Clopidogrel therefore remains an antiplatelet regimen of choice for the secondary prevention of recurrent ischaemic stroke in Japan. There appears to be no benefit from routine CYP2C19 genetic testing to guide the selection of prasugrel over clopidogrel. However, the generalisability of the findings to Japanese people older than 75 years or weighing less than 50 kg (the subject of the ongoing PRASTRO-II trial [JapicCTI-121901]), Japanese women (who comprised only 21% [797 of 3747] of participants in the PRASTRO-I trial), or other non-Japanese populations is unclear. Whether the results are applicable to higher doses of prasugrel, as used in other countries, is also unclear.

The quest continues for more effective antithrombotic therapies to reduce the proportion and severity of recurrent stroke. The thienopyridine ticagrelor has the advantage over clopidogrel and prasugrel of acting directly (without biotransformation) and binding reversibly to the platelet P2Y12 receptor for ADP. It prevents stroke in individuals with vascular risk factors[7] and might have a role in long-term secondary stroke prevention. A large trial (NCT03354429) is testing the safety and efficacy of adding ticagrelor to aspirin for prevention of new early stroke after acute transient ischaemic attack or ischaemic stroke. A trial of the combination of cilostazol with aspirin or clopidogrel compared with aspirin or clopidogrel alone for the long-term prevention of recurrent ischaemic stroke in 1884 Japanese high-risk patients with non-cardioembolic ischaemic stroke is due to report its results soon (NCT01995370). Combining long-term, low-dose anticoagulation (rivaroxaban at 2·5 mg, twice per day) with low-dose antiplatelet therapy (aspirin at 100 mg/day) is another promising antithrombotic strategy of secondary stroke prevention, given that it substantially reduced the rate of stroke, compared with aspirin monotherapy, in patients with stable peripheral and coronary artery atherosclerosis, including in a subgroup of patients with previous non-lacunar ischaemic stroke.[8] Other treatment paradigms that target the metabolic causes of plaque accumulation, the inflammatory causes of plaque instability and rupture,[9] and the activated form of coagulation factor XI (XIa),[10] an enzyme involved in thrombus propagation and stabilisation, are under investigation.

Graeme J Hankey
Medical School, Faculty of Health and Medical Sciences, The University of Western Australia, Harry Perkins Institute of Medical Research, QEII Medical Centre, Nedlands, Perth 6009, Australia
graeme.hankey@uwa.edu.au

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Dementia risk after transient ischaemic attack and stroke

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About 20% of patients who are admitted to hospital for stroke develop dementia within the first year after the event; incidence is higher in those with recurrent stroke and lower in those with first-ever stroke.[1] Furthermore, roughly one in ten patients with first-ever stroke already has dementia at event onset.[1] As survival rates after stroke increase, dementia has become a growing concern for patients, families, and health-care providers. Previous studies have identified predictors of post-stroke dementia, including age, low educational attainment, previous stroke, stroke severity, dysphasia, diabetes, atrial fibrillation, and leucoaraiosis on brain imaging.[1–3] However, this information mostly originates from hospital-based studies, which are prone to selection bias and other biases, including attrition. There are few data for dementia risk after transient ischemic attack or

minor stroke, which together account for about 70% of cerebrovascular events. Also, information is scarce about the extent to which the incidence of dementia after transient ischaemic attack or stroke is higher than age-specific dementia incidence in the general population.

In *The Lancet Neurology*, Sarah T Pendlebury and Peter M Rothwell report the incidence of and risk factors for dementia before and after transient ischaemic attack and stroke, in a population-based study of 92 728 people from Oxfordshire, UK.[4] They prospectively recruited 2305 patients with acute cerebrovascular events that occurred between 2002 and 2012, and followed up these patients for 5 years with regular interviews. The authors used several methods of case ascertainment and comprehensive measures to minimise attrition, and found a stepwise association between severity of the index event and both pre-event and post-event dementia, irrespective of age. The prevalence of pre-event dementia ranged from 4·9% (95% CI 3·4–6·9) in patients with a transient ischaemic attack to 20·6% (15·8–26·5) in those with severe stroke (ie, a score >10 on the US National Institutes of Health Stroke Scale [NIHSS]). The incidence of post-event dementia at one year was 5·2% (95% CI 3·4–7·0) after transient ischaemic attack and 34·4% (29·7–41·5) after severe stroke. These estimates should be kept in mind when counselling patients and families, organising care, planning trials, and interpreting trial findings. However, the results must also be viewed in the context of largely variable mortality rates in this study. In patients who did not have pre-event dementia, 176 (75%) of 235 with severe stroke died before the 5-year follow-up, compared with 141 (22%) of 655 with transient ischaemic attack. Indeed, competing-risk results suggest that the long-term risk of dementia might be greatest in patients with NIHSS scores of 3–10.

Compared with published UK population estimates of dementia, in Pendlebury and Rothwell's study the risk of dementia 1–5 years after severe stroke was 6·5 times higher, and after transient ischaemic attack was 1·5 times higher. These figures are important for counselling and long-term follow-up of patients. As expected, a substantial proportion of post-event dementia was diagnosed in the first year after the event, particularly in patients with severe stroke. This finding reflects the immediate effects of the index lesion on brain function, but could also relate to variations in stroke recurrence or secondary processes within the brain (eg, inflammation or secondary neurodegeneration). Detailed neuroimaging studies should help to disentangle these factors. The baseline predictors of post-event dementia identified by Pendlebury and Rothwell were mostly in line with those reported previously for post-stroke dementia,[1-3] except that atrial fibrillation was not associated with dementia risk, which is somewhat surprising in view of previous results.[1,5] As a notable finding, a score of less than 24 on the mini-mental state examination at baseline was among the strongest predictors of dementia risk, a finding that further emphasises the prognostic usefulness of early cognitive testing after cerebrovascular events.[6]

Pendlebury and Rothwell's findings provide an important reference for physicians, policy makers, and researchers. Yet several questions remain, including the potential utility of a simple risk score for post-event dementia; the rates and characteristics of, and predictors for, cognitive impairment not meeting the criteria for dementia; and the effect of mild cognitive impairment on quality of life after stroke. Clarification of the extent to which characteristics of the index lesion (eg, volume, number, location) and markers of pre-existing brain injury (eg, leucoaraiosis, brain atrophy) add to the prediction of cognitive decline beyond factors accessible by clinical examination is important. The generalisability of Pendlebury and Rothwell's findings to other ethnicities and health-care systems is also unclear. In the Reasons for Geographic and Racial Differences in Stroke (REGARDS) cohort,[7] acute declines in cognitive function after stroke were greater in survivors who were black and had cardioembolic or large artery stroke. Declines in global cognitive function during the years after stroke were greater in survivors residing outside the Stroke Belt (a region in southeastern USA which has been recognised to have an unusually high incidence of stroke).[7] How the prevalence of and risk factors for dementia in patients with primary intracerebral haemorrhage compare with those in patients with ischaemic events needs further investigation. In Pendlebury and Rothwell's study, there was some indication of a higher risk of post-event dementia after intracerebral haemorrhage compared with ischaemic stroke (although this difference was not significant).[4] The Prognosis of Intracerebral Haemorrhage (PITCH) study[8] identified various imaging features that predict risk of dementia, underscoring the value of integration of neuroimaging findings into risk-prediction models.

Additional work is needed to better understand the trajectories of cognitive function after transient ischaemic attack and stroke, including how the determinants of delayed-onset dementia (ie, dementia that manifests months or years from stroke) differ from those of immediate-onset dementia;[2] the mechanisms underlying the association between diabetes and dementia risk, and whether this risk can be modified by more intensive glycaemic control;[9] and whether the risk of dementia in patients with atrial fibrillation can be lowered by oral anticoagulation (which would be expected as a result of the effects on stroke prevention). Finally, whether the risk of post-event dementia can be reduced by acute stroke therapy needs to be investigated. Secondary analyses from the REVASCAT trial suggest that endovascular treatment in patients with anterior circulation proximal arterial occlusion improves cognitive outcomes, particularly in patients with good functional outcomes.[10]

Martin Dichgans
Institute for Stroke and Dementia Research, Klinikum der Universität München, Ludwig-Maximilians-Universität, Feodor-Lynen-Straße 17, D-81377, Munich, Germany; German Center for Neurodegenerative Diseases, Munich, Germany; and Munich Cluster for Systems Neurology (SyNergy), Munich, Germany
martin.dichgans@med.uni-muenchen.de

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Thymectomy in myasthenia gravis: when, why, and how?

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Myasthenia gravis is an autoimmune disease mediated by antibodies against proteins expressed in the neuromuscular junction; the main antigen is the acetylcholine receptor. In patients with myasthenia gravis, the thymus can have histological abnormalities, such as follicular hyperplasia or thymoma. Although thymectomy is standard treatment for patients with myasthenia gravis who have thymoma, whether the procedure is of any clinical benefit in patients without thymoma has been questioned for more than 40 years. Many retrospective studies showed that thymectomy might be clinically beneficial, and several meta-analyses supported these findings,[1,2] but a randomised clinical trial was needed. Prof Newsom-Davis (1932–2007), with courage and determination, was able to promote the organisation of an international randomised clinical trial to compare thymectomy plus prednisone with prednisone alone in patients with non-thymomatous myasthenia gravis. The results of the Thymectomy Trial in Non-Thymomatous Myasthenia Gravis Patients Receiving Prednisone (MGTX) were eagerly anticipated, and were first discussed at the MGTX Conference in Oxford, UK, in 2016. The study clearly showed that, after follow-up of 3 years, thymectomy plus prednisone significantly improved clinical outcomes compared with prednisone alone in patients with non-thymomatous myasthenia gravis.[3] In *The Lancet Neurology*, Gil I Wolfe and colleagues[4] now report the results of the two-year extension phase of MGTX, bringing the total follow-up to 5 years. The authors concluded that the benefits conferred by thymectomy plus prednisone, compared with prednisone alone, were still apparent after the 2 years of the extension study. This conclusion was reached on the basis of reductions in mean Quantitative Myasthenia Gravis scores (5·47 [SD 3·87] *vs* 9·34 [5·08]; p=0·0007]) and alternate-day prednisone doses (24 mg [SD 21]