

# Screening for dementia: Can screening bring benefits to those with unrecognised dementia, their carers and society? An appraisal against UKNSC criteria

A report for the  
UK National Screening Committee

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# Contents

|                                 |    |
|---------------------------------|----|
| Introduction .....              | 4  |
| The Condition .....             | 5  |
| The Test.....                   | 8  |
| The Treatment .....             | 16 |
| The Screening Programme .....   | 21 |
| Implications for policy.....    | 23 |
| Implications for research ..... | 24 |
| Appendix A .....                | 25 |
| References .....                | 28 |

## Introduction

1. This report reviews screening for all classes of dementia against the UK National Screening Committee (NSC) criteria for appraising the viability, effectiveness and appropriateness of a screening programme (NSC 2003). It is based on a literature search conducted by the NSC in August 2013 (Coles 2013). Full details of the search strategy are set out in Appendix A. It also draws substantially on a review of the evidence for screening for cognitive impairment published by the US Preventative Services Task Force (USPSTF) in October 2013.
2. The focus for this report is to assess 'the evidence for screening for all classes of dementia using cognitive assessment tools as a strategy to reduce morbidity from dementia and to increase the benefit to family and society'. The broad questions to be assessed are:
  - Are there any cognitive assessment tools that are sufficiently valid to be used for population screening for any class of dementia?
  - Are there any interventions that can be offered to people with screen-detected dementia that will reduce morbidity from dementia and/ or increase the benefit to family and society?
3. The population of interest in this review is people in living in the community who are not already suspected of having dementia.
4. In the current review we have used the most recent systematic reviews available. Thus, our primary source has been the 2013 systematic evidence review conducted by the USPSTF, supplemented by additional reviews identified through the NSC literature search that were either published after the USPSTF search date, or which provided additional relevant information that was not directly addressed by the USPSTF review. Individual studies were only used if they post-dated the search that the authors conducted for their systematic review on that topic.
5. A review of screening for Alzheimer's against the UK NSC criteria was completed in 2010. The current policy is that systematic population screening for Alzheimer's disease is not recommended. This current review has been expanded to include all classes of dementia.
6. The NICE clinical guideline on dementia includes the recommendation that general population screening for dementia should not be undertaken (NICE 2006; last updated 2012).
7. The United States Preventative Services Task Force (USPSTF) is currently reviewing their policy on screening for cognitive impairment in older adults (aged over 65 years). Their final recommendation statement (published March 2014) considered that the current evidence is insufficient to assess the balance of benefits and harms of screening for cognitive impairment (Moyer 2013).

## The Condition

### The condition should be an important health problem

8. Dementia is a progressive and largely irreversible clinical syndrome, characterized by impairment of mental function. As the condition progresses people with dementia can experience memory loss, language impairment, disorientation, changes in personality, difficulties with the activities of daily living, self-neglect, psychiatric symptoms (e.g. apathy, depression or psychosis) and out-of-character behaviour (NICE 2006).
9. People with dementia often have a range of complex needs with high levels of dependency and morbidity, which can challenge the skills and capacity of carers and services. As the condition progresses this can include behaviours such as aggression, restlessness and wandering, eating problems, incontinence, delusions and hallucinations and mobility problems (NICE 2006).
10. The number of patients with dementia in the UK has been estimated at 821,884 representing 1.3% of the UK population (Alzheimer's Research Trust 2010).
11. It has been estimated that dementia costs the UK economy £23 billion per year. This breaks down into £12.4 billion in costs for unpaid carers, £9 billion of social care costs, £1.2 billion of health care costs and £29 million in productivity losses (Alzheimer's Research Trust 2010).
12. In summary, dementia is a progressive clinical condition associated with a range of complex needs that can result in high levels of dependency and morbidity. This criterion is met.

### The epidemiology and natural history of the condition, including development from latent to declared disease, should be adequately understood and there should be a detectable risk factor, disease marker, latent period or early symptomatic stage

13. Dementia usually occurs in people aged over 65 years (late-onset dementia) but can occur in younger people (young-onset dementia).
14. The most common forms of late-onset dementia are Alzheimer's disease, accounting for approximately 60% of all cases, and vascular dementia and dementia with Lewy bodies, which together represent about 15-20% of cases. The most common forms of young-onset dementia are fronto-temporal dementia followed by Alzheimer's disease. Other diseases that may cause dementia include Parkinson's and Huntington's, HIV and AIDS, Korsakoff's syndrome, Creutzfeldt-Jakob disease, multiple sclerosis and motor neurone disease (Alzheimer's Research Trust 2010).
15. The early stages of Alzheimer's disease are associated with minor changes in abilities and behaviour such as short-term memory loss. The later stages are associated with more significant changes in ability and behaviour such as increasing forgetfulness and an increasing need for help with daily activities, usually to the point of complete dependence. In vascular dementia, patients can experience similar symptoms to that of Alzheimer's disease. However as these are usually associated with a series of small strokes, people with vascular dementia may develop symptoms suddenly, remain stable for some time and then quickly deteriorate, though they may experience a more gradual decline. Dementia with Lewy bodies is characterized by similar symptoms to those found in

Parkinson's disease, and people with fronto-temporal dementia experience progressive decline with extreme behaviour changes (Alzheimer's Research Trust 2010).

16. The rate of progression of cognitive decline varies with type of dementia, for example patients with Alzheimer's disease may show a decline of two points or less per year on the Mini Mental State Examination (MMSE). However, the rate of decline may be more rapid in other types of dementia, for example two to four points on the MMSE scale annually. The rate of decline may also vary as the disease progresses (Lin et al 2013).
17. Few cases of dementia are diagnosed in the early stages as many of the associated symptoms, such as memory loss, could be attributed to general aging or other conditions such as depression, diabetes, thyroid abnormalities or alcoholism (Alzheimer's Research Trust 2010).
18. Early diagnosis of dementia could potentially allow people with dementia and their carers to plan for the future whilst the patient still retains the capacity to participate in decision making, and to start any potential treatment earlier. It could also support the early education of caregivers on how to manage the patient, and the management of any co-morbid health conditions (Lin et al 2013).
19. The main risk factor for general cognitive decline and for Alzheimer's disease is increasing age (Lin et al 2013). The prevalence of dementia doubles with every five-year increase across the whole age range from 30 to 90 (Alzheimer's Society 2007). The prevalence of dementia at different ages is set out in Table 1:

**Table 1: Estimates of the population prevalence of dementia age 65 to 90+ (Alzheimer's Society 2007)**

| Age (years) | Prevalence (%) |
|-------------|----------------|
| 65-69       | 1.3            |
| 70-74       | 2.9            |
| 75-79       | 5.9            |
| 80-84       | 12.2           |
| 85-89       | 20.3           |
| 90-94       | 28.6           |
| 95+         | 32.5           |

20. A 2010 systematic review examined a range of factors for their potential association with risk for and possible prevention of cognitive decline (Plassman et al 2010). This review included observational studies with at least 300 participants and randomized controlled trials (RCT) with 50 or more participants, with follow up for at least one year. Participants were 50 years or older and drawn from the general population. There was some evidence from single RCTs supporting a decreased risk from physical exercise and cognitive training. There was also evidence from observational studies suggesting an increased risk associated with the apolipoprotein E  $\epsilon$ 4 allele, tobacco use and metabolic syndrome, and limited evidence from two observational studies for a decreased risk associated with a Mediterranean diet and vegetable consumption. The authors considered the overall quality of the available evidence to be low with heterogeneity between the categorization and definition of exposures and cognitive decline, and few studies that were designed to directly assess the association between specific exposures and cognitive decline.
21. A scoping review produced for NICE (NICE 2014b) considered the association between behavioural risk factors in mid-life and disease in later life, including dementia. This report drew a number of conclusions relevant to dementia (Lafortune 2014):

- There is consistent evidence that midlife physical activity has a beneficial effect on later life healthy aging, dementia, disability and other chronic disease outcomes, with beneficial effects reported for both men and women
- There is some consistent evidence (but from a limited number of studies) that a healthy diet in general or Mediterranean diet and fruit and vegetables have beneficial effects on late life outcomes and that higher consumption of saturated fat or processed and red meat in midlife is associated with poorer ageing, disability, dementia, frailty outcomes and non-communicable conditions
- Evidence specific to midlife alcohol consumption was mixed. Two studies reported moderate quality evidence of higher risk of dementia in non-drinkers and heavy drinkers compared to moderate drinkers
- There is consistent evidence that midlife smoking has a detrimental effect on later life dementia

### ***Mild cognitive impairment as an early symptomatic stage?***

22. Mild cognitive impairment (MCI) differs from dementia in that it is not severe enough to impact on independence in daily life, but may have some clinical value in predicting later dementia (Lin et al 2013).
23. The prevalence of MCI is difficult to assess due to differences in the criteria used to define the condition in different studies, and differences in sampling and methods of clinical assessment. Estimates for the prevalence of MCI vary considerably from 3% to 42% in adults aged 65 years and older (Lin et al 2013).
24. Blossom et al (2007) conducted a UK multi-centre prospective cohort study exploring the application of existing classifications of MCI and associated states (n=2,053 individuals without dementia). Population prevalence estimates for cognitive impairment varied from 0.1% to 42%, reflecting differences in the way that criteria were defined and operationalised.
25. A 2009 systematic review and meta-analysis included 41 cohort studies of at least three years duration on the progression of MCI to dementia (Mitchell et al 2009). The results from specialist clinical and community settings and for studies that did or did not use the original (1997) or revised (2001) Petersen et al criteria for MCI were analysed separately. The results from community studies are of most interest within the context of this paper on screening for dementia.
26. In community studies using the Petersen et al criteria for MCI, 21.9% (95%CI 7.3 to 41.6) converted to dementia over the observation period (range 3-10 years). For studies not using the Petersen et al criteria 22.7% (95%CI 14.2 to 32.6) converted to dementia over the observation period (range 3-8 years).
27. Five studies included a head-to-head comparison of the risk of dementia between individuals with MCI and age comparable controls, with a mean follow-up of 6 years. In these studies the annual conversion rate for people with MCI was 3.6% compared to 0.43% for healthy subjects. After correcting for sample size, the pooled relative risk was 13.8 (95%CI 8.44 to 22.6) (Mitchell et al 2009).
28. However, MCI may also return to normal cognition over time in 10 to 40% of individuals with MCI, and patients who revert to normal cognition may later progress to dementia, which complicates the ability to estimate progression to dementia (Lin et al 2013).
29. There are still some uncertainties around the natural history of dementia. Mild cognitive impairment has been suggested as a potential early symptomatic stage, however the results of a systematic review on the progression of MCI to dementia suggest that less

than a quarter of people with MCI had gone on to develop dementia over observation periods ranging from three to ten years. We did not identify any evidence to suggest that there is good understanding of which individuals with MCI will progress to dementia. This criterion is not met at present.

**All the cost-effective primary prevention interventions should have been implemented as far as practicable**

30. A review conducted for NICE (NICE 2014b) found no intervention studies delivered in mid-life that demonstrate an impact on dementia (Lafortune 2014). A review to assess the effectiveness and cost-effectiveness of primary interventions delivered in later life is underway with findings due to be available in 2015 (Lafortune 2014).
31. The potential association between cognitive decline and a wide range of factors has been investigated. However, as discussed above the overall quality of evidence in this area is considered to be low, so it is difficult to assess whether this criterion is met.

**If the carriers of a mutation are identified as a result of screening, the natural history of people with this status should be understood, including the psychological implications.**

32. This is not applicable to screening for dementia using cognitive assessment tools.

## The Test

33. This section considers evidence from systematic reviews that have compared tools for use in primary care or community settings with a population who are not already suspected of having dementia.
34. The evidence review conducted by the US Preventative Services Task Force included the question 'what is the test performance of screening instruments to detect cognitive impairment in elderly, community-dwelling primary care patients?' Studies were included that evaluated brief screening instruments that could be delivered by a clinician in primary care in 10 minutes or less, or self-administered in 20 minutes or less. Screening instruments could be administered to the patient or an informant (Lin et al 2013).
35. The 'gold standard' against which the screening tools were compared was formal diagnosis of dementia, or mild cognitive impairment as a potential early symptomatic stage.

**There should be a simple, safe, precise and validated screening test. The distribution of test values in the target population should be known and a suitable cut-off level defined and agreed**

36. Lin et al (2013) identified 12 brief instruments that have been studied more than once in good or fair quality studies (n=41) that evaluated their ability to detect dementia in primary care-relevant populations. All study participants were community-dwelling older adults selected from community or primary care practices. Only two of the 41 studies explicitly included people in assisted living or residential care facilities. Most studies had a majority of female participants.. All included studies had to include a reference standard for dementia, with the most common reference standards used being criteria from the 'Diagnostic and Statistical Manual of Mental Disorders' (DSM) III, DSM-IV or the National Institute of Neurological and Communicative Disorders and Stroke and Alzheimer's

Disease and Related Disorders Association. Formal diagnosis of dementia was based on a combination of history, examination, neuropsychological testing and expert consensus. Table 2 summarises the results for the ability of these instruments to detect dementia.

37. Lin et al also identified 27 good or fair quality studies investigating the accuracy of screening instruments to detect MCI in primary care-relevant populations. Of these, 15 studies excluded patients with dementia and so allowed estimation of their accuracy for MCI alone. The other 16 studies allowed estimation of the instrument's accuracy in detecting either MCI or dementia. There was more variation in the diagnostic criteria applied for MCI in these studies than in the studies assessing the accuracy of tools for diagnosing dementia, which limits the comparability of diagnostic estimates across studies. All studies included populations approximate to those in primary care, most of which were community-dwelling older adults. Two (of 27) studies explicitly included patients living in assisted living or residential care facilities. Almost all studies had a majority of female participants. Table 3 summarises the results for the ability of these instruments to detect either MCI alone, or MCI or dementia.
38. A number of other potential instruments were identified that appear promising (i.e. a sensitivity and specificity of >80%), but whose test performance has not been reproduced in other primary care-relevant populations. For dementia these include the 6-Item Screener, Visual Association Test, General Practitioner Assessment of Cognition (GPCOG), Activities of Daily Living/Instrumental Activities of Daily Living, Benton's Orientation Test, Delayed Recall Test and Short Concord Informant Dementia Scale. For mild cognitive impairment these include Ascertain Dementia 8 (AD8), abbreviated Fuld Object Memory Evaluation (FOME), St Louis University Mental Status Examination (SLUMS) and Computer Assessment of Mild Cognitive Impairment (CAMCI) (Lin et al 2013).

**Table 2: Summary of the results from a review of test performance of screening instruments to detect dementia in elderly, community-dwelling primary care patients (Lin et al 2013)**

| Test                                                                                                                                             | Number of studies and people                                                                      | Cut-off levels                                                                                             | Sensitivity                                                                             | Specificity                                                                        | Author's Conclusions                                                                                                                                                                                 |
|--------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Mini-Mental State Examination (MMSE)                                                                                                             | 14 studies;<br>n = 10,185<br><br>Mean age: 69 to 95 years<br><br>Dementia prevalence: 1.2% to 38% | No universally accepted cut-off value. Most commonly used cut-off points were 23/24 and 24/25 (out of 30). | Pooled estimate: 88.3% (95%CI 81.3 to 92.9)                                             | Pooled estimate: 86.2% (95%CI 81.8 to 89.7)                                        | Adequate test performance from many fair quality studies. A large body of literature suggests that a general cut-off level of 23/24 or 24/25 could be appropriate for most primary care populations. |
| Clock drawing test (CDT)                                                                                                                         | 7 studies;<br>n = 2,509<br><br>Mean age: 75 to 82 years<br><br>Dementia prevalence: 5% to 47.1%   | Different scoring methods and cut-off points used in the studies. Optimal cut-off point is unclear.        | Range: 67% to 97.9% (95% CI range 39 to 100)                                            | Range: 69% to 94.2% (95% CI range 54 to 97.1)                                      | Adequate test performance from good and fair quality studies, however the diagnostic accuracy will vary with the choice of scoring method and cut-off level.                                         |
| Verbal or category fluency tests<br><br>(participants have to say as many names as possible from a category in a given time, usually 60 seconds) | 6 studies;<br>n = 2,083<br><br>Mean age: 77 to 82 years<br><br>Dementia prevalence: 5% to 17.6%   | 12 or 13<br><br>14 or 15                                                                                   | Range: 37% to 89.5% (95% CI range 19 to 100)<br><br>57% to 88% (95% CI range 35 to 100) | Range: 62 to 97% (95% CI range 48 to 99)<br><br>43% to 94% (95% CI range 33 to 97) | A wide range of sensitivity and specificity results from good and fair quality studies.                                                                                                              |
| The short or full Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE)                                                           | 5 studies;<br>n = 1,108<br><br>Mean age: 72 to                                                    | Around 3.3 (average score out of 5) in 2 studies on the                                                    | Short IQCODE range: 75% to 81% (95% CI range                                            | Short IQCODE range: 68% to 80% (95% CI range                                       | Most well-studied of the informant-based screening tools with evidence from good and fair quality studies. However                                                                                   |

|                                                                                  |                                                                                                                                 |                                                                                 |                                                                               |                                                                                         |                                                                                                                                                               |
|----------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------|-------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                  | 78 years<br><br>Dementia prevalence not reported                                                                                | short IQCODE and 2 studies on the full IQCODE                                   | 41 to 100)<br><br>Full IQCODE range:<br>79% to 83%<br>(95% CI range 48 to 98) | 59 to 100)<br><br>Full IQCODE range:<br>65% to 90%<br>(95% CI range not reported to 95) | 95% CI are quite wide.                                                                                                                                        |
| The Memory Impairment Screen (MIS) and The Memory Impairment Screen by telephone | 4 studies;<br>n = 1,671<br><br>1 study;<br>n = 300<br><br>Mean age: 78 to 79 years<br><br>Dementia prevalence:<br>3.3% to 17.6% | 4 (out of 8)                                                                    | Range:<br>43% to 86%<br>(95% CI range 24 to 96)                               | Range:<br>93% to 97%<br>(95% CI range 56 to 100)                                        | Adequate test performance from good and fair quality studies. However, the 2 best quality studies showed very low sensitivity (43% and 49%)                   |
| Mini-Cog (includes the CDT plus a three-item word recall test)                   | 4 studies;<br>n = 1,570<br><br>Mean age: 79 years<br><br>Dementia prevalence:<br>3.3% to 40.2%                                  | Different cut-off points used in the studies. Optimal cut-off point is unclear. | Range:<br>76% to 100%<br>(95% CI range 54 to 100)                             | Range:<br>54% to 85.2%<br>(95% CI range 43 to 88.4)                                     | Adequate test performance from good and fair quality studies                                                                                                  |
| Abbreviated Mental Test (AMT)                                                    | 4 studies;<br>n = 824<br><br>Mean age: 69 to 76 years                                                                           | 7/8 (out of 10)                                                                 | Range:<br>42% to 100%<br>(95% CI range 31 to 99.8)                            | Range:<br>83% to 95.4%<br>(95% CI range 89 to 97.3)                                     | Limited reproducibility in similar primary care relevant populations from fair quality studies.<br><br>Sensitivity and specificity ranges are from 2 of the 4 |

|                                                                                                                         |                                                                                                                   |                                                                    |                                                         |                                                          |                                                                                                                                                                                                                                                    |
|-------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------|---------------------------------------------------------|----------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                         | Dementia prevalence: 4% to 29%                                                                                    |                                                                    |                                                         |                                                          | studies. The other studies had very wide 95% CI and suggested that optimal cut-off point may vary by language culture/ education.                                                                                                                  |
| Mental Status Questionnaire (MSQ) and Short Portable Mental Status Questionnaire (SPMSQ) <sup>1</sup><br><br>SPMSQ only | 2 studies; n = 522<br><br>2 studies; N=535<br><br>Mean age not reported<br><br>Dementia prevalence: 2.5% to 16.4% | Cut-off point not specified in 2 of the 4 studies                  | For SPMSQ Range: 92.3% to 100% (95% CI range 29 to 100) | For SPMSQ Range: 83.5% to 100% (95% CI range 76 to 100)  | Reasonable performance from fair quality studies, although very wide 95% CI. Only one study evaluated the MSQ or SPMSQ in English.<br><br>In the 2 studies that evaluated both the MSQ and SPMSQ both instruments had similar diagnostic accuracy. |
| The Free and Cued Selective Reminding Test (FCSRT)                                                                      | 2 studies; n = 734<br><br>Mean age: 79 years<br><br>Dementia prevalence: 18%                                      | 25 (mean score) (1 study)<br><br>Unknown (1 study)                 | 86% (95% CI 41 to 100)<br><br>100% (95% CI 92.6 to 100) | 73% (95% CI 56 to 96)<br><br>87.2% (95% CI 83.4 to 90.5) | The FCSRT has limited validation in a primary care-relevant population with wide confidence intervals around sensitivity and specificity.                                                                                                          |
| The 7-Minute Screen (7MS)                                                                                               | 2 studies; n = 553<br><br>Mean age: 77 to 79 years                                                                | Optimal cut-off point is unclear due to limitations in the studies | 100% (95% CI range 71.5 to 100)                         | Range: 95.1% to 100% (95% CI range 86.8 to 100)          | Very limited evidence from fair quality studies.                                                                                                                                                                                                   |

<sup>1</sup> The SPMSQ was derived from the MSQ with a few added questions (Lin et al 2013b)

|                                                 |                                                                                           |                                |                                           |                                           |                                                  |
|-------------------------------------------------|-------------------------------------------------------------------------------------------|--------------------------------|-------------------------------------------|-------------------------------------------|--------------------------------------------------|
|                                                 | Dementia prevalence: 8.1% to 11.5%                                                        |                                |                                           |                                           |                                                  |
| Telephone Interview for Cognitive Status (TICS) | 2 studies; n =677<br><br>Mean age: 79 to 81 years<br><br>Dementia prevalence: 9% to 14.1% | Optimal cut-off point unclear. | Range: 74% to 88% (95% CI range 54 to 96) | Range: 86% to 87% (95% CI range 81 to 91) | Very limited evidence from fair quality studies. |

**Table 3: Summary of the results from a review of test performance of screening instruments to detect either MCI alone, or MCI or dementia in elderly, community-dwelling primary care patients (Lin et al 2013)**

| Test                                                                                   | Number of studies and people                                                            | Most commonly reported cut-off levels                                                                              | Sensitivity                                                                                                            | Specificity                                                                                                            | Author's Conclusions                                                                                                                                                                                                                                                                                                                                                                  |
|----------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Mini-Mental State Examination (MMSE)                                                   | 15 studies; n = 5,758<br><br>Mean age: 73 to 83 years<br><br>MCI prevalence: 20% to 84% | 27-28 (out of 30) (to detect MCI)<br><br>27 (to detect MCI and dementia)<br><br>23-24 (to detect MCI and dementia) | Range: 46% to 60% (95% CI range 36 to 74)<br><br>71% (95%CI 48 to 89)<br><br>Range: 53% to 77% (95% CI range 43 to 85) | Range: 65% to 90% (95% CI range 56 to 99)<br><br>90% (95%CI 77 to 97)<br><br>Range: 70% to 92% (95% CI range 58 to 99) | The most studied instrument used to detect MCI with good and fair quality studies identified.<br><br>A cut-off point of 27 or 28 had a low and widely ranging sensitivity to detect MCI. A cut-off point of 23 or 24 appears to have a better sensitivity and specificity to detect MCI and dementia than most other screening instruments, however this was still less than optimal. |
| The short or full Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) | 4 studies: n=975<br><br>Mean age: 72 to                                                 | 3.3 (average score out of 5) (full version)                                                                        | Range: 71% to 83% (95% CI range 60.6 to not                                                                            | Range: 74.3% to 83% (95% CI range 62.4 to not                                                                          | Across different fair quality studies, IQCODE had relatively low sensitivity for detecting MCI.                                                                                                                                                                                                                                                                                       |

|                                                    |                                                                                               |                                                                                  |                                                        |                                                      |                                                                                                                                            |
|----------------------------------------------------|-----------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|--------------------------------------------------------|------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
|                                                    | 80 years<br><br>MCI prevalence:<br>10% to 45%                                                 | 3 (short version)                                                                | reported)<br><br>74.8% (95%CI<br>67.7 to 80.7)         | reported)<br><br>69.1% (95%CI<br>63.1 to 74.4)       |                                                                                                                                            |
| Clock drawing test (CDT)                           | 4 studies;<br>n=4,191<br><br>Mean age: 71 to<br>83 years<br><br>MCI prevalence:<br>14% to 48% | Different cut-off<br>points used in the<br>studies.                              | Range:<br>40.7% to 76%                                 | Range:<br>44% to 85%                                 | Fair quality studies suggest that<br>the CDT appears to have worse<br>sensitivity or specificity to detect<br>MCI than to detect dementia. |
| Mini-Cog                                           | 3 studies;<br>n=1,092<br><br>Mean age: 75 to<br>83 years<br><br>MCI prevalence:<br>7% to 79%  | Different cut-off<br>points used in the<br>studies.                              | Range:<br>50% to 84%                                   | Range:<br>? to 87.9%                                 | Good and fair quality studies<br>found different estimates for<br>sensitivity.                                                             |
| Telephone Interview for<br>Cognitive Status (TICS) | 3 studies;<br>n=568<br><br>Mean age: 75 to<br>81 years<br><br>MCI prevalence:<br>15% to 24%   | Each of the three<br>studies identified<br>a different optimal<br>cut-off point. | Range:<br>47% to 73%<br>(95% CI range<br>28 to 80)     | Range:<br>46% to 77%<br>(95% CI range<br>35 to 82)   | Fair quality studies arrived at<br>widely varied estimates for<br>sensitivity and specificity.                                             |
| MoCA                                               | 2 studies;<br>n=251<br><br>Mean age: 70 to<br>76 years<br><br>MCI prevalence:<br>20 to 24%    | 25/26 (out of 30)                                                                | Range:<br>80% to 100%<br>(95% CI range<br>56.3 to 100) | Range:<br>50% to 76%<br>(95% CI range<br>41 to 84.9) | Good and fair quality studies,<br>both of which used the Petersen<br>criteria for MCI.                                                     |

39. The mean age of participants varied across the included studies from 69 to 95 years. The prevalence of dementia and education level (when reported) also varied across studies.
40. The best studied test is the MMSE. It is known that the MMSE has different norms by age, education and ethnicity, however there is no universally accepted cut-off point based on age and education level (Lin et al 2013). The USPSTF review noted that although the sensitivity and specificity of the MMSE is likely to vary according to an individual's age and education, though they did not attempt to quantify such variation. They concluded that there is a large body of evidence to suggest that a general cut-off point of 23/24 or 24/25 could be appropriate for screening for dementia in most primary care populations (Lin et al 2013).
41. In summary, several brief screening instruments that could be delivered in primary care appear to have an adequate test performance for detecting dementia, but less good performance for detecting mild cognitive impairment. For many instruments the optimal cut-off point for detecting dementia or MCI was unclear and/ or a wide range of sensitivity and specificity scores was observed between the different studies. Therefore although there are tests that could potentially be used as screening tools further clarification is required around optimum cut-off levels. This criterion is partially met.

### **The test should be acceptable to the population**

42. In one US study where screening was offered to 8,342 veterans (using the mini-cog screening tool), 96.7% agreed to be screened (McCarten et al 2012). In another US study of 3,573 individuals the uptake was similarly high at 93% (Boustani et al 2005).
43. A systematic review assessing attitudes and preferences towards screening for dementia identified 29 studies (n=2,575) (Lafortune 2014; Martin 2014). This concluded that "overall the level of evidence is low, few large scale studies have been undertaken and none were conducted in representative samples ... nevertheless our findings suggest that population screening for dementia may not be acceptable to either the general public or health care professionals". It is not specified whether any of the included studies were conducted in the UK.
44. This criterion is not met.

### **There should be an agreed policy on the further diagnostic investigation of individuals with a positive test result and on the choices available to those individuals**

45. The National Institute for Health and Care Excellence (NICE) published a clinical guideline on dementia in 2006 (CG42), and last updated this is 2012. This states that a diagnosis of dementia should only be made after a comprehensive assessment and describes the elements that should be included within this comprehensive assessment.
46. This criterion is therefore met.

**If the test is for mutations the criteria used to select the subset of mutations to be covered by screening, if all possible mutations are not being tested, should be clearly set out**

47. This is not applicable to screening for dementia using cognitive assessment tools.

## The Treatment

**There should be an effective treatment or intervention for patients identified through early detection, with evidence of early treatment leading to better outcomes than late treatment**

48. A number of systematic reviews were identified that considered pharmacological and non-pharmacological interventions that aim to either permanently or temporarily prevent, slow or reverse cognitive decline. Non-pharmacological interventions aimed at carers or families are also discussed.

### Acetylcholinesterase inhibitors and memantine

49. Lin et al (2013) identified 54 fair and good quality trials (n=19,384) evaluating acetylcholinesterase inhibitors (AChEIs)<sup>2</sup> and 10 trials (n=4,517) of memantine, mostly in people with moderate Alzheimer's disease and with six months follow-up. The review authors concluded that AChEIs and memantine can achieve small improvements in global cognitive function (approximately 1 to 3 points on the ADAS-cog scale) in the short term. The review authors considered that the average effect of these changes may not be clinically meaningful using commonly accepted values to interpret the clinical importance of these changes. AChEIs also appeared to consistently improve measures of global functioning in people with Alzheimer's disease in the short term (up to 6 months). However, it was unclear if AChEIs can improve physical functioning, due to inconsistent and sparsely reported findings.

50. Four trials (n=1,960) involving people with MCI showed small statistically significant benefits in global cognitive functioning for donepezil and galantamine, but the clinical importance of this was unclear (Lin et al 2013).

51. Trials that looked at outcomes beyond six months generally reported outcomes that were consistent with the results at six months follow up. Two trials that evaluated donepezil for MCI did not find any significant differences in conversion to Alzheimer's disease at about three years (Lin et al 2013).

52. Side effects from AChEIs were fairly common, for example bradycardia and adverse events related to bradycardia. However, AChEIs did not appear to be associated with a higher number of serious adverse events. The rate of withdrawal or discontinuation was higher for AChEIs than placebo at approximately 15% (Lin et al 2013).

53. A 2012 Cochrane review (Russ & Morling 2012) looking specifically at the use of cholinesterase inhibitors (donepezil, galantamine and rivastigmine) in people with mild cognitive impairment included nine trials (n=5,149). A meta-analysis of three studies that reported on conversion to dementia found no strong evidence of benefit for cholinesterase inhibitors in preventing progression to dementia at one, two or three

<sup>2</sup> Donepezil (24 studies); Galantamine (12 studies); Rivastigmine (12 studies); Tacrine (6 studies).

years. The authors concluded that there is very little evidence that cholinesterase inhibitors affect progression to dementia or cognitive test scores in MCI.

### Other pharmacological treatments

54. Lin et al (2013) identified 26 good and fair quality trials (n=5,325) of other medications or supplements, primarily aimed at cardiovascular risk reduction to treat vascular dementia. These included low-dose aspirin, HMG-CoA reductase inhibitors (statins); non-steroidal anti-inflammatory drugs (NSAIDs); gonadal steroids and dietary supplements (including vitamins and omega-3 fatty acids). Most of these trials included people with mild to moderate dementia. These trials generally did not find evidence that these medications or supplements had any benefit on global cognitive or physical function in people with mild to moderate dementia or MCI. However, the authors noted that it was not possible to conduct any meaningful analysis of outcomes for important subgroups, for example by age, gender, ethnicity, type of dementia or level of cognitive impairment.
55. A 2012 Cochrane review on metal protein attenuating compounds (MPAC) for the treatment of Alzheimer's dementia (Sampson et al 2012) identified two trials of two different MPACs. A trial of clioquinil (PBT1) did not identify any significant difference in cognition, non-cognitive symptoms or clinical global impression at 36 weeks follow up and the authors noted that this drug has now been withdrawn from development. A trial of PBT2 (n=78) showed some benefit in Neuropsychological Test Battery (NBT) component tests of executive function, category fluency tests and trail making after 12 weeks. However no significant impact was found for cognition, or on the NTB composite, memory or executive scores. The authors concluded that larger trials are required to demonstrate cognitive efficacy.
56. A 2013 systematic review of the effect of any pharmacological intervention on well-being and quality of life included 15 trials, with follow up ranging from 12 weeks to one year (Cooper et al 2013). This review found a lack of evidence that any pharmacological intervention results in improvements in quality of life or well-being for people with dementia, with none of the trials reporting a significant benefit when comparing those taking a drug or its comparator. However, the authors did note that studies may have been underpowered to detect impact on quality of life.

### Non-pharmacological treatments

#### *Physical activity*

57. Lin et al (2013) identified 10 fair quality trials (n=1,033) of exercise interventions, six of which involved people with either mild MCI or dementia, and four of which involved people with mild to moderate dementia. The interventions included aerobic training, strength/resistance training, balance training (or some combination of these) or Tai Chi. The authors concluded that there was no consistent benefit on global cognitive or patient depression outcomes from exercise interventions. However, the limited number of trials and the heterogeneity of the populations and interventions made it difficult to exclude a clinically important benefit for exercise interventions.
58. Two trials (n=220) of multi-component, self-guided exercise found a very small benefit on global cognitive function for people with MCI at 12 to 18 months. However the benefit was only approximately one point on the MMSE or ADAS-cog scale, so this change may be of limited clinical benefit (Lin et al 2013).

#### *Cognitive interventions*

59. Lin et al (2013) identified 15 fair quality trials of cognitive intervention (n=1,128). Five of these trials involved people with MCI and two involved people with either MCI or dementia. The other eight trials involved people with mild to moderate dementia. The interventions included cognitive training, cognitive rehabilitation, and/or cognitive stimulation with or without motor skills training.
60. Overall, the review authors judged the findings of these trials to be inconsistent and of uncertain clinical significance due to the limited amount of evidence and wide confidence intervals. Cognitive training alone did not appear to improve global or memory-specific cognitive functioning at three to six months. However, a meta-analysis of six trials of cognitive stimulation, with or without cognitive training, did show a moderate improvement of global cognitive function in people with MCI or dementia at six to 12 months, albeit with wide confidence intervals (effect size: -0.59, 95%CI -0.93 to -0.25;  $I^2=52.7\%$ ). Only two of the eight trials that reported depression outcomes reported a small but statistically significant improvement (Lin et al 2013).
61. A 2012 Cochrane review focused on cognitive stimulation interventions aimed at improving cognition for people with mild to moderate dementia (Woods et al 2012). This review identified 15 trials of variable quality and included a meta-analysis of data from 718 participants. The authors found a clear and consistent benefit on cognitive function (SMD<sup>3</sup> 0.41, 95%CI 0.25 to 0.57) which remained evident at follow-up of one to three months after the treatment. Positive impacts were also seen on self-reported quality of life and well-being (SMD 0.38, 95%CI 0.11 to 0.65) and on staff ratings of communication and social interaction (SMD 0.44, 95%CI 0.17 to 0.71). However no evidence was found for improvements in the mood of participants or their ability to care for themselves or function independently, and there was no reduction in behaviour found difficult by staff or carers.

#### *Multidisciplinary care interventions*

62. Lin et al (2013) identified five good and fair quality studies of multidisciplinary care interventions involving assessment and care coordination (n=1,766). One of these studies involved people with MCI and dementia, the others involved people with mild to moderate dementia. None of the trials identified found a benefit for multidisciplinary care interventions for cognitive or physical function, health related quality of life or institutionalization.

#### *Education-only interventions*

63. Lin et al (2013) identified two fair quality trials of education-only interventions (n=741), both of which involved people with mild to moderate dementia. The education interventions were aimed at the healthcare staff caring for people with dementia and covered a variety of topics around treatment, communication with patients and families and effective working between healthcare professionals. Neither of the trials identified found a benefit for education-only interventions for cognitive or physical function, health related quality of life or institutionalization.

#### *Non-drug therapies*

64. A 2010 systematic review of published systematic reviews on non-drug therapies for dementia identified 33 reviews (Hulme et al 2010). The studies identified within these reviews were mostly based in community residential settings, usually did not identify a specific type or stage of dementia and were generally thought to have weak study designs and small sample sizes. Evidence was found to be lacking or inconclusive for acupuncture, animal assisted therapy, aromatherapy, behaviour management,

<sup>3</sup> SMD = standardised mean difference

cognitive stimulation/training, counselling, environmental manipulation<sup>4</sup>, light therapy, reality orientation, reminiscence therapy, multi-sensory stimulation, transcutaneous electrical nerve stimulation and validation therapy. However, there was more evidence for positive effects for massage/touch therapies for a short-term reduction in agitated behaviour, music therapy for reducing behavioural and psychological symptoms, and physical exercise for reducing behavioural and psychological symptoms and improving functional ability.

## Other treatments

65. A 2009 Cochrane review (Birks & Grimley Evans 2009) assessed the efficacy and safety of Ginkgo biloba for the treatment of people with dementia or cognitive decline, of any degree of severity, compared to placebo. This systematic review identified 36 trials published up to September 2007, most of which were small and of less than three months duration. There were nine more recent trials, with a total of 2,016 patients, which were of six months duration and were judged to generally be of adequate size and conducted to a reasonable standard. The results of these more recent trials showed inconsistent results for the effects of Ginkgo biloba compared to placebo on cognition, activities of daily living, mood, depression and carer burden. The review concluded that there was no consistent or reliable evidence that Ginkgo biloba has a predictable or clinically significant benefit for patients with dementia or cognitive impairment, or for a sub-group of patients with Alzheimer's disease.
66. Lin et al (2013) acknowledged that disease-modifying therapies to slow cognitive decline is an active area of current research with a number of therapies showing some promise, including intravenous immunoglobulin (IVIG), growth hormone-releasing hormone (GHRH) and immunotherapies targeting beta-amyloid.

## Impacts for carers, families or society

67. One of the goals of this review is to assess whether there are any interventions for people with screen-detected dementia that might increase the benefit to family and society. None of the abstracts of the 544 articles in the August 2013 UKNSC literature search contains any explicit mention of benefits to society as an outcome. However, we did identify a number of reviews that have considered the impact of treatments for people with dementia on carers and families.
68. Lin et al (2013) identified 59 fair to good quality trials (n=8,932) evaluating interventions primarily aimed at carers or the patient-carer dyad. Of these trials 52 evaluated interventions with a psycho-educational component and eight evaluated other interventions such as caregiver physical activity (3 trials), peer support (4 trials) and multidisciplinary assessments and treatment planning (1 trial). The patients included in these trials had mild to moderate dementia (mostly moderate dementia), were living in the community and required care.
69. The review authors found a generally consistent but small benefit for interventions including a psycho-educational component on caregiver burden and depression for people caring for patients with moderate dementia. The clinical significance of this benefit was unclear, although the authors did suggest that the wide effect estimates may suggest that some subpopulations experience clinically important benefits. However, none of the eight trials of other interventions showed a reduction in caregiver burden or depression outcomes (Lin et al 2013).

<sup>4</sup> This includes studies that manipulated the environment to effect changes in neuropsychiatric symptoms and inappropriate behaviours such as agitation and wandering through, for example, access to outdoor areas, sign-posting and use of mirrors.

70. Woods et al (2012), in their systematic review of cognitive stimulation interventions for mild to moderate dementia, included three studies which reported family caregiver outcomes, one of which taught family caregivers to deliver the cognitive stimulation. The effect sizes for anxiety, depression and caregiver burden were all close to zero and not statistically significant. The authors did note that there was no evidence of increased strain on family caregivers in the one study that trained the caregivers to give the intervention.
71. A 2012 systematic review on the effect of non-pharmacological interventions on quality of life or wellbeing (Cooper et al 2012) included 20 trials. Pooled analysis of studies reporting similar interventions found that family carer coping strategy-based interventions (SES<sup>5</sup> 0.24; 4 studies) and combined patient activity and family carer coping interventions (SES 0.84; 2 studies) might improve quality of life. However, none of the results of the individual trials were statistically significant alone.

## Summary

72. We identified a number of systematic reviews covering several potential treatments. Overall there was a lack of strong positive evidence for the benefit of the treatments considered for people with MCI or dementia or families/carers. When statistically significant results were found, the effect sizes were generally small which raises questions about the clinical significance of the findings. The studies identified included people with mild to moderate dementia and the application of the findings to screen detected cases is unclear. Importantly given that screening would detect early symptomatic cases, it is also not possible to determine whether early treatment leads to better outcomes than late treatment.
73. This criterion is not met at present. However, it should be noted that the evidence identified was often inconsistent or inconclusive rather than demonstrating negative effects, suggesting that further research may be beneficial.

## **There should be agreed evidence based policies covering which individuals should be offered treatment and the appropriate treatment to be offered**

74. The NICE clinical guideline on dementia includes recommendations for the identification, treatment and care of people with dementia and the support of carers (NICE 2006).
75. The NICE guideline includes recommendations that apply to all types of dementia in addition to recommendations on specific forms of dementia such as Alzheimer's disease.
76. This criterion is therefore met.

## **Clinical management of the condition and patient outcomes should be optimised in all health care providers prior to participation in a screening programme**

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<sup>5</sup> SES = standardised effect size

77. The National Institute for Health and Care Excellence clinical guideline on dementia makes recommendations for the identification, treatment and care of people with dementia and the support of carers (NICE 2006).
78. The NSC literature search did not identify any studies providing audit data on whether the NICE recommendations are being implemented in practice, so we cannot tell whether this criterion is met.

## The Screening Programme

**There should be evidence from high quality Randomised Controlled Trials that the screening programme is effective in reducing mortality or morbidity**

79. No trials on screening for dementia were identified in the NSC literature search.
80. The USPSTF review on screening for cognitive impairment in older adults (Lin et al 2013) did not identify any trials examining the direct effect of screening for cognitive impairment in primary care on patient or clinical decision making, on the health of the patient or caregiver or on societal outcomes.
81. The NSC literature search did identify a study from the United States assessing the effect of offering screening to 8,342 veterans on diagnosing cognitive impairment (McCarten et al 2012). Participants were aged 70 years or older and did not have a prior diagnosis of cognitive impairment. Of the 8,063 veterans screened, 2,081 had a positive screening test and were offered further evaluation. Following further evaluation 540 (7%) received a diagnosis of cognitive impairment, however, the percentage of screen positive individuals who did not complete the further evaluation was high (72%). Of the 1,501 who refused further evaluation 259 (17.3%) were known to have subsequently received a diagnosis of cognitive impairment in standard care.
82. This criterion is not met.

**There should be evidence that the complete screening programme (test, diagnostic procedures, treatment/ intervention) is clinically, socially and ethically acceptable to health professionals and the public**

83. The USPSTF review did not identify any studies that directly addressed any adverse psychological effects of screening or from false-positive or false-negative results (Lin et al 2013).
84. The percentage of those offered a screening test who agreed to take part was over 90% in two studies from the United states (Boustani et al 2005; McCarten et al 2012).
85. However, the uptake of further diagnostic tests by individuals who screened positive for cognitive impairment was fairly low in the same two US studies at 48% (n=483) and 28% (n=2,081) (Boustani et al 2005; McCarten et al 2012). Older patients and patients with higher screening scores (implying less cognitive impairment) were more likely to refuse further assessment (Boustani et al 2006).
86. It is not clear how transferable these US studies would be to a UK screening context, however low uptake of further diagnostic tests would have a significant negative impact on any screening programme.

87. This criterion is not met.

**The benefit from the screening programme should outweigh the physical and psychological harm (caused by the test, diagnostic procedures and treatment)**

88. The benefits of the earlier recognition of dementia could include confirming suspicions and ending uncertainty, increasing understanding of problems, giving access to support, promoting positive coping strategies, facilitating planning and fulfilment of short-term goals (Iliffe et al 2009). Potential hazards include restriction of activities, preoccupation with the diagnosis or hyper vigilance from family carers. Incorrect categorisation of some behaviours or cognitive changes as dementia could also lead to unnecessary distress from being given a serious but incorrect diagnosis and under-treatment of conditions such as depression (Iliffe et al 2009).
89. There are a number of potential benefits and risks associated with the earlier diagnosis of dementia but it is not currently clear whether the benefits outweigh the risks, so this criterion is not met.

**All other options for managing the condition should have been considered (e.g. improving treatment, providing other services), to ensure that no more cost effective intervention could be introduced or current interventions increased within the resources available.**

90. A 2009 paper identified three approaches that need considering in relation to improving the detection of dementia in primary care, namely enhancing professional skills, modifying service delivery and screening (Iliffe et al 2009). The authors considered that there was insufficient evidence of benefit to justify population screening and instead suggested national campaigns to improve public and professional understanding of dementia and implementation of best practice such as evidence based practice protocols or communication skills in talking to people with dementia might be a better use of resources.
91. A 2007 report looked at the gap between the number of people diagnosed with dementia in England and the estimated annual prevalence. This found that for the 65-69 age group, five people per 1,000 were diagnosed with dementia against an expected 13 per 1,000, and for people aged 80 years and over 60 per 1,000 were diagnosed of an expected 122, per 1,000 (National Audit Office 2007).
92. Potential barriers to diagnosis that may account for this gap include fear of the disease amongst patients or families, difficulty distinguishing between the symptoms of dementia and normal aging processes, a lack of confidence and training in diagnosing dementia amongst GPs and variation and inconsistency in the diagnostic tools available (Alzheimer's Research Trust 2010).
93. There are a number of potential actions that could be considered to improve the understanding, recognition and diagnosis of dementia without introducing a screening programme for dementia. This criterion is not met at present.

## Implications for policy

It is not appropriate to implement a national screening programme for dementia using cognitive assessment tools, because:

- Although there are several brief screening instruments for dementia or mild cognitive impairment that could potentially be delivered in primary care, a wide range of sensitivity and specificity scores have been observed between different studies and the optimum cut-off levels are uncertain.
- The prevalence rates for dementia vary for different age groups, which has an impact on the positive and negative predictive value of screening tests. The most studied screening test for dementia (MMSE) is estimated to have a pooled sensitivity of 88.3% and specificity of 86.2%. Using these values for test sensitivity and specificity, Table 4 demonstrates the impact that the prevalence estimates for dementia at different ages have on the positive and negative predictive values of MMSE test results.

**Table 4: Positive and negative predictive values at different ages for a test with a sensitivity 88.3% and specificity of 86.2%**

| Age (years) | Prevalence (%) | Positive predictive value (%) | Negative predictive value (%) |
|-------------|----------------|-------------------------------|-------------------------------|
| 65-69       | 1.3            | 7.8                           | 99.8                          |
| 70-74       | 2.9            | 16.0                          | 99.6                          |
| 75-79       | 5.9            | 28.6                          | 98.2                          |
| 80-84       | 12.2           | 38.0                          | 98.0                          |
| 85-89       | 20.3           | 62.0                          | 96.7                          |
| 90-94       | 28.6           | 71.9                          | 94.8                          |
| 95+         | 32.5           | 75.5                          | 93.9                          |

- This demonstrates that it is only in people aged 85 and above that a positive MMSE test result is likely to indicate that an individual has dementia. At ages below this the majority of people with a positive screening test result will be found not to have dementia on further evaluation.
- Mild cognitive impairment represents a potential early symptomatic stage. However, at least three-quarters of people who are found to have mild cognitive impairment on screening will not develop dementia over the next three to ten years (which is the longest duration of follow-up reported to date). Between ten and forty per cent of individuals with mild cognitive impairment return to normal cognitive function over time. Screening for mild cognitive impairment may therefore harm more people by falsely alarming them than it might help by allowing early intervention for cognitive decline. This is particularly relevant given that the evidence for early intervention is weak.
- The available evidence on the effectiveness of interventions for people with mild cognitive impairment or dementia, and for their families/ carers, is often inconsistent or inconclusive and when statistically significant effects are seen these are often small and of questionable clinical significance.
- Evidence from US studies suggests that the uptake of further diagnostic testing amongst people who receive a positive screening test is low, which would undermine the effectiveness of any screening programme. It is not clear at present whether this would also be the case within a UK context.

## Implications for research

Longer-term follow-up (beyond ten years) is needed to define the natural history of cognitive function in individuals who are screened for mild cognitive impairment. This will tell us whether the proportion of people with screen-detected mild cognitive impairment who go on to develop dementia (relative to the background incidence of dementia in those who do not have mild cognitive impairment on screening) rises to a level that could be considered to make screening justifiable.

Further evaluation in well-designed trials is needed of interventions that seek to reduce progression from mild cognitive impairment to dementia.

If further research on the natural history of cognitive function in individuals with screen-detected mild cognitive impairment, and on interventions that seek to reduce progression from mild cognitive impairment to dementia, suggests that a national screening programme might possibly be appropriate, further research will be needed to define the optimum cut-off levels for brief screening instruments that could be delivered in primary care or community settings, and on the acceptability of such a screening programme in the UK.

# Appendix A

**Knowledge update on screening for dementia**  
**Paula Coles, Information Scientist, 12<sup>th</sup> August 2013**

## BACKGROUND:

**SOURCES SEARCHED:** Medline, Embase, PsychINFO, Cochrane Library.

**DATES OF SEARCH:** January 2008 – August 2013 (All searches carried out on 12<sup>th</sup> August 2013).

## SEARCH STRATEGY:

1. (Mental status questionnaire or MSQ).tw.(435)
2. Category fluency test.tw.(52)
3. Memory impairment screen.tw.(44)
4. (6 item cognitive test or 6-CIT).tw.(3)
5. (Abbreviated mental test score or AMTS).tw.(178)
6. (Prueba cognitive de leganes or PCL).tw.(5714)
7. DEMTECT.tw.(22)
8. (Montreal cognitive assessment or MOCA).tw.(386)
9. Memory alteration test.tw.(11)
10. MINI-COG.tw.(62)
11. clock drawing test.tw.(400)
12. clock-drawing copy.tw.(0)
13. number transcoding task.tw.(2)
14. trail making test\$.tw.(1701)
15. verbal fluency.tw.(3170)
16. East Boston memory test.tw.(27 )
17. John Brown test.tw.(0)
18. word list delayed recall.tw.(15)
19. word list immediate recall.tw.(4 )
20. (General Practitioner Assessment of Cognition or GPCOG).tw.(11)
21. (Mini-Cognitive Assessment Instrument or Mini-COG).tw.(63)
22. 7 minute screen.tw.(17)
23. (Short form Informant Questionnaire on Cognitive Decline in the Elderly or short IQCODE).tw.(5)
24. (Bowles-Langley Technology or Ashford Memory Test).tw.(0)
25. Mental alteration test.tw.(0)
26. ((Short and Sweet Screening Instrument) or SASSI).tw.(36)
27. (Short Test of Mental Status or STMS).tw.(131)
28. (Rowland Universal Dementia Assessment Scale or RUDAS).tw.(23)
29. ((Time and change test) or T&C).tw.(35852)
30. Human Figure drawing.tw.(78)
31. Community screening interview for dementia.tw.(31)
32. Hopkins verbal learning test.tw.(193)
33. Observation list of possible early signs of dementia.tw.(2)
34. Rapid dementia screening test.tw.(1)
35. Neuropsychiatry unit cognitive screen.tw.(1)
36. Cambridge Examination for Mental disorders of the Elderly.tw.(66)
37. Short Cognitive Evaluation Battery.tw.(3 )
38. Cognitive Abilities Screening Instrument.tw.(104 )
39. Visual Association Test.tw.(15)
40. USPSTF Test.tw.(0)
41. Mental Test Score.tw.(138)
42. Deterioration Cognitive Observee.tw.(2)

43. (Cognitive decline and Cognitive impairment scales of the Psychogeriatric Assessment scales).tw.(0)
44. Functional Activities Questionnaire.tw.(78)
45. Modified mini-mental status test.tw.(0)
46. Short portable mental status questionnaire.tw.(216)
47. cognitive assessment tool\$.tw.(46)
48. exp Neuropsychological Tests/(70334)
49. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48(115031)
50. alzheimer\$.tw.(91532)
51. exp Dementia/(120121)
52. dementia.tw.(65297)
53. 50 or 51 or 52(165227)
54. Mass Screening/(82318)
55. detect\$3.tw.(1509946)
56. screen\$3.tw.(464483)
57. (test or tests or testing).tw.(1511333)
58. Early Diagnosis/(12501)
59. early diagnosis.tw.(50320)
60. 54 or 55 or 56 or 57 or 58 or 59(3138984)
61. systematic review.tw.(44641)
62. clinical trial.pt.(499770)
63. controlled clinical trial.pt.(88866)
64. meta analysis.pt.(49854 )
65. randomized controlled trial.pt.(382290)
66. 61 or 62 or 63 or 64 or 65(758807)
67. 49 and 53 and 60 and 66(922)
68. 67(922)
69. limit 68 to yr="2008 -Current"(329)

**Similar searches also carried out in Embase, PsycINFO, and the Cochrane Library.**

|                  |             |
|------------------|-------------|
| Medline          | 329         |
| Embase           | 395         |
| Cochrane Library | 332         |
| PsycINFO         | 508         |
| <b>Total</b>     | <b>1564</b> |

The above search strategy retrieved 1564 references in total. After duplicate references were removed a total of 1168 potentially relevant references were left. The title and abstracts of the remaining citations were scanned for relevance to screening for Alzheimer's disease and all classes of dementia using cognitive assessment tools, particularly focusing on the test and the treatment and the following question:

'Screening for all classes of dementia using cognitive assessment tools as a strategy to reduce the incidence/ and or morbidity and to increase the benefit to family and society.'

544 references were deemed to be relevant. The final set of references was then passed to the expert reviewer for further appraisal and possible inclusion in the review.

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |            |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| <b>Systematic reviews and meta-analysis</b><br>The condition (18)<br>Cognitive assessment tools (10)<br>Prevention (7)<br>Interventions (21)<br>Screening (1)<br>Guidelines and recommendations (5)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | <b>62</b>  |
| <b>Structured abstract</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | <b>5</b>   |
| <b>Non-systematic reviews</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | <b>4</b>   |
| <b>The condition</b><br>Epidemiology (15)<br>Chronic characteristics and progression (29)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | <b>44</b>  |
| <b>Cognitive assessment tools</b><br>Reviews (8)<br>Clock drawing test (30)<br>Brief assessments (21)<br>Memory assessments (18)<br>Montreal Cognitive Assessment (MoCA) (16)<br>Verbal fluency assessments (10)<br>Trail making assessments (7)<br>Use of technology (7)<br>Addenbrooke's cognitive examination (ACE) (5)<br>Activities of daily living assessments (4)<br>Picture based assessments (4)<br>The Cambridge Cognitive Examination (CAMCOG) (3)<br>Rowland Universal Dementia Assessment Scale (RUDAS) (3)<br>Alzheimer Disease Assessment Scale (ADAS-Cog) (2)<br>Consortium to Establish a Registry for Alzheimer's Disease – NP (CERAD-NP) (2)<br>DemTect (2)<br>Miscellaneous (17)<br>Combination of assessments (14)<br>Comparisons (33) | <b>206</b> |
| <b>Prevention</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | <b>19</b>  |
| <b>Caregiver burden/ interventions</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | <b>13</b>  |
| <b>The treatment</b><br>Reviews (4)<br>Cholinesterase inhibitors (35)<br>NMDA receptor antagonists (18)<br>Diabetes drugs (7)<br>Statins (4)<br>Antihypertensives (3)<br>Antipsychotics (3)<br>Cerebrolysin (3)<br>NSAIDs (3)<br>Cognitive rehabilitation (21)<br>Physical activity (12)<br>Diet (8)<br>Music therapy (6)<br>Combination of interventions (10)<br>Comparison of interventions (6)<br>Miscellaneous (23)<br>Supplements and complementary therapies (22)                                                                                                                                                                                                                                                                                     | <b>188</b> |
| <b>The screening programme</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | <b>2</b>   |
| <b>Total</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | <b>544</b> |

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