Population-based screening for dementia: controversy and current status

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Background
With our ageing population, the prevalence of dementia is expected to double every decade; global burden of disease is estimated to reach 81.1 million by 2040.1 However, by 2014 only around 40% of people with dementia in the UK were thought to have been diagnosed. There are government drivers to increase diagnosis in the National Dementia Strategy (2009)2 and the more recent focus on primary care diagnosis with GPs in England being paid £55 for each patient diagnosed and recorded with dementia.3 However, population screening for dementia is controversial,3 with concerns raised over why the government continues to push for ‘case finding’ in dementia after the UK National Screening Committee (UKNSC) recently reiterated its view that none of the current tests used in practice distinguished sufficiently between those with and without dementia.4

What is needed for screening?
Screening is defined as ‘a process of identifying apparently healthy people who may be at increased risk of a disease or condition’ with the aim that ‘they can then be offered information, further tests and appropriate treatment to reduce their risk and/or any complications arising from the disease or condition’.5 The UK screening criteria are based upon those laid down by the World Health Organization in 1968.6

In essence, the test should be cheap, easy to administer, nearly 100% sensitive in detecting all true positives and detection should lead to an effective and simple intervention. With a long preclinical phase most types of dementia would be amenable for intervention at an early stage, but there remain problems with identifying appropriate screening tools and effective treatments.

Tests for dementia and options for screening
There are difficulties with diagnosing ‘dementia’, not least because it is not a single disease entity. For most subtypes of dementia, the gold standard for diagnosis is neuropathology. Expert consensus using validated diagnostic criteria is an acceptable reference standard in research and clinical practice. However, as this involves a lengthy interview, cognitive testing, blood tests and appropriate neuroimaging it is not a simple screening test that could be applied to a whole population.7

Box 1. Wilson and Jungner criteria for population screening6

- The condition should be an important health problem
- The natural history of the condition should be understood
- There should be a recognisable latent or early symptomatic stage
- There should be a test that is easy to perform and interpret, acceptable, accurate, reliable, sensitive and specific
- There should be an accepted treatment recognised for the disease
- Treatment should be more effective if started early
- There should be a policy on who should be treated
- Diagnosis and treatment should be cost-effective
- Case-finding should be a continuous process

Biomarkers and neuroimaging
For Alzheimer’s disease there are some promising biomarkers – cerebrospinal fluid (CSF) amyloid / tau and neuroimaging. However, these are neither cheap, nor easy to administer to populations. Furthermore they do not have 100% sensitivity and specificity, eg the recently licensed amyloid positron emission tomography (PET) is also positive in other dementias, with one study identifying 51% positivity in Lewy body disease, 30% positivity in vascular dementia and 12% positivity in fronto-temporal dementia;8 a negative amyloid PET was found in 12% of those with clinical Alzheimer’s dementia and the likelihood of detecting incidental amyloid pathology increased with advancing age (in another study 44% of those aged over 90 years with positive amyloid PET had normal cognition).9

Magnetic resonance imaging (MRI) data have proved unhelpful in predicting who will develop dementia versus conventional risk modelling (using variables such as age, sex, education, cognition, physical function, smoking, alcohol use, cardiovascular disease, diabetes, systolic blood pressure, and the apolipoprotein genotype).10

Other problems with biomarkers include the lack of a standard
cut off point for differentiating between Alzheimer’s and control and variation in measurements between laboratories. Although there has been significant progress due to global collaborative research, the limitations mean that these tests remain unsuitable for use in population screening. Thus the only current option for population screening is cognitive screening tests.

**Cognitive screening tests**

Most of the tests have been validated in clinical rather than population samples. Additionally, few of these have been validated in primary care settings, where they are most likely to be used. There is also evidence of education, cultural or language bias in many of the tests used, making them unsuitable for whole population screening. Literature reviews have demonstrated a wide range of sensitivity and specificity scores for many of the tests, and optimum cut-off levels for dementia have not been validated in most.

<table>
<thead>
<tr>
<th>Cognitive screening test</th>
<th>Evidence for test</th>
<th>Pros</th>
<th>Cons</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMT</td>
<td>3 minutes to administer</td>
<td>Some studies had even wider ranging CIs for sens / spec suggesting optimal cut off points may vary by language, culture or education</td>
<td>Range: 42–100 (95% CI 31–99.8)</td>
<td>Range: 83–95.4 (95% CI 89–97.3)</td>
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<tr>
<td>CDT</td>
<td>2 minutes to administer</td>
<td>Different scoring methods and cut-off points used in various studies; optimal cut-off point unclear</td>
<td>Range: 67–97.9 (95% CI 39–100)</td>
<td>Range: 69–94.2 (95% CI 54–97.1)</td>
<td></td>
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<tr>
<td>GPCOG</td>
<td>4.5 minutes to administer Translated and validated in French and Italian</td>
<td>Population used to validate had 29% dementia prevalence (higher than 15% &gt;75s likely in GP sample) Some education bias Test performance not reproduced in primary care relevant populations</td>
<td>85&lt;sup&gt;12&lt;/sup&gt;</td>
<td>86&lt;sup&gt;12&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>MIS</td>
<td>4 minutes to administer Evaluated as having no education/language or cultural bias</td>
<td>Best quality studies showed worst sensitivity data (43% and 49%)</td>
<td>Range: 43–86 (95% CI 24–96)</td>
<td>Range: 93–97 (95% CI 56–100)</td>
<td></td>
</tr>
<tr>
<td>MMSE</td>
<td>Well known and understood</td>
<td>Educational/language/cultural bias Takes too long to administer (10mins)</td>
<td>Pooled estimate: 88.3 (95% CI 81.3–92.9)</td>
<td>Pooled estimate: 86.2 (95% CI 81.8–89.7)</td>
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</tr>
<tr>
<td>Mini COG (CDT plus 3- item word recall)</td>
<td>2-4 mins to administer Evaluated as having no education/language or cultural bias</td>
<td>Different cut off points between studies; optimal cut-off point unclear</td>
<td>Range: 76–100 (95% CI 54–100)</td>
<td>Range: 54–85.2% (95% CI 43–88.4)</td>
<td></td>
</tr>
</tbody>
</table>

Key: AMT – Abbreviated Mental Test score; CDT – Clock Drawing Test; GPCOG – General Practitioner Assessment of Cognition; MIS – Memory Impairment Screen; MMSE – Mini-Mental State Examination
Differences in prevalence rates for dementia between age groups mean that positive and negative predictive values (PPV / NPV) vary greatly depending on the age, with very low PPVs in younger age groups where the prevalence is lower. Many of the short cognitive screens assess only verbal, rather than verbal and performance (eg drawing, writing, manipulating) measures. Memory is by far the most tested function, but will not pick up all cases. Few tools include any assessment of executive function. Short tests are less sensitive for identifying rarer subtypes of dementia, including frontal dementias.

Research has shown that few GPs screen for dementia even in at-risk age groups or when cognitive decline is suspected, with lack of time, lack of a cure and lack of a suitable screening tool frequently cited as reasons. With GP consultations averaging 10 minutes, tools that take five minutes or less to administer are likely to be most used (see Table 1).

Several reviews have identified the Mini-cog, GPCOG and MIS as sensible tools, on the grounds that they were validated in a community, primary care or population sample, were simple and quick to administer and performed better than MMSE on misclassification rates and negative predictive value. However, even these have widely varying sensitivity rates for picking up true positives. GPCOG data have still not been reproduced in a primary care setting.

Self-administered tests such as Test Your Memory (TYM) and tests which assessed functional status or activities of daily living were not included in many reviews as they were not considered cognitive tests, but it is possible that these are options for identifying early dementia.

The independent UK NSC review\(^7\) concluded that there were several brief screening instruments that could be used in primary care, which had an adequate test performance in detecting dementia but cut-off points were often not validated and that wide ranges of sensitivity and specificity were seen between studies.

**Current consensus**

Available research and opinion currently suggests that the use of screening tests in the general population, even in those over a certain age, is not helpful. This is partly related to the intrinsic characteristics of the cognitive screening tools, which are not particularly sensitive, especially for identifying the early stages of dementia. False positives could lead to unnecessary treatments (potentially leading to harms) and increased treatment costs; they may also lead to undertreatment of differential diagnoses including depression. False negatives could lead to misleading reassurance. There remains a lack of understanding of the natural progression of dementia from latent to declared disease, including how mild cognitive impairment (MCI) fits into this picture and which individuals with MCI may progress to dementia, hence identifying prodromal illness is still elusive.\(^2\)

However, the crux of the argument remains that there is no meaningful disease-modifying treatment for dementia; interventions such as controlling cardiovascular risk factors for vascular dementia and memory enhancing drugs for Alzheimer’s dementia are argued to have little overall benefit, with early diagnosis only bringing ‘stress and fear’.\(^15\) As well as a lack of medical therapies, it is felt that there is a general lack of talking therapies and social support for both patients and carers, which may be of benefit in improving quality of life. The National Dementia Strategy remarked upon a ‘marked reluctance’, particularly in primary care, to be involved in dementia diagnosis due to the belief that little can be done, concerns about their own competency and concerns about the availability of resources.\(^16\) This should be weighed against evidence that suggests that early diagnosis followed by brief educational intervention significantly improved quality of life for both patients and carers, as well as delaying institutionalisation (which recouped the costs of the memory assessment service).\(^17\)

**Changing the playing field?**

Longer term research in the follow-up of patients with MCI is likely to give us more information about the natural history of dementia and whether the proportion of people moving from MCI to dementia is likely to make screening justifiable. The advent of the first disease-modifying agents which may prevent progression from MCI to dementia, or improve prognosis in dementia, likely to come first in the realm of Alzheimer’s disease, would then alter the balance in favour of screening.

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**Declaration of interests**

No conflicts of interest were declared.

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