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Abstract

The present study evaluated the short Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE 2-year version) against a single item concerning informant's perception of patient's memory, as screening tools for CIND not dementia (CIND) and dementia. Data were drawn from the Aging, Demographics, and Memory Study, which is a national study that was specifically designed to provide population-based estimates of cognitive impairment and dementia in the United States. The study employed a comprehensive dementia evaluation that yielded an expert consensus-based diagnosis. Receiver-operating curves, sensitivity, specificity, negative predictive value, and positive predictive value were calculated. Both the IQCODE and the single-item instrument demonstrated only mild-to-moderate abilities to discriminate between cognitively intact individuals and individuals with CIND. Whereas the ability of the IQCODE to discriminate between cognitively intact individuals and individuals with dementia was moderate, the single-item instrument showed an adequate ability to distinguish between cognitively intact individuals and individuals with dementia. Therefore, for screening purposes, asking informants a single question concerning patients' memory is sufficient. However, if additional data concerning patients' strengths and weaknesses are needed, the IQCODE may be desirable.

Keywords

screening, dementia, cognitive impairment, psychometrics

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Introduction

Early recognition of cognitive impairment not dementia (CIND) and dementia is important for several reasons and has received considerable attention in the past few decades.^{1,2} For instance, there are, currently, several pharmacological interventions with known efficacy in delaying the progression of cognitive impairment. These agents are particularly effective in the early stages of the disease.³ In addition, an appropriate dementia diagnosis allows families to adjust according to patient's situation and to prepare for future deterioration.⁴ Moreover, certain medical procedures and medications may be unwarranted in the case of CIND or dementia and may even exacerbate cognitive deficits.^{5,6}

More recently, efforts have been taken to integrate informant reports with brief cognitive screens in order to enhance screening capacity for dementia and CIND. Informant reports rely on the judgment of a significant other concerning the patient's condition. The informant is usually asked to compare the patient's current condition to past functioning.⁷ Whereas traditional cognitive screens require the cooperation of the patient,

informant reports rely solely on the informant and, thus, can be particularly useful when the administration of a cognitive screen is not feasible.⁸ An additional advantage is that unlike cognitive screens, informant reports are independent of prior academic achievements and premorbid intelligence.⁹

Research has shown that informant reports provide data that are somewhat independent of patients' functioning on the cognitive screen.¹⁰ Yet, informant reports have shown to be as effective as cognitive screens in detecting CIND or dementia.¹⁰ Moreover, researchers have shown that combining cognitive screens with informant reports results in improved screening accuracy.^{10,11} Using informant reports is particularly warranted

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if the *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition [DSM-IV]) dementia diagnosis criteria are employed, as these criteria require not only the presence of cognitive impairment but also the presence of functional impairment,¹² which is most often assessed by an informant. Nevertheless, informant reports (regardless of number of items) also have several limitations, with the most notable being the fact that they are considered as an indication not only of patients' true cognitive functioning but also of informants' mental status as well as of the relationship between patients and informants.^{13,14}

The Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) is probably the most well-known informant self-report measure.¹⁵ The measure has been used worldwide and has been recommended for use in combination with screening measures such as the Mini-Mental Status Examination (MMSE).¹⁰ The measure is considered to represent a single perceived impairment construct.⁷ It has shown to correlate with a variety of cognitive tests¹⁶ and neuroanatomic changes^{17,18} and to discriminate between cognitively intact individuals and individuals with dementia^{7,19,20} and CIND.²¹ The measure has also shown to predict future impairment.²¹

The present study evaluates the use of the short version of the IQCODE, which contains 16 items, against a single-item informant screen. The study compares the ability of the 2 instruments to discriminate between cognitively intact versus individuals with CIND or individuals with dementia. Screening tools should demonstrate high sensitivity by yielding as few false negatives as possible (ie, those individuals who have the condition should be identified as such). On the other hand, specificity (ie, the number of true negatives detected) could be slightly lower, as these screening tools are considered the first line of testing and should be followed up by a multidisciplinary evaluation. The study provides sensitivity, specificity, positive predictive value, and negative predictive value for several cutoff points of the short version of the IQCODE and the single-item informant instrument. Both measures are evaluated against an expert consensus-based diagnosis of CIND or dementia, obtained by the Aging, Demographics, and Memory Study (ADAMS), a national study that was specifically designed to provide population-based estimates of CIND and dementia in the United States.²²

Methods

Sample

The ADAMS sample was drawn from the Health and Retirement Study (HRS), which is a nationally representative sample of individuals 50 years and older (<http://hrsonline.isr.umich.edu/>). Participants in the HRS take part in a biennial interview that covers a range of topics including income, wealth, work, retirement, health, health care utilization, and so on. The ADAMS is funded by the National Institute of Aging and is conducted by a research team from Duke University. The study

was approved by the Institutional Review Board of Duke University and the University of Michigan.

The HRS provided a sample frame for the ADAMS. The HRS includes data of more than 30 000 individuals. Initial baseline participation was approximately 80% and the reinterview participation rate ranges between 92% and 95%. In order to construct ADAMS, a group of 1770 HRS respondents, 70 year or older were sampled from the 2000 to 2002 HRS waves. This sample was stratified based on the cognitive assessment measure, completed by either a respondent or a proxy as part of the HRS. Stratification was performed in order to ensure a range of cognitive abilities. The cognitively intact group was also stratified by age (70-79 vs >80) and sex. Of the initial sample, 856 respondents (56% response rate of surviving target sample) completed the first wave of the ADAMS interviews. A detailed description of study procedure can be found elsewhere.²²

The ADAMS clinical assessment protocol consisted of a 3- to 4-hour in-person structured assessment conducted by a nurse and a neuropsychology technician. Neuropsychology technicians were from Duke University and were trained by a PhD-clinical neuropsychologist. All testing was scored by 2 technicians in addition to a final review by a neuropsychologist. The protocol required the participation of both a respondent and an informant, familiar with respondent's daily life and history. Respondents completed a neuropsychological battery (eg, selected sections of the Consortium to Establish a Registry for Alzheimer's Disease (CERAD), MMSE, Trail Making Test A & B, Digit Span, Shipley Vocabulary Test, etc.), a self-report depression measure, a standardized neurologic examination, physiological testing, and genetic testing. Prior neuroimaging and laboratory results from physicians were also obtained. Informants provided a detailed chronological account of patient's condition, medical history, medication use, neuropsychiatric symptoms, cognitive and functional impairment, family history of memory problems, and data concerning care provision. For a detailed account of study procedure, see Langa et al.²²

Instruments

The IQCODE. This is an informant self-report measure designed to assess patient's current cognitive performance relative to past performance. The ADAMS used the 16-item, short version, which has shown good psychometric properties similar to the full-scale version.²³ The original version asks the informants to report current cognitive functioning in relation to 10 years ago. However, the version used in the ADAMS study asks to compare current functioning to 2 years ago. For instance, informants are asked "compared with 2 years ago, how is your friend or relative at remembering things about family and friends, such as occupations, birthdays, and addresses?" Change is rated on a 5-point scale, ranging from 1 (*much better*) to 5 (*much worse*). A composite mean score is calculated, with a higher score representing worse perceived cognitive functioning. Cronbach α in the present study was .97.

Table 1. Sample Characteristics by Dementia Diagnosis

	Cognitive Intact (256)	CIND (185)	Dementia (206)	P
Age	77.38 (0.32)	80.52 (0.54)	83.67 (0.71)	<.001
Gender				
Female	134 (58.7%)	90 (53.4%)	136 (67.9%)	.18
Education	12.48 (0.20)	10.81 (0.26)	10.04 (0.34)	<.001
MMSE	27.90 (0.14)	24.96 (0.28)	15.76 (0.65)	<.001
IQCODE	2.98 (0.02)	3.19 (0.02)	3.90 (0.08)	<.001
Single item	1.87 (0.04)	2.75 (0.06)	4.02 (0.07)	<.001
Informant is a spouse	120 (49.6%)	67 (38.3%)	34 (16.7%)	<.001

Abbreviations: CIND, cognitive impairment not dementia; IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; MMSE, Mini-Mental Status Examination.

A single-item informant report. As part of the overall informant report questionnaire, informants were asked to rate respondents' memory: "how would you rate your friend's or relative's memory at the present time?" Response option is on a 5-point scale, ranging from 1 (*excellent*) to 5 (*poor*), with a higher score indicating worse perceived memory.

Mini-Mental State Examination²⁴. The MMSE is a commonly used 19-item assessment screening measure of mental status. The MMSE evaluates orientation, recall and recent memory, abstract thinking, attention and calculation, and objection identification. The MMSE has a maximum score of 30, with high scores representing better performance. In the present study, it was used as a crude indicator of cognitive functioning.

Procedure

Cognitive diagnosis. Research diagnosis was obtained through a consensus panel of a Duke University geropsychiatrist, neurologist, neuropsychologist, and cognitive neuroscientist, who were all blind to HRS respondents' initial cognitive stratum. Information from the in-home assessment was integrated with medical records and neuroimaging results to produce a final diagnosis broadly categorized as dementia, CIND, or normal cognitive function. The diagnosis of dementia was largely based on the *Diagnostic and Statistical Manual of Mental Disorders* (Third Edition Revised [*DSM-III-R*]) and on the *DSM-IV* criteria. Cognitive impairment not dementia was defined as functional impairment per respondent or informant report that did not meet criteria for dementia or performance on neuropsychological measures that was below expectations and ≥ 1.5 standard deviations (SDs) below published norms.²²

Analysis

Descriptive statistics were conducted. In addition, the correlations between the 2 informant instruments, level of education, and the MMSE were calculated. These analyses were weighted to account for nonparticipation rate and sample methodology. Next, receiver–operating curves (ROCs)²⁵ were used to compare the discriminative ability of the instruments.^{26,27} An area under the curve of 1.0 represents perfect discriminative ability, whereas an area of 0.5 represents worthless ability. The statistical

comparison between the curves was conducted using the *roccomp* command in STATA 11, which relies on the Jackknife method.²⁸ Analyses were conducted separately to determine the ability of the instruments to distinguish between cognitively intact individuals and individuals with CIND and between cognitively intact individuals and individuals with dementia. In an additional sensitivity analysis, the 2 instruments were evaluated against those 229 individuals with a diagnosis of probable or possible Alzheimer disease versus those identified as cognitively intact. Subsequently, ROCs were adjusted for age, gender, education, and total MMSE score. These analyses were conducted using the *comproc* command in STATA 11. This procedure estimates the performance of the measures conditional on the covariates. A Wald statistic which divides the observed difference between the 2 measures by its standard error (SE) is compared to the standard normal distribution to obtain a *P* value. Standard errors are obtained by bootstrapping.²⁹

Recommended cutoff scores for the IQCODE range between 3.3 and 4.0 according to study,¹⁵ whereas the single item does not have a recommended cutoff. Therefore, sensitivity, specificity, positive predictive value, and negative predictive value were calculated for several cutoff scores of the instruments. A decision concerning an appropriate cutoff point is not solely statistical but involves clinical judgment. For instance, in the case of a screening instrument, a need for high sensitivity often outweighs the need for high specificity.

Results

The final sample consisted of 647 (75.5%) respondents, who went through a dementia workup, had a total MMSE score, and complete informant reports. Overall, 206 respondents were diagnosed with dementia, 185 met CIND criteria, and the remaining 256 were classified as cognitive intact. There were significant differences between the 3 groups on IQCODE score and the single-item score, with the group having dementia demonstrating the highest (worse) scores on both instruments, and the cognitively intact group demonstrating the lowest (best) scores on both instruments. The cognitively intact group had the highest MMSE score (indicating less impairment) relative to the other 2 groups. There were also significant age differences between the groups, with the cognitively intact group

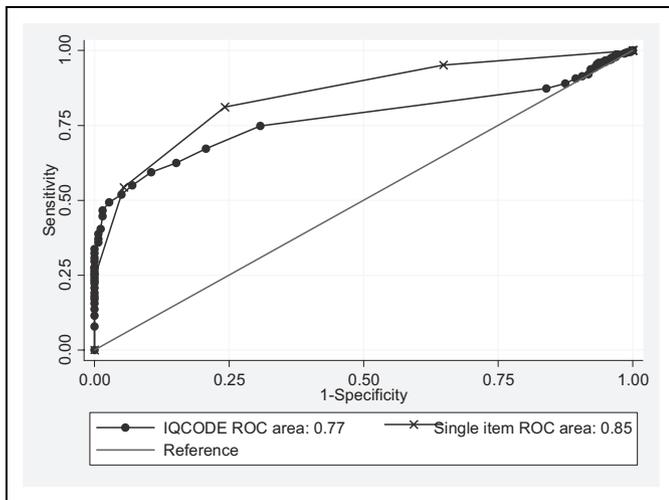


Figure 1. Areas under the curve of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) and the single-item instrument for discriminating between cognitive impairment not dementia (CIND) and cognitively intact individuals.

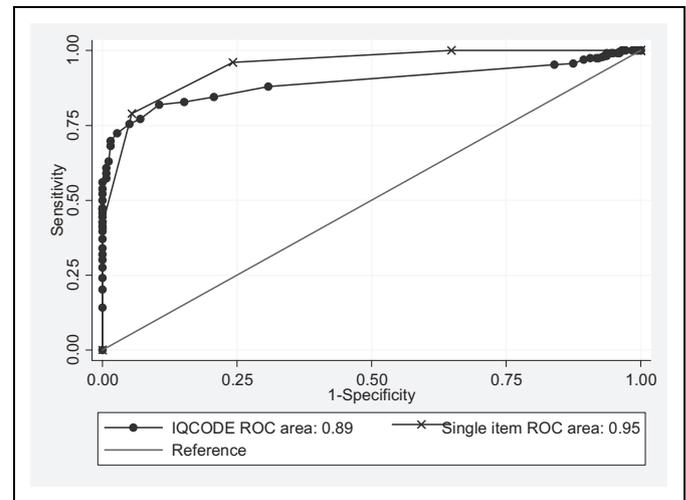


Figure 2. Areas under the curve of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) and the single-item instrument for discriminating between individuals with dementia and cognitively intact individuals.

being the youngest, and the group with dementia being the oldest. The cognitively intact group was significantly more educated than the other 2 groups. There were no gender differences across groups (see Table 1).

The overall correlation between the IQCODE and the single item was significant ($r = .57, P < .001$). The correlations between the IQCODE and education ($r = .01, P = .68$) was not significant, but the correlation between the single item and education ($r = -.18, P < .001$) was significant. Finally, there were significant correlations between the IQCODE and the MMSE total score ($r = -.44, P < .001$) and between the single item and the MMSE total score ($r = -.53, P < .001$).

IQCODE versus a single-item informant instrument. The ability of the 2 instruments to discriminate between cognitively intact individuals and individuals with CIND was moderate. The area under the curve of the IQCODE (0.77, SE = 0.02) was significantly worse than the area under the curve of the single item (0.85, SE = 0.01; $P < .001$; see Figure 1). After adjusting for age, gender, education, and total MMSE score, results remained consistent, but the difference between the areas under the curve of the 2 measures was nonsignificant: area under the curve of the IQCODE (0.75, SE = 0.04) and area under the curve of the single item (0.81, SE = 0.03; $P = .28$).

With regard to the discrimination between cognitively intact individuals and individuals with dementia, the areas under the curve indicated moderate-to-good discriminative ability for the IQCODE and the single-item instrument, respectively. The area under the curve of the IQCODE (0.89, SE = 0.01) was significantly worse than the area under the curve of the single item (0.95, SE = 0.008; $P < .001$; see Figure 2). After adjusting for age, gender, education, and total MMSE score, results remained consistent, but the difference between the areas under the curve of the 2 measures was nonsignificant: area under the

curve of the IQCODE (0.87, SE = 0.05) and area under the curve of the single item (0.92, SE = 0.04; $P = .43$).

An additional sensitivity analysis evaluated the ability of the 2 measures to discriminate between cognitively intact individuals and individuals with a diagnosis of possible or probable Alzheimer disease. This analysis resulted in comparable findings, with the area under the curve of the IQCODE (0.89, SE = 0.01) being significantly smaller than the area under the curve of the single item (0.95, SE = 0.009; $P < .001$).

Cutoff scores for the IQCODE and the single item. Table 2 outlines several potential cutoff points for the IQCODE and the single-item informant instrument. The table demonstrates improved ability for both instruments to discriminate between cognitively intact individuals and individuals with dementia relative to individuals with CIND. As expected, discriminative ability varied by the cutoff score used. Using 2.7 as a cutoff score on the IQCODE resulted in adequate sensitivity but low specificity. A cutoff score of 3 on the IQCODE resulted in worse sensitivity (failing to identify 105 individuals as having CIND) but improved specificity (erroneously identifying 79 individuals as having CIND). Using 3.3 as a cutoff score resulted in low sensitivity and high specificity. A similar trend was found for the IQCODE when used to discriminate between cognitively intact individuals and individuals with dementia.

Using a cutoff score of 1 on the single-item instrument to discriminate between cognitively intact individuals and individuals with CIND resulted in adequate sensitivity (erroneously missing only 22 individuals with CIND) but poor specificity (erroneously misclassifying 177 patients with intact cognitive functioning as having CIND). A cutoff of 2 on the single-item instrument resulted in comparable sensitivity and specificity, failing to identify as many as 86 patients as having CIND and erroneously identifying 67 individuals with intact

Table 2. Comparing the Ability of the IQCODE and the Single Item to Discriminate Between Cognitively Intact Individuals and Individuals With CIND and Between Cognitively Intact Individuals and Individuals With Dementia Across Different Cutoff Scores

	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)
CIND vs intact				
IQCODE >2.7	92.1	8.2	91.8	7.9
IQCODE >3.0	74.8	69.0	30.9	25.1
IQCODE >3.3	55.1	92.6	7.4	44.9
Single item >1	95.1	34.9	65.0	4.8
Single item >2	81.1	75.3	24.6	18.8
Single item >3	54.9	94.8	5.1	45.0
Dementia vs intact				
IQCODE >2.7	97.4	8.2	91.7	2.6
IQCODE >3.0	87.9	69.0	30.9	12.0
IQCODE >3.3	77.1	92.9	7.0	22.8
Single item >1	100	34.9	65.0	0
Single item >2	95.7	75.3	24.6	4.2
Single item >3	79.0	94.8	5.1	20.9

Abbreviations: CIND, cognitive impairment not dementia; IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly.

cognitive functioning as having CIND. Sensitivity decreased, but specificity improved, when a cutoff score of 3 was used. A similar trend was found for the single-item when used to discriminate between cognitively intact individuals and individuals with dementia (see Table 2).

Discussion

The use of informant measures has several advantages especially when the respondent is unable to complete the cognitive screen or when premorbid intelligence or academic achievements are likely to complicate the interpretation of the results of the cognitive screen.^{8,9} Brevity plays an important role in determining whether or not an instrument is used. Nevertheless, the ability of a tool to discriminate cases from noncases is of utmost importance. Therefore, the present study evaluated the use of 2 brief informant-based instruments to screen for CIND and dementia. The present study shows that both the IQCODE and the single-item instrument have only mild-to-moderate abilities to discriminate between cognitively intact individuals and individuals with CIND. Whereas the ability of the IQCODE to discriminate between cognitively intact individuals and individuals with dementia is moderate, the single-item instrument shows an adequate ability to distinguish between cognitively intact individuals and individuals with dementia. This may suggest that for screening purposes, there is no need to use an elaborated measure such as the IQCODE, but instead a single question regarding patient's functioning should suffice.

The most notable finding of the present study is the superior properties of the single item relative to the short version of the IQCODE. The single-item instrument outperforms the

IQCODE both in discriminating between cognitively intact individuals and individuals with CIND and in discriminating between cognitively intact individuals and individuals with dementia. This could be possibly due to the specific focus of the single item on present memory functioning relative to the broader focus of the IQCODE, which encompasses a variety of cognitive domains over a period of 2 years. Given the brevity of the single-item instrument and its improved discriminative ability, it represents a strong alternative to the IQCODE. Nonetheless, screening instruments are used not only to discriminate between noncases and cases (eg, cognitively intact vs individuals with CIND or dementia) but also to assess areas of strength and weakness and to monitor progress over time. For these various purposes, a single-item informant instrument is inadequate, whereas the short version of the IQCODE may provide rich information about various aspects of patients' perceived cognitive functioning.

An important limitation of both instruments is their relative low specificity. For screening purposes, the need for high sensitivity outweighs specificity. However, the potential trade-off between sensitivity and specificity, as identified in the present study, suggests that in order to avoid missing cases and, thus, maintain a high sensitivity (a low false negative rate) there is a need to use a relatively low cutoff point. As such, both instruments result in a high number of false positives. Although the consequences of being classified as a false positive with regard to dementia or CIND are less detrimental than being classified as a false positive in other situations,³⁰ going through a dementia evaluation carries consequences to the individual, his or her family, and the public.³¹ Thus, the choice of a specific cutoff for these screening instruments should reflect these aspects and is highly dependent on the characteristics of the specific setting. Because past research suggested that cognitive complaints often reveal neurological deficits that are not detected in a dementia evaluation,¹⁸ it is still possible that the false positives identified by these instruments actually present with cognitive deficits that might be of significance in the future.

The study has several limitations that should be addressed. First, the study evaluated the discriminative ability of the 2 instruments, but not their predictive ability. It is possible that a significant portion of the false positives identified in this study will develop dementia or CIND in future follow-ups. In addition, past research has found the 2-year version of the IQCODE to have lower psychometric properties than the 10-year version.³² This might explain the relative superiority of the single-item instrument in the present study. In addition, unlike past research, the present study did not evaluate the added value of informant instruments to commonly used cognitive screens. Finally, it is important to note that the shortcomings of informant reports are likely present both in the single-item measure and in the IQCODE.^{13,14} Nevertheless, the present study shows that for screening purposes asking informants a single question concerning the patient's cognitive state is a sensitive method. Therefore, asking a single question concerning patient's perceived memory functioning appears to be superior to the short version of the IQCODE for screening purposes.

Declaration of Conflicting Interests

The author declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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