Mini-Cog for the diagnosis of Alzheimer's disease dementia and other dementias within a secondary care setting

Review information

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What's new

Date	Event	Description

History

Date	Event	Description

Abstract

Background

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Plain language summary

[Summary title]

[Summary text]

Background

Target condition being diagnosed

Alzheimer's disease (AD) and related forms of dementia are common among older adults with a prevalence of 8% in individuals over age 65 years increasing to a prevalence of approximately 43% in adults aged 85 years and older (Thies 2012). Given the increasing number of older adults in most developing countries, the prevalence of dementia is expected to increase considerably in the coming years. Currently, an estimated 5.4 million Americans are diagnosed with AD and this number is expected to increase to 6.7 million by 2025 (Thies 2012). Alzheimer's disease and related forms of dementia are currently incurable and result in considerable direct and indirect costs, both in terms of formal health care and lost productivity from both the affected individual and their caregivers (Thies 2012). There are several benefits to diagnosing AD and related dementias early in the disease course. Most individuals with dementia, and their caregivers, would prefer to know a diagnosis of dementia, and earlier diagnosis of AD allows for individuals with AD to make decisions regarding future planning while they retain the capacity to do so (Prorok 2013). A diagnosis of dementia is also necessary to access certain services and supports for individuals and their caregivers, and pharmacological treatments such as cholinesterase inhibitors (Birks 2006; Rolinski 2012) or memantine (McShane 2006; Wilkinson 2012) may provide temporary symptomatic improvement in cognitive and functional symptoms for individuals with mild to moderate AD.

The diagnosis of AD is clinical and based on a history of decline in cognition with deficits in memory and at least one other area of cognitive functioning (for example apraxia, agnosia, or executive dysfunction). There must be a decline from a previous level of functioning which results in significant social or occupational impairment (American Psychiatric Association 2000; McKhann 2001). A definitive diagnosis of AD can only be achieved at autopsy, but a clinical diagnosis using standardized criteria is associated with a sensitivity of 81% and a specificity of 70% when compared to autopsy proven cases (Knopman 2001).

Approximately 50% to 80% of all individuals with dementia are ultimately classified as AD (Blennow 2006; Brunnstrom 2009; Canadian Study of Health and Aging 1994). While patients with dementias share common characteristics, subtle differences can help to provide a diagnosis in the absence of neuropathological examination. Vascular dementias may occur more abruptly or present with a step-wise decline in cognitive functions over time, and account for approximately 15% to 20% of dementias (Canadian Study of Health and Aging 1994; Feldman 2003; Lobo 2000). Dementia with a mixed vascular and Alzheimer's disease pathology is present in 10% to 30% of cases (Brunnstrom 2009; Crystal 2000; Feldman 2003). A smaller proportion of dementias are associated with dementia with Lewy bodies (Brunnstrom 2009) or Parkinson's disease dementia (Aarsland 2005). Patients experiencing frontotemporal dementia account for a smaller proportion of dementias (4% to 8%) and often present with problems in executive function and changes in behaviour, while memory is relatively preserved early in the disease course (Brunnstrom 2009; Greicius 2002).

Index test(s)

The Mini-Cog is a brief cognitive test consisting of two components, a delayed three word recall and the clock drawing test (Borson 2000). The Mini-Cog was initially developed in a community setting to provide a relatively brief cognitive screening test that was free of educational and cultural biases. Different scoring algorithms were tested to determine which combination had the optimal balance of sensitivity and specificity (McCarten 2011; Scanlan 2001). The Mini-Cog takes approximately three to five minutes to complete in routine practice (Borson 2000; Holsinger 2007; Scanlan 2001). The Mini-Cog has been reported to have little potential for bias with education or language (Borson 2000; Borson 2005).

Clinical Pathway

Dementia typically begins with subtle cognitive changes and progresses gradually over the course of several years. There is a presumed period when people are asymptomatic although the disease pathology may be progressing. Individuals or their relatives may first notice subtle impairments of short-term memory or other areas of cognitive functioning. Gradually, the severity of cognitive deficits become apparent resulting in difficulty completing complex activities of daily living such as management of finances and medications, or operating motor vehicles (Njegovan 2001). The attribution of cognitive symptoms to normal aging may cause delays in the diagnosis and treatment of AD or other types of dementia. Therefore, there is a need for accurate brief cognitive screening tests to help distinguish between the cognitive changes associated with normal aging and changes that might indicate a dementia. In a secondary care setting, individuals are typically referred from primary care or community health services for further evaluation of possible memory complaints. Therefore, most individuals in secondary care settings would likely have some cognitive complaints or symptoms at the time of evaluation. Secondary care settings that would frequently use the Mini-Cog or other screening tests would include neurology, geriatric medicine, geriatric psychiatry services or memory clinics. Typically, individuals who are assessed in secondary care settings would receive more detailed neuropsychological testing along with other investigations that are needed in order to confirm a diagnosis of dementia.

Prior test(s)

As the Mini-Cog is recommended to be used as an initial screening test for dementia it is unlikely that individuals will have any testing completed prior to the administration of the Mini-Cog.

Role of index test(s)

Most older adults with memory complaints will first present to their general practitioner or other primary healthcare provider (for example nurses or a nurse practitioner). Primary healthcare providers may then refer an individual to a secondary care setting such as a neurologist, geriatrician, or geriatric psychiatrist. Some countries have also recommended that brief cognitive screening tests be administered to all older adults in order to help screen for undetected or asymptomatic cognitive impairment (Cordell 2013) although routine screening of older adults for dementia is controversial. We would anticipate that the Mini-Cog would be utlized as a screening test to guide further evaluation of cognitive complaints for individuals in secondary care and not as a diagnostic test in most instances.

Alternative test(s)

We are not including alternative tests in this review because there are currently no standard tests available for the diagnosis of dementia.

The Cochrane Dementia and Cognitive Improvement Group (CDCIG) is in the process of conducting a series of diagnostic test accuracy reviews of biomarkers and scales (see the list below). Although the CDCIG is conducting reviews on individual tests compared to a reference standard, we plan to compare our results in an overview.

- Positron emission tomography F-2-fluoro-2-deoxy-D-glucose (^{18}F-FDG-PET)
- Positron emission tomography Pittsburg compound-C (^{11}C-PIB-PET)
- Structural magnetic resonance imaging (sMRI)
- Neuropsychological tests (Mini-Mental State Examination (MMSE); Montreal Cognitive Assessment (MoCA))
- Informant interviews (Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE); AD8 Dementia Screening Interview)
- Apolipoprotein E e4 (APOE e4)
- Fluoropropil-carbomethoxy-iodophenil-tropane single-photon emission tomography (FP-CIT SPECT)

Rationale

Cognitive diagnostic tests are required to assess cognition and assist in diagnosing conditions such as mild cognitive impairment and dementia. Comprehensive evaluation, conducted by psychologists or dementia specialists such as general psychiatrists, geriatric psychiatrists, geriatricians, or neurologists, using standardized diagnostic criteria would be the reference standard for assessing cognition and diagnosing dementia in older adults. However, access to these specialized resources is scarce and expensive and as such they are not practical to be used routinely in the evaluation of cognitive complaints (Pimlott 2009; Yaffe 2008). While there are some cognitive tests that can be performed by healthcare providers who are not dementia specialists, many of these tests are time consuming and may not be practical to use as a first-line cognitive screen in secondary care settings. As such, brief but relatively accurate cognitive screening tests are required for healthcare providers in secondary care settings to identify individuals who may require more in-depth evaluation of cognition. In secondary care settings, brief cognitive screening tests may be used to guide subsequent evaluations or to complement more detailed evaluations.

Utilizing a standard cognitive screening test like the Mini-Cog also promotes effective communication between healthcare providers. Sensitivity and specificity of such tests vary depending upon the setting in which they are utilized (Holsinger 2007). Some studies have found that in primary care the majority of older adults with dementia are undiagnosed (Boustani 2005; Sternberg 2000). In addition, many primary care providers have difficulty in accurately diagnosing dementia, and mild dementia is particularly under-diagnosed (van den 2011). Early diagnosis and treatment of dementia can have clinical benefits for the patient, their community, and the healthcare system (Bennett 2003; Prorok 2013; Thies 2012). Accurate diagnosis of dementia is also important in order to initiate dementia therapeutics including both non-pharmacological treatments and pharmacological treatments such as cholinesterase inhibitors (Birks 2006; Rolinski 2012) or memantine (McShane 2006). A brief and simple cognitive screening test such as the Mini-Cog that could be used in secondary care settings would allow healthcare professionals or lay people to initially screen older adults for the presence of dementia. Individuals that screen positive for cognitive impairment on the Mini-Cog may then be further investigated for the presence of dementia using additional cognitive tests or other investigations. Given that the Mini-Cog is brief, widely available, easy to administer, and has been reported to have reasonable test accuracy properties (Brodaty 2006; Lin 2013) it may be well suited for use as an initial cognitive screening test in secondary care. The Mini-Cog has been recommended as a suitable cognitive screening test for primary care in some countries (Cordell 2013). The current review will examine the diagnostic accuracy of the Mini-Cog in secondary care settings. Separate DTA reviews are being undertaken for community and primary care settings (Fage 2013).

Objectives

To determine the diagnostic accuracy of the Mini-Cog for detecting Alzheimer's disease dementia and related dementias in a secondary care setting.

Secondary objectives

To investigate the heterogeneity of test accuracy in the included studies and potential sources of heterogeneity. These potential sources of heterogeneity will include the baseline prevalence of dementia in study samples, thresholds used to determine positive test results, the type of dementia (Alzheimer's disease dementia or all causes of dementia), and aspects of study design related to study quality.

We will also identify gaps in the evidence where further research is required.

Methods

Criteria for considering studies for this review

Types of studies

We included all cross-sectional studies with well-defined populations that utilized the Mini-Cog as an index cognitive screening test compared to a reference standard. Included studies utilized a reference standard to determine whether or not a dementia was present. Included studies also utilized the Mini-Cog as a screening test and not for confirmation of diagnosis. Some studies utilized the test on patients with a previously known diagnosis of AD or a related dementia, but when possible, studies administered the index and reference tests to individuals where their diagnosis is not already known.

Participants

Study participants were sampled from a secondary care setting and may or may not have ultimately been diagnosed with AD or a related dementia. Participants may have had cognitive complaints or dementia at baseline although their cognitive status should not be known to the individual administering the Mini-Cog or the reference standard. Studies on participants with a developmental disability which prevented them from completing the Mini-Cog were excluded. Studies including participants in either a community or primary care setting were excluded as these are the topic of other reviews (Fage 2013).

Index tests

Mini-Cog test

The Mini-Cog consists of a three word recall task and the clock drawing test. The standard scoring system involves assigning a score of zero to three points on the word recall task for the correct recall of 0, 1, 2, or 3 words, respectively. The clock drawing test is scored as being either 'normal' or 'abnormal'. A positive test on the Mini-Cog (that is dementia) is assigned if either the delayed word recall score is zero out of three, or if the delayed recall score is either one or two and the clock drawing test is abnormal. A score of three on the delayed word recall or one to two on the delayed word recall with a normal clock drawing is a negative test (that is no dementia) (Borson 2000).

Studies had to include the results of the Mini-Cog. If multiple scoring algorithms were utilized the differences in results was explored through subgroup analysis.

Target conditions

Target conditions included any stage of AD or other types of dementia including vascular dementia, dementia with Lewy bodies, Parkinson's disease dementia, or frontotemporal dementia.

Reference standards

While a definitive diagnosis can only be made post-mortem at autopsy, there are clinical criteria for the diagnosis of most forms of dementia. All dementia diagnostic criteria require that an individual has deficits in multiple areas of cognition that results in impairment in daily functioning and is not caused by either the effects of a substance or general medical condition. We have included several potential reference standards for the diagnosis of all-cause dementia or specific types of dementia. All-cause dementia is commonly diagnosed using criteria such as the Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV) criteria for dementia (American Psychiatric Association 2000), the DSM-5 (American Psychiatric Association 2013) criteria for major neurocognitive disorder, or the International Classification of Diseases (ICD) diagnosis of dementia (World Health Organization 2010). The standard clinical diagnostic criteria commonly used for Alzheimer's disease dementia include the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria for probable or possible dementia (McKhann 1984; McKhann 2011). Diagnostic criteria for other types of dementia will include the National Institute of Neurological Disorders and Stroke and Association Internationale pour la Recherché et l'Enseignement en Neurosciences (NINCDS-AIREN) criteria for vascular dementia (Roman 1993), standard criteria for dementia with Lewy bodies (McKeith 2005) and for frontotemporal dementia (McKhann 2001). The evaluation often includes laboratory investigations, many of which are useful for excluding alternative diagnoses (Feldman 2008). Additional procedures to help confirm the diagnosis include specific findings on neuroimaging (either computed tomography (CT) or magnetic resonance imaging (MRI)). These investigations are typically used to confirm the diagnosis rather than rule out the possibility of dementia. While these clinical criteria for dementia are considered the reference standard for the purpose of our review, the sensitivity and specificity of these clinical reference standards may vary when compared to neuropathological criteria for dementia (Nagy 1998).

Search methods for identification of studies

Electronic searches

We searched MEDLINE (OvidSP), EMBASE (OvidSP), BIOSIS previews (Web of Knowledge), Science Citation Index (ISI Web of Knowledge), PsycINFO (Ovid SP), LILACS (BIREME), and the Cochrane Dementia Group register of diagnostic test accuracy studies that is under development. See Appendix 1 for the search strategy used in MEDLINE (OvidSP) and to view the 'generic' search that is run regularly for the Cochrane Dementia and Cognitive Improvement Group register of diagnostic test accuracy studies. Similarly, structured search strategies was designed using search

terms appropriate for each database. Controlled vocabulary such as MeSH terms and EMTREE were used where appropriate. There was no attempt to restrict studies based on sampling frame or setting in the searches that were developed. This is to maximize sensitivity and allow inclusion on the basis of population-based sampling to be assessed at testing (see 'Selection of studies'). Search filters (collections of terms aimed at reducing the number need to screen) were not used as an overall limiter because those published have not proved sensitive enough (Whiting 2011). No language restriction was applied to the electronic searches, and we used translation services as necessary.

A single review author with extensive experience in systematic reviews performed the initial searches. Screening of abstracts and titles were conducted by two independent authors.

Searching other resources

The reference lists of all relevant studies were searched for additional relevant studies. These studies were also used to search the electronic databases to identify additional studies through the use of the related article feature. We asked research groups authoring studies used in the analysis for any unpublished data.

Data collection and analysis

Selection of studies

Included studies had to:

1. Make use of the Mini-Cog as a cognitive diagnostic tool.

2. Include patients from a secondary care setting who may or may not have dementia or cognitive complaints. Case-control studies will not be included in this review.

3. Clearly explain how a diagnosis of dementia was confirmed according to a reference standard such as the DSM IV-TR or NINCDS-ADRDA at the same time or within the same four week time period that the Mini-Cog was administered. Formal neuropsychological evaluation was not required for a diagnosis of dementia.

4. Report estimates of test reproducibility, if completed within the study.

Articles were first selected based on the abstracts and titles. Two independent review authors located selected articles and assessed for inclusion. Disagreements were settled by a third author.

Data extraction and management

Two review authors extracted the following data from all included studies:

- Author, journal, and year of publication.
- Scoring algorithm for the Mini-Cog including cut-points used to define a positive screen. Method of Mini-Cog administration including who administered and interpreted the test, their training, and whether or not the readers of the Mini-Cog and reference standard were blind (masked) to the results of the other test.
- Reference criteria and method used to confirm diagnosis of AD or a related dementia.
- Baseline demographic characteristics of the study population including age, gender, ethnicity, spectrum of presenting symptoms, comorbidity, educational achievement, language, baseline prevalence of dementia, country, ApoE status, methods of participant recruitment and sampling procedures.
- Length of time between administration of index test (Mini-Cog) and reference standard.
- The sensitivity and specificity, and positive and negative likelihood ratios of the index test in defining dementia.
- Version of translation (if applicable).
- Prevalence of dementia in the study population.

Assessment of methodological quality

We used the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) criteria to assess data quality (Whiting 2011). The QUADAS-2 criteria contain assessment domains for patient selection, index test, reference test, and flow and timing. Each domain has suggested signalling questions to assist with the risk of bias assessment for each domain. The potential risk of bias associated with each domain is rated as being at high, low, or uncertain risk of bias. In addition, we performed an assessment of the applicability of the study to the review question for each domain using the guide provided in the QUADAS-2. We used a standardized risk of bias template to extract data on the risk of bias for each study using the form provided by the UK Support Unit Cochrane Diagnostic Test Accuracy group. See Appendix 2 for details of the QAUDAS-2. The quality assessment results were summarized using the methodological quality summary table and methodological summary graph in RevMan.

Statistical analysis and data synthesis

We performed statistical analysis as per the Cochrane guidelines for diagnostic test accuracy reviews (Macaskill 2010). Two-by-two tables were constructed separately for the Mini-Cog results for Alzheimer's disease dementia and all-cause dementia where this information was available.

We entered data from individual studies including the true positives (TP), true negatives (TN), false positives (FP), and false negatives (FN) into RevMan. We then calculated the sensitivity, specificity, and positive and negative likelihood ratios as well as measures of statistical uncertainty (for example 95% confidence intervals) in RevMan from the raw data. Data from each study was presented graphically by plotting sensitivities and specificities on a coupled forest plot. If there were explicit thresholds across included studies we planned to use the bivariate random-effects approach for meta-analysis of the sensitivity and specificity (Reitsma 2005). If multiple thresholds were reported

for the Mini-Cog, we planned to use the hierarchical summary receiver operating characteristic (HSROC) method of Rutter and Gastconis for meta-analysis (Rutter 2001). The diagnostic odds ratio (DOR) was calculated for each study. The typical algorithm used to score the Mini-Cog is explicit in how the results should be scored. However, where variation from this scoring scheme was encountered in the literature, the analysis plan changed to incorporate multiple average threshold points.

Investigations of heterogeneity

The potential sources of heterogeneity included baseline prevalence of cognitive impairment in the target population, the cut-points used to determine a positive test result, the reference standard used to diagnose dementia, the type of dementia (Alzheimer's disease dementia or all-cause dementia), the severity of dementia in the study sample, and aspects related to study quality.

We performed subgroup analyses to investigate the effects of the sources of heterogeneity. These involved visual examination of the forest plot of sensitivity and specificity and the ROC plot within each subgroup (for example baseline prevalence, type of dementia, etc). Additionally, we performed a formal analysis using the HSROC model. If necessary, this model was extended to include covariates to assess whether threshold, accuracy, or the shape of the ROC curve varied with patient or study characteristics. If the number of studies was limited, we investigated the effect of each source of heterogeneity by using covariates to estimate differences in both the accuracy and threshold parameters; the underlying shape of the summary ROC curve was assumed to be constant.

Sensitivity analyses

If not already explored as part of the investigation of heterogeneity, above, we performed a sensitivity analysis in order to investigate the influence of study quality on overall diagnostic accuracy of the Mini-Cog test. In this analysis we omitted studies at high risk of bias.

We also determined the impact of individual studies on summary outcome measures.

Assessment of reporting bias

We did not investigate reporting bias because of current uncertainty about how it operates in test accuracy studies and the interpretation of existing analytical tools such as funnel plots.

Results

Results of the search

The results of the literature search are summarized in Figure 1. A review of the electronic databases initially in September 2012 identified 108 articles. This search was updated in January 2013 adding an additional 106 and a second update was completed in February 2015 which identified another 34 potentially relevant citations. The same search strategy was employed for this review that was used in separate reviews of the Mini-Cog in the community setting () and primary care setting. After removal of duplications a total of 144 abstracts and citations were reviewed by two authors for inclusion criteria and suitability for inclusion in the final review.

A total of 40 full-text articles were reviewed for eligibility to be included in the final review. Of these 40 articles, 36 were excluded due to a lack of a reference standard (N=15), failure to include the Mini-Cog as an index text (N=5), duplicate publications (N=6), incorrect setting (N=7), or lack of sufficient data to be included in in the review (N=3).

The final search resulted in four studies being included (including five separate research reports). The characteristics of the studies are outlined in Summary of findings table 1.

Methodological quality of included studies

The results of the QUADAS-2 assessment for the four included studies are presented in Figure 4. Filho 2009 was judged as being at high risk of bias in the patient selection and flow and timing domains. This was because a consecutive, random sample of patients was not used, the study did not avoid inappropriate exclusions, and not all patients were included in the analysis. For Clionsky 2010 and Steenland 2008, it was unclear whether or not a consecutive, random sampling of patients was employed, but this did not introduce a risk of bias in paient selection. It was also unclear if the Mini-Cog was interpreted with or without knowledge of the reference standard assessment in Clionsky 2010, but risk of bias was still judged to be low. Alternatively, it was unclear if the reference standard assessment was interpreted with or without knowledge of the Mini-Cog results in Filho 2009, but again the risk of bias was judged to be low. There was unclear risk of bias in the conduct or interpretation of the reference standard assessment for Steenland 2008.

An additional feature common across all four included studies that may have introduced other potential sources of bias was the index test employed. All studies used a version of the Mini-Cog that was derived from the three-word recall and clock drawing test components of a larger neuropsychological test (i.e. the MMSE), and furthermore, Filho 2009 utilized a modified threshold for its index test. The accuracy of the Mini-Cog may have been affected when the result of the Mini-Cog stemmed from more comprehensive testing compared to when the component tests were administered by themselves.

Findings

There were four study reports, each on unique study populations, that were selected for the final review (Clionsky 2010, Filho 2009, Milian 2012, Steenland 2008). The characteristics of these studies are summarized in the Characteristics of included studies section of this review. Additional features of these studies are also summarized in Summary of findings table 1. The baseline prevalence of dementia in the overall study samples varied from 32.2% (Filho 2009) to 90.2% (

Clionsky 2010). All studies utilized the original scoring system proposed by Borson et al (Borson 2000), except Filho 2009, in which a modified threshold was used.

Meta-analysis of the diagnostic test accuracy of the Mini-Cog was planned, although due to the small number of studies, methodological limitations, and heterogeneity of included studies we did not perform a meta-analysis. The extracted data, including sensitivity, specificity and forest plots for the Mini-Cog in each study, are summarized in Summary of findings table 1 and in the forest plot presented in Figure 2. The sensitivities of the Mini-Cog in the individual studies were reported as 0.67 (Clionsky 2010), 0.60 (Filho 2009), 0.87 (Milian 2012), and 0.72 (Steenland 2008). The specificity of the Mini-Cog for each individual study was 0.88 (Clionsky 2010), 0.65 (Filho 2009), 1.00 (Milian 2012), and 0.13 (Steenland 2008). The values for the positive and negative predictive values and positive and negative liklihood ratios for the individual studies are summarized in the Summary of findings table 1 and in Figure 2.

The use of meta-analysis to arrive at pooled estimates for the diagnostic test accuracy was not performed due to the small number of studies, heterogeneity, and overall poor quality of the included studies. The study specific sensitivity and specificity were plotted in a forest plot (Figure 2) and the summary test characteristics of the individual studies were plotted in a graph (Figure 3).

Discussion

Summary of main results

Strengths and weaknesses of the review

Applicability of findings to the review question

Authors' conclusions

Implications for practice

Implications for research

Acknowledgements

Contributions of authors

BF wrote the draft of the protocol and contributed to revisions of the protocol. DS, SG, NH, NS, CC and VN all contributed to revising the protocol and the final protocol. HN assisted with drafting the final version of the manuscript and with data extraction.

Declarations of interest

The authors have no conflicts of interest to declare.

Differences between protocol and review

Published notes

Characteristics of studies

Characteristics of included studies

Clionsky 2010

Patient Selection

A. Risk of Bias	
Patient Sampling	Patients were selected from medical records in neuropsychology and geriatric psychiatry practices between 2005 - 2008
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk

B. Concerns regarding applicability	
Patient characteristics and setting	Patient population was heterogenous in gender with an average age of 78.2 years old
Are there concerns that the included patients and setting do not match the review question?	Low concern

Index Test

Index tests	Mini-Cog scored according to original criteria in Borson 2000

All tests

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	Clinical diagnosis of dementia was determined based on the criteria of DSM-IV by 1 of 6 licensed psychologists. Psychologists were blind from Mini-Cog results. Patients were evaluated based on their age and education adjusted neuropsychological test scores, medical and psychiatric history and interview with a family informant.
Is the reference standards likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk

B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern

Flow and Timing

A. Risk of Bias	
Flow and timing	All patients received both index tests and reference standard.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk

Notes

Notes	

Filho 2009

Patient Selection

A. Risk of Bias	
Patient Sampling	Convenient sample of 306 individuals, 65 years old or older, seeking medical treatment as outpatients at Internal Medicine Clinic of the Policlinica Piquet Carneiro at Rio de Janeiro State University Hospital. Sampling limited by the number of consenting individuals and number of screening spots open for each day. Occassionally, patients return next day to finishing their testing.
Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	No
Could the selection of patients have introduced bias?	High risk

B. Concerns regarding applicability	
Patient characteristics and setting	Patients seeking general medical treatment were invited to participate. Those over 65 years old without serious visual and auditory deficient, mental illness affecting their understanding of testing procedures were not eligible for the screening tests. Non-native Portuguese speakers and elders with hand movement difficulties were excluded.
Are there concerns that the included patients and setting do not match the review question?	Unclear

Index Test

Index tests	Mini-Cog testing as described by Borson (2000) with a modified threshold for diagnosing dementia. A threshold of 2/3 was chosen instead of the 3/5 threshold as described by Borson (2000)

All tests

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	No
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	Diagnosis of dementia based on the formal criteria of DSM-IV evaluated based on clinical impression and neuropsychological evaluation, which includes some components of the index tests, as agreed upon between geriatrician and neuropsychologist.
Is the reference standards likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk

B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern

Flow and Timing

A. Risk of Bias	
Flow and timing	No intervention/ treatment occurred between index test and the reference standard. Ocassionally, the index test and reference tests were administered on different days. Patients who were lost in follow up and those who did not finish their evaluation were excluded.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	High risk

Notes

Notes	

Milian 2012

Patient Selection

A. Risk of Bias	
Patient Sampling	Patient selected retrospectively from all admitted patients to the Memory Clinic of the Departent of Psychiatry and Psychotherapy of the University Hospital of Tubingen between 2004 to 2009.
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk

B. Concerns regarding applicability	
Patient characteristics and setting	Patient sample composed of older adults from both gender, with normal visual acuity and sufficient hearing, wide education range. Patients with severe handicap affecting required tasks, mild cognitive impairment and depressive episodes were excluded from this analysis. Also, patients with underlying neurological and psychiatric disorder unrelated to the diagnosis of dementia were excluded.
Are there concerns that the included patients and setting do not match the review question?	Low concern

Index Test

Index tests	Mini-Cog administered with original scoring, as per Borson 2000.

All tests

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	Diagnosis of dementia based on the formal criteria of DSM-IV, ICD-10 of Mental & Behavior Disorder by the WHO and NINCDS-ADRDA
Is the reference standards likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk

B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern

Flow and Timing

A. Risk of Bias	
Flow and timing	The index test and reference standard were determined in succession by blinded assessors.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk

Notes

Notes	

Milian 2013

Patient Selection

A. Risk of Bias	
Patient Sampling	Memory clinic
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk

B. Concerns regarding applicability	
Patient characteristics and setting	Not specified
Are there concerns that the included patients and setting do not match the review question?	Low concern

Index Test

Index tests	The Mini-cog was completed by the individuals completing the reference standard. The scoring was standard scoring and the 3 word recall was derived from the MMSE.

All tests

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	Diagnosis of dementia according to ICD-10, NINCDS-ADRDA conducted by two psychiatrists
Is the reference standards likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk

B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern

Flow and Timing

A. Risk of Bias	
Flow and timing	The interval between index and reference were not specified and no description of patient drop outs were provided.
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Low risk

Notes

Notes	

Steenland 2008

Patient Selection

A. Risk of Bias	
Patient Sampling	Patients without prior history of dementia were sampled from the outpatient Geriatric Medicine Clinic at Wesley Woods Center of Emory University of Medicine. Patients were also sampled from registry of research volunteers at the Emory Alzheimer's Disease Research Center.
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk

B. Concerns regarding applicability	
Patient characteristics and setting	Patients suspected of possible cognitive deficits, or family expressed concern about cognitive decline were referred by geriatricians.
Are there concerns that the included patients and setting do not match the review question?	Low concern

Index Test

Index tests	Mini-Cog scored according to original scoring algorithm as per Borson 2000.

All tests

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	Clinical diagnosis of dementia based on evaluations by two experienced behavioral neurologists individually reviewing clinical history of all participants and neuropsychologists' impression.
Is the reference standards likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk

B. Concerns regarding applicability	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear

Flow and Timing

A. Risk of Bias	
Flow and timing	All patients completed both the index test and reference standard at the same time.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	Low risk

Notes

Notes	

Footnotes

Characteristics of excluded studies

Chen 2011

Reason for exclusion	Participants were not without dementia or cognitive complaints at baseline. Study did not receive gold standard evaluation using standardized diagnostic criteria.

Dash 2004

Reason for exclusion	Participants were not without dementia or aconative complaints at baseline. Study did not receive gold standard evaluation using standardized diagnostic criteria.

Del Ser 2000

Reason for exclusion	Study did not use Mini-Cog as index test. Participants were not without dementia or cognitive complaints at baseline.

Dougherty Jr 2010

Reason for exclusion	Participants were not without dementia or cognitive complaints at baseline.

Sonnett 2012

Reason for exclusion	Study did not receive gold standard evaluation using standardized diagnostic criteria.

Wilber 2005

Reason for exclusion	Study did not receive gold standard evaluation using standardized diagnostic criteria.

Wright 2011

Reason for exclusion	Study did not use Mini-Cog as Index test.

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

Summary of results tables

1 New Summary of findings table

Title: Mini-Cog for the diagnosis of Alzheimer's disease dementia and other dementias within a secondary care setting				
Population	Patients from secondary care setting			
Setting	Studies with patients recruited from secondary care settings and evaluated using the Mini-Cog and reference standard were included.			
Index Test	Mini-Cog was derived from CDT and 3 word recall from the MMSE. Standard scoring was used.			
Reference Standard	Clinical diagnosis of dementia using recognized standardized dementia criteria.			
Studies	Cross-sectional studies were included.			
Study	Accuracy (95% CI)	Number of participants	Dementia prevalence	Implications
Clionsky 2010	Sensitivity: 0.67 (0.63 to 0.71) Specificity: 0.88 (0.76 to 0.95) Positive LR: 5.58 Negative LR: 0.375	572	90.2%	
Filho 2009	Sensitivity: 0.60 (0.48 to 0.72) Specificity: 0.65 (0.57 to 0.73) Positive LR: 1.71 Negative LR: 0.615	211	32.2%	
Milian 2012	Sensitivity: 0.87 (0.83 to 0.90) Specificity: 1.00 (0.94 to 1.00) Positive LR: 0.00 Negative LR: 0.13	502	87.3%	
Steenland 2008	Sensitivity: 0.72 (0.58 to 0.83) Specificity: 0.13 (0.06 to 0.24) Positive LR: 0.83 Negative LR: 2.15	125	45.6%	

Footnotes

Additional tables

1 Characteristics of included studies

Study ID	Country	Participants(N)	Setting	Mini-Cog scoring	Dementiadiagnosis	Dementiaprevalence	Notes

Footnotes

References to studies

Included studies

Clionsky 2010

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Ongoing studies

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Wright DW, Navarez H, Kilgo P, Laplaca M, Robinson A, Fowler S, et al. A Novel Technology to Screen for Cognitive Impairment in the Elderly. American Journal of Alzheimer's Disease and Other Dementias 2011;26(6):484-91.

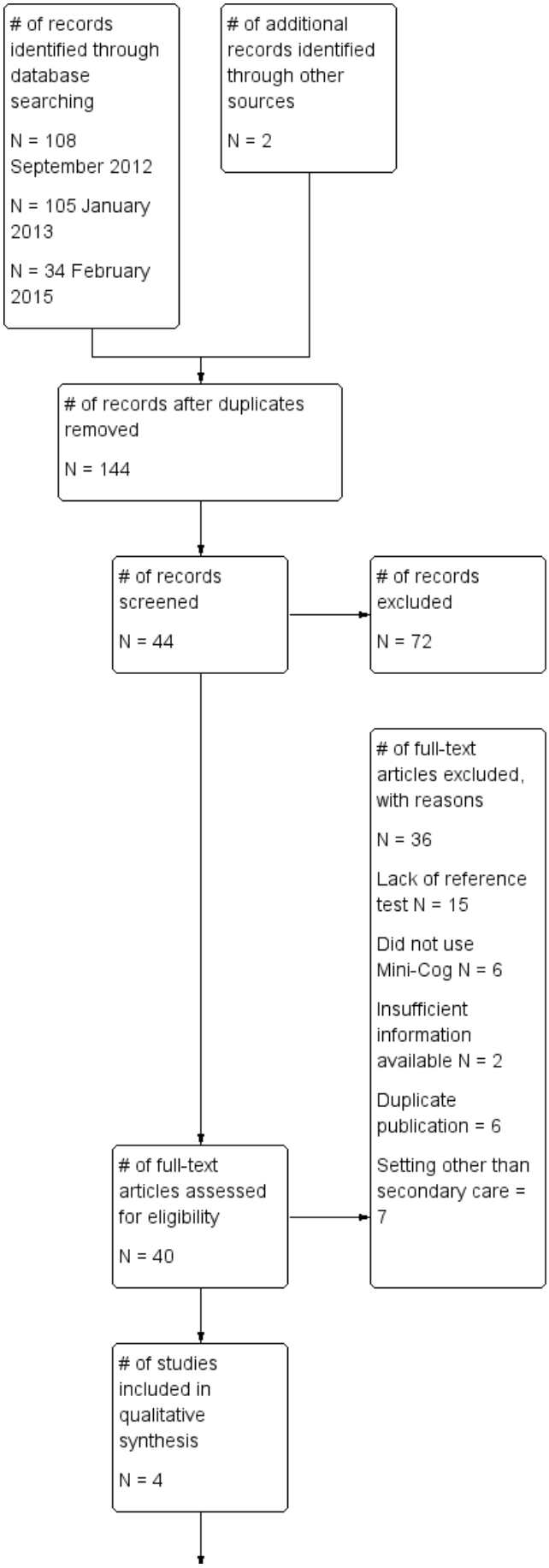
Data and analyses

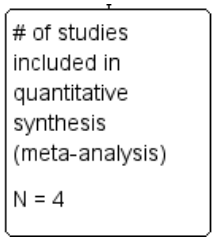
Data tables by test

Test	Studies	Participants
1 Mini-Cog in Tertiary Setting	4	1410

Figures

Figure 1

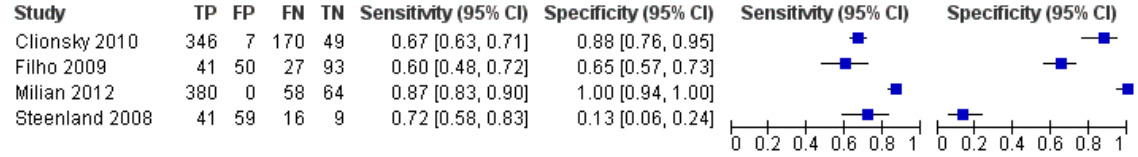




Caption

Study flow diagram.

Figure 2 (Analysis 1)

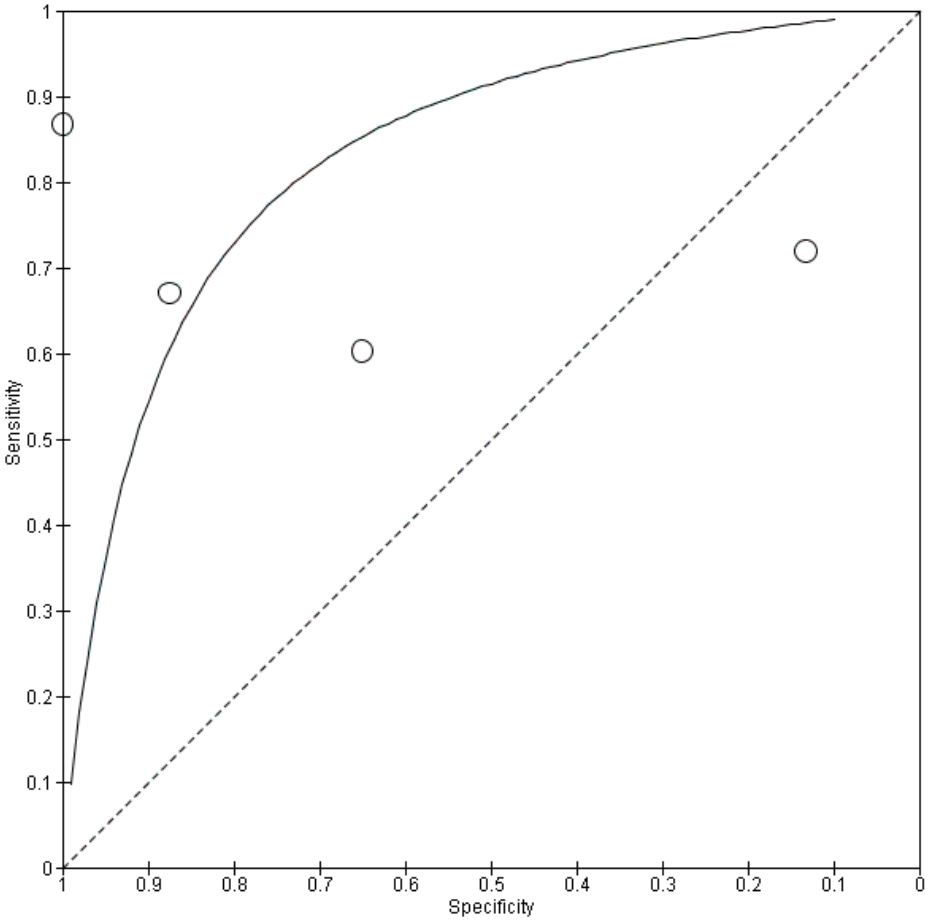


Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Clionsky 2010	346	7	170	49	0.67 [0.63, 0.71]	0.88 [0.76, 0.95]
Filho 2009	41	50	27	93	0.60 [0.48, 0.72]	0.65 [0.57, 0.73]
Milian 2012	380	0	58	64	0.87 [0.83, 0.90]	1.00 [0.94, 1.00]
Steenland 2008	41	59	16	9	0.72 [0.58, 0.83]	0.13 [0.06, 0.24]

Caption

Forest plot of 1 Mini-Cog in Tertiary Setting.

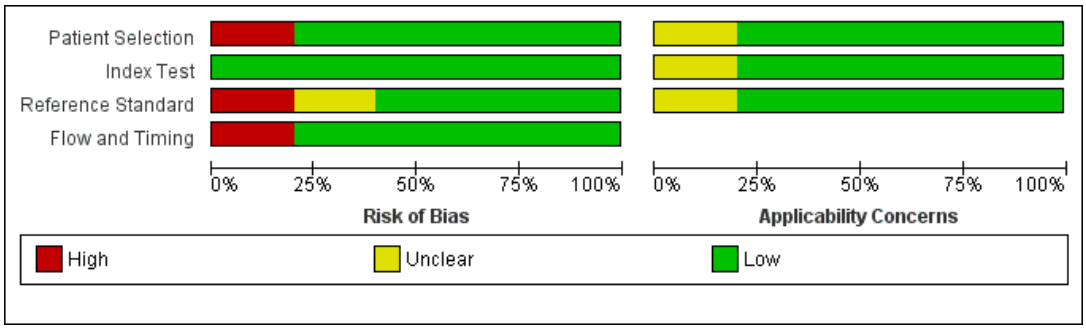
Figure 3 (Analysis 1)



Caption

Summary ROC Plot of 1 Mini-Cog in Tertiary Setting.

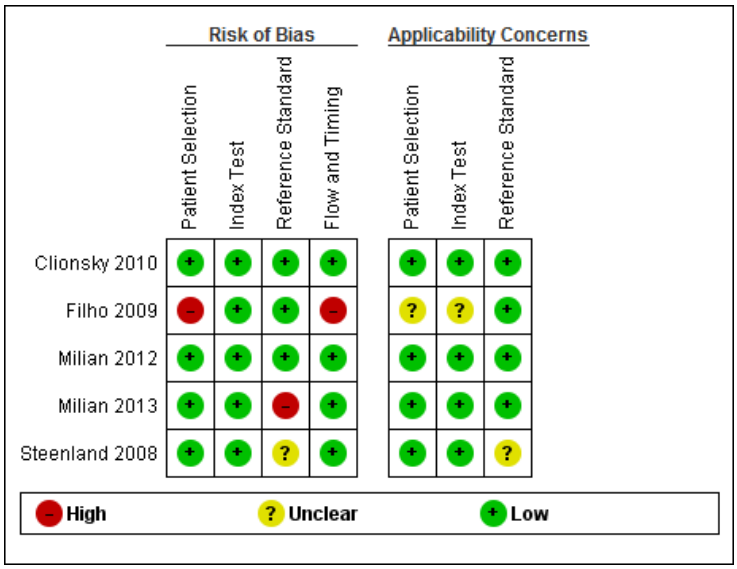
Figure 4



Caption

Risk of bias and applicability concerns graph: review authors' judgements about each domain presented as percentages across included studies

Figure 5



Caption

Risk of bias and applicability concerns summary: review authors' judgements about each domain for each included study

Sources of support

Internal sources

- No sources of support provided

External sources

- No sources of support provided

Feedback

Appendices

1 MEDLINE search strategy

The Mini-Cog search will utilize only one search concept: the index test (Mini-Cog):

1. "mini-Cog".ti,ab.
2. minicog.ti,ab.
3. (MCE and (cognit* OR dement* OR screen* OR Alzheimer*)).ti,ab.
4. or/1-3

The MEDLINE generic search run for the CDCIG DTA register:

1. "word recall".ti,ab.
2. ("7-minute screen" OR "seven-minute screen").ti,ab.
3. ("6 item cognitive impairment test" OR "six-item cognitive impairment test").ti,ab.
4. "6 CIT".ti,ab.
5. "AB cognitive screen".ti,ab.

6. "abbreviated mental test".ti,ab.
7. "ADAS-cog".ti,ab.
8. AD8.ti,ab.
9. "inform* interview".ti,ab.
10. "animal fluency test".ti,ab.
11. "brief alzheimer* screen".ti,ab.
12. "brief cognitive scale".ti,ab.
13. "clinical dementia rating scale".ti,ab.
14. "clinical dementia test".ti,ab.
15. "community screening interview for dementia".ti,ab.
16. "cognitive abilities screening instrument".ti,ab.
17. "cognitive assessment screening test".ti,ab.
18. "cognitive capacity screening examination".ti,ab.
19. "clock drawing test".ti,ab.
20. "deterioration cognitive observee".ti,ab.
21. ("Dem Tect" OR DemTect).ti,ab.
22. "object memory evaluation".ti,ab.
23. "IQCODE".ti,ab.
24. "mattis dementia rating scale".ti,ab.
25. "memory impairment screen".ti,ab.
26. "minnesota cognitive acuity screen".ti,ab.
27. "mini-cog".ti,ab.
28. "mini-mental state exam*".ti,ab.
29. "mmse".ti,ab.
30. "modified mini-mental state exam".ti,ab.
31. "3MS".ti,ab.
32. “neurobehavio?ral cognitive status exam*”.ti,ab.
33. "cognistat".ti,ab.
34. "quick cognitive screening test".ti,ab.
35. "QCST".ti,ab.
36. "rapid dementia screening test".ti,ab.
37. "RDST".ti,ab.
38. "repeatable battery for the assessment of neuropsychological status".ti,ab.
39. "RBANS".ti,ab.
40. "rowland universal dementia assessment scale".ti,ab.
41. "rudas".ti,ab.
42. "self-administered gerocognitive exam*".ti,ab.
43. ("self-administered" and "SAGE").ti,ab.
44. "self-administered computerized screening test for dementia".ti,ab.
45. "short and sweet screening instrument".ti,ab.
46. "sassi".ti,ab.
47. "short cognitive performance test".ti,ab.
48. "syndrome kurztest".ti,ab.
49. ("six item screener" OR “6-item screener”).ti,ab.
50. "short memory questionnaire".ti,ab.
51. ("short memory questionnaire" and "SMQ").ti,ab.
52. "short orientation memory concentration test".ti,ab.

53. "s-omc".ti,ab.
54. "short blessed test".ti,ab.
55. "short portable mental status questionnaire".ti,ab.
56. "spmsq".ti,ab.
57. "short test of mental status".ti,ab.
58. "telephone interview of cognitive status modified".ti,ab.
59. "tics-m".ti,ab.
60. "trail making test".ti,ab.
61. "verbal fluency categories".ti,ab.
62. "WORLD test".ti,ab.
63. "general practitioner assessment of cognition".ti,ab.
64. "GPCOG".ti,ab.
65. "Hopkins verbal learning test".ti,ab.
66. "HVLT".ti,ab.
67. "time and change test".ti,ab.
68. "modified world test".ti,ab.
69. "symptoms of dementia screener".ti,ab.
70. "dementia questionnaire".ti,ab.
71. "7MS".ti,ab.
72. ("concord informant dementia scale" or CIDS).ti,ab.
73. (SAPH or "dementia screening and perceived harm*").ti,ab.
74. or/1-73
75. exp Dementia/
76. Delirium, Dementia, Amnestic, Cognitive Disorders/
77. dement*.ti,ab.
78. alzheimer*.ti,ab.
79. AD.ti,ab.
80. ("lewy bod*" or DLB or LBD or FTD or FTLD or “frontotemporal lobar degeneration” or “frontaltemporal dement*).ti,ab.
81. "cognit* impair*".ti,ab.
82. (cognit* adj4 (disorder* or declin* or fail* or function* or degenerat* or deteriorat*)).ti,ab.
83. (memory adj3 (complain* or declin* or function* or disorder*)).ti,ab.
84. or/75-83
85. exp "sensitivity and specificity"/
86. "reproducibility of results"/
87. (predict* adj3 (dement* or AD or alzheimer*)).ti,ab.
88. (identif* adj3 (dement* or AD or alzheimer*)).ti,ab.
89. (discriminat* adj3 (dement* or AD or alzheimer*)).ti,ab.
90. (distinguish* adj3 (dement* or AD or alzheimer*)).ti,ab.
91. (differenti* adj3 (dement* or AD or alzheimer*)).ti,ab.
92. diagnos*.ti.
93. di.fs.
94. sensitivit*.ab.
95. specificit*.ab.
96. (ROC or "receiver operat*").ab.
97. Area under curve/
98. ("Area under curve" or AUC).ab.
99. (detect* adj3 (dement* or AD or alzheimer*)).ti,ab.

100. sROC.ab.
101. accura*.ti,ab.
102. (likelihood adj3 (ratio* or function*)).ab.
103. (conver* adj3 (dement* or AD or alzheimer*)).ti,ab.
104. ((true or false) adj3 (positive* or negative*)).ab.
105. ((positive* or negative* or false or true) adj3 rate*).ti,ab.
106. or/85-105
107. exp dementia/di
108. Cognition Disorders/di [Diagnosis]
109. Memory Disorders/di
110. or/107-109
111. *Neuropsychological Tests/
112. *Questionnaires/
113. Geriatric Assessment/mt
114. *Geriatric Assessment/
115. Neuropsychological Tests/mt, st
116. "neuropsychological test*".ti,ab.
117. (neuropsychological adj (assess* or evaluat* or test*)).ti,ab.
118. (neuropsychological adj (assess* or evaluat* or test* or exam* or battery)).ti,ab.
119. Self report/
120. self-assessment/ or diagnostic self evaluation/
121. Mass Screening/
122. early diagnosis/
123. or/111-122
124. 74 or 123
125. 110 and 124
126. 74 or 123
127. 84 and 106 and 126
128. 74 and 106
129. 125 or 127 or 128
130. exp Animals/ not Humans.sh.
131. 129 not 130

2 QUADAS-2

Domain	Patient selection	Index test	Reference standard	Flow and timing
Description	Describe methods of patient selection: describe included patients (prior testing, presentation, intended use of index test and setting)	Describe the index test and how it was conducted and interpreted	Describe the reference standard and how it was conducted and interpreted	Describe any patients who did not receive the index test(s) and/or reference standard or who were excluded from the 2 x 2 table (refer to flow diagram): describe the time interval and any interventions between index test(s) and reference standard
Signalling questions (yes, no, unclear)	Was a consecutive or random sample of patients enrolled? Was a case-control design avoided? Did the study avoid inappropriate exclusions?	Were the index test results interpreted without knowledge of the results of the reference standard? If a threshold was used, was it pre-specified?	Is the reference standard likely to correctly classify the target condition? Were the reference standard results interpreted without knowledge of the results of the index test?	Was there an appropriate interval between index test(s) and reference standard? Did all patients receive the same reference standard? Were all patients included in the analysis?
Risk of bias: (high, low, unclear)	Could the selection of patients have introduced bias?	Could the conduct or interpretation of the index test have introduced bias?	Could the reference standard, its conduct, or its interpretation have introduced bias?	Could the patient flow have introduced bias?
Concerns regarding applicability: (high, low, unclear)	Are there concerns that the included patients do not match the review question?	Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Are there concerns that the target condition as defined by the reference standard does not match the review question?	—

Anchoring statements to assist with assessment of risk of bias

Domain 1: patient selection

Risk of bias: could the selection of patients have introduced bias? (high, low, unclear)

Was a consecutive or random sample of patients enrolled?

Where sampling is used, the methods least likely to cause bias are consecutive sampling or random sampling, which should be stated and/or described. Non-random sampling or sampling based on volunteers is more likely to be at high risk of bias.

Weighting: high risk of bias

Was a case-control design avoided?

Case-control study designs have a high risk of bias, but sometimes they are the only studies available especially if the index test is expensive and/or invasive. Nested case-control designs (systematically selected from a defined population cohort) are less prone to bias but they will still narrow the spectrum of patients that receive the index test. Study designs (both cohort and case-control) that may also increase bias are those designs where the study team deliberately increase or decrease the proportion of subjects with the target condition, for example a population study may be enriched with extra dementia subjects from a secondary care setting.

Weighting: high risk of bias

Did the study avoid inappropriate exclusions?

We will automatically grade the study as unclear if exclusions are not detailed (pending contact with study authors). Where exclusions are detailed, we will grade the study as 'low risk' if exclusions are felt to be appropriate by the review authors. Certain exclusions common to many studies of dementia are: medical instability; terminal disease; alcohol/substance misuse; concomitant psychiatric diagnosis; other neurodegenerative condition. However if 'difficult to diagnose' groups are excluded this may introduce bias, so exclusion criteria must be justified. For a community sample we would expect relatively few exclusions. We will label post hoc exclusions 'high risk' of bias.

Weighting: high risk of bias

Applicability: are there concerns that the included patients do not match the review question? (high, low, unclear)

The included patients should match the intended population as described in the review question. If not already specified in the review inclusion criteria, setting will be particularly important – the review authors should consider population in terms of symptoms; pre-testing; potential disease prevalence. We will classify studies that use very selected subjects or subgroups as having low applicability, unless they are intended to represent a defined target population, for example, people with memory

problems referred to a specialist and investigated by lumbar puncture.

Domain 2: index test

Risk of bias: could the conduct or interpretation of the index test have introduced bias? (high, low, unclear)

Were the index test results interpreted without knowledge of the reference standard?

Terms such as 'blinded' or 'independently and without knowledge of' are sufficient and full details of the blinding procedure are not required. This item may be scored as 'low risk' if explicitly described or if there is a clear temporal pattern to the order of testing that precludes the need for formal blinding, i.e. all (neuropsychological test) assessments were performed before the dementia assessment. As most neuropsychological tests are administered by a third party, knowledge of dementia diagnosis may influence their ratings; tests that are self administered, for example using a computerized version, may have less risk of bias.

Weighting: high risk of bias

Were the index test thresholds pre-specified?

For neuropsychological scales there is usually a threshold above which subjects are classified as 'test positive'; this may be referred to as threshold, clinical cut-off or dichotomisation point. Different thresholds are used in different populations. A study is classified as at higher risk of bias if the authors define the optimal cut-off post hoc based on their own study data. Certain papers may use an alternative methodology for analysis that does not use thresholds and these papers should be classified as not applicable.

Weighting: low risk of bias

Were sufficient data on (neuropsychological test) application given for the test to be repeated in an independent study?

Particular points of interest include method of administration (for example self completed questionnaire versus direct questioning interview); nature of informant; language of assessment. If a novel form of the index test is used, for example a translated questionnaire, details of the scale should be included and a reference given to an appropriate descriptive text, and there should be evidence of validation.

Weighting: low risk of bias

Applicability: are there concerns that the index test, its conduct, or interpretation differ from the review question? (high, low, unclear)

Variations in the length, structure, language, and/or administration of the index test may all affect applicability if they vary from those specified in the review question.

Domain 3: reference standard

Risk of bias: could the reference standard, its conduct, or its interpretation have introduced bias? (high, low, unclear)

Is the reference standard likely to correctly classify the target condition?

Commonly used international criteria to assist with clinical diagnosis of dementia include those detailed in DSM-IV and ICD-10. Criteria specific to dementia subtypes include but are not limited to NINCDS-ADRDA criteria for Alzheimer's dementia; McKeith criteria for Lewy Body dementia; Lund criteria for frontotemporal dementias; and the NINDS-AIREN criteria for vascular dementia. Where the criteria used for assessment are not familiar to the review authors and the Cochrane Dementia and Cognitive Improvement Group this item should be classified as 'high risk of bias'.

Weighting: high risk of bias

Were the reference standard results interpreted without knowledge of the results of the index test?

Terms such as 'blinded' or 'independent' are sufficient and full details of the blinding procedure are not required. This may be scored as 'low risk' if explicitly described or if there is a clear temporal pattern to order of testing, that is, all dementia assessments performed before (neuropsychological test) testing.

Informant rating scales and direct cognitive tests present certain problems. It is accepted that informant interview and cognitive testing is a usual component of clinical assessment for dementia, however specific use of the scale under review in the clinical dementia assessment should be scored as high risk of bias.

Weighting: high risk of bias

Was sufficient information on the method of dementia assessment given for the assessment to be repeated in an independent study?

Particular points of interest for dementia assessment include the training and expertise of the assessor, whether additional information was available to inform the diagnosis (for example, neuroimaging, other neuropsychological test results), and whether this was available for all participants.

Weighting: variable risk, but high risk if method of dementia assessment not described

Applicability: are there concerns that the target condition as defined by the reference standard does not match the review question? (high, low, unclear)

There is the possibility that some methods of dementia assessment, although valid, may diagnose a far smaller or larger proportion of subjects with disease than in usual clinical practice. For example, currently the reference standard for vascular dementia may under-diagnose compared to usual clinical practice. In this instance the item should be rated as having poor

applicability.

Domain 4: patient flow and timing

Risk of bias: could the patient flow have introduced bias? (high, low, unclear)

Was there an appropriate interval between the index test and reference standard?

For a cross-sectional study design, there is potential for the subject to change between assessments, however dementia is a slowly progressive disease, which is not reversible. The ideal scenario would be a same-day assessment, but longer periods of time (for example several weeks or months) are unlikely to lead to a high risk of bias. For delayed-verification studies the index and reference tests are necessarily separated in time given the nature of the condition.

Weighting: low risk of bias

Did all subjects receive the same reference standard?

There may be scenarios where subjects who score 'test positive' on the index test have a more detailed assessment for the target condition. Where dementia assessment (or reference standard) differs between subjects this should be classified as high risk of bias.

Weighting: high risk of bias

Were all subjects included in the final analysis?

Attrition will vary with study design. Delayed verification studies will have higher attrition than cross-sectional studies due to mortality, and it is likely to be greater in subjects with the target condition. Dropouts (and missing data) should be accounted for. Attrition that is higher than expected (compared to other similar studies) should be treated as a high risk of bias. We have defined a cut-off of greater than 20% attrition as being high risk but this will be highly dependent on the length of follow-up in individual studies.

Weighting: high risk of bias

Graphs

Mini-Cog in Tertiary Setting

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Clionsky 2010	346	7	170	49	0.67 [0.63, 0.71]	0.88 [0.76, 0.95]
Filho 2009	41	50	27	93	0.60 [0.48, 0.72]	0.65 [0.57, 0.73]
Milian 2012	380	0	58	64	0.87 [0.83, 0.90]	1.00 [0.94, 1.00]
Steenland 2008	41	59	16	9	0.72 [0.58, 0.83]	0.13 [0.06, 0.24]