrointestinal or other bleeds, metabolic disturbances, perioperative stroke) and are more sensitized to the potential for these events, leading to a lower clinician threshold to cease causal medication. Infection becomes an increasingly important cause of death in the very elderly, and thus, stroke secondary preventative measures may have less of a role, the exception perhaps being influenza vaccination. Given the uncertainty of the value of secondary prevention for the frail (particularly, those with disability or dementia), an alternative approach may be to assess the risks and benefits of Deprescribing individual medications to clarify their role in this situation. Such RCTs are currently underway.

In looking after very elderly patients, we cannot merely consider stroke prevention in isolation. The prevention (or delaying the onset) of cancer and dementia is also means of compressing morbidity. The recent Lancet Commission on Dementia[48] includes some of the prevention strategies discussed here (stopping smoking, encouraging exercise, avoiding obesity, treatment of hypertension).

Future Directions

In stroke prevention for the very elderly, there is evidence of undertreatment (thromboprophylaxis of those in AF) and overtreatment (the widespread use of statins for nursing home residents), and these evidence-practice gaps should be closed. As our stroke populations age, we need to ensure that upper age limits are avoided in future RCTs and epidemiological research, and trialists need to be more inclusive and ensure that frailty and comorbidity are quantified at baseline.

Disclosures

Dr Lindley has received honoraria from Pfizer and Covidien for occasional speaking fees.

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