(non-routine) investigations and the extra costs that would be involved.[8]

High-risk patients who could benefit from surgical intervention still need to be identified; these might be patients who are least likely to take prescribed medicines reliably, or those with chronic long-term conditions such as diabetes. Large-scale evidence is needed, and long-term trial follow-up of stroke risk is important. The balance of risk and long-term benefit will be reported again in future trials, including CREST-2, which will include evidence on 4-year stroke risk from unoperated tight stenosis.[9] New stenting technology (such as transcarotid artery revascularisation) is still untested in a randomised trial, although this approach has become widely adopted by US surgeons.[10]

Many patients with symptomatic or asymptomatic carotid artery stenosis undergo surgical interventions every year. When strokes from carotid stenosis occur without warning, about half these patients are seriously disabled or die, and surgery or stenting to prevent future events is not indicated for these patients with disability. Asymptomatic patients with severe stenosis have similar risk factors to those with heart disease, and population screening is not currently recommended. Although stenting and surgery have similar 5-year risks and benefits, the stroke risk for those on medical treatment alone will need further evidence from long-term follow-up, to enable comparison of all three treatments over 10 years.

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1 Brott TG, Calvet D, Howard G, et al. Long-term outcomes of stenting and endarterectomy for symptomatic carotid stenosis: a preplanned pooled analysis of individual patient data. *Lancet Neurol* 2019; **18:** 348–56.
2 Halliday A, Bulbulia R, Bonati LH, et al. Second asymptomatic carotid surgery trial (ACST-2): a randomised comparison of carotid artery stenting versus carotid endarterectomy. *Lancet* 2021; **398:** 1065–73.
3 Reiff T, Eckstein H-H, Mansmann U, et al. Carotid endarterectomy or stenting or best medical treatment alone for moderate-to-severe asymptomatic carotid artery stenosis: 5-year results of a multicentre, randomised controlled trial. *Lancet Neurol* 2022; **21:** 877–88.
4 Eckstein HH, Reiff T, Ringleb P, et al. SPACE-2: a missed opportunity to compare carotid endarterectomy, carotid stenting, and best medical treatment in patients with asymptomatic carotid stenoses. *Eur J Vasc Endovasc Surg* 2016; **51:** 761–65.
5 Brott TG, Howard G, Roubin GS, et al. Long-term results of stenting versus endarterectomy for carotid-artery stenosis. *N Engl J Med* 2016; **374:** 1021–31.
6 Rosenfield K, Matsumura JS, Chaturvedi S, et al. randomized trial of stent versus surgery for asymptomatic carotid stenosis. *N Engl J Med* 2016; **374:** 1011–20.
7 Howard DPJ, Gaziano L, Rothwell PM. Risk of stroke in relation to degree of asymptomatic carotid stenosis: a population-based cohort study, systematic review, and meta-analysis. *Lancet Neurol* 2021; **20:** 193–202.
8 Naylor AR, Ricco JB, de Borst GJ, et al. editor's choice - management of atherosclerotic carotid and vertebral artery disease: 2017 Clinical Practice Guidelines of the European Society for Vascular Surgery (ESVS). *Eur J Vasc Endovasc Surg* 2018; **55:** 3–81.
9 Howard VJ, Meschia JF, Lal BK, et al. Carotid revascularization and medical management for asymptomatic carotid stenosis: protocol of the CREST-2 clinical trials. *Int J Stroke* 2017; **12:** 770–78.
10 Schermerhorn ML, Liang P, Eldrup-Jorgensen J, et al. Association of transcarotid artery revascularization *vs* transfemoral carotid artery stenting with stroke or death among patients with carotid artery stenosis. *JAMA* 2019; **322:** 2313–22.

Long-term disability after transient ischaemic attack or minor stroke

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Disability is not an unexpected outcome after a stroke and, in people aged 75–80 years, functional decline is a common outcome, which can be associated with other comorbidities. Whether disability is an inevitable result of normal ageing, and if the process of functional decline can be prevented or halted, are questions that remain to be answered.

In *The Lancet Neurology*, Cristina Hobeanu and colleagues[1] report 5-year follow-up data from TIAregistry.org, an international, prospective observational registry that included 3105 patients with transient ischaemic attack or minor ischaemic stroke and no disability (modified Rankin Scale [mRS] score of ≤1) at baseline,[2] with the aim to investigate factors associated with poor functional outcome. All study sites that provided data for the registry had dedicated care systems for people with transient ischaemic attack, with care delivered by stroke specialists. Prescription and sustained use of pharmacological secondary prevention were high in this population, probably higher than in any clinical setting.

Despite having no disability immediately after transient ischaemic attack or minor stroke, more than one in five patients (710 [22·9%] of 3105) had developed

disability (mRS score of >1) by 5 years of follow-up, frequently after recurrent stroke.[1] Patients with new disability were, on average, 11 years older (mean age 74·9 years [SD 10·8] at baseline) than those without disability (age 63·9 years [12·6]). Living alone also contributed to the risk of new disability. Recurrent stroke or intracranial haemorrhage had occurred in 184 (25·9%) of 710 patients with disability at 5 years, compared with 144 (6·0%) of 2395 patients who did not have disability. These strokes occurred despite the reported high and sustained use of pharmacological secondary prevention in the cohort. Patients with disability at 5 years had a far higher burden of risk factors, including smoking, alcohol consumption, and cardiovascular comorbidities compared with those without disability at 5 years.

Findings of the 2018 US National Health Interview Survey[3] showed that a physical difficulty (defined as respondents answering at least once "very difficult" or "can't do at all" after performing nine physical activities) was present in 19·0% of people aged 45–64 years, in 30·0% of those aged 65–74 years, and in 48·6% of those aged 75 years or older. From this perspective, the increase in disability after transient ischaemic attack or minor stroke that was recorded by Hobeanu and colleagues[1] is not high—most likely because only patients with an mRS score of 0–1 at baseline were included in the cohort. The aim in clinical care, however, is not to achieve average disability, but to reduce disability to a minimum in every individual presentation.

Hobeanu and colleagues[1] also reported that the risk of long-term disability was reduced by half with regular physical activity before the index event. It is well known that physical activity after stroke reduces the risk of recurrent stroke and poor outcome in a dose-dependent manner.[4] However, people with stroke seem less physically active than people of the same age without stroke.[5] These findings therefore highlight the importance of reducing physical inactivity and identifying efficient means of doing so.[6]

Development of new and effective drugs for prevention of stroke, including factor XIa inhibitors,[7] could provide better risk reduction for patients who adhere to treatment compared with available drugs. Nevertheless, improvements in drug treatment alone are unlikely to halt stroke incidence. The risk factors and causes of stroke are heterogeneous, as are outcomes after stroke, implying that the absolute benefit of a specific drug—as well as the risk–benefit ratio—will vary between patients. One approach could be to investigate secondary prevention on the basis of risk factors and cause of stroke, which could entail interventions targeting specific subgroups—eg, patients with large-vessel disease. This approach could also include provision of appropriate support for patients with risk factors (eg, living alone) and focus on non-pharmacological interventions, including regular physical activity.

The findings reported by Hobeanu and colleagues[1] highlight that, even in people with excellent early outcome after transient ischaemic attack and who were receiving pharmacological secondary prevention, functional decline at 5 years is frequent and often related to recurrent stroke. The incidence of strokes and the number of people living with stroke are increasing and expected to rise for years to come.[8] Presently, it is unlikely that most stroke patients (even in high-income regions, such as Europe) receive the dedicated care that was provided for the cohort reported by Hobeanu and colleagues. Implementation of primary and secondary prevention with a population-wide strategy are urgently needed and would be highly cost-effective for societies.[9,10]

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1 Hobeanu C, Lavallée PC, Charles H, et al. Risk of subsequent disabling or fatal stroke in patients with transient ischaemic attack or minor ischaemic stroke: an international, prospective cohort study. *Lancet Neurol* 2022; **21:** 889–98.
2 Amarenco P, Lavallée PC, Tavares LM, et al. Five-year risk of stroke after TIA or minor ischemic stroke. *N Engl J Med* 2018; **378:** 2182–90.
3 National Center for Health Statistics. Crude percentages of any physical difficulty for adults aged 18 and over, United States, 2015–2018. National Health Interview Survey. July 18, 2022. https://www.cdc.gov/nchs/nhis/ADULTS/www/index.htm (accessed Aug 22, 2022).
4 Hou L, Li M, Wang J, et al. Association between physical exercise and stroke recurrence among first-ever ischemic stroke survivors. *Sci Rep* 2021; **11:** 13372.
5 Krarup L-H, Truelsen T, Pedersen A, et al. Level of physical activity in the week preceding an ischemic stroke. *Cerebrovasc Dis* 2007; **24:** 296–300.
6 Boysen G, Krarup L-H, Zeng X, et al. ExStroke Pilot Trial of the effect of repeated instructions to improve physical activity after ischaemic stroke: a multinational randomised controlled clinical trial. *BMJ* 2009; **339:** b2810.
7 Heitmeier S, Visser M, Tersteegen A, et al. Pharmacological profile of asundexian, a novel, orally bioavailable inhibitor of factor XIa. *J Thromb Haemost* 2022; **20:** 1400–11.
8 Wafa HA, Wolfe CDA, Emmett E, Roth GA, Johnson CO, Wang Y. Burden of stroke in Europe. *Stroke* 2020; **51:** 2418–27.
9 Owolabi MO, Thrift AG, Mahal A, et al. Primary stroke prevention worldwide: translating evidence into action. *Lancet Public Health* 2022; **7:** e74–85.
10 Bertram MY, Sweeny K, Lauer JA, et al. Investing in non-communicable diseases: an estimation of the return on investment for prevention and treatment services. *Lancet* 2018; **391:** 2071–78.