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BRIEF REPORT

Diagnostic performance of the six-item cognitive impairment test as first-step screening for dementia: a meta-analysis

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Abstract

Objective: Dementia, a slowly progressive disease, is poorly diagnosed. One reason is that it is difficult to use the screening tools. The six-item cognitive impairment test (6-CIT) is brief, with six items, and has a confirmed scoring system that can easily be used by an average individual. This review aimed to analyze the predictive validity of the 6-CIT including comparisons with other tools such as the Mini-Mental State Examination (MMSE).

Methods: Literature searches were performed on the MEDLINE, EMBASE, CINAHL, and PsycArticles using the dementia and 6-CITas keywords. The Quality Assessment of Diagnostic Accuracy Studies-2 was applied to assess the risk of bias.

Results: Seven studies with 6,831 participants that met the selection criteria were included. The pooled sensitivity of the 6-CIT analyzed in seven studies was 0.82 (95% CI 0.73–0.89), the pooled specificity was 0.87, and the summary receiver operating characteristic (sROC) curve was 0.90 (SE = 0.04). The diagnostic performance of the 6-CIT and MMSE was compared in three studies. The pooled sensitivity of the 6-CIT was 0.85, the pooled specificity was 0.91, and the sROC curve was 0.91, whereas the MMSE values were 0.70, 0.93, and 0.68, respectively.

Conclusion: This review presents evidence that the 6-CIT has excellent dementia screening performance and could be used as a potential alternative to the MMSE. The 6-CIT may provide an opportunity for early detection of dementia.

Keywords: Dementia; cognitive dysfunction; neuropsychological tests; sensitivity and specificity; meta-analysis

Introduction

As the global increase in the prevalence of dementia is presenting key health and social challenges, the National Health Service of England (NHS England, 2015a) published a report on dementia diagnosis and management, stating that primary care settings should appropriately diagnose dementia. Emphasizing that dementia is a slowly progressive disease, a two-step process for assessing dementia was proposed in which the first screening used a standardized tool to distinguish depression, delirium, drugs, and memory changes due to natural aging, and then the cause of dementia was identified (Stähelin, Monsch & Spiegel, 1997). In this process, the Six-Item Cognitive Impairment Test (6-CIT) was suggested as one of the tools that could be used as a dementia screening tool in primary care settings (NHS England, 2015a).

The 6-CIT is a very brief dementia screen test developed in 1983 by Katzman et al., and consists of six items: three questions asking for the year, month, and time, listing the months of the year backwards, the name and address memory phrase, and counting down from 20 to 1. It takes

3–4 min to perform and covers several cognitive domains such as orientation, memory, and concentration. Additionally, it is easy to interpret because a score of 8 or higher indicates significant dementia. The questions are so clear that they can be used without error when translated into languages from other cultures; therefore, even those who are not physicians can easily use them with minimal training (Katzman et al., 1983).

NHS England emphasized the need to assess dementia first in primary care (NHS England, 2015a), but this is also required in acute care hospitals (Timmons et al., 2015). Dementia patients often receive acute care without a prior diagnosis. Hospitals also need screening tests for assessing cognitive impairment in older adult inpatients (O'Sullivan, O'Regan & Timmons, 2016). It also provides the benefit of avoiding potential safety issues in the course of care or during discharge (Timmons et al., 2015). Because of its brevity and simplicity, the 6-CIT can be efficiently used in both primary and secondary care settings as well as community (NHS England, 2015b).

The 6-CIT has been used to screen for cognitive function (Alves Apóstolo et al., 2018), but unlike the Mini-Mental State Examination (MMSE), its diagnostic performance for dementia screening has not been quantitatively reviewed (O'Sullivan et al., 2016). This study, which was based on the existing studies comparing the 6-CIT with the MMSE and other screening tools, was conducted to analyze the predictive validity of the 6-CIT as the first step in dementia screening.

Methods

This study was conducted according to the guidelines of the Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy (Bossuyt, Davenport, Deeks, Gatsonis & Wisniewski, 2013) and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 Statement (Page et al., 2021).

The MEDLINE, Embase, CINAHL, and PsycArticles databases were searched on August 17, 2021. The key search terms were dementia and 6-CIT. In dementia, MeSH terms for each type of dementia were used, and in the 6-CIT, free text was used. An example of the search strategy is provided in Supplementary Table 1.

The inclusion criteria were as follows: (i) *types of studies*: studies (e.g., cohort and cross-sectional studies) that reported diagnostic accuracy results; (ii) *types of participants*: studies that targeted patients with mild cognitive impairment (MCI) or any type of dementia; (iii) *indexed tests*: studies using the 6-CIT. The cutoff scores of the 6-CIT have applied the values suggested in each study; (iv) *gold standards*: studies in which dementia or cognitive impairment was diagnosed using international guidelines such as the Diagnostic and Statistical Manual of Mental Disorders (DSM), the International Classification of Diseases, Tenth Revision (ICD-10), or Petersen's criteria (Petersen et al., 1999); (v) *types of outcomes*: studies reporting true positive (TP), false positive (FP), false negative (FN), and true negative (TN) results that could be used to calculate sensitivity and specificity. Age and language were not limited in the literature search process.

The quality of the selected studies was assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2). The following information was extracted from the selected literature: year of publication, author, location, setting, age, sample size, the gold standard, blinding, cutoff scores for the 6-CIT and other tools, and TP, FP, FN, and TN values.

The meta-analysis was conducted using MetaDiSc 1.4 (Zamora, Abraira, Muriel, Khan & Coomarasamy, 2006) and the Meta DTA program (Freeman et al., 2019; Patel, Cooper, Freeman & Sutton, 2021). Based on the TP, FP, FN, and TN described in the 2×2 contingency table, screening accuracy was evaluated by yielding pooled sensitivity, and specificity with 95% confidence intervals (CIs). The data were analyzed with a bivariate random effect model. The summary receiver operating characteristic (sROC) curve statistics were presented graphically through the area under the curve (AUC). The AUC values were interpreted as follows. An

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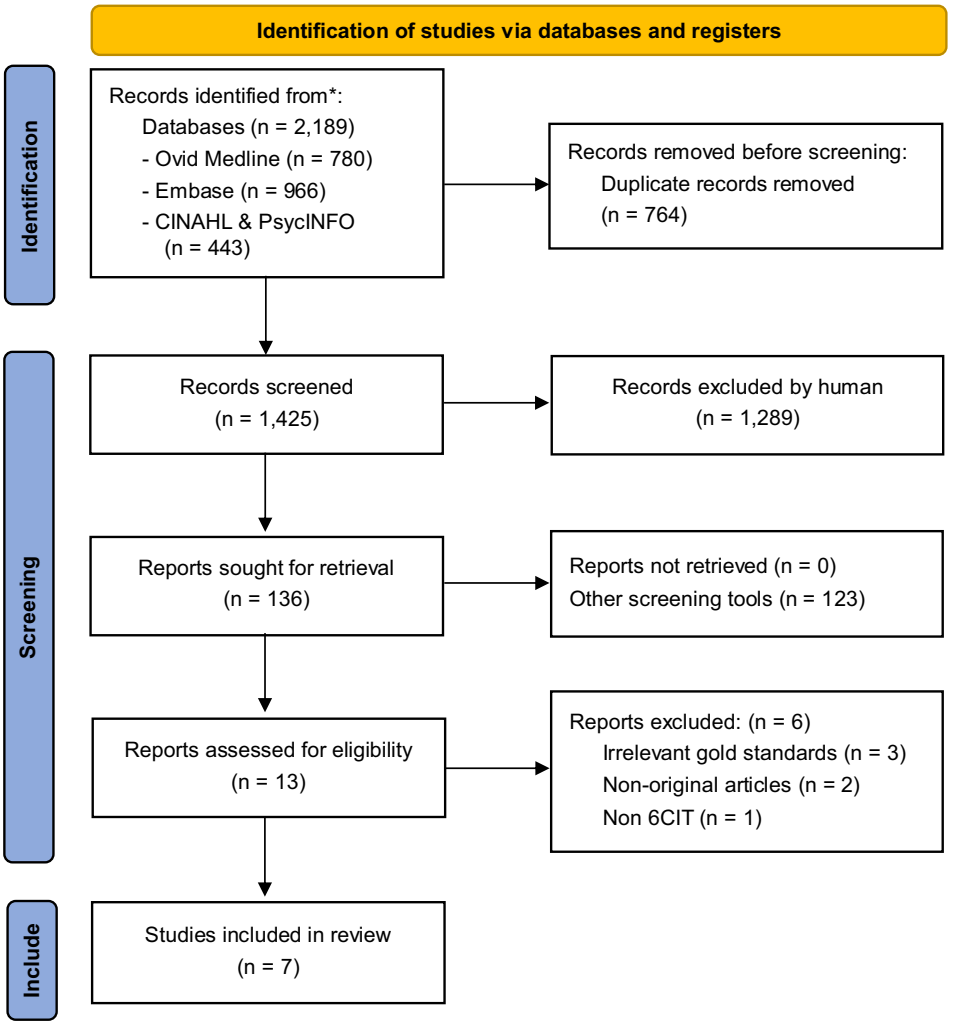

Figure 1. Flow diagram of article selection. This flow diagram developed by Preferred Reporting Items for Systematic Reviews and Meta-Analysis 2020. Figure 1 depicts the flow of information through the different phases of a systematic review. It maps out the number of records identified, included and excluded, and the reasons for exclusions.

AUC of 0.5 was a non-informative test, $0.5 < AUC \leq 0.7$ was low accurate, $0.7 < AUC \leq 0.9$ was moderate accurate, $0.9 < AUC < 1$ was high accurate, and an AUC of 1 was a perfect test (Greiner, Pfeiffer & Smith, 2000). The Q^* value represents the point at which sensitivity and specificity are equal in the sROC curve, with a value of 1 indicating accuracy of 100% (Walter, 2002).

Results

Selection process and risk of bias

A total of 2,189 papers were found in the four databases. Of them, 764 studies were duplicated, and the inclusion and exclusion criteria were applied to 1,425 studies. After excluding 1,418 (99.5%) studies, seven studies were selected for inclusion in the study. The study selection process is detailed in the PRISMA 2020 flow diagram (Fig. 1).

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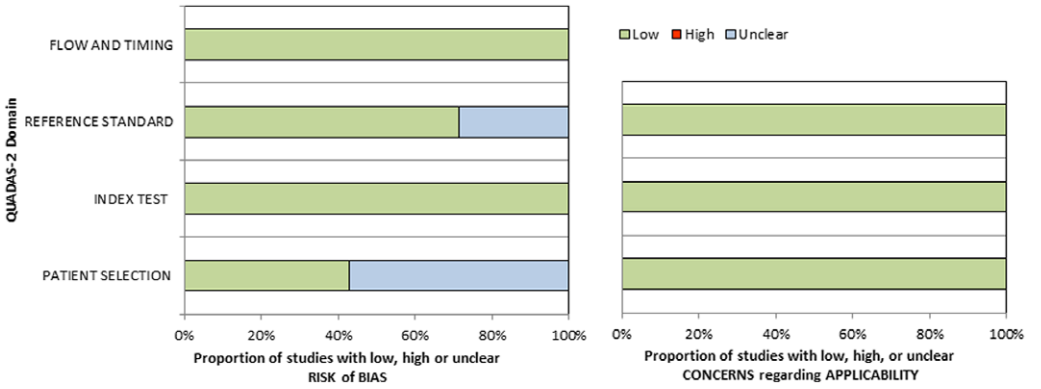

Figure 2. Quality assessment results of the selected studies by QUADAS-2. Graphical display for presenting results of QUADAS-2 for assessing the quality of studies.

As a result of assessing the quality of the selected studies, three studies (Abdel-Aziz & Larner, 2015; Hessler et al., 2017; Larner, 2021) were found to have a low risk of bias in all domains and items. In the patient selection domain, three studies were random samples (Hessler et al., 2017) or consecutive samples (Abdel-Aziz & Larner, 2015; Larner, 2021) and the rest were unclear. Five studies (Abdel-Aziz & Larner, 2015; Hessler et al., 2017; Larner, 2021; O'Sullivan et al., 2018) on which blinding was performed had a low risk of bias in the index test domain and the reference standard domain. All studies were assessed as low risk in flow and timing and the application of each domain because the same tests were performed on the patients (Fig. 2).

Summary of the included studies

A total of seven studies verified the predictive validity of the 6-CIT, and the total number of participants was 6,681. Abdel-Aziz & Larner (2015) analyzed dementia and MCI. The age of the participants was 65 years or older, except for in two studies (Abdel-Aziz & Larner, 2015; Larner, 2021). The studies were mainly published in the UK, and two studies were in Germany (Hessler et al., 2014; Hessler et al., 2017), one in Ireland (O'Sullivan et al., 2018). There were 100 or more participants in each study, and there were two large-scale studies (Hessler et al., 2014; Hessler et al., 2017) with more than 1,000 people. The optimal cutoff scores for the 6-CIT presented in each study ranged from 8 to 11. In five studies, the 6-CIT and other tools including the MMSE (Abdel-Aziz & Larner, 2015; Brooke & Bullock, 1999; Upadhyaya, Rajagopal & Gale, 2010), the Ascertain Dementia (AD8) (Larner, 2021), and the 4 'A's test (4AT) (O'Sullivan et al., 2018) were compared (Table 1).

Predictive validity of the 6-CIT in selected studies

The predictive validity of the 6-CIT was assessed for 6,681 participants across seven studies. The prevalence was 32.0%. The sensitivity and specificity ranged from 0.49 to 0.90 and 0.62 to 1.00, respectively. In the meta-analysis, the pooled sensitivity of the 6-CIT was 0.82 (95% CI, 0.73–0.89), the pooled specificity was 0.87 (95% CI, 0.73–0.95), and the sROC AUC was 0.90 (SE = 0.04). The Q^* value was 0.83 (SE = 0.04) (Table 2 and Fig. 3).

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Table 1. Characteristics of Selected Studies

Year	Authors	Location	Participants	Age	Female (%)	Total (*n*)	Gold standard	Blind	Tools	Cut off	2 × 2 Table				Value (95% confidence interval)	
											TP	FP	FN	TN	Sensitivity	Specificity
2021	Larner et al.	UK	New patients in memory clinic	59.0 ± 19.0	46.9	177	DSM-IV	Yes	6-CIT	8	44	48	7	78	0.86 (0.74–0.93)	0.62 (0.53–0.70)
									AD8	2	49	112	2	14	0.96 (0.87–0.99)	0.11 (0.07–0.18)
2018	O'Sullivan et al.	Ireland	ED attendees aged ≥70 years	77.0	51.3	415	DSM-V	Yes	6-CIT	8/9	62	71	12	223	0.84 (0.74–0.90)	0.76 (0.71–0.80)
									4AT	1/2	61	43	21	290	0.74 (0.64–0.83)	0.87 (0.83–0.90)
2017	Hessler et al.	Germany	Inpatients aged ≥65 years	78.6 ± 7.4	53.7	1,440	DSM-IV	Yes	6-CIT	10/11	238	59	32	1,111	0.88 (0.84–0.91)	0.95 (0.94–0.96)
2015	Abdel-Aziz et al.	UK	New dementia patients in clinic	57.0 ± 19.5	49.4	245	DSM-IV	Yes	6-CIT	10	42	43	6	154	0.88 (0.75–0.94)	0.78 (0.72–0.83)
									MMSE	22	13	19	9	109	0.59 (0.39–0.77)	0.85 (0.78–0.90)
			New MCI patients in clinic						6-CIT	9	44	39	23	91	0.66 (0.54–0.76)	0.70 (0.62–0.77)
									MMSE	25	22	21	21	64	0.51 (0.37–0.65)	0.75 (0.65–0.83)
2014	Hessler et al.	Germany	Adults aged ≥55 years who live in community	67.7 ± 7.8	59.1	3,908	ICD-10	Unclear	6-CIT	7/8	259	338	269	3,042	0.49 (0.45–0.53)	0.90 (0.89–0.91)
2010	Upadhyaya et al	UK	Older people referred to the local mental health team	79.3 ± 7.2	64.1	209	ICD-10	Unclear	6-CIT	10/11	129	11	14	55	0.90 (0.84–0.94)	0.83 (0.73–0.90)
									MMSE	23/24	114	9	29	57	0.80 (0.72–0.85)	0.86 (0.76–0.93)
1999	Brooke et al.	UK	Outpatients	73.8 ± 9.4	67.2	287	Clinical diagnosis	Yes	6-CIT	7/8	137	0	15	135	0.90 (0.84–0.94)	1.00 (0.97–1.00)
									MMSE	23/24	120	0	32	135	0.79 (0.72–0.85)	1.00 (0.97–1.00)

This is a summary table of the seven studies included in this review.

Abbreviations: TP, true positive; FP, false positive; FN, false negative; TN, true negative; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders-fourth edition; 6-CIT, Six-item Cognitive Impairment Test; AD8, Ascertain Dementia; ED, emergency department; 4AT, 4 'A's test; MMSE, Mini-Mental State Examination; MCI, mild cognitive impairment; ICD-10, International Classification of Diseases-Tenth Revision.

Table 2. Summary Results of Meta-analysis

Subjects	Studies (*k*)	Subjects (*n*)	Prevalence (%)	Pooled diagnostic test accuracy (95% confidence interval)		Summary ROC curve			
				Sensitivity	Specificity	AUC	SE	Q*	SE
6-CIT	7	6,831	32	0.82 (0.73–0.89)	0.87 (0.73–0.95)	0.90	0.04	0.83	0.04
6-CIT vs. MMSE									
6-CIT	3	741	44	0.85 (0.75–0.92)	0.91 (0.60–0.99)	0.91	0.06	0.84	0.07
MMSE	3	646	42	0.70 (0.57–0.81)	0.93 (0.69–0.99)	0.68	0.19	0.63	0.15
6-CIT vs. other tools									
6-CIT	2	592	24	0.85 (0.77–0.91)	0.70 (0.60–0.79)				
Other tools	2	592	24	0.89 (0.62–0.98)	0.48 (0.05–0.94)				

This is the meta-analysis result of the 6-CIT, and compared with other tools.
Abbreviations: ROC curve, receiver operating characteristic curve; AUC, area under the curve; SE, standard error, 6-CIT, Six-item Cognitive Impairment Test; MMSE, Mini-Mental State Examination.

Compared predictive validity of the 6-CIT and other tools

The 6-CIT versus the MMSE

The predictive validity of the MMSE compared to the 6-CIT was assessed for 741 participants in three studies (four cases). The sensitivity ranged from 0.66 to 0.90 for the 6-CIT, 0.51 to 0.80 for the MMSE, respectively. The specificity ranged from 0.70 to 1.00 for the 6-CIT, 0.75 to 1.00 for the MMSE, respectively. The pooled sensitivity of the 6-CIT was 0.85 (95% CI, 0.75–0.92), the pooled specificity was 0.91 (95% CI, 0.60–0.99), the sROC AUC was 0.91 (SE = 0.06), and the Q* value was 0.84 (SE = 0.07). In contrast, the pooled sensitivity of the MMSE was 0.70 (95% CI, 0.57–0.81), the pooled specificity was 0.93 (95% CI, 0.69–0.99), the sROC AUC was 0.68 (SE = 0.19), and the Q* value was 0.63 (SE = 0.15) (Fig. 4).

The 6-CIT versus other tools

The predictive validity of other tools compared to the 6-CIT was assessed for 592 participants in two studies. The pooled sensitivity of the 6-CIT was 0.85 (95% CI, 0.77–0.91), and the pooled specificity was 0.70 (95% CI, 0.60–0.79). And the pooled sensitivity of the other tools analyzed with the AD8 and 4AT was 0.89 (95% CI, 0.62–0.98), and the pooled specificity was 0.48 (95% CI, 0.05–0.94) (Fig. 5).

Discussion

The dementia screening tool can quantitatively assess the degree of cognitive impairment and is useful for measuring changes in cognitive function through repeated examinations. Dementia is a progressive disease; hence, it is difficult for family members or acquaintances to detect it accurately as well as in a timely (Grand, Caspar & Macdonald, 2011). Thus, the 6-CIT comprising six items has some advantages because it could easily and frequently check for dementia. The most widely used mental state examination worldwide is the MMSE (Arevalo-Rodriguez et al., 2015). This study was intended to quantitatively identify the dementia screening performance of the 6-CIT in seven studies compared with the MMSE which have been well proven through various researches.

In the studies included in this review, the 6-CIT was used for the early identification of cognitive function in older adults living in the community or patients who visited or were admitted to primary and secondary care settings. Since the 6-CIT is a dementia screening tool targeting the

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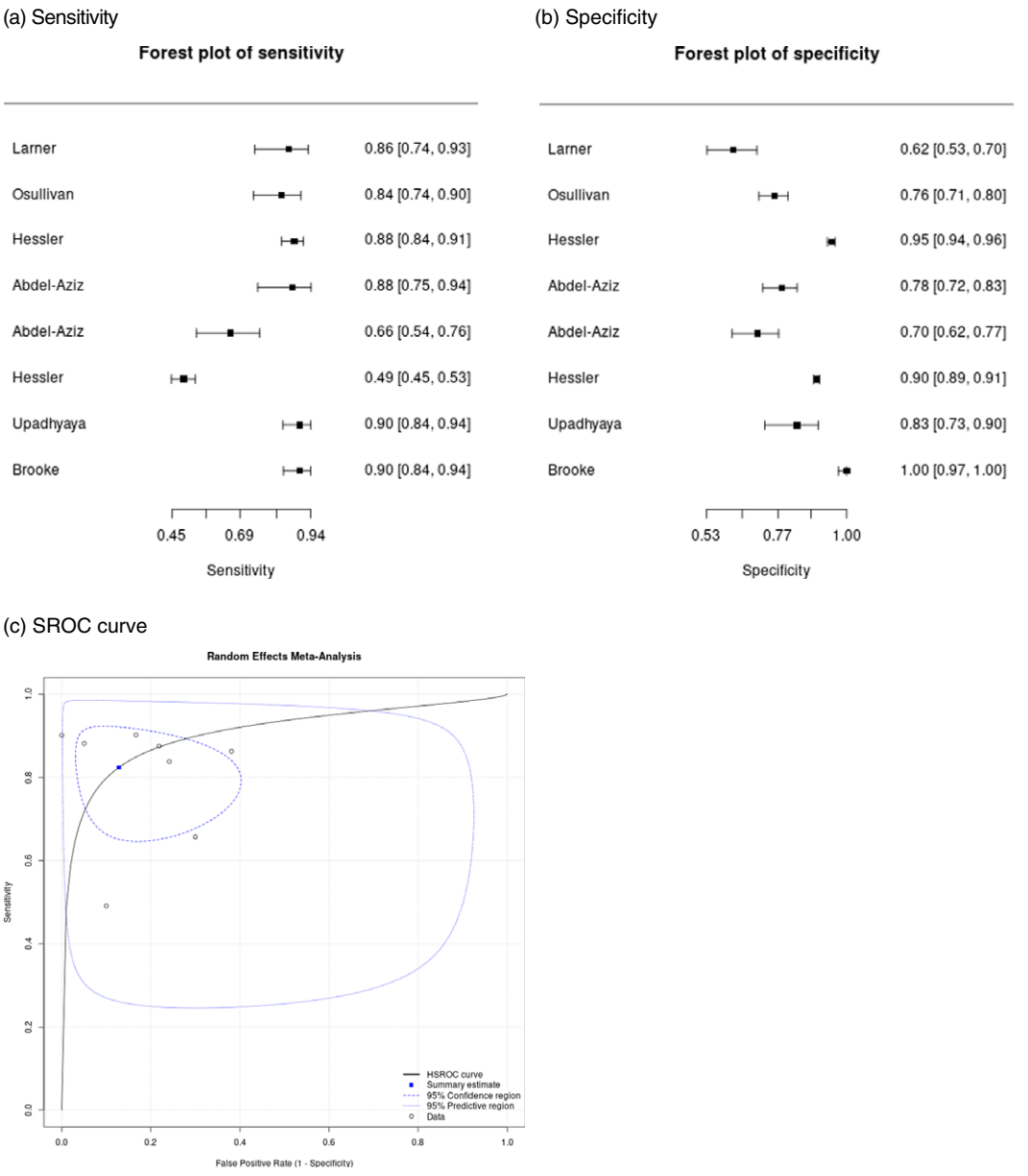

Figure 3. Predictive validity of the 6-CIT. The forest plot summarizes the results of the pooled sensitivity and specificity of the 6-CIT in selected studies.

older adult population, it was interpreted that the characteristics of these participants were similar to those of the environment in which 6-CIT was practically applied. In addition, since 6-CIT has a quantified scoring system, it was determined that the risk of bias in the procedure of the test would be low.

In the meta-analysis, the 6-CIT of all included studies had the pooled sensitivity of 0.82, the pooled specificity of 0.87, and the sROC AUC of 0.90. In comparison with the MMSE, the sROC AUC for the 6-CIT was 0.91, indicating a highly accurate test. The results of this review provide evidence that the 6-CIT demonstrates an excellent diagnostic performance for screening

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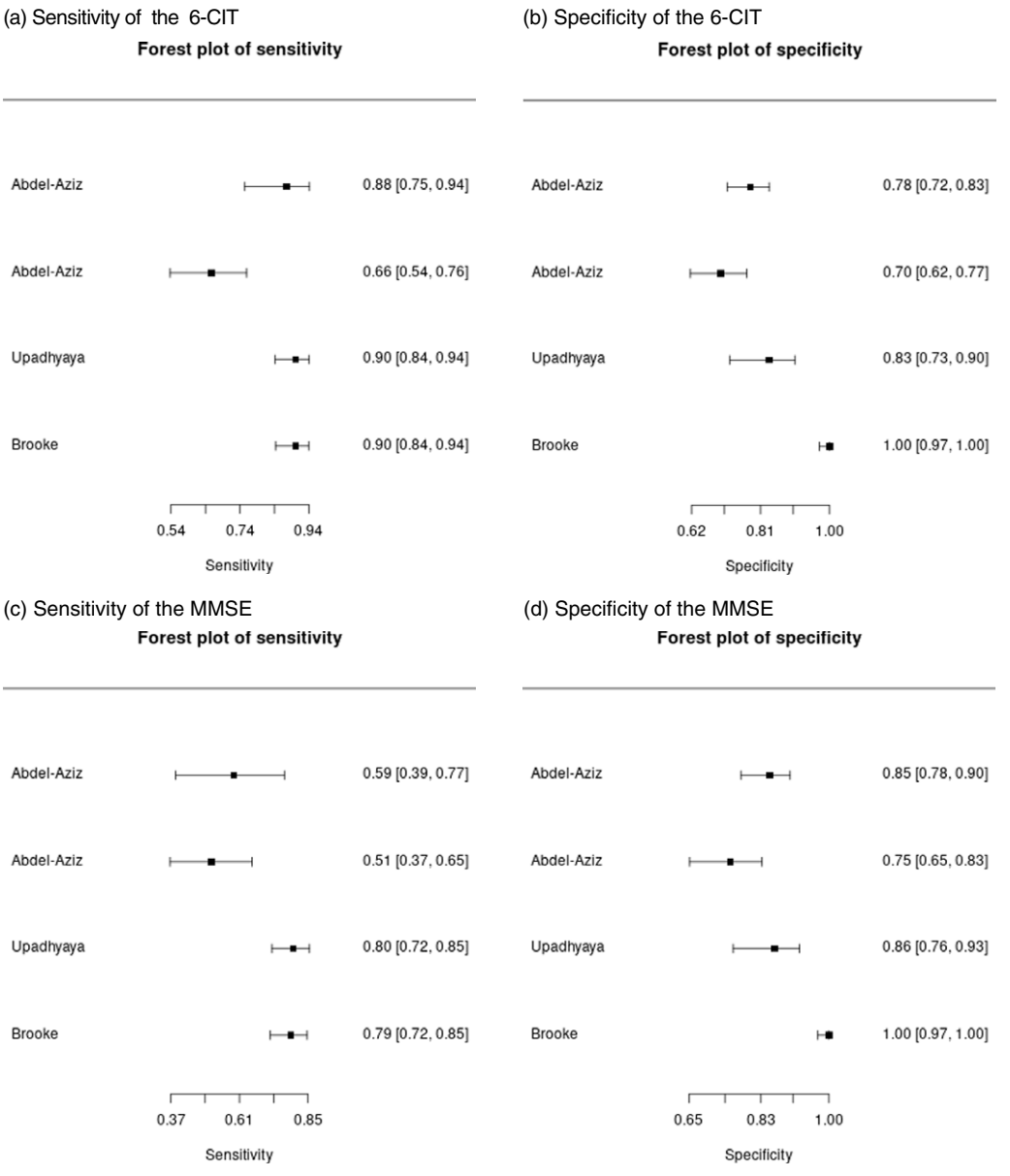

Figure 4. Predictive validity of the 6-CIT vs. the MMSE. The forest plot summarizes the results of the pooled sensitivity and specificity in the 6-CIT versus the MMSE.

dementia. The advantage of the 6-CIT over other neuropsychological assessments is that it is very simple and easily accessible. The cognitive domains that neuropsychological assessments usually evaluate are memory, attention, processing speed, reasoning, judgment, problem-solving, and spatial and language functions (Harvey, 2012). In comparison, the 6-CIT assesses only the domains of orientation, memory, and concentration (Katzman et al., 1983). Nevertheless, the findings of this review outline the excellent diagnostic performance of the 6-CIT, which highlights the clear advantage of using it as a quick and easy first screener when dementia is suspected in practice.

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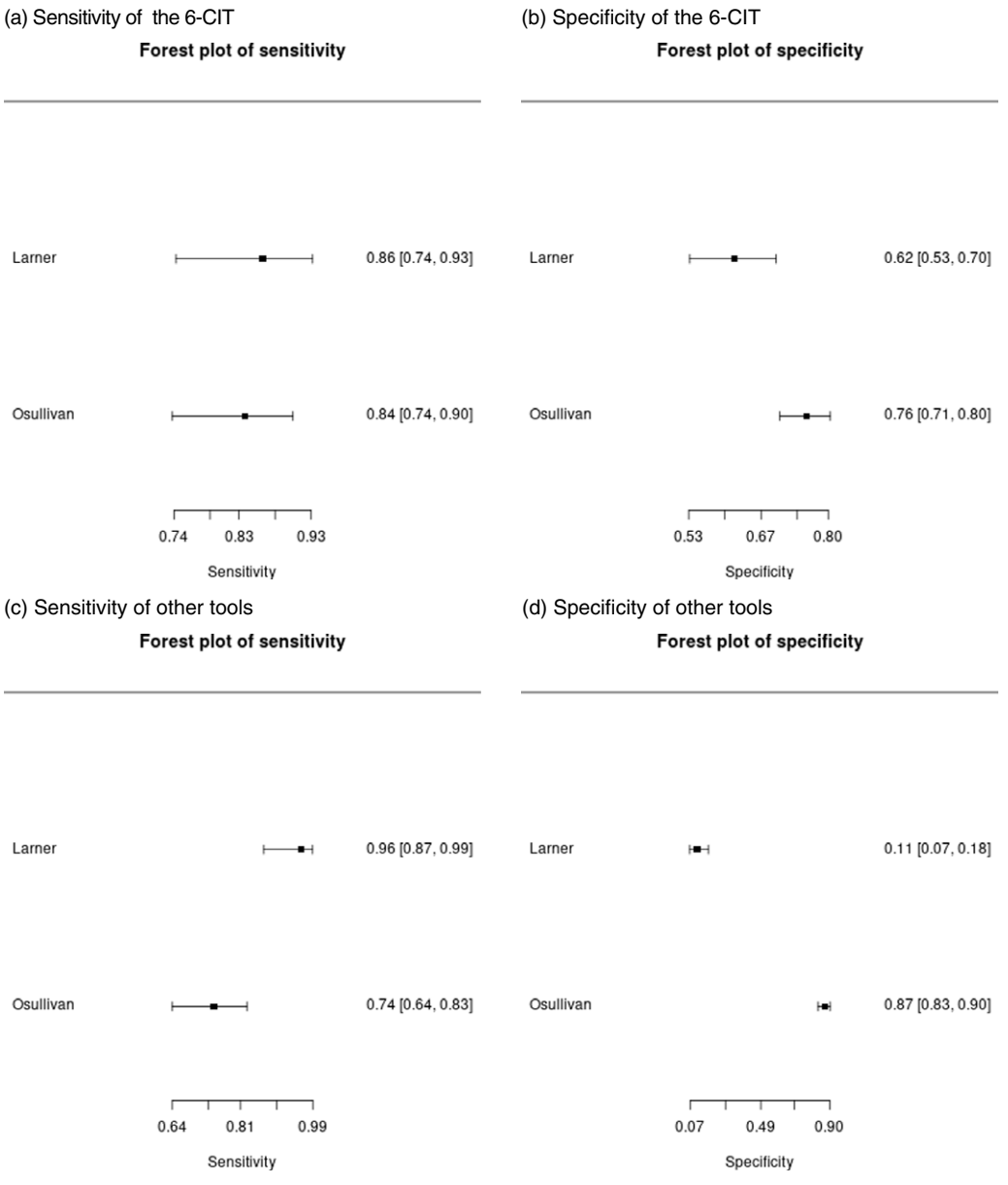

Figure 5. Predictive validity of the 6-CIT vs. other tools. The forest plot summarizes the results of the pooled sensitivity and specificity in the 6-CIT versus other tools.

In comparison with the MMSE, the pooled sensitivity of the 6-CIT was 0.85, which was higher than that of the MMSE (0.70), and the pooled specificity was 0.91, similar to that of the MMSE (0.93). The sROC AUC of the 6-CIT was 0.91, which was interpreted as highly accurate, whereas the SROC AUC of the MMSE was 0.68, which showed a relatively low diagnostic performance. There are many neuropsychological assessments, but among them, the MMSE is the most used and well-tested tool. However, the MMSE is affected by education level, and is difficult to apply a consistent cutoff score, and takes too much time to use in primary care (Matallana et al., 2011). There are also limitations when translating items from other cultures (Shim, Yang, Kim, Park &

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Kim, 2017). However, the questions of the 6-CIT are simple and clear sentences; hence, there would be no translation errors (Katzman et al., 1983; O'Sullivan et al., 2016). This review provides evidence that the dementia screening performance of the 6-CIT is relatively superior compared to that of the MMSE. Thus, we can suitably use it in any country. In comparison to other tools (AD8 and 4AT), the pooled sensitivity was similar at 0.85, but the pooled specificity of the 6-CIT at 0.70 was better than that of the other tools at 0.48.

In this study, the cutoff score of the 6-CIT applied in each study was used as it is. The 6-CIT has a quantified scoring system, and some websites can automatically calculate the measured scores. In the selected studies, a cutoff score of 10 or 11 was applied to patients with dementia or referred patients, and a cutoff score of 8 or 9 was applied to general participants for cognitive function screening. This was interpreted as a result showing that the scoring system that Katzman distinguished according to cognitive function (Katzman et al., 1983) was consistently applied in practice.

This review has certain limitations. The number of studies included in the review was small: seven articles. Comparison with the MMSE was done using three studies (four cases) and that with other tools was done using two studies. Thus, this study confirmed that the diagnostic performance of the 6-CIT was comparable to that of other tools, but it could not explain its potential benefits like when the use of the 6-CIT might be advantageous instead of the MMSE, and when the use of the 6-CIT is not suitable. The studies selected for this review did not consider differences in dementia subtypes. In addition, the use of the 6-CIT tends to be limited to some countries. All studies included in this review were published in three countries: four studies were from the UK, two from Germany, and one was from Ireland. Therefore, it also needs to be assessed in countries with different cultures.

Many of the older adults with dementia remain undiagnosed. Dementia, for which there is no treatment, is one of the early symptoms of cognitive decline (Knopman & Petersen, 2014). Considering the social and psychological effects of dementia, dementia screening should be easy and fast. This study presents evidence that the 6-CIT had excellent dementia screening performance and could be used as an alternative to the MMSE. The questions of the 6-CIT are very clear; hence, any country can correctly translate it into their own language. Cognitive impairment can be linked to adverse events that threaten the safety of older adults. The 6-CIT may provide an opportunity for early detection of dementia in people at potential risk. The 6-CIT, which is easy for anyone to use, can easily and quickly detect patients with cognitive impairment in the community or primary and secondary care settings and provide useful information for care.

Supplementary materials. For supplementary material for this article, please visit https://doi.org/10.1017/BrImp.2022.22

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Conflicts of interest. There are no conflicts to disclose.

Ethical standards. Not applicable.

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