The use of wide-scale mental agility testing to identify people at risk of dementia: crucial or harmful?

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ABSTRACT The prevalence of dementia in the UK is rising rapidly and is predicted to double over the next 30 years. The NHS in England has been told to push for a rapid rise in dementia diagnosis rates, so that by 2015, two out of three cases are identified. The Prime Minister has raised the ‘dementia challenge’ as a priority for the NHS. While there is agreement on the need for action, debate arises over the nature of that intervention. Some, including Professor Alessi, argue that tools exist to support the diagnosis of mild cognitive impairment and they should be used because the disease is amenable to interventions. He believes that we need a shift in knowledge and attitude from thresholds to a continuum of cognitive impairment, from late to early stages and from effects to causes. The Montreal Cognitive Assessment (MoCa) should become part of the routine NHS Health Check after people reach age 40. Dr Fox argues on the other hand that widespread testing could lead to unnecessary anxiety and panic among those at risk and that funding should be focused on learning more about the early stages of dementia. While the concept of early testing is appealing, there is a large knowledge gap; instruments in use have not been tested in pre-dementia patients and have limited validity. While there is debate over the approach, we can agree that the economic and social impacts of this condition need to be addressed sooner rather than later.

KEYWORDS Diagnosis, prevention, testing, dementia

DECLARATIONS OF INTERESTS Dr Fox is part of an NHS England task force on improving diagnosis. He is also a coordinator of a Medical Research Council prevention and screening platform in dementia research group. Dr Fox was funded by the Alzheimer’s Society for a systematic review on screening in dementia. Dr Alessi is the lead on preventable dementia for Public Health England. Dr Ahluwalia reports he will be a co-applicant on a grant request to the NIHR (to be submitted) looking to study the role of vascular risk factor modification on dementia prevention.

Wide-scale mental agility testing should not be introduced to identify people at risk of dementia

C Fox

ABSTRACT There are increasing pressures to consider diagnosing dementia at an early pre-syndrome stage where it is suggested prevention strategies could be deployed. However there are problems with current assessment tools and there is no good evidence that any preventative strategy is effective in dementia; rather that there are general health benefits. This paper will consider the problems and suggest the key considerations for those making such decisions.

With the level of dementia globally currently at 44 million and by 2050, 135 million people, the need for game changing interventions is recognised by governments and scientists the world over.1,2 Sadly attempts over the last 20 years, with considerable investment, have yet to progress to that goal.3 Current pharmacologic therapy for Alzheimer’s dementia only provides the minority of patients short-term improvement, for a perhaps six to 18 months.2
DIAGNOSTIC DEAD ENDS

There is a new focus on exploring the very early/pre-dementia states. Indeed the 5th edition of the *Diagnostic and Statistical Manual of Mental Disorders (DSM 5)* has introduced a new category of minor neurocognitive disorder. This goes beyond normal issues of ageing. To be diagnosed with this disorder, there must be changes that impact cognitive functioning which are usually observed by the individual, a close relative, or other knowledgeable informant, such as a friend, colleague, or clinician, or they are detected through objective testing – where any formal testing clinical evaluation lies more than one standard deviation below appropriate norms. Under this definition nearly one in five people will be defined as having this disorder. The introduction of routine memory testing could increase the levels of people so labelled if started from age 40 onwards.

So what would this mean? This would label people with a condition that has as yet no treatment and there is no definitive phenotyping on those who will progress to dementia. The majority of people so labelled will either remain stable and some may even improve over time. This risks harm in creating worry and over-investigating patients who need no such response.

Specific impacts include:

1. For the individual there is recognition that this could lead to anxiety and depression, stigma, the loss of life/health insurance coverage, driving privileges, or employment. They could develop identity concerns, for example ‘will I be able to support my family?’ and feelings of loss, anger, uncertainty, and frustration.

2. For the family of the person so tested, this could have a devastating impact on relationships and financial concerns.

PREVENTION: OPPORTUNITY VERSUS UNKNOWNS

The greatest risk factor for dementia is age, with a doubling of the rate of people with both Alzheimer’s and vascular dementia every five years over the age of 65. The commonest late-onset dementias are moderately heritable. Most individual genes increase risk by only a small amount; the apolipoprotein e4 allele confers a three- to four-fold increase in risk for Alzheimer’s and a smaller increase in the risk of vascular dementia. Genes and dementias are understood in 500 families but 35 million people worldwide have dementia. Genes can best be seen as impacting on a small number of high-risk mendelian families; the majority are low-risk.

There is a growing area of research looking at preventative strategies for dementia. However there are complications, as evidence suggests that while hypertension, raised cholesterol and obesity in midlife increase the risk for later onset of dementia, blood pressure levels, cholesterol and body mass index fall progressively before the onset of the dementia (Table 1). Hence people with dementia have lower blood pressure levels, cholesterol and body mass than others. Therefore, early primary prevention may be the most effective intervention. Preventive trials indicate that statins and antihypertensive treatment do not seem to lower the incidence of dementia when initiated in older people, but there have been no long-term trials from midlife onwards. In addition there is a lack of any

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**TABLE 1 Cochrane-registered prevention reviews, January 2014**

<table>
<thead>
<tr>
<th>Review</th>
<th>Comment</th>
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<tbody>
<tr>
<td>Cognitively impaired</td>
<td></td>
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<tr>
<td>Cognitive training</td>
<td>No difference active vs control</td>
</tr>
<tr>
<td>Diabetes management</td>
<td>No conclusions</td>
</tr>
<tr>
<td>Physical activity</td>
<td>Protocol stage</td>
</tr>
<tr>
<td>Donepezil/galantamine/rivastigmine</td>
<td>Little evidence</td>
</tr>
<tr>
<td>Folic acid/B12</td>
<td>Folic acid use with B12 in those with high homocystine may benefit</td>
</tr>
<tr>
<td>Ginkgo biloba</td>
<td>No evidence</td>
</tr>
<tr>
<td>Procaine</td>
<td>No evidence</td>
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<tr>
<td>Lecithin</td>
<td>One small study showed benefit on cognition</td>
</tr>
<tr>
<td>Melatonin</td>
<td>No evidence</td>
</tr>
<tr>
<td>Nicergoline</td>
<td>No evidence</td>
</tr>
<tr>
<td>Piracetam</td>
<td>More research needed</td>
</tr>
<tr>
<td>Vinpocetine</td>
<td>Inconclusive</td>
</tr>
<tr>
<td>Vitamin B12</td>
<td>No evidence</td>
</tr>
<tr>
<td>Vitamin B6</td>
<td>No evidence</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>Should not be used</td>
</tr>
<tr>
<td>Cognitively intact</td>
<td></td>
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<tr>
<td>Cognitive training</td>
<td>No difference active vs control</td>
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<tr>
<td>Diabetes management</td>
<td>No evidence</td>
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<tr>
<td>Blood pressure</td>
<td>Late life no convincing evidence</td>
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<tr>
<td>L-Carnitine</td>
<td>Protocol stage</td>
</tr>
<tr>
<td>Dehydroepiandrosterone</td>
<td>No evidence</td>
</tr>
<tr>
<td>Hormone replacement therapy</td>
<td>Insufficient evidence</td>
</tr>
<tr>
<td>Omega 3 fish oils</td>
<td>No benefit</td>
</tr>
<tr>
<td>Procaine</td>
<td>No evidence</td>
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<tr>
<td>Statins</td>
<td>Not recommended</td>
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<td>Statins</td>
<td>Not recommended</td>
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<tr>
<td>Statins</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Vitamin B6</td>
<td>No evidence of benefit</td>
</tr>
</tbody>
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*The use of wide-scale mental agility testing to identify people at risk of dementia: crucial or harmful?* J R Coll Physicians Edinb 2014; 44:30–5 © 2014 RCPE
randomised clinical trials replicating observational studies, which have implemented prevention strategies for dementia using identified risk-modifying behaviors.

Secondary prevention of vascular dementia, for example using angiotensin-converting enzyme inhibitors, can significantly prevent further strokes and subsequent cognitive decline. Studies with non-steroidal anti-inflammatory drugs, vitamin E and folic acid/vitamin B12 aiming to prevent dementia among the general elderly population, or to prevent worsening of symptoms among individuals with dementia, have mostly failed. These negative findings may reflect the effect on observational studies of reverse causality; for example, those with early stages of cognitive decline are probably less likely to eat well and take part in exercise. Other confounders include personality and co-morbid conditions. These studies have included middle aged participants and the failure of these trials may mean that attempts to prevent dementia need to start earlier than midlife, and last longer, than any so far conducted.

So, as yet there are no specific evidence-based prevention strategies recommended to prevent dementia and the optimal time to start is unclear — old age, middle age or childhood.

Based on statistical associations, current suggestions for reducing the risk for dementia throughout the lifespan include:

1. Avoid passive parental smoking in childhood.
2. Detect and treat attention deficit hyperactivity disorder in adolescence and adulthood.
3. Stay in education to adulthood/working age.
4. Optimise diet and nutrition.
5. Exercise regularly.
6. Detect and treat depression, thyroid disease, hormone and vitamin deficiencies from adulthood to old age.
7. Avoid smoking.
8. Maintain a healthy weight from middle age onwards.
10. Maintain cognitive activity from middle age onwards.
11. Use cognitive compensation strategies and devices in retirement.

Before population-based recommendations can be made we need to demonstrate causality, efficacy, and ultimately, cost-effectiveness in large scale randomised controlled trials of sufficient duration.

**ROUTINE TESTING**

The concept of regular testing from age 40 onwards is conceptually appealing, however there is a large knowledge gap. The measures currently available are many and varied. There are several competing concepts in the development of tools that have use in routine testing: they have to be sensitive and specific and valid in the population. Instruments in current use have not been tested in pre-dementia populations and therefore have limited validity in the decades before the usual presentation of dementia. Technology platforms such as diagnostic support aids offer an important solution but need further research as there are accuracy and reliability issues with consequent help-seeking behaviours being reduced due to false negative (and thus reassuring) results, or generating unnecessary distress by false positive results.

Several limitations of online instruments are recognised. First, in an effort to keep them brief (and encourage completion), content has to be restricted, which can escalate the false positive rate. Second, although internet-based assessments are becoming increasingly prevalent and results demonstrate good validity, the conditions of administration are not controlled and there is no way to ensure legitimate results. It is certainly feasible that some participants in validation studies of online measures do not respond truthfully to questions or violate instructions to obtain higher scores on the memory test. Alternatively, poor performances may be due to environmental distractors or waning motivation, rather than genuine memory impairment. Serious issues may arise if people believe incorrectly that any online screening test is valid and behave in accordance with the results, as there is the potential to decrease help-seeking behaviours in the case of false negative errors, or cause unnecessary distress if false positive errors occur. In addition, the resulting effect of further investigations on the health service in terms of time and cost for no benefit at present, appears futile.

**CONCLUSIONS**

While testing from age 40 years alongside routine co-morbidity screening appears logical there are serious consequences for patients, their families, society and the healthcare system. Misdiagnosis rates of 41% in working age people have recently been reported.

We have to be mindful there are vested interests advocating earlier routine testing including:

- Geneticists looking for genes that can be patented.
- Companies selling their memory tests.
- Pharmaceutical companies looking for more ‘diagnosed’ persons with dementia to increase use of ‘treatment’ drugs.
- Pharmaceutical companies marketing neuroimaging testing.

We may, as was stated at the G8 Dementia Conference, achieve a pharmaceutical breakthrough which could help
some patients, but many believe that what is needed is more research on the tools, on people with early cognitive impairment and on the harms and benefits. If we can prepare the ground then when a breakthrough occurs, society will be ready to respond. This requires randomised controlled trials in large samples and for extended periods; three to four years of follow-up studies would provide the answers to many as yet unasked questions. Without a sound scientific basis we risk harming people and wasting time and money to the detriment of the entire healthcare system.20

**SELECTED REFERENCES**


2 Department of Health. G8 dementia summit concludes with international agreement to work together [Internet]. London: Department of Health; 2013 [cited 2014 Jan 24]. Available from: http://dementiachallenge.dh.gov.uk/2013/12/12/g8-dementia-summit-agreements/


Wide-scale mental agility testing should be introduced to identify people at risk of dementia

C Alessi, S Ahluwalia, V Hachinski

The Secretary of State for Health in the UK published his state of the nation report on dementia in November 2013. It is predicted that with a rapidly ageing population, the prevalence of dementia is likely to increase over the next 30 years and to rise sharpest in those from ethnic minorities; it accounts for 2.5% of premature years of life lost and costs the English economy nearly £19 billion per year. Its social impact is profound, with nearly 550,000 people acting as carers for those with dementia.

The standard approach to diagnosing dementia in patients with early symptoms is based on the mini-mental state examination (MMSE). However, this test is both time consuming, and more importantly, misses nearly 80% of patients with mild cognitive impairment i.e. those with memory problems but without significant functional disability. Annually, 10–15% of patients with mild cognitive impairment go on to develop dementia associated with functional deficits.

The issue of early diagnosis is mired in controversy as evidenced by the recent lively discussion generated by Coutier et al’s article in the British Medical Journal. This variance in opinion about the need for an early diagnosis of dementia is reflected in the rates of diagnosis for people living with dementia varying from 39% in the worst performing areas to 75% in the best performing areas.

In the past decade a number of valid and reliable tools have emerged to support the diagnosis of mild cognitive impairment. These include the memory impairment screen, the General Practitioner Assessment of Cognition, and the Montreal Cognition Assessment test. These tools are based upon the assessment of higher order executive functions (e.g. mental agility testing) and take less than 10 minutes i.e. the standard length of a GP consultation.

These tools will increasingly play an important role as evidence emerges that the prevalence of dementia may be dropping, possibly as a result of early intervention. The Cognitive Function and Aging Study and another study by Christensen et al. compared prevalence in two population cohorts born more than 10 years apart from the United Kingdom and Denmark. The researchers used the same diagnostic and methodological techniques for studying both population cohorts. Both study groups found reductions in the prevalence of dementia in the cohort born later. It suggests that the disease process is amenable to interventions. The authors identify a number of reasons for the differences seen in prevalence rates. These include the role of better lifestyles (including healthier diets and exercise), more intellectually stimulating environments and the modification of vascular risk factors.

The link between neurodegenerative and vascular factors is supported by neuropathological studies. Toledo et al. studied the association between neurodegenerative conditions and cerebrovascular changes through an analysis of pathological specimens of patients diagnosed with dementia. The size of the population was large, with more than 6,000 patient brain tissues studied. They found that changes related to cerebrovascular disease were common in aged patients diagnosed with dementia, and that these changes were higher in patients with Alzheimer’s compared to other neurodegenerative conditions with a prevalence ranging from 60% in frontotemporal dementia to 80% in Alzheimer’s. The results of this study and others support the notion that cerebrovascular and neurodegenerative processes are ‘mutually influencing and closely interacting’.

Current evidence on interventions for slowing the progression of dementia are mixed. Chertkow et al. reviewed the current state of evidence in the treatment of mild cognitive impairment. There was strong evidence for benefit from treating hypertension, but no benefit associated with use of aspirin or lipids. There is no randomised control trial data for managing other vascular risk factors and their influence on the development or progression of dementia.

Studies involving cholinesterase inhibitors and N-methyl-D-asparate (NMDA) receptor inhibitors did not show any influence on the development of cognitive impairment in the elderly. Similarly, hormonal therapy, anti-inflammatories, vitamin E, and ginkgo biloba had no effect on progression in patients with mild cognitive impairment. By contrast, evidence from randomised control trials of exercise and cognitive stimulation therapy demonstrated positive benefit in improving executive functions and mixed evidence of progression of dementia.

The variations in levels of diagnosis and care provided in general practice have also been explored through research. Attitudes of GPs to early diagnosis, levels of knowledge about dementia and its treatment, and the organization of care all have an impact on variation seen in the UK.
Connolly et al.\textsuperscript{14,15} assessed the quality of care provided to patients with dementia in general practice. Their results pointed to the poorer quality of care provided to patients with vascular dementia. This included a greater likelihood of inappropriate monitoring and prescribing of medications. Patients with vascular dementia were more likely to receive poorer care if they were registered with a single-handed GP surgery. Ahmad et al.\textsuperscript{16} identified that older GPs were more likely to be more confident in diagnosing dementia but less likely to identify benefits from early intervention, whereas younger GPs were more likely to believe that more could be done. All GPs felt that there was a need for greater training in dementia, and that their knowledge levels were low.

The emergent evidence from epidemiological, neuropathological, and therapy orientated research poses a number of challenges for clinicians and researchers. There is an urgent need through research to understand the contribution of vascular mechanisms to the development of dementia, the role of multi-modal vascular modification in patients at risk of developing dementia, identify non-invasive approaches to diagnose and monitor progression of dementia and the influence of therapies on the course of dementing illness, and the most effective organisational and contractual approaches to improving access and care for patients with dementia.

The current state of the literature does not provide us with enough evidence to argue for a systematic screening programme in asymptomatic adults. However, we would argue that there is much that clinicians can do now. The potential to delay or even prevent symptoms of dementia is something primary care needs to be engaged in by actively managing vascular risk. The availability of tools for recognising mild cognitive impairment offers the opportunity to identify and monitor those at greatest risk of developing dementia; the emergent role of neurovascular disease as a key contributor to dementia offers the opportunity to intervene in slowing its progression through the judicious use of tested therapies such as better blood pressure control and psychological and social interventions. All this is dependent upon acknowledging and recognising that dementia is a condition for which something can be done. This shift in knowledge and attitude among clinicians is long overdue. Emphasis needs to shift from thresholds to a continuum of cognitive impairment, from late to early stages and from effects to causes.\textsuperscript{17}

REFERENCES


