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Evidence-based Synthesis Program

A Systematic Evidence Review of the Signs and Symptoms of Dementia and Brief Cognitive Tests Available in VA

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PREFACE

HSR&D's Evidence-based Synthesis Program (ESP) was established to provide timely and accurate syntheses of targeted healthcare topics of particular importance to VA managers and policymakers, as they work to improve the health and healthcare of Veterans. The ESP disseminates these reports throughout VA.

HSR&D provides funding for four ESP Centers and each Center has an active VA affiliation. The ESP Centers generate evidence syntheses on important clinical practice topics, and these reports help:

- develop clinical policies informed by evidence,
- the implementation of effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures, and
- set the direction for future research to address gaps in clinical knowledge.

In 2009, an ESP Coordinating Center was created to expand the capacity of HSR&D Central Office and the four ESP sites by developing and maintaining program processes. In addition, the Center established a Steering Committee comprised of HSR&D field-based investigators, VA Patient Care Services, Office of Quality and Performance, and VISN Clinical Management Officers. The Steering Committee provides program oversight and guides strategic planning, coordinates dissemination activities, and develops collaborations with VA leadership to identify new ESP topics of importance to Veterans and the VA healthcare system.

Comments on this evidence report are welcome and can be sent to Nicole Floyd, ESP Coordinating Center Program Manager, at nicole.floyd@va.gov.

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EVIDENCE REPORT

BACKGROUND

In 2004, the Office of the Assistant Deputy Under Secretary for Health for Policy and Planning estimated that the total number of Veterans with dementia would be as high as 563,758 in FY 2010.[1] A cost analysis of data from the VA determined that the average annual cost of care for a patient with dementia was $19,522 in FY 1999.[2]

Broad-based dementia screening programs have not been widely advocated given lack of evidence that earlier detection will improve health outcomes.[3, 4] When implemented, screening programs have been associated with high false positive rates, patient hesitation to undergo diagnostic confirmation, and high cost per case identified.[5] Furthermore, several studies have suggested the public is concerned about the implications of dementia screening.[6-8]

The alternative to systematic screening is a case-finding approach in which clinicians initiate diagnostic assessment of dementia when patients and/or their caregivers describe symptoms or present with signs suggestive of dementia. However, with current case-finding approaches, the diagnosis of dementia is often missed in primary care practice.[9-11]

Improving the accuracy of case-finding techniques depends both on an understanding of signs and symptoms that help distinguish patients with dementia from those without, and the reliability of brief assessment tests that can be incorporated into primary care practice when appropriate. Currently, several organizations have issued statements including signs and symptoms that should prompt a diagnostic evaluation for dementia.[12] However, these recommendations are based largely on expert opinion.

One objective of this review, then, is to determine which signs and symptoms help distinguish demented patients from those without dementia. The second objective of this review is to compare the relative accuracy and usability of 6 brief dementia assessment methods available for use in VA.

METHODS

TOPIC DEVELOPMENT

This review was requested by the VHA Dementia Steering Committee (DSC) and commissioned by the Department of Veterans Affairs' Evidence-based Synthesis Program (ESP). The DSC served as the technical expert panel for guiding topic development and reviewing drafts of the report.

In 2007, a workgroup of expert VA clinicians identified 6 brief mental status measures as possible alternatives to the Mini-Mental State Examination (MMSE): Blessed Orientation-Memory-Concentration (BOMC) Test, Mini-Cog, Montreal Cognitive Assessment (MoCA), General Practitioner Assessment of Cognition (GPCOG), St. Louis University Mental Status (SLUMS) Exam, and Short Test of Mental Status (STMS). The MMSE, a widely-used clinical instrument for detecting cognitive impairment, requires payment or permission before it can be reproduced or distributed, under copyright by the Psychological Assessment Resources (PAR). The 6 alternative measures were selected by an internal VA panel on the basis of brevity, applicability in a range of settings including primary care, accuracy in detecting cognitive disturbance, and availability for use in VA clinical and research settings without payment of royalty fees. The instruments are available on an internal VA website: http://vaww.mentalhealth.va.gov/mmse.asp.

The objectives of this review are to address the following questions:

Key Question #1. What signs and symptoms should prompt VA providers to assess cognitive function as part of an initial diagnostic workup for dementia?

Key Question #2. Which measures of cognitive function provide the optimal sensitivity, specificity, and time to completion among the measures available to VA providers?

Key Question #3. What are adverse consequences of using these measures?

These questions were explored within the following contexts:

Population: Adults without prior diagnosis of dementia.

Interventions to be compared: Six specific measures that VA has identified as alternatives to MMSE: BOMC, Mini-Cog, GPCOG, STMS, SLUMS, and MoCA.

Outcomes: Likelihood for patients to be appropriately diagnosed and treated for dementia; and adverse consequences of assessment, such as depression and anxiety.

Settings: Primary general medicine, mental health, geriatric clinics, specialty clinics, and extended-care settings.

SEARCH STRATEGY

We conducted searches in MEDLINE (PubMed), PsychINFO, CINAHL, HAPI, and AGELINE databases for cross-sectional studies comparing demented to non-demented participants, published from database inception through July 2009. Appendix A provides the search strategy in detail. We obtained additional articles from systematic reviews, reference lists of pertinent studies, reviews, editorials, and by consulting experts. All citations were imported into an electronic database (EndNote X2).

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STUDY SELECTION

Two reviewers assessed for relevance the abstracts of citations identified from literature searches. Full-text articles of potentially relevant abstracts were retrieved for further review. Each article retrieved was reviewed using the eligibility criteria shown in Appendix B.

Eligible articles had English-language abstracts and provided primary data relevant to the key questions. Eligibility criteria varied depending on the question of interest, as described below.

To evaluate the signs and symptoms of dementia, we determined the prevalence of signs/symptoms potentially associated with dementia in cross-sectional studies that compared patients with newly diagnosed, mild to moderate dementia with non-demented participants. We excluded studies with only demented individuals or only non-demented individuals, studies that did not provide prevalence data regarding signs and symptoms, and studies that did not use a reference standard to confirm the diagnosis of dementia. Because we were assessing signs and symptoms of prevalent dementia, we excluded studies on signs and symptoms that predicted future dementia.

To evaluate the 6 cognitive tests selected for use in VA, we included diagnostic accuracy studies that compared the performance of the index test against a reference standard for dementia diagnosis, such as DSM-IV. We included studies that compared demented patients with cognitive normal patients, or that included patients with mild cognitive impairment in either the demented or non-demented group. We excluded studies that assessed the performance of the index test for detecting mild cognitive impairment only. We included observational studies on the adverse effects of cognitive assessment.

DATA ABSTRACTION

For each study we abstracted the following: study design, objectives, setting, population characteristics, subject eligibility and exclusion criteria, number of subjects, the standard diagnostic criteria used, and the severity of and type of dementia. For Key Question #1, we additionally abstracted the prevalence of the sign/symptom among demented patients and among non-demented patients. For Key Question #2, we additionally abstracted the proportion of subjects with dementia; the cognitive measure and cut-off score used; the cognitive groups compared; subgroups analyzed (e.g. age, education, race); sensitivity and specificity; the administration time of the test; and any additional test characteristics such as inter-rater reliability, test-retest reliability, and internal consistency. Positive and negative likelihood ratios with 95% confidence intervals were calculated using STATA version 10.1.

QUALITY ASSESSMENT

We assessed the quality of studies using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) criteria for evaluating diagnostic accuracy studies.[13] Each sign or symptom was considered a diagnostic test, and the QUADAS criteria were used for quality assessment for these studies as well. The QUADAS tool includes 14 criteria that assess applicability, validity, and potential sources of bias, with each item scored as "yes," "no," or "unclear". Appendix C lists the QUADAS criteria in detail. We did not calculate an overall quality score for each study, since the importance of individual items varies according to context, and the use of summary scores for reviews of diagnostic studies is problematic.[14] We noted selected characteristics of studies that may affect quality.

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DATA SYNTHESIS

We constructed evidence tables showing the study characteristics and results for all included studies for Key Questions #1 and #2. We critically analyzed studies to compare their characteristics, methods, and findings. We compiled a summary of findings for each key question, and drew conclusions based on qualitative synthesis of the findings.

PEER REVIEW

A draft version of this report was sent to the technical advisory panel and additional peer reviewers. Reviewer comments and our responses are found in Appendix D.

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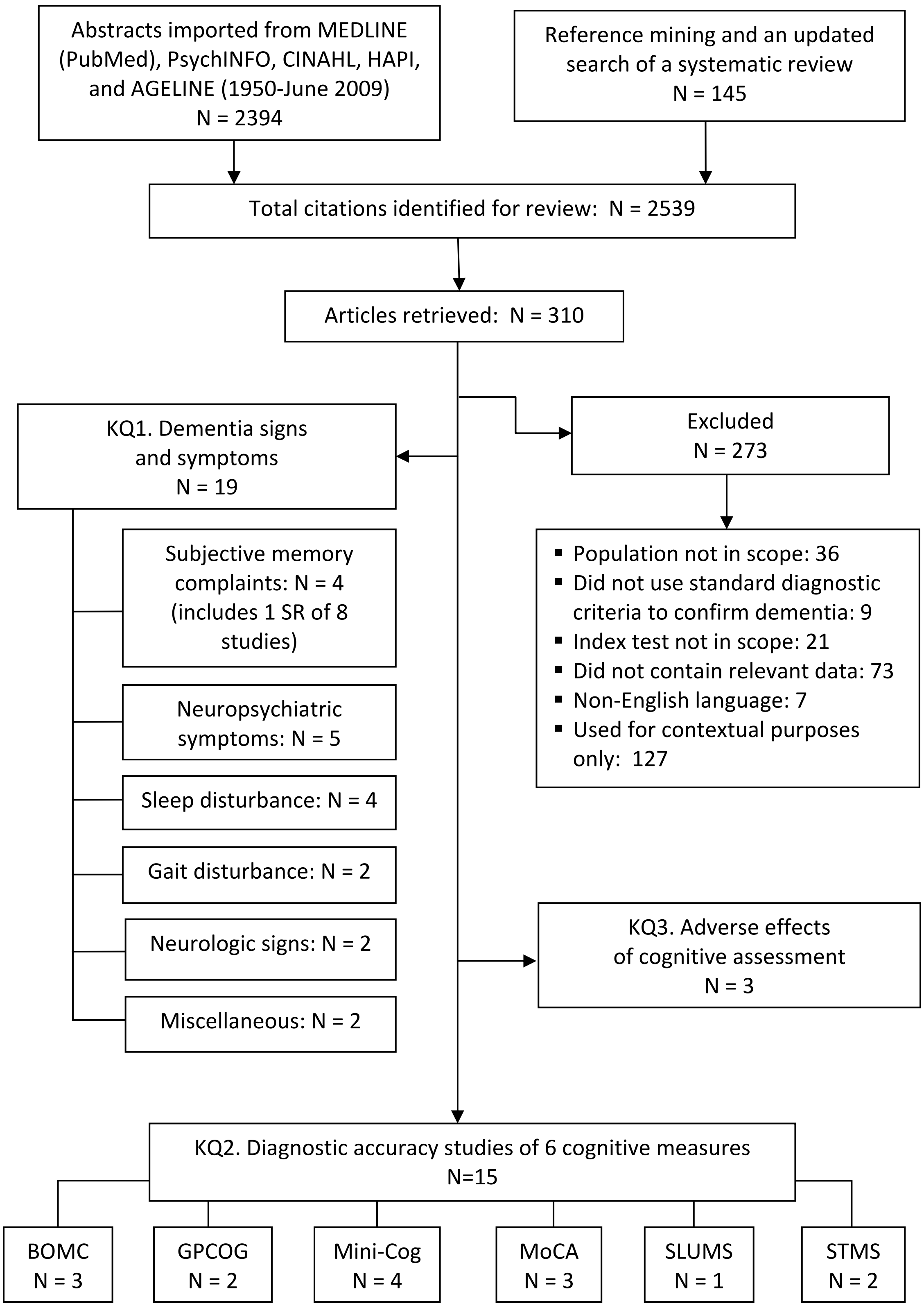
RESULTS

LITERATURE SEARCH

We reviewed 2,394 titles and abstracts from the electronic search, an additional 88 from reference mining, and 57 from conducting an update search of a relevant systematic review.

After applying inclusion/exclusion criteria at the abstract level, we retrieved 310 full-text articles for further review. Of the full-text articles, we rejected 273 that did not meet our inclusion criteria (Figure 1). We included 18 studies and 1 systematic review in synthesizing evidence for key question #1. For key question #2, we evaluated the results of 15 diagnostic accuracy studies of the 6 VA cognitive measures. To address key question #3, we included 3 cross-sectional studies on the acceptability of dementia screening and diagnostic workup.

Figure 1. Literature Flow



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KEY QUESTION #1. What signs and symptoms should prompt VA providers to assess cognitive function as part of an initial diagnostic workup for dementia?

Studies that examined signs and symptoms in demented and non-demented individuals are shown in the table below. The findings for each sign/symptom are described following Table 1.

Table 1. Study characteristics, sensitivity, and specificity of dementia signs and symptoms

Sign/ symptom	N of subjects, setting, country, dementia prevalence, type, and severity (MMSE if available)	Sensitivity of sign/symptom (unless otherwise specified)	Specificity of sign/symptom (unless otherwise specified)	Comments
Subjective memory complaints – self-reported [15]	Total pooled N = 9,148 Meta-analysis of 8 studies, U.S. Largely population based samples Dementia prevalence: 8.8% Severity: NR	Range: 31 – 96%.	Range: 30 – 98%	Good quality review, but methodologic flaws and study heterogeneity limit confidence in pooled results. Many of the included studies had methodologic flaws.
Subjective memory complaints – self-reported [16]	N = 339 Primary care, U.S. Dementia prevalence: 9.7% Type: NR Severity: NR	Self-reported SMC: 15.2% (5/33)	Self-reported SMC: 93.5% (285/305)	Depended on chart documentation of a self-reported symptom – may grossly underestimate the prevalence of the symptom and inflate specificity.
Subjective memory complaints – self-reported [17]	N = 358 Community based sample, U.S. Dementia screen positive (MMSE < 25): 31.0% Dementia type: NR CDR < 1: 61.8% CDR 1-3: 23.5% CDR > 3: 14.7%	Self-reported SMC (patients with CDR ≥ 1): 29.5%	Self-reported SMC: 82.2%	Subjects screened with MMSE so prevalence of dementia is higher than would be expected in pure population sample. Prevalence of SMC in patients with CDR = 0.5 (questionable dementia) was 24.8%.
Subjective memory complaints – informant reported [18]	N = 482 Community based sample, U.S. Dementia prevalence: NC Dementia type: AD CDR 0: 32.8% CDR 0.5: 34.2% CDR 1: 33.0%	Self-reported SMC (patients with CDR ≥ 1): 75.3% Informant-reported SMC (patients with CDR ≥ 1): 98.1%	Self-reported SMC (including patients with questionable dementia in control group): 35.6% Self-reported SMC (excluding patients with questionable dementia): 56.3% Informant-reported SMC (excluding patients with questionable dementia): 86.1%	The only study using single question assessment of informant-reported SMC. Self-reported SMC correlated with depressive symptoms.

Sign/ symptom	N of subjects, setting, country, dementia prevalence, type, and severity (MMSE if available)	Sensitivity of sign/symptom (unless otherwise specified)	Specificity of sign/symptom (unless otherwise specified)	Comments
Neuro-psychiatric symptoms [19]	N =1,563 randomly selected from community, Brazil Dementia prevalence: 6.8% AD: N = 60 CIND: N = 25 Randomly selected healthy controls: N = 78 MMSE: 15.5 ± 4.9	Sensitivities AD v CIND + control: Delusion 11.7% (7/60) Hallucination 8.3% (5/60) Agitation/aggression 20% (12/60) Depression 38.3% (23/60) Anxiety 25% (15/60) Elation 5% (3/60) Apathy 53.3% (32/60) Disinhibition 16.7% (10/60) Irritability 23.3% (14/60) Aberrant motor behavior 10% (6/60) Sleep disturbance 38.3% (23/60) Appetite alteration 23.3% (14/60)	Specificities AD v CIND + control: Delusion 100% (103/103) Hallucination 100% (103/103) Agitation/aggression 94.2% (97/103) Depression 87.4% (90/103) Anxiety 89.3% (92/103) Elation 100% (103/103) Apathy 96.1% (99/103) Disinhibition 100% (103/103) Irritability 96.1% (99/103) Aberrant motor behavior 100% (103/103) Sleep disturbance 91.2% (94/103) Appetite alteration 99.0% (102/103)	Dementia patients were older and less well-educated.
Neuro-psychiatric symptoms [20]	N = 682 Cross-sectional substudy of cardiovascular health study, U.S. Patients (at 3 of 4 sites) from pool considered "high-risk" for AD and non-AD dementia Dementia prevalence: 33.4% (24% if risk-screened patients excluded) MCI prevalence: 27.2% Severity: NR	Dementia (%) vs MCI* Delusions 18% (65/362) v 3.1 v 2.4 Hallucinations 10.5% (38/362) v 1.3 v 0.6 Agitation/aggression 30.3% (110/362) v 11.3 v 2.9 Depression 32.3% (117/362) v 20.1 v 7.2 Anxiety 21.5% (78/362) v 9.9 v 5.8 Euphoria 3.1% (11/362) v 0.6 v 0.3 Apathy 35.9% (130/362) v 14.7 v 3.2 Disinhibition 12.7% (46/362) v 3.1 v 0.9 Irritability 27.0% (98/362) v 14.7 v 4.6 Aberrant motor behavior 16% (58/362) v 3.8 v 0.4 Sleep disturbance 27.4% (99/362) v 13.8 v NA Eating disturbance 19.6% (71/362) v 10.4 v NA	Dementia vs MCI: Delusions 96.9% (310/320) Hallucinations 98.7% (316/320) Agitation/aggression 88.7% (284/320) Depression 79.9% (256/320) Anxiety 90.1% (290/320) Euphoria 99.4% (318/320) Apathy 85.3% (273/320) Disinhibition 96.9% (310/320) Irritability 85.3% (273/320) Aberrant motor behavior 96.2% (308/320) Sleep disturbance 86.2% (276/320) Eating disturbance 89.6% (287/320)	Higher dementia prevalence since nearly half the participants had high pre-test probability of cognitive disturbance. Non-demented population data derived from a different cohort.
Neuro-psychiatric symptoms [21]	N = 1002 Community, U.S. Dementia prevalence (MMSE screen positive): 18.4% Predominantly AD and vascular dementia Severity: NR	Sensitivities: Delusions 18.5% (61/329) Hallucinations 13.7% (45/329) Depression 23.7% (78/329) Anxiety 17.0% (56/329) Apathy 27.4% (90/329) Irritability 20.4% (67/329) Agitation/aggression 23.7% (78/329) Disinhibition 9.1% (30/329) Aberrant motor behavior 14.3% (47/329)	Specificities: Delusions 97.0% (653/673) Hallucinations 99.3% (668/673) Depression 92.7% (624/673) Anxiety 93.3% (628/673) Apathy 96.6% (650/673) Irritability 95.1% (640/673) Agitation/aggression 96.9% (652/673) Disinhibition 98.8% (665/673) Aberrant motor behavior 98.4% (662/673)	Population-based design and high participation rates. Subjects screened with MMSE so prevalence of dementia is higher than would be expected in pure population sample.

Sign/ symptom	N of subjects, setting, country, dementia prevalence, type, and severity (MMSE if available)	Sensitivity of sign/symptom (unless otherwise specified)	Specificity of sign/symptom (unless otherwise specified)	Comments
Depression (DSM-IV) [22]	N = 1260 Cross-sectional substudy of general population cohort study, Finland Dementia prevalence: 8.9% Mainly AD and vascular dementia MMSE: 17.0 in those without dementia documented in chart 12.7 in those with dementia documented in chart	32% (36/112)	81.8% (929/1136)	Population-based design and high participation rates are strengths. Study mainly looked at rates of documentation in chart.
Depression [23]	N = 86 Specialty center, U.S. Dementia prevalence: NC Dementia type: NR MMSE/CDR: NR	Mild, moderate or severe depression according to Hamilton Rating Scale for Depression: 40.9%	Mild, moderate or severe depression according to Hamilton Rating Scale for Depression: 88%	
Sleep disturbance [24]	N = 310 Memory clinic, U.S. Dementia prevalence: 50% Type: NR Severity: NR	Poor sleep quality (PSQI > 5): 34.2% (53/155)	Poor sleep quality (PSQI > 5): 40% (62/155)	Subtypes of dementia not reported.
Sleep disturbance [25]	N = 662 Specialty clinic, U.S. Dementia prevalence: NC Dementia type AD MMSE: 19.2 ± 6.2	Subjective sleep problems: 27.6% (71/258)	Subjective sleep problems: 82.7% (320/393)	Non-demented patients self-reported information, while caregivers of demented patients often reported information for demented subgroup.
Sleep disturbance [26]	N = 641 Population-based sample of persons ≥ 81 yo, Sweden Dementia prevalence: NR Type: NR Severity: NR	Subjective sleep disturbance (Comprehensive Psychopathological Rating Scale): 17.8% N not reported	Subjective sleep disturbance: 73.1%	Unclear duration of dementia diagnosis, little information about cohort.

Sign/ symptom	N of subjects, setting, country, dementia prevalence, type, and severity (MMSE if available)	Sensitivity of sign/symptom (unless otherwise specified)	Specificity of sign/symptom (unless otherwise specified)	Comments
REM sleep behavior disorder [27]	N = 65 Movement disorder clinic, U.K. Parkinsons Disease Severity: NR	Sensitivity: 77% (10/13)	Specificity: 73% (38/52)	Applicable to Parkinson's dementia only. Unclear proportion of dementia diagnoses that were made retrospectively. Convenience sample. RBD diagnosed with questionnaire, not polysomnography.
Gait disorders [28]	N = 245, age > 65 Specialty clinics, U.K. Dementia prevalence: NC AD, vascular, Parkinsons, and DLB Cambridge Examination for Mental Disorders of the Elderly Cognitive subsection score: Control: 94.0 ± 4.7 AD: 59.0 ± 14.5 Vascular dementia: 61.7 ± 18.3 Parkinsons: 63.9 ± 16.3 DLB: 59.7 ± 15.0	Gait or balance disorder (Tinetti score < 7 or balance score < 22): AD – 10/40 (25%) Vascular dementia – 31/39 (79%) Parkinson's – 43/46 (93%) DLB – 24/32 (75%)	Specificity: 93% (39/42)	Convenience sample. Not clear if reference standard was applied to all controls.
Gait disorders [29]	N = 110 Specialty clinic, U.S. Dementia prevalence: NC Type: AD MMSE: 21/55 mild dementia (CDR 1) 20/55 moderate dementia (CDR 2) 14/55 severe dementia (CDR 3)	Disequilibrium 58% (32/55) Wide-based gait 31% (17/55) Short-stepping gait 35% (19/55) Resistance to passive movement 18% (10/55)	Disequilibrium 64% (35/55) Wide-based gait 85% (47/55) Short-stepping gait 84% (46/55) Resistance to passive movement 98% (1/55)	Convenience sample. Purposive sampling of mild, moderate, and severe dementia. Prevalence of frontal gait disorder correlated with severity of dementia.
Neurologic signs [30]	N = 647, Age > 75 Community, Australia Dementia type: NR Severity: NR	Signs associated with dementia in a regression model (p < .05): rigidity, spasticity, snout/grasp reflex, impaired vibration sense		Major methodologic flaws. Selection criteria, index test, and standard criterion not well described. Large number of variables tested in regression model.

Sign/ symptom	N of subjects, setting, country, dementia prevalence, type, and severity (MMSE if available)	Sensitivity of sign/symptom (unless otherwise specified)	Specificity of sign/symptom (unless otherwise specified)	Comments
Neurologic signs [31]	N = 182 Multi-site (primary care, specialty, and community), U.S. Dementia prevalence: NC Type: AD MMSE: 20.9 ± 5.3	Sensitivities: Release signs – 54.7% (52/95) Olfaction – 20.2% (19/95) Stereognosis† and graphesthesia‡ - 22.1% (21/95) Abnormal gait – 33.7% (32/95)	Specificities: Release signs – 90.8% (79/87) Olfaction – 90.7% (79/87) Stereognosis and graphesthesia – 98.9% (1/87) Abnormal gait – 92.9% (6/87)	Convenience sample. Mean estimated duration of Sx nearly 3 years in dementia group. Not clear if "healthy" defined by self-report or by standard criterion.
Pulse pressure [32]	N = 192 Memory clinic (cases) and community (controls), Korea Dementia prevalence: 63.1% Type: AD MMSE: 16.2 ± 5.8	Mean pulse pressure, cases: 58.9 ± 16.0	Mean pulse pressure, controls: 54.3 ± 11.3	Convenience samples taken from two different populations, with case patients enrolled from a memory clinic.
Driving ability [33]	N = 75 Neurology clinic, U.S. Cross-sectional study from a larger longitudinal study of driving and AD Dementia prevalence: NC MMSE: Mild AD: 21.5 ± 3.9 Very mild AD: 24.9 ± 3.6	Self-reported less than "safe" driving ability: 6% (3/50)	Self-reported less than "safe" driving ability: specificity: 100% (24/24)	Not a population-based sample. Focused mainly on correlation between self-rated and on-road driving performance in demented patients.

*Controls taken from a different cohort, therefore figures represent comparison of demented patients to those with MCI

†Stereognosis = the ability to perceive the form of an object by using the sense of touch

‡Graphesthesia = the ability to recognize a number or letter written on the skin by the sensation of touch

Abbreviations: AD = Alzheimer 's disease, CIND = Cognitively impaired non-demented, DLB = Dementia with Lewy bodies, MCI = Mild cognitive impairment, NC = cannot be calculated, PSQI = Pittsburgh Sleep Quality Index, SMC = subjective memory complaints, Sx = symptoms

Subjective memory complaints

Summary of findings (Table 1)

Epidemiologic studies suggest subjective memory complaints (SMC) – in most cases elicited with single- or multi-item questionnaires, rather than spontaneous – are common in community-living elderly adults.[34, 35] The ability, however, of subjective memory complaints to discriminate effectively between healthy elderly adults and those with dementia is uncertain. We examined cross-sectional studies comparing rates of SMC between persons with dementia and healthy elderly controls.

Conclusions from this body of evidence should be tempered by methodologic flaws in some of the studies, as well as variability across studies in populations included and methods used for memory complaint elicitation. We found patient-reported SMC did not reliably distinguish demented from non-demented individuals. Patient-reported SMC were poorly sensitive for detecting dementia and only moderately specific. In populations with low prevalence of dementia, the absence of SMC may have some utility in excluding a diagnosis of dementia given its relatively high negative predictive value in these settings. Informant-reported memory complaints may better distinguish demented from non-demented individuals.

Detailed description

One recently published systematic review found 8 cross-sectional studies which compared elicited patient-reported SMC in demented and non-demented persons.[15] All studies were community-based and ranged in size from 156 to 3,220 participants. A number of the included studies had substantial flaws which reduce the strength of conclusions that can be drawn from this body of literature. Three studies established a dementia diagnosis using a widely-accepted gold standard.[36-38] One of the studies used a less widely-accepted cognitive evaluation,[39] and another study used an informant interview to establish a diagnosis.[40] Three of the studies used only brief assessment methods to validate the diagnosis of dementia.[41-43] Because of significant heterogeneity among studies, the pooled results cannot be used with any degree of confidence.

Of the 3 studies that used a widely-accepted gold standard to establish a dementia diagnosis,[36-38] one was mainly a study of different subtypes of mild cognitive impairment (MCI) and the number of patients with dementia was very low.[38] Tobiansky, et al.[36] and St. John, et al.[37] both examined large community-based samples, but used different methods for eliciting SMC: 1 study used a 9-item questionnaire,[36] while the other study simply asked whether participants had had memory loss during the past year.[37]

We found several more recent studies that were not included in the Mitchell review. One community-based study found a very low sensitivity of 15.2%, but a relatively high specificity of 93.5%.[16] However, these rates were likely a reflection of the method of SMC ascertainment, which relied on retrospective chart review. A multi-site primary care study of patients with largely mild dementia found patient-reported SMC also did not distinguish well between demented and non-demented participants.[17] Of note, investigators did find greater discrepancies between patient interview results and chart notes among patients with more severe dementia.

In contrast to patient-reported SMC, a small body of evidence suggests informant-reported SMC may better distinguish demented from non-demented individuals. One study of patients with mild and very mild Alzheimer's type dementia (AD) found informant complaints of memory loss (using a single question assessment) more reliably correlated with dementia than patient

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complaints (sensitivity of informant complaints 98.1%, specificity 86.1%).[18] Furthermore, patient-reported SMC did not predict future onset of dementia, whereas informant-reported SMC were associated with an increased risk of future dementia, a finding similar to a prior longitudinal study.[44] Patient complaints of memory loss in this study were closely associated with depressive symptomatology, findings that corroborate those of older studies.[44, 45]

Table 2 uses data from 2 of the self-reported SMC studies and the informant-reported memory complaint study to compare positive and negative predictive values in hypothetical populations with differing prevalence rates of dementia. All 3 studies suggest in populations with low rates of dementia, the lack of memory complaints may help exclude a dementia diagnosis, and the lack of informant memory complaints may most reliably exclude a diagnosis of dementia.

Table 2. Sensitivity, specificity, and predictive values of memory complaints in selected studies

Population	Sensitivity	Specificity	Prevalence assumption	Positive Predictive Value	Negative Predictive Value
Community sample[37]	58.0%	76.0%	10% 50% 75%	21.2% 70.7% 87.9%	94.2% 64.4% 37.6%
Community sample[36]	46.0%	97.0%	10% 50% 75%	63.1% 93.9% 97.9%	94.2% 64.2% 37.5%
Community sample – informant-reported memory complaints[18]	98.1%	86.1%	10% 50% 75%	43.8% 87.5% 94.6%	99.7% 97.7% 82.7%

A brief informant questionnaire, which combines 3 questions on informant-reported memory complaints with 5 questions covering other domains, including judgment and financial management, has been evaluated in demented and non-demented individuals. The questionnaire – the AD8 – discriminated well between demented and non-demented individuals (area under the curve 0.92; 95% CI 0.88 – 0.95).[46] The same authors later compared the utility of informant-administered to patient-administered AD8 and found both distinguished demented from non-demented individuals, but the informant-administered questionnaire performed better.[47]

Neuropsychiatric symptoms

Summary of findings

We found 3 community-based studies which used the Neuropsychiatric Inventory (NPI)[48] to compare neuropsychiatric symptoms in demented and non-demented persons. In general, neuropsychiatric symptoms were poorly sensitive but moderately to highly specific for dementia. Apathy was the most common neuropsychiatric symptom reported in demented persons and was present much less frequently in non-demented persons. Depression and anxiety were common in both groups, suggesting the presence of either symptom would not be useful in reliably ruling in or ruling out a diagnosis of dementia.

Detailed description

One well-conducted study included elderly residents of Cache County, Utah, and used a modified, more sensitive version of the Mini-Mental State Exam (MMSE) to identify a subpopulation at higher risk for dementia; and also included a randomly selected MMSE screen negative population.[21] All participants underwent a comprehensive cognitive assessment and were categorized as demented or non-demented according to DSM-IV criteria. The prevalence of dementia (18.4%) in this study reflects the use of MMSE as an initial screen and is higher than would be expected in the general population. Neuropsychiatric symptoms were more common in demented than non-demented individuals and 61% of demented individuals had had at least one behavorial symptom in the last month. Over 1 in 4 people with dementia were reported to display apathy, compared to less than 1 in 20 non-demented people. Depression was least helpful in distinguishing healthy elderly controls (specificity 92.7%).

Another study used a subsample of data from the Cardiovascular Health Study, and nearly half the participants had a high pre-test probability of cognitive dysfunction, which was reflected in the study's high prevalence of dementia (33.4%).[20] The study cohort included persons with dementia and mild cognitive impairment (MCI), but the non-demented comparison group was derived from a separate cohort in which sampling methods may have been different. Therefore, we only report sensitivity and specificity data comparing persons with dementia to persons with MCI. As expected, the specificities were lower, suggesting a higher likelihood of neuropsychiatric symptom presence in persons with MCI than healthy controls.

A community-based Brazilian study with a lower prevalence of dementia also had largely similar findings, but findings from this study may be less generalizable to VA populations in the United States.[19]

One population-based study focused on accuracy of dementia documentation in medical records of persons with and without dementia, but included the prevalence rates of depression in demented and non-demented people.[22] Similar to other studies, depression had a low sensitivity and specificity for dementia (32.0% and 81.8%, respectively). These results were similar to a small, older study of depression in demented and non-demented persons.[23]

Sleep disturbance

We found 4 studies comparing the frequency of sleep disturbance in patients with and without dementia. One of these studies compared the frequency of REM Sleep Behavior Disorder (RBD) in a convenience sample of Parkinson's disease patients with and without dementia, and is not applicable to patients with other types of dementia.[27]

The remaining 3 studies examined sleep disturbance in persons with and without dementia, mainly of Alzheimer's type.[24-26] In general, sleep disturbance is a commonly reported symptom in both demented and non-demented individuals, and does not discriminate the groups well. In fact, 2 of the studies found a higher prevalence of sleep disturbance complaints in non-demented than in demented persons.[24, 26] Results from the third study are more difficult to interpret because sleep disturbance questionnaires were completed by caregivers of demented participants, whereas non-demented participants in the control group completed the questionnaires themselves.[25] The body of evidence is limited by differences in definition of sleep disturbance, disparate patient populations and settings, and limited direct applicability to primary care settings.

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Gait disturbance

Summary of findings

Only 2 studies have compared gait disturbance frequency in persons with and without dementia. Gait disturbances are probably useful in distinguishing different subtypes of dementia, but there is little evidence that gait disturbances can clearly distinguish demented from non-demented individuals.

Detailed description

Early presence of gait disturbance had been thought an uncommon finding in AD and, in fact, is cited as a factor negatively associated with the diagnosis in the NINCDS-ADRDA criteria for AD.[49] One small study examined the prevalence of various types of gait disturbance in patients with various stages of AD and in a poorly defined control population.[29] They found that cautious gait was a common finding in both early stage AD and in healthy controls. Findings consistent with frontal gait disturbance, on the other hand, were more common with increasing severity of disease, but very uncommon in healthy participants.

The second study compared gait and balance disorder frequency between persons with different dementia subtypes and also to healthy controls.[28] Not surprisingly, gait and balance disorders were significantly more common in persons with vascular, Lewy-body, and Parkinson's dementia than in persons with AD. Gait and balance disturbance was slightly more prevalent in persons with AD than in controls (odds ratio 4, 95% CI 1.1 – 17).

Neurologic signs

Several physical exam findings may be more common in persons with AD than healthy controls. In one study using a convenience sample of persons with mild AD, release signs, olfactory deficit, impaired sense of touch, and an abnormal gait were all more common in persons with AD.[31] The only finding, however, that was highly specific for AD was stereognosis (the ability to perceive the form of an object by using the sense of touch) and graphesthesia (the ability to recognize writing on the skin purely by the sensation of touch), with sensitivity of 22.1% and specificity of 98.9%. None of the signs were very sensitive for dementia, though release signs were present in over half the participants with AD (sensitivity 54.7%).

Another study using a population-based sample also examined a number of neurologic signs and found that rigidity, spasticity, and frontal release signs were associated with dementia in a regression model.[30] The study findings were somewhat consistent with the aforementioned study; however, the study evaluated a large number of signs in a regression model and it is possible some of the findings reflect a chance finding given the multiple variables examined.

Miscellaneous

The final 2 studies provide interesting preliminary data but are not part of a robust enough body of evidence to draw firm conclusions. One study examined the relationship between pulse pressure and AD, and found higher mean pulse pressure among persons with AD compared with their non-demented counterparts (58.9 vs. 54.3, $p < 0.05$). The result suggests higher pulse pressure was associated with increased white matter changes.[32] However, the study has some methodologic flaws, the most important being the case and control groups were derived from different populations.

One study focused primarily on the correlation between self-reported and on-road driving performance, but did examine self-reported rating of "safe" driving ability in patients with and without dementia.[33] Most demented persons rated themselves as safe drivers even though informants and driving instructors were much less likely to rate their driving as safe. The sensitivity of less than safe driving ability for identifying dementia is, not surprisingly, very low.

KEY QUESTION #2. Which measures of cognitive function provide the optimal sensitivity, specificity, and time to completion, among the measures available to VA providers?

Summary of findings

All 6 measures available in VA test for recall ability, and 5 of the 6 measures assess executive function by means of a clock drawing test. The assessment of other cognitive domains, such as orientation, abstraction, and aphasia, varies among the 6 measures.

The Mini-Cog has the shortest administration time of all 6 tests and has been validated in a large sample of the general population. Sensitivity ranged from 76% to 99%, and specificity ranged from 83% to 93% in analyses that excluded patients with MCI.

The SLUMS test was studied in a VA population and found to have high sensitivity (98-100%) and specificity (98-100%) with adjustment for education. The SLUMS takes longer to administer than other tests. It was developed more recently than the other tests and has not been widely studied.

The STMS has been studied in a primary care setting. The STMS had sensitivity ranging from 86% to 95%, and specificity was highest (93.5%) when cut-off score was adjusted for age. The STMS was evaluated in 2 samples and has not been widely studied.

The GPCOG has been evaluated in a primary care setting, and includes separate sections for patient and informant. The sensitivity of the components ranged from 82% to 98%, but the informant section by itself had low specificity (49-66%). The specificity of the combined score and 2-stage method ranged from 77% to 86%.

The BOMC was evaluated in a bi-racial population sample, and found to misclassify more blacks than whites as impaired. Specificity ranged from 38% to 94%, and sensitivity ranged from 69% to 100%, although the inclusion of patients with previously diagnosed dementia might have inflated the sensitivity in 2 studies.

The MoCA has the longest administration time among the 6 tests, and had low specificity in 2 of 3 studies (35-50%). The MoCA has been evaluated in a memory clinic population, but has not been studied in a general practice setting.

Table 3 summarizes the strengths and limitations of each test. Detailed findings are provided in the pages that follow.

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Table 3. Pros and cons of 6 brief mental status measures available for use in VA

Test	Pros	Cons
BOMC	▪ Studied in a general population sample and 2 specialty clinic settings	▪ Low specificity (38-77%) in 2 of 4 studies ▪ Race and education biases in 1 study
GPCOG	▪ Studied in a primary care setting ▪ Education bias found absent ▪ The combined score and 2-stage method had higher sensitivity and specificity than patient and informant sections separately	▪ Informant section alone has low specificity (49-66%)
Mini-Cog	▪ Shortest administration time (2-4 minutes) ▪ Studied in a general population sample ▪ High specificity (83-93%) in studies that excluded MCI from comparator group ▪ Education and language/race biases found absent in U.S. samples	▪ May be inappropriate for populations with extremely low levels of education or literacy
MoCA	▪ Studied in a memory clinic population ▪ High sensitivity (94-100%)	▪ Longest administration time (10-15 minutes) ▪ Low specificity (35-50%) in 2 of 3 studies
SLUMS	▪ Studied in a VA geriatric clinic population ▪ High sensitivity and specificity (98-100%) ▪ Adjusts cut-off score for education	▪ Longer administration time (7 minutes) ▪ Evaluated in only 1 study
STMS	▪ Studied in a primary care setting ▪ Shorter administration time (5 minutes) ▪ High specificity (93.5%) using age-adjusted cutoff scores	▪ Evaluated in 2 studies

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Detailed description

The literature search identified 16 primary studies that assessed the test performance of one or more of the 6 brief cognitive assessments against a standard criterion for diagnosing dementia. Table 4 shows the study characteristics and the test performance results for each cognitive measure. Positive and negative likelihood ratios were calculated using the reported results for sensitivity and specificity, with the exception of 1 study,[50] for which sensitivity and specificity results were derived from a systematic review compiled in 2003 for the U.S. Preventive Services Task Force (USPSTF).[51]

The BOMC test was assessed in 4 studies reported in 6 publications,[50-55] the GPCOG in 2 studies,[56, 57] the Mini-Cog in 3 studies,[58-60] the MoCA in 3 studies,[61-63] SLUMS in 1 study,[64] and STMS in 2 studies.[65, 66]

The cognitive measures were studied in a variety of populations, including primary care, specialty clinics, and residential care/assisted living facilities. The prevalence of dementia varied with study setting (Table 4). Prevalence is not shown for studies that used a constructed sample (e.g. dementia cases matched 1:1 with controls) or that recruited subjects from heterogeneous settings. The prevalence of dementia in Table 4 is defined as the proportion of demented patients in the analyzed sample.

In some studies, subjects with MCI were excluded from the analysis.[58, 60, 61, 64] In other studies, subjects with MCI were included in the non-demented comparison group,[60] or were combined with dementia patients for the assessment of test performance.[62] The inclusion of subjects with MCI in the analysis could negatively affect the operating characteristics of the index test. Combining MCI with dementia would decrease sensitivity if MCI patients were more likely than dementia patients to be misclassified as unimpaired. Conversely, including MCI in the non-demented group would decrease specificity if MCI patients were more likely than cognitively normal subjects to be misclassified as demented.

Table 4. Study characteristics and test performance results for the BOMC, GPCOG, Mini-Cog, MoCA, SLUMS, and STMS

Sample/setting (Reference)	Dementia (%)	Comparison	N total	Cut-off Score	Sens.	Spec.	+LR (95%CI)	-LR (95% CI)
BOMC								
Population sample*[52]	16.9	Black race only: demented v. non-demented	83	11	1.0	0.382	1.56 (1.27-1.91)	0.0881 (0.0057-1.37)
	3.7	White race only: demented v. non-demented	81	11	1.0	0.785	3.95 (2.27-6.88)	0.161 (0.012-2.15)
Memory clinic†‡[53]	83.3	Combined dementias v. normal	282	7/6	0.91	0.63	2.52 (1.72-3.69)	0.14 (0.0883-0.222)
				10/9	0.83	0.77	3.55 (2.11-5.97)	0.222 (0.161-0.307)
Neurology clinic*†‡[54]	33.1	Combined dementias v. normal	133	10/11	0.886	0.944	15.8 (6.69-37.2)	0.12 (0.0527-0.275)
Mixed settings†§[50, 51]	||	Combined dementias v. normal	321	NR	0.69	0.9	7 (4.06-12.1)	0.346 (0.279-0.428)
GPCOG								
General practice: patients aged 75+, and patients aged 50-74 with memory complaints[56]	29.1	Patient section only; demented v. non-demented	282	7/8	0.82	0.7	2.72 (2.15-3.45)	0.261 (0.164-0.417)
		Informant section only	202	4/5	0.89	0.66	2.62 (2.06-3.34)	0.155 (0.0718-0.333)
		Combined score	202	10/11	0.82	0.83	4.85 (3.3-7.12)	0.224 (0.131-0.384)
		Two-stage method	246	---	0.85	0.86	6.14 (4.18-9.02)	0.177 (0.103-0.306)
Mixed settings†¶[57]	||	Patient section only; definite dementia v. normal (excludes MCI)	118	<=7	0.982	0.672	2.95 (2.06-4.22)	0.0259 (0.0037-0.182)
		Informant section only	80	<=4	0.942	0.491	1.82 (1.24-2.66)	0.114 (0.0351-0.367)
		Combined score; definite dementia v. normal (excludes MCI)	80	<=10	0.981	0.774	4.09 (2.03-8.23)	0.0239 (0.0034-0.169)
Mini-Cog								
Population sample[58]	6.4	Demented v. normal (excludes MCI)	1119	2/3	0.76	0.89	6.95 (5.61-8.62)	0.265 (0.175-0.402)
Residential care/assisted living, without history of dementia¶#[60]	37.7	Dementia v. (MCI + no cognitive impairment)	146	2/3	0.87	0.54	1.89 (1.48-2.41)	0.236 (0.115-0.484)
Mixed settings; enriched in ethnic minorities, demented patients†[59]	||	Combined dementias v. normal (excludes MCI)	300	2/3	0.969	0.828	5.65 (3.92-8.14)	0.0377 (0.0159-0.0897)
MoCA								
Memory clinic†[61]	72.7 48††	Dementia v. non-demented (excludes MCI)	44	<26	0.94	0.5	1.88 (1.06-3.32)	0.125 (0.0291-0.536)

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Sample/setting (Reference)	Dementia (%)	Comparison	N total	Cut-off Score	Sens.	Spec.	+LR (95%CI)	-LR (95% CI)
Mixed settings†**[62]	||	Combined (dementia + MCI) v. normal	118	<=26	0.97	0.35	1.51 (1.27-1.79)	0.0647 (0.0091-0.46)
Patients with history of mild dementia v. controls†[63]	||	Mild AD v. normal (excludes MCI)	183	26	1.0	0.87	7.24 (4.33-12.1)	0.0062 (3.9e-04-0.098)
SLUMS								
VA-GRECC patients aged 60+¶[64]	16.5 12.6††	Education <HS: Dementia v. normal (excludes MCI)	164	19.5	1.0	0.98	38.7 (13.7- 109)	0.0183 (0.0012-0.286)
	15.4 11.3††	Education >=HS: Dementia v. normal (excludes MCI)	358	21.5	0.98	1.0	592 (37.1-9442)	0.0268 (0.0055-0.13)
STMS								
Newly diagnosed dementia v. controls in primary care†[66]	||	Dementia v. normal (excludes MCI)	248	<29	0.864	0.884	7.45 (4.67-11.9)	0.154 (0.096-0.248)
				By age: 60-69: 30 70-79: 29 80-89: 28 >90: 27	0.864	0.935	13.2 (7.01-25)	0.146 (0.091-0.234)
Patients with history of dementia v. non-demented controls from a neurology clinic†¶[65]	||	Combined dementias v. no dementia (excludes MCI)	180	<=29	0.92	0.914	10.7 (5.5-20.8)	0.088 (0.0431-0.18)
		AD v. no dementia (excludes MCI)	160		0.955	0.914	11.1 (5.71-21.6)	0.049 (0.0162-0.148)
		Aged 60+ only: Combined dementias v. no dementia (excludes MCI)	109		0.947	0.879	7.82 (3.11-19.6)	0.0599 (0.0229-0.157)

* Sample may have included prevalent dementia; sensitivity may be overestimated.
† May not be applicable to primary care populations.
‡ Unclear whether clinic patients were randomly or consecutively sampled.
§ Sensitivity and specificity were calculated in the USPSTF 2003 report[51] based on an AHCPR 1996 meta-analysis.[55]
|| Mixed clinic/community or constructed sample. Prevalence could not be calculated.
¶ Interpretation of index test and reference standard were not fully blinded.
# Non-demented comparison group includes subjects with mild cognitive impairment.

** Subjects with dementia and MCI are compared with cognitively normal subjects.
†† Prevalence of dementia in the total sample that comprised patients with dementia, MCI, and no cognitive impairment. MCI patients were otherwise excluded from the results shown.
Abbreviations: +LR = Positive Likelihood Ratio; -LR = Negative Likelihood Ratio; AD = Alzheimer's Disease; BOMC = Blessed Orientation-Memory-Concentration Test; GPCOG = General Practitioner Assessment of Cognition; MCI = Mild Cognitive Impairment; MoCA = Montreal Cognitive Assessment; Sens. = Sensitivity; SLUMS = St. Louis University Mental Status Exam; Spec. = Specificity; STMS = Short Test of Mental Status

Table 5 on the following page provides descriptive characteristics of the 6 tests, including the time to administer and the cognitive domains assessed.[67] All 6 measures test for recall ability, and assessment for executive function by means of a clock drawing test is a component in all measures except the BOMC. The assessment of other cognitive domains, such as orientation, abstraction, math, and language skills, varies among the 6 measures.

Table 5 also shows characteristics of the tests that were reported in some but not all studies. These include inter-rater reliability; test-retest reliability; internal consistency; and the effects of education, race, and language on test performance. Among the 6 measures, only the Mini-Cog and BOMC were examined for differences by race or language in a biracial or multi-ethnic sample.

In addition, Table 5 displays the sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio from a selected study for each cognitive measure. These representative studies were selected based on applicability to the settings that the samples were drawn from: the general population in the case of the BOMC and Mini-Cog; primary care or a geriatric clinic in the case of the GPCOG, SLUMS, and STMS; and a memory clinic population in the case of the MoCA.

Table 5. Cognitive domains, biases, and other characteristics of BOMC, GPCOG, Mini-Cog, MoCA, SLUMS, and STMS

	BOMC	GPCOG		Mini-Cog	MoCA	SLUMS		STMS
Cognitive domain								
Orientation (e.g. time/place)	X	X			X	X		X
Registration/recall	X	X		X	X	X		X
Remote memory						X		
Praxis, visuospatial		X		X	X	X		X
Aphasia, verbal fluency					X			X
Attention	X				X	X		X
Abstraction					X	X		X
Executive function		X		X	X	X		X
Biases detected								
Education bias	Yes[52, 53]	No[56, 57]		No[59, 68]	Yes*[62]	No[64]		Yes[66]
Language/race bias	Yes[52]	---		No[59, 68]	---	---		Yes†[65]
Performance results from selected studies‡	[53]	[56]		[58]	[61]	[64]		[66]
Sensitivity	0.83	Patient only: 0.82	Two-stage: 0.85	0.76	0.94	<HS: 1.0	HS+: 0.98	Age-based cutoff: 0.86
Specificity	0.77	0.7	0.86	0.89	0.5	0.98	1.0	0.935
+LR (95%CI)	3.55 (2.11-5.97)	2.72 (2.2-3.5)	6.14 (4.2-9.0)	6.95 (5.6-8.6)	1.88 (1.0-3.3)	38.7 (13.7- 109)	592 (37.1-9442)	13.2 (7.0-25)
-LR (95%CI)	0.222 (0.161-0.307)	0.261 (0.16-0.42)	0.177 (0.10-0.31)	0.265 (0.18-0.40)	0.125 (0.03-0.54)	0.0183 (0.001-0.29)	0.0268 (0.006-0.13)	0.146 (0.09-0.23)
Other characteristics								
Time to administer, mean or range (min)	4-6	Patient: 2-5 Informant: 1-3		2-4	10-15	7		5
Inter-rater reliability	---	Adequate[56]		Adequate[59]	---	---		---
Test-retest reliability	Adequate[53, 54]	Adequate[56]		---	Adequate[63]	---		---
Internal consistency	---	Adequate[56]		---	Adequate[63]	---		---

* The effect of education on the MoCA was correctable by the inclusion of a 1-point education correction for individuals with 12 or fewer years of education.[62]

† Study authors note that a severe language disturbance would preclude use of the STMS. The test could be administered with the help of interpreters to patients who do not speak English.

‡ A representative study for each cognitive measure was selected based on applicability to the setting that the sample was drawn from: the general population in the case of the Mini-Cog; primary care or a geriatric clinic for the GPCOG, SLUMS, and STMS; and a memory clinic population for the BOMC and the MoCA.

Abbreviations: <HS = less than high school education; HS+ = high school or more education.

BOMC

The BOMC is a 6-item measure derived from the Blessed Information-Memory-Concentration Test.[69] The items are weighted for a total maximum score of 28, and include current date (month, year) and time, counting backwards from 20 to 1, reciting the months of the year in reverse order, and recalling a previously repeated 5-element address.[50] Test-retest reliability of the BOMC was assessed and found adequate in 2 studies.[53, 54] The administration time is 4 to 6 minutes.

The BOMC was assessed in a population-based sample, a memory clinic, a neurology clinic, and in a study with mixed settings (Table 4). Two studies used a cutoff score of 11 (11 or more errors on the weighted 28-point scale indicates impairment),[52, 54] but the cut-off score of 10/9 (given as best score for demented group/worst score for non-demented group) yielded the maximum results for both sensitivity (83%) and specificity (77%) in a study of patients in a memory clinic.[53] Although the sensitivity of the BOMC was found to be 100% in the population-based study,[52] this result may be inflated due to the inclusion of subjects with pre-existing dementia in the sample.

In a population-based subsample from the Established Populations for Epidemiologic Studies of the Elderly (EPESE) cohort, the BOMC was found to misclassify a greater proportion of Africans Americans as demented compared with whites.[52] Specificity was only 38.2% for blacks, compared with 78.5% for whites in this study. Less educated subjects were more likely to be classified as impaired, and the effect of education did not vary by race. The lack of adjustment for education in this study limits interpretation of the observed racial differences. Other studies have reported an association between race and cognitive test scores that persists after controlling for education, suggesting that additional factors such as socioeconomic status, comorbidity, health habits, and social factors, may contribute to the observed racial differences.[70]

GPCOG

The GPCOG contains separate sections for patient and informant. The patient section includes items testing time orientation (3 points, including a clock drawing test), awareness of a news story within the previous week (1 point), and recall of a name and an address (5 points). The informant section includes 6 items that ask an informant to make a comparison between the participant's current function and that from a few years ago. The cognitive and informant sections can be scored separately, together, or sequentially. In the sequential or 2-stage method, the informant section is not required for participants who score >8 (considered cognitively intact) or <5 (considered impaired). For participants who score 5 to 8 (inclusive) on the cognitive section, scores of <=3 on the informant section indicate cognitive impairment.[56]

The GPCOG was assessed in a primary care setting[56] and in subjects recruited through various settings including memory clinics, an Alzheimer's respite program, and other clinics.[57] In the first study, 67 general practitioners in 4 regional divisions in Australia administered the GPCOG to 283 patients aged 75 and older, as well as community-dwelling patients aged 50 to 74 with memory complaints. The prevalence of dementia in the sample was 29.1%. The components of the GPCOG were assessed separately and in combination: patient section only, informant section only, combined score from patient and informant sections, and the 2-stage method. The sensitivity of each ranged from 82% to 89%. The specificity was lower for the informant section only (66%), and the patient section only (70%), compared with the combined score (83%) or 2-stage method (86%). In the study of mixed settings, the sensitivity of the individual or combined sections was higher, ranging from 94.2% to 98.2%; but the specificity was lower: 49% for the informant section, 67.2% for the patient section, and 77.4% for the combined score.[57]

Mini-Cog

The Mini-Cog combines 2 cognitive tasks (3-item word memory and clock drawing) with a sequential scoring method; and was developed in a community sample that overrepresented dementia cases, persons of low education and nonwhite ethnicity, and non-English speakers.[68] We identified 3 studies that assessed the operating characteristics of the Mini-Cog.[58-60] In each of these studies, the results of the Mini-Cog were derived from longer tests that were administered to determine whether the minimum data elements that make up the Mini-Cog would perform as well as or better than the longer, more complex diagnostic tests. The operating characteristics of the Mini-Cog by itself may differ in practice from the research studies included in this review.

Of the 6 VA measures, the Mini-Cog takes the least time to administer (2 to 4 minutes) and has been validated in a large (N=1119), age-stratified, random sample of the general population aged 65 and older (mean age 73.1). The prevalence of dementia in the sample was 6.4%, and the sensitivity and specificity of the Mini-Cog were 0.76 and 0.89, respectively.[58]

In a sample that had proportionally more demented patients (62%)[59] than in the general population (6.4%),[58] the Mini-Cog had higher sensitivity (97% v. 76%) but similar specificity (83% v. 89%). No association was found between education or language on Mini-Cog test performance in a study that included ethnic minorities in the U.S., although both education and language were significantly associated with MMSE test performance in the same sample.[68] In a study of adults aged 65+ in residential care and assisted living facilities who did not have a chart-documented diagnosis of dementia, 37.7% of residents met criteria for probable dementia using DSM-IV criteria. The sensitivity of the Mini-Cog in this sample was 87% and the specificity was 54%.[60] This study included subjects with MCI in the non-demented comparator group, potentially causing a decrease in specificity.

Studies of the Mini-Cog among ethnic minority groups with mixed linguistic and educational backgrounds found that the effects of low education and literacy on the accuracy of the Mini-Cog were weak or absent.[59, 68] In one study, Asian Americans constituted 48% of the sample, African Americans 22%, Hispanics 17%, and white non-Hispanic 7%. The mean years of education were 11.5 among normal subjects, 10.4 among subjects with MCI, and 8.5 among demented subjects in this study.[59] The Mini-Cog performed less accurately in a study of elderly with low education in Brazil, of whom 76% had less than 5 years of schooling and 25% were illiterate.[71] Given that the Mini-Cog was developed to facilitate cognitive screening in primary care settings in first-world countries, the authors of the Mini-Cog suggest that in populations with extremely low levels of education or literacy, informant-based screening or individualized function-based screening might be preferable to the use of cognitive screening tests.[72]

MoCA

The MoCA is a 1-page, 30-point test, and has the longest administration time (10 to 15 minutes) among the 6 tests. Short-term memory recall is assessed by 2 learning trials of 5 nouns and delayed recall after approximately 5 minutes. Visuospatial tasks include a clock-drawing task and a 3-dimensional cube copy. Multiple aspects of executive functions are assessed using an alternation task adapted from the Trail Making B task, a phonemic fluency task, and a 2-item verbal abstraction task. Attention, concentration, and working memory are evaluated using a sustained attention task, a serial subtraction task, and digits forward and backward. Language is assessed using a 3-item confrontation naming task with low-familiarity animals (lion, camel, rhinoceros), repetition of 2 syntactically complex sentences, and the aforementioned fluency task. Finally, orientation to time and place is evaluated.[63] The tests, along with instructions for administering and scoring, are available in 30 languages.[73]

Three studies evaluated the test performance of the MoCA.[61-63] One was a prospective study of 67 consecutive patients seen in a memory clinic. In this sample, 48% were determined to have dementia, 34% had MCI, and 12% had an identifiable psychiatric illness that explained subjective memory complaints or had no objective evidence of memory loss.[61] The other 2 studies recruited subjects from mixed settings[62] or used a case-control sample,[63] and prevalence could not be determined. The MoCA has not been validated in a primary care population or a sample representative of the general population.

Although the sensitivity of the MoCA was high (94% to 100%), the specificity of the MoCA was low, ranging from 35% to 50% in 2 of the 3 studies. Individuals with <=12 years of education performed significantly worse on the MoCA ($p<0.05$). The effect of education, however, was correctable by the inclusion of a 1-point education correction for individuals with 12 years or less of education.[62]

SLUMS

The SLUMS examination is a 30-point, 11-item scale that includes tasks corresponding to attention, numeric calculation, immediate and delayed recall, animal naming, digit span, clock drawing, figure recognition/size differentiation, and immediate recall of facts from a paragraph.[64] The average administration time is 7 minutes.

The SLUMS test was studied in a population of 702 U.S. Veterans aged 60+ in a VA geriatric clinic.[64] The prevalence of dementia in the total sample, including subjects with MCI, was 11.6%. The study stratified subjects by level of education, and determined that the optimal cutoff score was 19.5 for subjects with less than high school education and 21.5 for subjects with high school or more education. Sensitivity and specificity were both high (98% to 100%) with this adjustment for education level.

STMS

The STMS is a 38-point, 8-item scale that tests orientation, attention, immediate recall, arithmetic, abstraction, construction, information, and delayed (approximately 3 minutes) recall.[66] The administration time is approximately 5 minutes.

The STMS was assessed in 2 studies that used a constructed sample of demented patients and non-demented controls. In one study, the demented group included 87 outpatients with mild to moderate severity and mean duration of 3.26 years, ranging from newly diagnosed to 10.3 years.[65] Ninety-three non-demented controls were recruited from consecutive patients who came to the neurologic practice for consultation during a 10-week period. Using a cutoff score of <=29, the sensitivity and specificity of the STMS were high in this study, but generalizability to the primary care setting is limited.

The second study drew consecutive, newly identified dementia patients (n=110) and controls matched on age and sex (n=138) from a primary care clinic.[66] This study compared the test performance using a cutoff of 29 with an age-adjusted cutoff score that raised the cutoff to 30 for ages 60-69, and lowered the cutoff by 1 point with each advancing age decade. Adjusting the cutoff score for age did not affect the sensitivity (86.4%), but improved the specificity of the STMS from 88.4% to 93.5%. To observe the effect of education without the confounding effects of dementia, the correlation of STMS total score with age and education was calculated within the control group only. The STMS appeared to be modestly influenced by age and education, with correlations of -0.34 (P = .0001) for age and 0.41 (P = .0001) for education. The study authors additionally noted that a severe language disturbance would preclude the use of the STMS.

KEY QUESTION #3. What are adverse consequences of using these measures?

Summary of findings

We found no evidence on adverse effects of the 6 cognitive tests of interest to VA. Three cross-sectional studies assessed the acceptability of dementia screening or diagnostic workup among older adults. The studies reported that high proportions of older adults were unwilling to be routinely tested for memory problems, or to undergo further diagnostic assessment for dementia after having positive results on cognitive screening tests. One survey determined that 80% of respondents wanted to know if they had dementia, but only 57% would agree to routine testing by a physician. Perceived harms included worry about losing insurance and fear of losing drivers license. The high refusal rates of screening and diagnostic workup indicate the need for further research to understand the psychological burden associated with cognitive tests and assessment for dementia.

Detailed description

The USPSTF 2003 review determined that most articles on the adverse effects of screening for dementia dealt primarily with genetic screening for increased risk of AD and the impact of disclosing the diagnosis of dementia.[74] Potential harms include psychological morbidity such as depressed mood, suicide, suicidal attempts and thoughts, and anxiety; as well as possible discrimination due to insurers and employers gaining access to screening results.[6, 74]

Our review found no literature on the adverse effects of the 6 cognitive tests of interest to VA. We found 2 studies that assessed the acceptability of dementia screening among older adults,[6,7] and 1 study that assessed refusal of diagnostic workup for dementia after screening.[8] Because the studies were cross-sectional surveys, we did not rate them for quality.

In 1 study, a mailed, self-administered questionnaire sent to residents of continuous care retirement communities (CCRCs) determined that the majority of respondents (51%) were not willing to be tested regularly for memory problems.[6] The questionnaire was sent to 500 residents aged 50 and older in two CCRCs in North Carolina, and excluded residents of assisted living and nursing homes, where the prevalence of diagnosed dementia would be greater. The survey contained 20 questions that addressed socio-demographic and health status, memory problems, depression, and medications; and also asked whether the respondent would like to be tested

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on a regular basis for memory problems and depression in 2 separate questions. Forty-nine percent of respondents were willing to be tested regularly for memory problems, and only 40% were interested in being screened regularly for depression. Acceptance of depression screening was highly correlated with acceptance of screening for memory problems: 97% of participants who were willing to accept routine depression screening would also accept routine screening for memory problems, whereas only 17% of those not willing to accept depression screening would accept routine memory screening. The study did not explore the reasons why residents were unwilling to be screened regularly for dementia, but the study investigators suggested that the high refusal rate indicates the need for further research to understand the psychological burden due to dementia screening, social stigmatization, health and long-term care insurance, employment discrimination, mistrust in the health care system in managing other medical conditions, institutionalization, and losing driving privileges.

In a screening and diagnosis study led by the same investigator, nearly half of patients with positive screening results refused diagnostic workup for dementia.[8] In this study, 3,340 patients aged 65 and older received cognitive screening, regardless of whether cognitive complaints were present, in 7 primary care practice centers in Indianapolis. Four hundred and thirty-four patients were eligible for diagnostic assessment, having made at least one error on a 6-item screening test[75] and subsequently scoring <=24 on a modified version of the Community Screening Instrument for Dementia.[76] Forty-eight percent of the patients with positive screening results refused further assessment for dementia. The proportion of refusals did not significantly differ between men (46.2%) and women (48.5%), or between African Americans (46.3%) and whites (50.4%), although the likelihood of refusal varied among age-race groups. Patients who made mistakes on orientation items were more willing to undergo the diagnostic assessment than those who did not make such mistakes. The study authors suggest that this finding may reflect the individual's perception as to whether or not s/he is likely to have the illness, in that patients who perceive themselves as asymptomatic may be less likely to desire to undergo a clinical evaluation.

A third study, published as an abstract,[7] sought to capture attitudes and perspectives toward dementia screening among 234 non-demented dwelling older adults (mean age 75) in North Carolina. This survey determined that 80% of respondents wanted to know if they had dementia, but only 57% would agree to routine testing by a physician. Perceived harms included worry about losing insurance (40%), and fear of losing drivers license (81%). Regression analysis determined that acceptance of routine dementia screening was associated with acceptance of routine screening for colon cancer ($p<0.001$), acceptance of routine depression screening ($p<0.001$), a belief that early detection improves treatment of dementia ($p<0.001$), and a fear that dementia leads to nursing home placement ($p<0.038$). The study investigators suggest that broad-based screening for early dementia may require targeted educational interventions regarding its benefits.

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DISCUSSION

SIGNS AND SYMPTOMS OF DEMENTIA

Efforts to improve dementia case finding in general practice settings may be hampered by the protean manifestations of the disease, and the low sensitivity of many of the signs and symptoms encountered in practice. The utility of these signs and symptoms in effectively triaging patients for further diagnostic assessment would depend on the relative value placed on reducing false positive findings as compared to increasing dementia detection rates and reducing false negative rates. Determining the long-term benefits and harms of earlier and increased rates of dementia detection has been debated in the literature, but is largely beyond the scope of this review.

All of the signs and symptoms we evaluated were poorly sensitive in detecting mild dementia. This may reflect inter-individual variation in clinical manifestations of dementia, variations in the methods for detecting these signs and symptoms, or simply a reflection of the almost subclinical nature of early dementia.

The best studied of these symptoms are subjective memory complaints (SMC), which are theoretically attractive as a very brief initial assessment method in general practice settings. However, the presence of self-reported SMC does not correlate well with existing dementia. On the other hand, most cognitively intact persons do not have SMC, which may mean that in low prevalence settings, lack of SMC may be useful in identifying patients who could forego further dementia assessment. One potential consequence of routinely eliciting SMC in general practice patients is the likely high rate of false positives. If the finding of SMC would trigger further evaluation for dementia, this could lead to significant time pressures in general practice settings given that many of the “brief” assessment methods require 2 to 10 minutes to complete.

Of note, several large prospective cohort studies in different populations have found that elicited SMC are very common but of questionable significance, as they may not predict future cognitive decline.[77-79] Rather, studies have suggested self-reported SMC are associated with depression, anxiety, physical health and personality traits.[18, 45, 77]

Informant-reported memory complaints may better differentiate demented from non-demented individuals[18] and may be a promising area of inquiry for future case-finding approaches. The AD8 may be a promising very brief assessment instrument based partly on informant-reported memory complaints.[46] A number of additional studies have found that caregivers of demented patients are reliably able to assess their cognitive deficits.[45, 80-82] However, most of these studies have evaluated the use of longer questionnaires which may take some time to administer, and function almost as a proxy dementia screening tool.

Some neuropsychiatric symptoms such as apathy, hallucinations, and delusions are relatively uncommon in healthy elderly people and may suggest the need for further evaluation when present. Depression and anxiety, on the other hand, do not seem to be useful in distinguishing demented from non-demented individuals.

BRIEF MEASURES OF COGNITIVE FUNCTION AVAILABLE TO VA

The 6 measures available in VA all test for memory impairment, while apraxia and executive function (including a clock drawing test) are assessed in all measures except the BOMC. The assessment of other cognitive domains such as orientation, abstraction, and aphasia varies among the 6 measures (Table 5). A 2007 review by Holsinger, et al. discusses the cognitive domains in the DSM-IV criteria for dementia, and describes tasks used to assess each domain.[67]

Among the 6 tests, the Mini-Cog has the shortest administration time (2 to 4 minutes), and has been studied in a large population sample as well as in multi-ethnic samples. Sensitivity and specificity were high in 2 studies, while poor specificity in a third study may have resulted from inclusion of subjects with MCI.

The SLUMS examination had very high sensitivity and specificity in a VA population, and it allows for adjustment for education. However, the SLUMS has a longer administration time (approximately 7 minutes) compared with other tests, and has only been evaluated in 1 study.

The other 4 tests had various strengths and limitations. The STMS had high sensitivity and specificity in a primary care setting, but has been evaluated in only 2 studies. The GPCOG is unique in that it allows for the input of an informant; however, the specificity of the informant section by itself was low (49-66%). The BOMC was evaluated in a bi-racial population sample, and was found to misclassify more blacks than whites as impaired. Specificity varied widely among studies of the BOMC. The MoCA has the longest administration time among the 6 tests, and had low specificity (35-50%) in 2 of 3 studies.

LIMITATIONS

Our review does not address the relative value of various signs or symptoms in predicting future dementia. Also, because we excluded studies involving only patients with mild cognitive impairment (MCI) and because few included studies enrolled patients with very mild or very early dementia, these results may not be readily applicable to case-finding approaches designed to detect those patients with the earliest manifestations of disease.

The scope of this review was limited to the 6 brief cognitive measures identified as priorities for VA. There are many other cognitive measures available that are not covered in this review. Few studies have assessed the 6 instruments in VA populations, and though some of the study populations may be similar to VA populations, applicability to VA settings cannot be directly assumed. The adverse consequences of the 6 cognitive measures have not been studied.

FUTURE RESEARCH RECOMMENDATIONS

Consequences of expanded case-finding efforts

The utility and consequences of a targeted case-finding approach in VA primary care settings should be assessed. For instance, the utility of routinely asking about memory problems followed by a brief dementia assessment method in patients with a positive response should be studied. It would be critical in such a study to carefully assess both the rate and consequences of false-positive results, as well as the cost and time used to find one additional confirmed case of dementia.

The psychologic, financial, and quality of life consequences of both true- and false-positive dementia diagnoses should be more rigorously evaluated. High refusal rates of screening and diagnostic workup indicate the need for further research to understand the psychological burden associated with cognitive tests and assessment for dementia.

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The role of caregivers in evaluating patients for dementia

The value of routinely asking patient caregivers about memory problems as an alternative to patient-reported memory complaints should be studied as well. Given a limited amount of literature suggesting informant characteristics may impact the reliability of informant report,[82] future studies of informant-administered instruments should also analyze the impact of the informant's relationship to the patient on the diagnostic utility of the instrument.

The reliability and validity of very brief informant assessment instruments such as the AD8 should be evaluated in different settings.

Evaluating combinations of signs and symptoms

Many of the signs and symptoms we examined were reported in isolation. Studies that examine the diagnostic utility of groups of signs and symptoms should be conducted.

Provider response to self-reported subjective memory complaints

Though the value of routine screening for dementia remains an active area of debate, subjective memory complaints are common enough that future studies, quality improvement, and education improvement efforts should ensure primary care providers are trained to feel comfortable having sensitive and holistic discussions with patients and their caregivers about memory loss. Studies should also address whether an assessment negative for dementia following a subjective memory complaint can be therapeutically useful.

Dementia and depression

Rates and consequences of the misclassification of dementia as depression (and vice versa) should be further studied.

Operating characteristics of the cognitive measures available in VA

The SLUMS and STMS tests have not been widely studied. Further studies are needed to assess the operating characteristics of these tests in various settings.

Of the 6 measures, only the BOMC and Mini-Cog have been evaluated in multi-ethnic samples. Further studies are needed to assess whether race or language biases affect the performance of the other cognitive measures.

Clinical utility of the cognitive measures available in VA

The perceived clinical utility of the GPCOG and Mini-Cog was examined in a narrative review and found to be equally high.[83] A similar survey among VA providers would be useful for determining preferences and utilities of the 6 measures available in VA. Because clinicians may need to use these assessment tools in busy primary care practices, studies should assess the instruments' ease of use, time to completion, and adverse effects in real-world VA settings.

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