A Systematic Evidence Review of the Signs and Symptoms of Dementia and Six Brief Cognitive Tests

Devan Kansagara MD, MCR
Michele Freeman, MPH
Portland Evidence-based Synthesis Program
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Disclosure

The findings and conclusions in this report are those of the authors who are responsible for its contents. The findings and conclusions in this report do not necessarily represent the views of the Department of Veterans Affairs.

VA Evidence-based Synthesis Program (ESP)

- Funding: VA Office of R&D, HSRD Service
- Products: Evidence synthesis reports on health care topics important to VA leaders, managers and policy makers for quality improvement.
- Purpose: Inform VA clinical policy, develop clinical practice guidelines, future research, performance measures, and drug formulary decisions.
- Sites: 4 VA medical centers with systematic review expertise: Portland, West LA, Durham, Minneapolis
- Topics: Identified by HSR&D planning and oversight committee; may be nominated using form on ESP website:
  http://www.hsrd.research.va.gov/publications/esp/TopicNomination.cfm

VA-ESP partnerships

- Planning and oversight committee
  - Representatives from HSRD, PCS, OQP, and VISN Clinical Management Officers.
  - Oversees and guides strategic planning, coordinates dissemination activities, identify priority topics, and assure quality of reports.
- Technical expert group
  - Recruited for each topic to provide content expertise
  - Guides topic development, reviews drafts of report
- External peer reviewers
  - Review and comment on draft report
  - Published authors, key experts in a field, may hold a range of opinions on the topic

Current report

A Systematic Evidence Review of
the Signs and Symptoms of Dementia
and Brief Cognitive Tests Available in VA
(April, 2010)

Full report available on ESP website:
http://www.hsrd.research.va.gov/publications/esp/dementia.pdf

Dementia Steering Committee

- Convened in 2006 by the VHA Office of Geriatrics and Extended Care in PCS to make recommendations on comprehensive, coordinated care for Veterans with dementia
- Identified priority topics for evidence review, to help VA identify evidence-based approaches or research needed to improve dementia care:
  1. Dementia warning signs and cognitive tests available in VA
  2. Non-pharmacological treatment of behavioral symptoms
  3. Evidence-based caregiver interventions

Background note: The DSC identified 7 priority topics. We did evidence reviews on the top 3.

These were the other 4 topics:

4. Evidence-based functional maintenance programs
5. Co-occurring dementia and depression
6. Management of vascular risk factors
7. Neuroimaging

Topic development

- Dementia steering committee (DSC)
  - Nominator and technical expert panel
  - Key questions, scope, and work plan were developed and refined in conjunction with DSC

Background

- Dementia is a common and costly condition in VA
  - Nearly 600,000 Vets with dementia
  - Up to 267,483 with incident dementia
  - Average annual cost $19,522/patient

Background

- Broad-based dementia screening programs have not been widely advocated
  - Lack of strong evidence that earlier detection will improve health outcomes
  - Screening programs may be costly and inaccurate
  - Public may be concerned about potential negative implications of dementia screening

U. S. Preventive Services Task Force. Ann Int Med, Sep 2003;103(9):87.
Boustani M, *Journal of General Internal Medicine.* Jul 2005;20(7):572-577.
Boustani M, *Int J Geriatr Psychiatry.* Sep 2003;18(9):780-786.

Regardless of the controversies surrounding dementia screening, there may be opportunities to improve case-finding approaches.

Background: case-finding vs. screening

- By definition, screening involves widespread testing of asymptomatic individuals
- Case-finding refers to targeted evaluation of individuals with higher probabilities of having disease

Background: case-finding

- Diagnosis of dementia is often missed in primary care practice, suggesting case finding approaches can be improved
- One approach to case-finding for dementia is to target evaluations such as brief cognitive assessments to patients presenting with signs or symptoms suggestive of dementia

Background: brief cognitive assessment tools

- Many available with varied operating characteristics
- VA is interested in alternatives to Mini-mental State Examination (MMSE) given proprietary issues
- VA workgroup in 2007 identified 6 brief cognitive tests as possible alternatives to MMSE: BOMC, Mini-Cog, MoCA, GPCOG, SLUMS, STMS

Full names of tests:

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

Short Test of Mental Status (STMS)

Review objectives

- Determine which signs and symptoms help distinguish persons with dementia from those without
- Compare the relative accuracy and usability of 6 brief dementia assessment methods available for use in VA

Key questions

1) What signs and symptoms should prompt VA providers to assess cognitive function as part of an initial diagnostic workup for dementia?
2) Which measures of cognitive function provide the optimal sensitivity, specificity, and time to completion among the measures available to VA providers?
3) What are adverse consequences of using these measures?

Literature search

- Cross-sectional studies comparing demented to non-demented participants
  - MEDLINE, PsychINFO, CINAHL, HAPI, Cochrane and AGELINE
  - Search dates: database inception → July 2009
  - Additional sources:
    - bibliographies, expert reviewers, editorials

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.

Study selection – Key question 1

- Included studies that:
  - compared patients with newly diagnosed, mild to moderate dementia with non-demented participants

Study selection – Key question 1

- Excluded studies that:
  - Included ONLY demented or non-demented participants
  - Did not present prevalence data
  - Did not use a reference standard (eg – DSM IV) for dementia diagnosis
  - Assessed signs/symptoms predictive of FUTURE dementia

Study selection – Key question 2

- Included studies that:
  - compared the performance of the index test against a reference standard for dementia diagnosis
  - compared demented patients with cognitively normal patients
  - included patients with mild cognitive impairment in either the demented or non-demented group
- Excluded studies that:
  - assessed the performance of the index test for detecting mild cognitive impairment only

Study selection – Key question 3

- Included any observational study assessing potential adverse consequences of cognitive assessment

Quality assessment

- QUADAS tool
  - 14 items designed for diagnostic accuracy studies
  - Assesses applicability, validity, and potential sources of bias
  - Quantitative score reporting discouraged

Whiting P, *BMC Med Res Methodol.* Nov 10 2003;3:25.

Examples of items in the QUADAS tool: Is the reference standard likely to correctly classify patients?

Is time period between reference standard and test in question short enough?

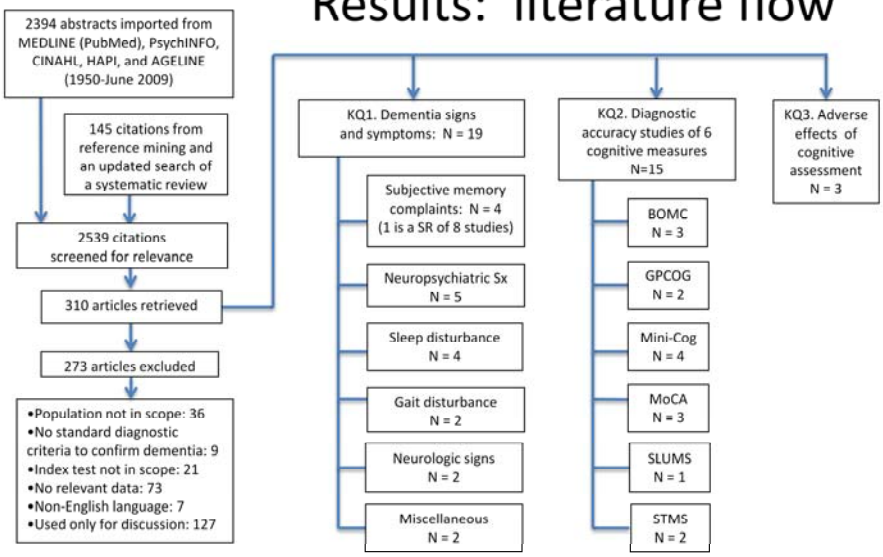
Did patients receive the same reference standard regardless of test result?

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

Data abstraction

- Signs/ symptoms
  - N of subjects, setting, country
  - Dementia prevalence, type, and severity
  - Sensitivity and specificity
- Six cognitive measures available in VA
  - N, population sample or clinical setting
  - Dementia prevalence
  - Cut-off score used
  - Sensitivity and specificity
  - Positive and negative likelihood ratios

Results: literature flow



Dementia signs and symptoms

- Subjective memory complaints and neuropsychiatric symptoms were best studied
- Depression, gait disorders, sleep disturbance, and neurologic signs were also studied
- Overall, a limited body of evidence suggesting none of these signs/symptoms reliably distinguish demented from non-demented patients

Subjective memory complaints (SMC)

- Context:
  - SMC are very common in general population
    - 34 – 56%
    - Not clear they are associated with risk of future dementia
- Most studies evaluate *elicited* rather than *spontaneous* SMC

Eliciting SMC means the investigators asked patients and/or caregivers whether or not they had experienced memory loss over a certain time period. There were various methods for eliciting SMC, most involving 1-3 brief questions. As applied in these studies, the elicitation of SMC is, in a sense, a form of screening.

Subjective memory complaints

- One systematic review of eight studies
  - Only two of these studies met our inclusion criteria
- Three additional studies
  - One examined chart documentation of SMC
  - One conducted in a MMSE-screened population
  - One assessed single-question informant-reported SMC

We relied on one systematic review by Mitchell et al from 2008. They used reliable methods to identify studies, however, they were more inclusive than we would have been in selecting studies.

Brief stats review

- Sensitivity: The proportion of truly diseased persons in the screened population who are identified as diseased by the screening test—that is, the true-positive rate
- Specificity: The proportion of truly nondiseased persons who are identified as such by the screening test—that is, the true-negative rate
- Positive Predictive Value: The proportion of people with a positive test who have the disease
- Negative Predictive Value: The proportion of people with a negative test who are free of disease.

Before we move on to selected results, I just wanted to briefly review some basic terminology.

Subjective memory complaints

Population	Sensitivity	Specificity	Prevalence assumption	Positive Predictive Value	Negative Predictive Value
Community sample (a)	58.0%	76.0%	10% 50% 75%	21.2% 70.7% 87.9%	94.2% 64.4% 37.6%
Community sample (b)	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 (c)	98.1%	86.1%	10% 50% 75%	43.8% 87.5% 94.6%	99.7% 97.7% 82.7%

(a) St. John, 2003; (b) Tobiansky, 1995; (c) Carr, 2000

These are the three best conducted and most representative of the SMC studies. The first two studies assessed self-reported SMC, while the third study by Carr et al assessed a single-item informant-reported SMC question. The table shows their sensitivity/specificity and then the predictive values of the test based on theoretic prevalence assumptions. As you can see, when the prevalence of dementia is low – as might be seen in a younger, primary care practice, a negative test result is very good at identifying patients without dementia. However, the value of a positive test result is much less, except in very high prevalence populations. The informant-reported SMC study found the best performance, but this has not been widely studied.

Neuropsychiatric symptoms

- Three community-based studies
- Apathy was the most common neuropsychiatric symptom reported in demented persons
  - Sensitivity: 27 – 53%
  - Specificity: 85 – 97%
- Depression and anxiety were common in both groups and likely not useful in reliably ruling in or ruling out a diagnosis of dementia.

In general, neuropsychiatric symptoms were poorly sensitive but moderately to highly specific for dementia. Some methodologic issues – two of the studies included a portion of cohort with + MMSE screen → higher dementia prevalence rates. One of the studies used a non-demented patient population from a different cohort.

Other signs/symptoms

- Sleep disturbance, gait disturbance, neurologic signs were also studied
  - No consistent evidence that these signs correlated well with dementia
  - Limited body of evidence
  - Stereognosis and grapesthesia were both highly specific for dementia
    - Only one study

Inability to perceive the form of an object by sense of touch.

Inability to recognize writing on the skin by sense of touch alone.

Methods: KQs 2 & 3

- Target population: Adults without prior diagnosis of dementia
- Outcomes
  - Likelihood for patients to be appropriately diagnosed and treated for dementia
  - Adverse consequences of assessment such as depression and anxiety
- Settings: excluded only acute care settings

6 brief cognitive measures: test characteristics

	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

All 6 measures test for recall ability.

A clock drawing test is included in all tests except BOMC.

Assessment of other cognitive domains, such as orientation, abstraction, math, and language skills, varies among the 6 measures.

6 cognitive tests: other characteristics

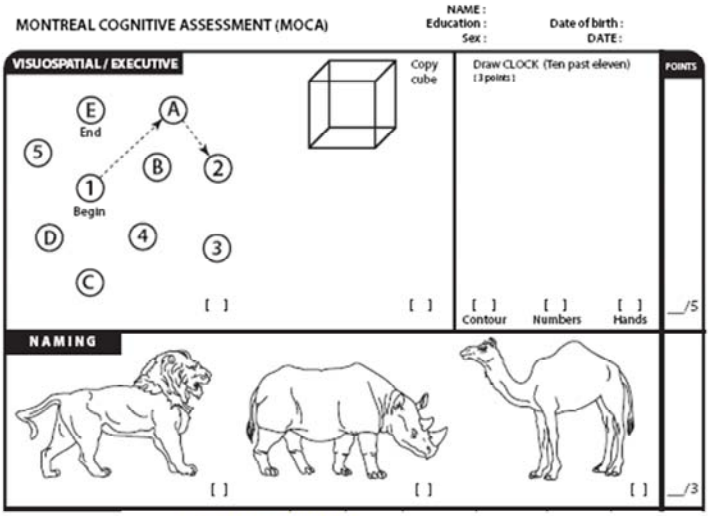
Other characteristics	BOMC	GPCOG	Mini-Cog	MoCA	SLUMS	STMS
Time to administer, mean or range (min)	4-6	Patient: 2-5 Informant: 1-3	2-4	10-15	7	5
Education bias	Yes	No	No	Yes*	No	Yes
Language/race bias	Yes	---	No	---	---	Yes†

*The effect of education on the MoCA was correctable by the inclusion of a 1-point correction for individuals with 12 or fewer years of education.
†The authors of the study noted that a severe language disturbance would preclude the use of the STMS.

Among the 6 tests, the Mini-Cog has the shortest administration time (2 to 4 minutes).

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.

Test example: MoCA



MONTREAL COGNITIVE ASSESSMENT (MOCA)

NAME :
Education :
Sex :
Date of birth :
DATE :

VISUOSPATIAL / EXECUTIVE

Copy cube

Draw CLOCK (Ten past eleven) [3 points]

POINTS

E End
A
5
B
2
1 Begin
D
4
3
C

[ ] [ ]

[ ] Contour [ ] Numbers [ ] Hands

/5

NAMING

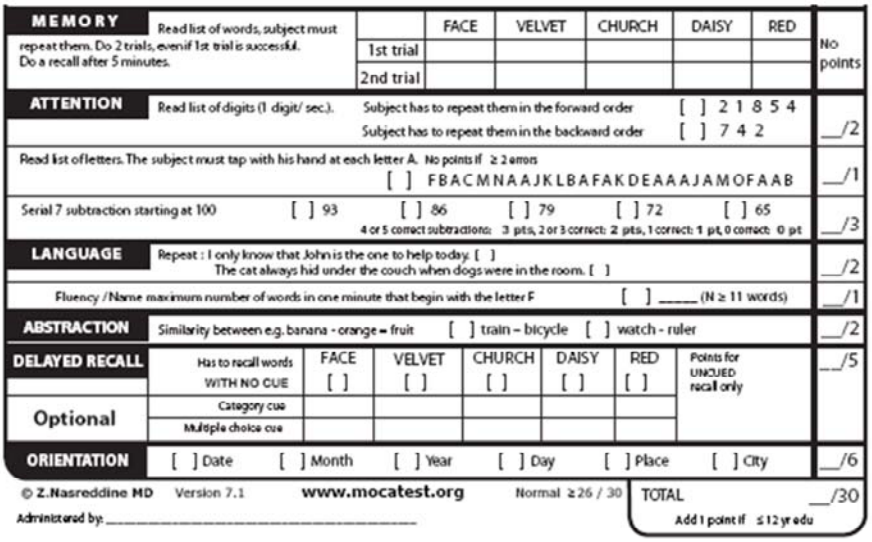
[ ] [ ] [ ]

/3

Excerpt from MoCA, available at www.mocatest.org. The MoCA test may be used, reproduced, and distributed without permission for clinical/educational use by universities/foundations/health professionals/ hospitals/clinics/public health institutes.

Example of brief cognitive measure: excerpt from the MoCA

Test example: MoCA (cont'd)



MEMORY Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.		FACE	VELVET	CHURCH	DAISY	RED	No points
	1st trial						
	2nd trial						
ATTENTION Read list of digits (1 digit/ sec.).	Subject has to repeat them in the forward order [ ] 2 1 8 5 4						
	Subject has to repeat them in the backward order [ ] 7 4 2						__/2
Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors [ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B							__/1
Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65 4 or 5 correct subtractions: 3 pts, 2 or 3 correct: 2 pts, 1 correct: 1 pt, 0 correct: 0 pt							__/3
LANGUAGE Repeat : I only know that John is the one to help today. [ ] The cat always hid under the couch when dogs were in the room. [ ]							__/2
Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words)							__/1
ABSTRACTION Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler							__/2
DELAYED RECALL	Has to recall words WITH NO CUE	FACE [ ]	VELVET [ ]	CHURCH [ ]	DAISY [ ]	RED [ ]	Points for UNCUED recall only	__/5
Optional	Category cue						
	Multiple choice cue						
ORIENTATION [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City							__/6
© Z.Nasreddine MD Version 7.1 **www.mocatest.org** Normal ≥ 26 / 30							TOTAL __/30
Administered by: _____							Add 1 point if ≤ 12 yr edu

Excerpt is 2nd half of MoCA. Shows scoring method and adjustment for education.

6 cognitive measures: summary of findings

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, education biases found 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/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, language/race biases found absent in US samples.	May be inappropriate for patients with extremely low levels of education or literacy.
MoCA	Studied in a memory clinic population. High sensitivity (94-100%).	Longest administration time (10-15 m). 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 min). 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.

Among the 6 tests, the Mini-Cog has the shortest administration time, 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.

Key question 3 – adverse consequences

- No studies evaluated adverse consequences associated with the use of any of the six assessment tools

Adverse consequences

- Three cross-sectional studies assessed the acceptability of dementia screening or diagnostic workup among older adults.
  - high proportions of older adults were unwilling to be routinely tested for memory problems,
  - many refused further diagnostic assessment for dementia after having positive results on cognitive screening tests

For example, in one study, only 57% of respondents would agree to routine testing for dementia.

Of note, these were mainly studies about dementia screening and are not 100% applicable to our key questions.

Limitations

- We do not address the risk of future dementia
- These studies may not apply to case-finding approaches designed to detect the earliest stages of disease
- We only studied six of the available cognitive instruments, though others exist and are used

We excluded studies of MCI patients only and most studies did not include populations with very mild or very early dementia.

Future research suggestions

- What are the consequences of expanded case-finding efforts?
- What is the role of caregivers/informants in evaluating patients for dementia?
- What is the diagnostic yield of *groups* of signs/symptoms?

Future research suggestions

- How should providers respond to SMC?
  - Is there therapeutic value to a negative cognitive assessment in patients presenting with SMC?
- What are the rates of consequences of the misclassification of dementia as depression and vice versa?
- What are the operating characteristics of the SLUMS and STMS in different populations?
- What is the clinical utility of the cognitive measures available in VA?

Clinical utility → provider satisfaction, workflow, time to completion, ease of use etc.

Questions?

- If you have further questions, feel free to contact Devan Kansagara MD:

  503-220-8262, x 51838

  Devan.Kansagara@va.gov