

## EDITORIALS

## How early can cognitive decline be detected?

Possibly when people are in their 40s, so preventive efforts need to start much earlier

Francine Grodstein *associate professor of medicine*

Department of Medicine, Brigham and Women's Hospital, Boston, MA 02115, USA

In the linked study (doi:10.1136/bmj.d7622), Singh-Manoux and colleagues present new analyses that track changes in cognitive function in several cohorts of men and women aged 45-70 years within the Whitehall II study.<sup>1</sup> The study has several strengths including repeated measures of cognitive function over a decade of follow-up across multiple cognitive domains. Using these data, the authors convincingly show that decline can be detected in almost all the cognitive domains tested during follow-up, even in the youngest participants—those aged 45-49 years.

To understand the importance of the findings it is necessary to appreciate the link between cognitive function and the clinical syndrome of dementia. Although cognitive function is not itself a defined clinical entity, and it can be difficult to understand the meaning of small changes in cognition over time, previous data show that modest differences in cognitive performance in earlier life predict larger differences in risk of dementia in later life. For example, in one neuropathological study, cognitive performance strongly predicted a pathological diagnosis of Alzheimer's disease over six years of follow-up, with an overall diagnostic accuracy of 75%.<sup>2</sup> Consistent findings have been observed over much longer follow-up periods. For example, in the Framingham study, performance on tests of verbal memory strongly predicted the development of Alzheimer's disease up to 22 years later—each one standard deviation difference in baseline performance increased the risk of Alzheimer's disease by 60% (relative risk 1.57, 95% confidence interval 1.31 to 1.87).<sup>3</sup>

Thus, Singh-Manoux and colleagues' study suggests that it may be possible to identify those at increased risk of dementia as early as in their 40s (although no existing studies track the risk of dementia according to cognitive status at such young ages, so the findings can only be extended in theory from older people to the younger adults in the Whitehall II study). This finding potentially has profound implications for prevention of dementia and public health. As yet, there is no cure for dementia, and accumulating evidence indicates that effective interventions will need to be administered long before marked neurodegeneration has occurred.<sup>4</sup>

By pinpointing cognitive decline in younger adults, Singh-Manoux and colleagues have set a new benchmark for

future research, and eventually clinical practice. That is, efforts to prevent dementia may need to start in adults as young as 45 years. Most current research into dementia has focused on people of 65 years and older. The major challenge will be to design prospective research studies that include much younger age groups—a dramatic change from the status quo. The main difficulty of achieving this will be the modest differences in cognition that are expected across risk factors for cognitive decline in middle aged people (in contrast to the larger differences at older ages).

Research that aims to understand risk factors for, and determinants of, cognitive decline beginning at middle age will need to incorporate relatively large sample sizes, probably tens of thousands of participants, to be able to detect the variables that influence brain health at these younger ages. The use of face to face cognitive interviews, the current standard in the field, will be difficult for such large investigations.

Some research exists in the evaluation of new research methods for assessing cognitive function in large samples,<sup>5</sup> such as the use of telephone cognitive batteries. Validation studies comparing results from telephone instruments versus face to face cognitive interviews have shown the resulting data to be similar.<sup>5</sup> Telephone instruments have important strengths, especially for large studies, including their ease of administration and modest cost. But they also have weaknesses, such as the inability to conduct certain neuropsychological tests over the phone (for example, tests that require visual cues). However, future research might explore ways in which certain tests could be adapted for telephone use. Other options, especially in younger people, include the use of computerised cognitive assessments, which could be done at the participant's convenience and have other strengths including the uniformity of administration and scoring.<sup>6</sup> Wide use of computers in cognitive assessments, especially in younger populations, has not yet been attempted, however, and more research is needed to evaluate its effectiveness fully.

We are entering a new era of research and prevention in dementia. There is probably greater hope of identifying ways to intervene in the development of dementia, but the challenge will be to change the status quo and find creative approaches to a slightly different research agenda.

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