



Accuracy of the Informant Questionnaire on Cognitive Decline in the Elderly for Detecting Preexisting Dementia in Transient Ischemic Attack and Stroke

A Population-Based Study

Astrid C. van Nieuwkerk, MD*; Sarah T. Pendlebury¹, BMBCh, DPhil*; Peter M. Rothwell¹, FMedSci; for the Oxford Vascular Study

BACKGROUND AND PURPOSE: Prestroke dementia prevalence is high and impacts outcome. Although the IQCODE (Informant Questionnaire on Cognitive Decline in the Elderly) is being used to assess prestroke cognition, data on its validity for prestroke dementia are lacking. We studied the accuracy of the short-form (16-item) IQCODE for pre-event dementia in a population-based study of all transient ischemic attack (TIA)/stroke.

METHODS: All patients with TIA/stroke in a defined population of $\approx 92\,720$ (Oxford Vascular Study, 2002–2017) with IQCODE were included. IQCODE questionnaires were given to participants at baseline interview with instructions to pass to an informant for completion and return by post. Diagnosis of pre-event dementia was defined as prior diagnosis of dementia, or dementia by the *Diagnostic and Statistical Manual of Mental Disorders-IV* criteria on study interview and hand-searching of the entire medical record blinded to IQCODE. Reliability of the IQCODE for dementia was determined by the area under the receiver operating characteristic curve, sensitivity and specificity, stratified by age, event severity, and first-ever stroke.

RESULTS: Among 2059 interviewed survivors, IQCODE were returned in 1068 (mean age/SD=72.9/12.3, 47% TIA, 52.3% male, 68 [6.4%] pre-event dementia). Area under the receiver operating characteristic curve for IQCODE for pre-event dementia was 0.94 (95% CI, 0.90–0.97, $P<0.001$) with similar results by age: 0.92, 0.88 to 0.96, <65 years; 0.94, 0.83 to 1.00, 65 to 74 years; 0.95, 0.92 to 0.99, 75 to 84 years; 0.89, 0.82 to 0.96, ≥ 85 years. The optimal cutoff score overall was >3.48 (sensitivity=89.7%; specificity=84.2%) but was nonsignificantly higher for major stroke (National Institutes of Health Stroke Scale score ≥ 3) than minor stroke/TIA (>3.85 versus >3.47). Performance was similar in patients with first-ever stroke (area under the receiver operating characteristic curve, 0.92 [0.88–0.97]; sensitivity=85.7%; specificity=84.8% for cutoff >3.48). All 16-IQCODE questions discriminated between dementia and no dementia (all $P<0.001$) with the greatest differences seen for finances, using gadgets, arithmetic, and learning new things.

CONCLUSIONS: IQCODE has excellent accuracy for detecting preexisting dementia in TIA and stroke with the pattern of deficits suggesting prominent executive dysfunction.

GRAPHIC ABSTRACT: An online [graphic abstract](#) is available for this article.

Key Words: cognition ■ dementia ■ diagnosis ■ interview ■ medical record ■ prevalence ■ survivors

Correspondence to: Sarah T. Pendlebury, Wolfson Centre for Prevention of Stroke and Dementia, Wolfson Bldg, John Radcliffe Hospital, Headley Way, Oxford OX3 9DU, United Kingdom. Email sarah.pendlebury@ndcn.ox.ac.uk

*A.C. van Nieuwkerk and S.T. Pendlebury are joint first authors.

This article was sent to Kazunori Toyoda, Guest Editor, for review by expert referees, editorial decision, and final disposition.

The Data Supplement is available with this article at <https://www.ahajournals.org/doi/suppl/10.1161/STROKEAHA.120.031961>.

For Sources of Funding and Disclosures, see page 1289.

© 2021 The Authors. *Stroke* is published on behalf of the American Heart Association, Inc., by Wolters Kluwer Health, Inc. This is an open access article under the terms of the [Creative Commons Attribution](#) License, which permits use, distribution, and reproduction in any medium, provided that the original work is properly cited. *Stroke* is available at www.ahajournals.org/journal/str

Nonstandard Abbreviations and Acronyms

AUROC	area under the receiver operating characteristic curve
IQCODE	Informant Questionnaire on Cognitive Decline in the Elderly
OXVASC	Oxford Vascular Study
TIA	transient ischemic attack

Cognitive impairment is associated with increased risk of stroke and of more severe stroke.^{1,2} The prevalence of prestroke dementia ranges from 5% in transient ischemic attack (TIA) to 21% in severe major stroke (National Institutes of Health Stroke Scale score >10).¹ Prestroke cognitive decline also increases the risk of death from stroke and of poststroke dementia.^{3–6}

However, identifying pre-TIA/stroke cognitive status at the time of the index cerebrovascular event may be difficult. Although some patients will have a documented dementia diagnosis, rates of undiagnosed dementia are high: around one-half of hospitalized people aged ≥75 years have moderate/severe cognitive impairment but only around 20% have a diagnosis of dementia.^{7,8} Pre-existing dementia can be excluded in patients with good cognitive function after TIA/stroke but for cognitively impaired patients, a retrospective assessment of cognition will be required. In such cases, indirect assessment via relatives or caregivers is necessary facilitated by structured tools including the IQCODE (Informant Questionnaire on Cognitive Decline in the Elderly), Eight-item Informant Interview to Differentiate Aging and Dementia (AD-8), and the general practitioner assessment of cognition, the latter being used in primary care settings.^{9–14}

The IQCODE measures global cognitive decline across a range of areas and is largely unaffected by occupation or education.^{9,10,12} It was developed to assess community-dwelling older adults, in whom Alzheimer disease is the most common dementia subtype and amnesic deficits are prominent. Each IQCODE item is scored on an ordinal 5-point scale score (1–5), and the average score across all items is calculated. Higher scores indicate cognitive decline. There is no consensus on the optimal cutoff for dementia which may vary according to the population characteristics and as with all cognitive screening tests, there is a trade-off between sensitivity and specificity.^{10,12} The IQCODE is available as 16- and 26- item versions that have similar validity and high internal consistency and test-retest reliability in non-stroke settings.^{10,12} However, previous validation studies had possible selection bias and limited reporting of IQCODE application, missing data, and incomplete questionnaires.^{10–12} There are also few data on differential item patterns across dementia subtypes.

The IQCODE has not been validated for prestroke dementia in cerebrovascular populations¹⁵ although it has been used to quantify or exclude pre-event dementia in stroke studies using variable cutoffs (3.30, 3.35, 4.00).^{4,5,16–20} We, therefore, assessed the accuracy of the IQCODE for pre-TIA/stroke dementia, and the effect of event severity and informant characteristics, in a population-based observational study of all TIA and stroke.

METHODS

Data Availability

Any requests for data will be considered by P.M. Rothwell (peter.rothwell@ndcn.ox.ac.uk).

Study Background

This study was conducted within the ongoing OXVASC (Oxford Vascular Study, 2002–) a longitudinal, prospective, population-based incidence study of all acute vascular events in a defined population of ≈92 720 in 9 primary care practices with around 100 general practitioners in Oxfordshire, United Kingdom.^{21,22} OXVASC is approved by the local Oxfordshire clinical research ethics committee (CO.043). Written consent is obtained at inclusion for study interview and follow-up, including review of all primary care and hospital records and death certificates. Where a patient is unable to give consent, assent from a relative is obtained.

Patients with TIA or minor stroke are referred by their primary care physician or the emergency department to the daily OXVASC emergency clinic staffed by a dedicated OXVASC clinical team. Patients with major stroke are admitted to the regional acute stroke unit at the John Radcliffe Hospital, Oxford, covering the study population area and are seen as soon as possible after admission by a member of the study team. Ascertainment of TIA and stroke approaches 100% of events reaching medical attention.^{21,22} Diagnosis and management are reviewed by the same senior neurologist (P.M. Rothwell) in all patients. Major stroke is defined as National Institutes of Health Stroke Scale score of 3 or greater, as this corresponds broadly to the inpatient versus outpatient population.²³

Participants

The current study included consecutive patients recruited during 2 periods when the IQCODE was included in the OXVASC study protocol (April 1, 2002, to February 31, 2004; March 31, 2010, to March 31, 2017). All patients with a stroke (ischemic and hemorrhagic) or definite/probable TIA, as adjudicated by P.M. Rothwell, were included.

Baseline interview was done using a structured proforma which included: medical history, risk factors, family history, medication, functional, and cognitive assessment. Reasons for lack of interview or cognitive test were documented. When a patient could not be interviewed (eg, because of aphasia, delirium, or dementia), a relative or caregiver was interviewed instead. Brain and vascular imaging were done at baseline.

The validated 16-item short IQCODE in English was given to the patient during the baseline interview.¹⁰ The patient was

instructed to ask someone they had known for at least 10 years to complete the form, and post it back. Patients were free to choose any informant. Informants were asked to score cognitive function over the last 10 years up to just before the index event. Each item was scored on a 5-item scale: 1: much improved, 2: a bit improved, 3: not much change, 4: a bit worse, 5: much worse. Informants or patients were called by a research nurse if the IQCODE was not returned within 2 weeks, or if they had very low scores or missing items. From 2010 onwards, the IQCODE included questions about the relationship of the informant to the patient.

Pre-event dementia diagnosis was made as described previously¹ (and see also methods in the [Data Supplement](#)) using the following information blinded to the IQCODE assessment: (1) baseline clinical assessment by study clinician; and (2) any dementia diagnosis, and related consultations and investigations, where available, in the primary care record, with hand-searching of the entire record including individual consultations, clinic letters, and hospitalization documentation.¹ The diagnosis of pre-event dementia was made by a senior study physician with expertise in dementia (S.T. Pendlebury) using the *Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV* criteria.¹ Dementia subtype diagnoses were recorded where available (eg, in the primary care or hospital records or clinic letters).

Statistical Analysis

Demographic and clinical characteristics were compared for patients with versus without IQCODE, using χ^2 or ANOVA as appropriate. We included IQCODEs with missing items and calculated mean item scores by dividing by the number of completed items.

Performance of individual IQCODE items was evaluated by calculating the difference in mean item scores of patients with versus without dementia and statistical significance was tested with ANOVA. Items were subsequently ranked in order of the differences in mean item scores between subjects with versus without dementia.

Validation of the IQCODE for pre-event dementia was done according to STARDdem criteria.²⁴ Reliability was determined using the area under the receiver operating characteristic curve (AUROC). Optimal cutoffs were calculated using Youden's index.²⁵ Sensitivity, specificity, positive, and negative predictive values were determined. AUROC, accuracy, and mean item scores were stratified by age, event severity, and dementia subtype (Alzheimer versus vascular), and subgroups were compared using ANOVA. We evaluated the differences between AUROCs with Z tests.²⁶ We also compared mean item scores and AUROC between patients who had the IQCODE but who were untestable with a direct-to-patient cognitive test (abbreviated mental test score [AMTS], Mini-Mental State Examination [MMSE], or Montreal Cognitive Assessment [MoCA]) and patients who had both IQCODE and a direct-to-patient test.

We performed sensitivity analyses omitting IQCODEs with missing items and where mean item scores were <3.00 (indicating cognitive improvement over 10 years). To exclude any possibility of incorporation bias, that is, that IQCODE had been used in the pre-event dementia diagnosis, we also performed analyses including only those patients with a dementia subtype

diagnosis since all such patients had received their dementia diagnosis from a specialist other than S.T. Pendlebury. Statistical significance was set at 0.05 and 95% CIs were derived as $\pm 1.96 \times$ the SE of the estimate. All analyses were done in SPSS for Windows 25.0.

RESULTS

Of 2400 patients (mean age/SD=73.6/13.6 years, 1180 female) with a definite or probable TIA or stroke over the 9 year study period, 2248 survived to ascertainment, of whom 2059 (92%) were interviewed and given an IQCODE to pass on to a relative or carer to complete and return by post. Questionnaires were returned in 1068 (52%; Figure and Table 1). The mean/SD age of interviewed patients with IQCODE (72.9/12.3 years) was similar to that of the 991 interviewed patients without a returned IQCODE (72.6/14.8, $P=0.70$) but those without IQCODE had more stroke (591, 59.6% versus 569, 53.3%, $P=0.004$), major stroke (271, 27.0% versus 212, 19.9%, $P<0.0001$), previous stroke (141, 14.3% versus 70, 6.6%, $P<0.0001$), hospitalization for the event (508, 51.2% versus 367, 34.3%, $P<0.0001$), and low baseline cognitive score (313/831 versus 299/968, $P<0.0001$ of those who had a baseline cognitive test, Table 1 in the [Data Supplement](#)).

Of the 1068 completed IQCODEs, all 16 items were completed in 1025 (96%) and in the remaining 43, 30 (70%) had only one item missing. Most commonly left unanswered were items 14-handling financial matters ($n=12$; 1.1%) and 1-remembering things about family and friends ($n=11$; 1.0%). The question about the nature of the informant was completed in 529 IQCODEs: 251 (65%) were spouses, 104 (27%) children, 20 friends (5%), 7 siblings (2%), 1 parent (0.2%), and 1 (0.2%) grandchild.

Mean/SD item score for all 1068 IQCODEs was 3.23/0.55 with median (interquartile range) 3.13 (3.00–3.38). The reference standard of a clinical pre-event dementia diagnosis was present in 68/1068 (6.4%) patients. Mean/SD item score in pre-event dementia was 4.34/0.59 versus 3.15/0.46 for no dementia ($P<0.0001$). AUROC for IQCODE and pre-event dementia was 0.94 (0.90–0.97, $P<0.001$) with optimal cutoff >3.48 showing optimal trade-off between sensitivity and specificity (sensitivity=89.7%, 79.9%–95.8%; specificity=84.2%, 81.8%–86.4%, Table 2). Results were similar by age (0.92, 0.88–0.96, <65 years; 0.94, 0.83–1.00, 65–74 years; 0.95, 0.92–0.99, 75–84 years; 0.89, 0.82–0.96, >84 years) and when analyses were restricted to patients with first-ever stroke (AUROC=0.92, 0.88–0.97, sensitivity=85.7%, 72.8%–94.1%; specificity=84.8%, 82.4%–87.0% for cutoff >3.48). Notably, the IQCODE had high negative predictive value with negative predictive value approaching 100 (Table 2). In contrast, positive

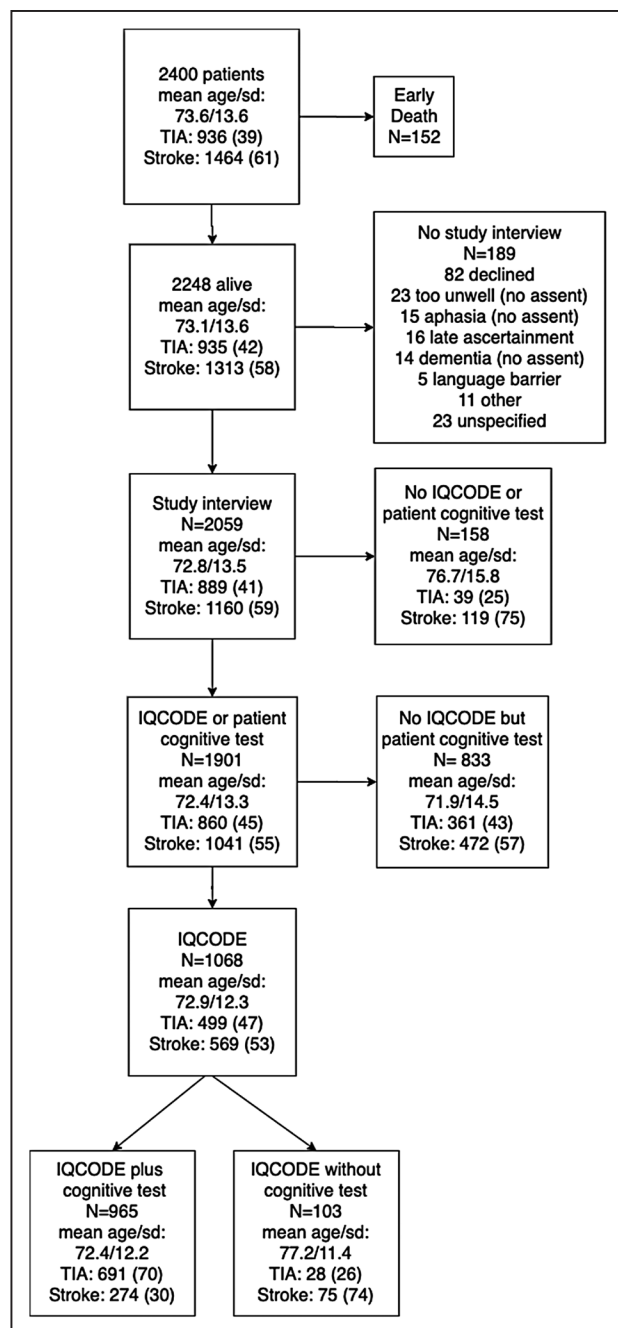


Figure. Flow chart showing the number and characteristics of all the transient ischemic attack (TIA) and stroke patients in the source population, and for all survivors, interviewed vs not interviewed, with vs without Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE), and with vs without direct-to-patient cognitive test (abbreviated mental test score, Mini-Mental State Examination, and Montreal Cognitive Assessment).

predictive value was much lower reaching a high of 51.5 (44.0–58.8) for cutoffs of >4 .

Patients with major stroke ($n=205$) had higher mean item scores than those with minor stroke ($n=364$) and TIA ($n=499$): mean/SD score=3.33/0.70 versus 3.19/0.51 and 3.22/0.50, $P=0.01$. Prevalence of

pre-event dementia was 5.0% (25/499) in TIA, 4.7% (364/499) in minor stroke and 12.7% (26/205) in major stroke with AUROCs of 0.92 (0.85–1.00, $P<0.001$), 0.95 (0.91–1.00, $P<0.001$), and 0.92 (0.87–0.97, $P<0.001$), respectively. Optimal cutoffs for identification of pre-event dementia were >3.47 for TIA and minor stroke and >3.85 for major stroke although differences were nonsignificant (Table 2).

Among the 1068 patients with IQCODE, 103 were untestable (Table 1 and Figure) with a direct-to-patient cognitive test (AMTS, MMSE, or MoCA). Compared with the 965 testable patients, untestable patients were older (mean age/SD=77.2/11.4 years versus 72.4/12.2 years, $P<0.0001$) with less TIA/minor stroke and more major stroke ($P<0.0001$), hospitalization (75, 72.8% versus 274, 28.4%, $P<0.001$), pre-event dementia (12, 11.7% versus 56, 5.8%, $P=0.02$), and IQCODEs scoring ≥ 3.48 (29, 28.2% versus 190, 19.7%, $P=0.04$; Table 1 and Figure). However, AUROCs for preexisting dementia were similar in testable and untestable patients: 0.93 (0.90–0.97) and 0.93 (0.87–1.00), respectively.

Mean item scores in incomplete IQCODEs were comparable to those of fully completed questionnaires (3.28 versus 3.23, $P=0.52$). Sensitivity analyses showed that test accuracy was unaffected by removal of IQCODEs with missing items: sensitivity=88.9% and specificity=84.2% for cutoff of >3.48 . The 117 patients with mean IQCODE score below 3.00 (indicating cognitive improvement over the last 10 years) were younger than those with mean scores ≥ 3.00 : mean age/SD=68.6/12.6 years versus 73.4/12.1 years ($P<0.001$). Excluding these 117 patients did not significantly change accuracy: sensitivity=91.0%, specificity=82.1% for cutoff of >3.48 . Among 68 pre-event dementia cases, 40 had a prior diagnosed dementia subtype. To rule out possible effects of incorporation bias, we performed a further sensitivity analysis excluding dementia patients without a documented dementia subtype. Accuracy of the IQCODE did not significantly change: cutoff >3.48 had 92.5% sensitivity and 84.0% specificity.

All 16-IQCODE items differed significantly for patients with versus without pre-event dementia both overall and after stratification for event severity (all $P<0.001$; Table 3 and Table II in the Data Supplement). Items 14-finance, 9-gadgets, 15-arithmetic, and 10-learning new things had the biggest mean differences between those with versus without pre-event dementia. The best discriminating item 14-handling financial matters alone had AUROC of 0.89 (Figure I in the Data Supplement). When stratified by event severity, major stroke showed greatest differences between dementia versus no dementia in items that might be considered as requiring greater executive function (items 14, 9, 15, 10), whereas TIA and minor stroke showed a more mixed pattern (items 9, 15, 14, 10/2/3; Table II in the Data Supplement).

Table 1. Baseline Characteristics of All Patients With IQCODE Stratified by Whether They Were Untestable or Testable Using With a Direct-to-Patient Cognitive Test

	All with IQCODE, N=1068	Untestable with cognitive test, N=103*	Testable with cognitive test, N=965*	P value
Age	72.9/12.2	77.2/11.4	72.4/12.2	<0.0001
Sex	558 (52.2)	52 (50.5)	506 (52.4)	0.71
Education <12 y	536 (50.2)	22 (21.4)	514 (53.3)	<0.0001
TIA	499 (46.7)	30 (29.1)	469 (48.6)	<0.0001
Minor stroke	364 (34.1)	21 (20.4)	343 (35.5)	
Major stroke	205 (19.2)	52 (50.5)	153 (15.9)	
PICH	28 (2.6)	7 (6.8)	21 (2.2)	<0.0001
In-patient	349 (32.7)	75 (72.8)	274 (28.4)	<0.0001
Previous stroke	74 (6.9)	11 (10.7)	63 (6.5)	0.10
Pre-event dementia	68 (6.4)	12 (11.7)	56 (5.8)	0.02
IQCODE mean/SD	3.23/0.55	3.27/0.77	3.23/0.52	0.48
IQCODE >3.48	219 (20.5)	29 (28.2)	190 (19.7)	0.04
IQCODE >3.6	168 (15.7)	22 (21.4)	146 (15.1)	0.10

Numbers are n (%) unless otherwise specified. IQCODE indicates Informant Questionnaire on Cognitive Decline in the Elderly; PICH, primary intracerebral hemorrhage; and TIA, transient ischemic attack.

*Mini-Mental State Examination, Montreal Cognitive Assessment, or abbreviated mental test score at baseline.

Among the 40 patients with known dementia subtypes, there were 17 (42.5%) with Alzheimer disease, 16 (40.0%) with vascular dementia, 3 (7.5%) with Lewy Body disease or Parkinson dementia, 2 (5.0%) with mixed dementia, and 2 (5.0%) with other. There were no significant differences in mean item scores across dementia subtypes ($P=0.50$). Although there were no significant differences in question performance between vascular and Alzheimer disease subgroups, Alzheimer patients were worse at remembering things about family and in

doing arithmetic whereas vascular dementia patients were worse in handling money, dealing with finances, and making decisions (Table 4).

DISCUSSION

The IQCODE had excellent accuracy for identifying pre-event dementia with an overall optimal cutoff of >3.48. Only 3% returned IQCODEs were incomplete, and of these, two-thirds had only 1 item missing. Missing items did not affect test accuracy. Patients with IQCODE who were untestable with a cognitive test were older and had more dementia suggesting that the IQCODE provided cognitive information in otherwise untestable patients and, therefore, mitigates selection bias. The pattern of deterioration across individual items suggested executive-type deficits especially in those with major stroke, in keeping with dementia with a vascular component.

To our knowledge, this is the first study to validate the IQCODE against a reference standard of prior clinical diagnosis of pre-TIA/stroke dementia. The original IQCODE validation found an optimal cutoff >4.0 with sensitivity of 92.7% and specificity of 88.1% but compared moderate/severely affected Alzheimer patients with community volunteers and was at risk of bias.⁹ The cutoff of >4.0 has subsequently been used to exclude preexisting dementia in stroke studies^{4,5,16–20} but our findings suggest that this will have resulted in some cases of dementia being included. The higher optimal cutoff we observed for major stroke than for TIA or minor stroke may be the result of more advanced/more severe dementia in those presenting with major stroke.¹ Just over a tenth of IQCODEs had a mean item score <3.00, indicating cognitive improvement. Studies in nonstroke populations rarely found low scores since aging is usually

Table 2. IQCODE Accuracy and 95% CIs for Pre-Event Dementia Using Different Cutoffs for All Patients, and Stratified by TIA, Minor Stroke, and Major (NIHSS ≥3) Stroke

IQCODE accuracy for pre-event dementia						
IQCODE cutoff	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	False negative	False positive
All, N=1068						
>3.30	92.7 (83.7–97.6)	71.8 (68.9–74.5)	18.3 (16.6–20.1)	99.3 (98.4–99.7)	0.282	0.074
>3.48	89.7 (79.9–95.8)	84.2 (81.8–86.4)	24.9 (24.7–31.3)	99.2 (98.4–99.6)	0.158	0.103
>3.50	89.7 (79.9–95.8)	84.2 (81.8–86.4)	24.9 (24.7–31.3)	99.2 (98.4–99.6)	0.158	0.103
>3.60	82.4 (71.2–90.5)	88.8 (86.7–90.7)	33.3 (28.9–38.1)	98.7 (97.8–99.2)	0.112	0.176
>4.00	77.9 (66.2–87.1)	95.0 (93.5–96.3)	51.5 (44.0–58.8)	98.5 (97.6–99.0)	0.050	0.221
TIA, N=499, optimal cutoff						
>3.47	88.0 (68.8–97.5)	86.1 (82.7–89.1)	25.0 (20.3–30.3)	99.3 (97.9–99.8)	0.750	0.007
Minor stroke, N=364, optimal cutoff						
>3.47	94.1 (71.3–99.9)	83.2 (78.8–87.0)	21.6 (17.5–26.4)	99.7 (97.7–100.0)	0.784	0.003
Major stroke, N=205, optimal cutoff						
>3.85	84.6% (65.1–95.6)	91.1% (85.9–94.8)	57.9 (45.6–69.3)	97.6 (94.3–99.0)	0.421	0.024

IQCODE indicates Informant Questionnaire on Cognitive Decline in the Elderly; NIHSS, National Institutes of Health Stroke Scale; NPV, negative predictive value; PPV, positive predictive value; and TIA, transient ischemic attack.

Table 3. Mean Scores of Each IQCODE Item for Pre-Event Dementia Versus No Dementia ($P<0.0001$ for All 16 Items)

	Dementia mean (95% CI)	No dementia mean (95% CI)	Mean difference	Rank difference
1: Family	4.24 (4.02–4.44)	3.14 (3.10–3.18)	1.10	13
2: Recent	4.51 (4.37–4.66)	3.28 (3.23–3.32)	1.24	5
3: Conversation	4.56 (4.41–4.71)	3.33 (3.28–3.37)	1.23	6
4: Address	4.03 (3.82–4.24)	3.00 (2.97–3.03)	1.03	16
5: Day and month	4.22 (4.03–4.41)	3.07 (3.04–3.11)	1.15	10
6: Things kept	4.16 (3.97–4.36)	3.14 (3.11–3.18)	1.02	15
7: Different place	4.56 (4.39–4.72)	3.34 (3.30–3.38)	1.22	7
8: Machines	4.14 (3.94–4.33)	3.04 (3.00–3.07)	1.10	14
9: Gadget	4.61 (4.45–4.76)	3.25 (3.20–3.29)	1.36	2
10: New things	4.52 (4.33–4.70)	3.26 (3.22–3.30)	1.26	4
11: Story	4.24 (4.04–4.43)	3.11 (3.07–3.14)	1.13	11
12: Decisions	4.36 (4.17–4.55)	3.17 (3.13–3.21)	1.19	8
13: Money	4.22 (4.02–4.43)	3.03 (3.00–3.06)	1.19	9
14: Finances	4.48 (4.30–4.66)	3.12 (3.08–3.16)	1.36	1
15: Arithmetic	4.44 (4.26–4.62)	3.09 (3.05–3.12)	1.35	3
16: Intelligence	4.36 (4.17–4.55)	3.22 (3.11–3.18)	1.12	12

Rank difference is rank based on mean difference from highest to lowest. IQCODE indicates Informant Questionnaire on Cognitive Decline in the Elderly.

associated with stable or declining cognition.²⁷ Mistakenly scoring early recovery after stroke as improvement might explain these low scores. Patients with low scores were younger, and young patients are more likely to improve after stroke.²⁸

IQCODE items about finances, money, arithmetic problems, and learning new things discriminated best between TIA/stroke patients with and without

preexisting dementia but in previous nonvascular validation studies, memory items were also important.^{9,10} There have been few studies on IQCODE-item performance across different dementia subtypes. One study reported that executive items showed differences between frontotemporal dementia and Alzheimer disease.²⁹ However, none of the 16 items differentiated between Alzheimer disease and vascular dementia subtypes in

Table 4. Mean Item Scores and 95% CIs for Pre-Event Dementia by Diagnosed Subtype (Alzheimer Versus Vascular Dementia)

	Alzheimer disease, N=17, mean (95% CI)	Vascular dementia, N=16, mean (95% CI)	P value	Mean difference	Rank difference
1: Family	4.44 (4.05–4.83)	4.06 (3.61–4.52)	0.19	0.38	1
2: Recent	4.71 (4.40–5.01)	4.50 (4.22–4.78)	0.30	0.21	7
3: Conversation	4.71 (4.40–5.01)	4.69 (4.37–5.01)	0.93	0.02	16
4: Address	4.12 (3.68–4.56)	4.00 (3.56–4.44)	0.69	0.12	13
5: Day and month	4.41 (4.05–4.78)	4.25 (3.89–4.61)	0.51	0.16	10
6: Things kept	4.31 (3.85–4.78)	4.13 (3.70–4.55)	0.53	0.18	9
7: Different place	4.76 (4.48–5.05)	4.56 (4.23–4.90)	0.34	0.20	8
8: Machines	4.31 (3.89–4.74)	4.19 (3.79–4.59)	0.65	0.12	13
9: Gadget	4.63 (4.24–5.01)	4.69 (4.37–5.01)	0.79	0.06	15
10: New things	4.47 (4.06–4.88)	4.69 (4.37–5.01)	0.37	0.22	6
11: Story	4.29 (3.86–4.73)	4.44 (4.10–4.77)	0.59	0.15	11
12: Decisions	4.38 (3.95–4.80)	4.63 (4.36–4.89)	0.30	0.25	4
13: Money	4.13 (3.65–4.60)	4.50 (4.11–4.89)	0.20	0.37	2
14: Finances	4.44 (4.00–4.87)	4.69 (4.37–5.01)	0.33	0.25	4
15: Arithmetic	4.71 (4.40–5.01)	4.44 (4.16–4.71)	0.25	0.27	3
16: Intelligence	4.59 (4.22–4.95)	4.44 (4.16–4.71)	0.49	0.15	11

Rank difference is rank based on mean difference from highest to lowest.

our study, possibly because of small numbers although there were some qualitative differences: patients with Alzheimer disease showed the biggest mean score difference in items associated with memory whereas vascular dementia patients scored worst on items requiring executive function.

Informants were most often spouses (60%–65%) or children (27%–30%) in keeping with the few studies that have reported informant details.^{30–32} The IQCODE was completed and returned in just over half of interviewed patients which is comparable to previous studies: lack of suitable informants may affect 12% to 40% inpatients.^{31–33} Since poor social interaction is associated with higher dementia incidence, this group might be at high risk resulting in a lower measured dementia rate in those with IQCODE versus the population as a whole.³⁴

Overall, the IQCODE would appear a valid tool for use in stroke research to exclude patients with prestroke dementia in studies of the prevalence and predictors of poststroke dementia. The IQCODE may also be useful in clinical practice to guide rehabilitation strategies: for example, patients with preexisting dementia may not benefit from cognitive rehabilitation and could be identified using an IQCODE score favoring specificity over sensitivity to ensure that patients without dementia were not excluded inappropriately. The IQCODE may also provide clinically useful prognostic information: patients with prestroke dementia may be more likely to have a substantial Alzheimer disease component and, therefore, ongoing poststroke decline than those with poststroke dementia and normal IQCODE who may show a more fixed deficit pattern with slower progression. Similarly, patients with abnormal IQCODE not reaching the threshold for dementia are at greater risk of future dementia after stroke as shown in previous studies^{5,6,35} although it remains unclear whether this is independent of baseline cognitive test score. In terms of the implications for clinical practice, the IQCODE findings may help in counseling patients and carers regarding the cognitive prognosis, likelihood of recovery and response to rehabilitation. In addition, studies in Alzheimer disease suggest that cognitive decline may be slowed by treatment of vascular risk factors and the acute TIA/stroke event provides an opportunity to properly address these through robust secondary prevention measures to reduce both the risk of future cerebrovascular events and dementia.³⁶

Strengths of our study include the large sample, population-based design, and limited exclusion criteria. We also performed a number of sensitivity analyses including for the effects of possible incorporation bias. Limitations include the fact that, despite the robust study design, the IQCODE was completed and returned less often in inpatients with more severe stroke and previous stroke in whom rates of pre-event dementia are higher, resulting in a lower rate of pre-event dementia (6.4%) in those with IQCODE than in the cohort overall (9.8%).¹ We did

not specifically examine feasibility, cost, and acceptability in our study, but available data from elsewhere suggest that these are favorable.¹² In addition, in keeping with previous studies, we analyzed the IQCODE as a nominal mean item score which assumes that the difference between each item is equal, when in fact it is an ordinal 5-point scale.^{10–12} We did not screen informants for cognitive problems or depression, anxiety, stress, or carer burden^{11,31} or stipulate any requirement regarding the amount of time informants should spend in the company of the patient.³³ Finally, informant characteristics were only available for later subjects in our study.

In conclusion, the IQCODE has high accuracy for identifying pre-TIA/stroke dementia, with optimal cut-off >3.48. However, the cutoff used in practice will vary according to whether greater sensitivity or specificity is preferred, and whether major stroke versus minor stroke or TIA is being assessed. Further studies are required to examine the patterns of item performance in different dementia subtypes, the impact of informant characteristics, and the predictive value of the IQCODE for post-stroke cognitive decline.

ARTICLE INFORMATION

Received July 24, 2020; final revision received November 25, 2020; accepted January 4, 2021.

Affiliations

Wolfson Centre for Prevention of Stroke and Dementia, Nuffield Department of Clinical Neurosciences, John Radcliffe Hospital and University of Oxford, United Kingdom (A.S.v.N., S.T.P., P.M.R.). National Institute for Health Research (NIHR) Oxford Biomedical Research Centre, John Radcliffe Hospital, United Kingdom (S.T.P.).

Acknowledgments

S.T. Pendlebury is supported by the National Institute for Health Research (NIHR) Oxford Biomedical Research Centre (BRC). P.M. Rothwell is supported by the NIHR Oxford BRC and the Wellcome Trust.

Sources of Funding

This study was supported by Wellcome Trust, Wolfson Foundation, British Heart Foundation, National Institute for Health Research (NIHR), and NIHR Oxford Biomedical Research Centre.

Disclosures

None.

Supplemental Materials

Tables I and II
Figure I

REFERENCES

1. Pendlebury ST, Rothwell PM; Oxford Vascular Study. Incidence and prevalence of dementia associated with transient ischaemic attack and stroke: analysis of the population-based Oxford Vascular Study. *Lancet Neurol*. 2019;18:248–258. doi: 10.1016/S1474-4422(18)30442-3
2. Rostamian S, Mahinrad S, Stijnen T, Sabayan B, de Craen AJ. Cognitive impairment and risk of stroke: a systematic review and meta-analysis of prospective cohort studies. *Stroke*. 2014;45:1342–1348. doi: 10.1161/STROKEAHA.114.004658
3. Hénon H, Durieu I, Lebert F, Pasquier F, Leys D. Influence of prestroke dementia on early and delayed mortality in stroke patients. *J Neurol*. 2003;250:10–16. doi: 10.1007/s00415-003-0917-3

4. Barba R, Morin MD, Cemillán C, Delgado C, Domingo J, Del Ser T. Previous and incident dementia as risk factors for mortality in stroke patients. *Stroke*. 2002;33:1993–1998. doi: 10.1161/01.str.0000017285.73172.91
5. Hénon H, Durieu I, Guerouaou D, Lebert F, Pasquier F, Leys D. Poststroke dementia: incidence and relationship to prestroke cognitive decline. *Neurology*. 2001;57:1216–1222. doi: 10.1212/wnl.57.7.1216
6. Pendlebury ST, Rothwell PM. Prevalence, incidence, and factors associated with pre-stroke and post-stroke dementia: a systematic review and meta-analysis. *Lancet Neurol*. 2009;8:1006–1018. doi: 10.1016/S1474-4422(09)70236-4
7. Pendlebury ST, Klaus SP, Mather M, de Brito M, Wharton RM. Routine cognitive screening in older patients admitted to acute medicine: abbreviated mental test score (AMTS) and subjective memory complaint versus Montreal Cognitive Assessment and IQCODE. *Age Ageing*. 2015;44:1000–1005. doi: 10.1093/ageing/afv134
8. Sampson EL, Blanchard MR, Jones L, Tookman A, King M. Dementia in the acute hospital: prospective cohort study of prevalence and mortality. *Br J Psychiatry*. 2009;195:61–66. doi: 10.1192/bjp.bp.108.055335
9. Jorm AF, Jacomb PA. The Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE): socio-demographic correlates, reliability, validity and some norms. *Psychol Med*. 1989;19:1015–1022. doi: 10.1017/s0033291700005742
10. Jorm AF. A short form of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE): development and cross-validation. *Psychol Med*. 1994;24:145–153. doi: 10.1017/s003329170002691x
11. Jorm AF. The Informant Questionnaire on cognitive decline in the elderly (IQCODE): a review. *Int Psychogeriatr*. 2004;16:275–293. doi: 10.1017/s1041610204000390
12. Harrison JK, Fearon P, Noel-Storr AH, McShane R, Stott DJ, Quinn TJ. Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) for the diagnosis of dementia within a secondary care setting (Review). *Cochrane Database Syst Rev*. 2015;3:CD010772.
13. Galvin JE, Roe CM, Powlisha KK, Coats MA, Muich SJ, Grant E, Miller JP, Storandt M, Morris JC. The AD8: a brief informant interview to detect dementia. *Neurology*. 2005;65:559–564. doi: 10.1212/01.wnl.0000172958.95282.2a
14. Brodaty H, Pond D, Kemp NM, Luscombe G, Harding L, Berman K, Huppert FA. The GPCOG: a new screening test for dementia designed for general practice. *J Am Geriatr Soc*. 2002;50:530–534. doi: 10.1046/j.1532-5415.2002.50122.x
15. McGovern A, Pendlebury ST, Mishra NK, Fan Y, Quinn TJ. Test accuracy of informant-based cognitive screening tests for diagnosis of dementia and multidomain cognitive impairment in stroke. *Stroke*. 2016;47:329–335. doi: 10.1161/STROKEAHA.115.011218
16. Banerjee G, Wilson D, Ambler G, Osei-Bonsu Appiah K, Shakeshaft C, Lunawat S, Cohen H, Yousry T Dr, Lip GYH, Muir KW, et al; CROMIS-2 Collaborators. Cognitive impairment before intracerebral hemorrhage is associated with cerebral amyloid angiopathy. *Stroke*. 2018;49:40–45. doi: 10.1161/STROKEAHA.117.019409
17. Klimkowicz A, Dziedzic T, Polczyk R, Pera J, Słowik A, Szczudlik A. Factors associated with pre-stroke dementia: the cracow stroke database. *J Neurol*. 2004;251:599–603. doi: 10.1007/s00415-004-0384-5
18. Laible M, Horstmann S, Möhlenbruch M, Schueler S, Rizos T, Veltkamp R. Preexisting cognitive impairment in intracerebral hemorrhage. *Acta Neurol Scand*. 2017;135:628–634. doi: 10.1111/ane.12646
19. Sachdev PS, Brodaty H, Valenzuela MJ, Lorentz L, Looi JC, Berman K, Ross A, Wen W, Zagami AS. Clinical determinants of dementia and mild cognitive impairment following ischaemic stroke: the Sydney Stroke Study. *Dement Geriatr Cogn Disord*. 2006;21:275–283. doi: 10.1159/000091434
20. Lefebvre C, Deplanque D, Touzé E, Hénon H, Parnetti L, Pasquier F, Gallai V, Leys D; SAFE II investigators. Prestroke dementia in patients with atrial fibrillation. Frequency and associated factors. *J Neurol*. 2005;252:1504–1509. doi: 10.1007/s00415-005-0900-2
21. Coull AJ, Silver LE, Bull LM, Giles MF, Rothwell PM; Oxford Vascular (OXVASC) Study. Direct assessment of completeness of ascertainment in a stroke incidence study. *Stroke*. 2004;35:2041–2045. doi: 10.1161/01.STR.0000137605.48864.2f
22. Rothwell PM, Coull AJ, Silver LE, Fairhead JF, Giles MF, Lovelock CE, Redgrave JN, Bull LM, Welch SJ, Cuthbertson FC, et al; Oxford Vascular Study. Population-based study of event-rate, incidence, case fatality, and mortality for all acute vascular events in all arterial territories (Oxford Vascular Study). *Lancet*. 2005;366:1773–1783. doi: 10.1016/S0140-6736(05)67702-1
23. Paul NL, Koton S, Simoni M, Geraghty OC, Luengo-Fernandez R, Rothwell PM. Feasibility, safety and cost of outpatient management of acute minor ischaemic stroke: a population-based study. *J Neurol Neurosurg Psychiatry*. 2013;84:356–361. doi: 10.1136/jnnp-2012-303585
24. Noel-Storr AH, McCleery JM, Richard E, Ritchie CW, Flicker L, Cullum SJ, Davis D, Quinn TJ, Hyde C, Rutjes AW, et al. Reporting standards for studies of diagnostic test accuracy in dementia: the STARDdem Initiative. *Neurology*. 2014;83:364–373. doi: 10.1212/WNL.0000000000000621
25. Youden WJ. Index for rating diagnostic tests. *Cancer*. 1950;3:32–35. doi: 10.1002/1097-0142(1950)3:1<32::aid-cnrc2820030106>3.0.co;2-3
26. Xhou X-H, Obuchowski NA, McClish DK. *Statistical Methods in Diagnostic Medicine, Second edition*. Wiley; 2011.
27. Reichenheim M, Sanchez MA, Lourenço RA. Re-assessing the dimensional structure of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE): empirical evidence for a shortened Brazilian version. *BMC Geriatr*. 2015;15:93. doi: 10.1186/s12877-015-0098-9
28. Knoflach M, Matosevic B, Rücker M, Furtner M, Mair A, Wille G, Zangerle A, Werner P, Ferrari J, Schmidauer C, et al; Austrian Stroke Unit Registry Collaborators. Functional recovery after ischemic stroke—a matter of age: data from the Austrian Stroke Unit Registry. *Neurology*. 2012;78:279–285. doi: 10.1212/WNL.0b013e31824367ab
29. Larner AJ. Can IQCODE differentiate Alzheimer's disease and frontotemporal dementia? *Age Ageing*. 2010;39:392–394. doi: 10.1093/ageing/afq014
30. Tang WK, Chan SS, Chiu HF, Wong KS, Kwok TC, Mok V, Ungvari GS. Can IQCODE detect poststroke dementia? *Int J Geriatr Psychiatry*. 2003;18:706–710. doi: 10.1002/gps.908
31. Harald A. Nygaard, Naik M, Geitung JT. The Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) is associated with informant stress. *Int J Geriatr Psychiatry*. 2009;24:1185–1191.
32. Bloomfield K, John N. Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) completion on an acute care ward for the elderly: a brief study of informant characteristics. *Int Psychogeriatr*. 2012;24:1700–1701. doi: 10.1017/S1041610212000415
33. Harwood DM, Hope T, Jacoby R. Cognitive impairment in medical inpatients. II: Do physicians miss cognitive impairment? *Age Ageing*. 1997;26:37–39. doi: 10.1093/ageing/26.1.37
34. Kuiper JS, Zuidersma M, Oude Voshaar RC, Zuidema SU, van den Heuvel ER, Stolk RP, Smidt N. Social relationships and risk of dementia: a systematic review and meta-analysis of longitudinal cohort studies. *Ageing Res Rev*. 2015;22:39–57. doi: 10.1016/j.arr.2015.04.006
35. Leys D, Hénon H, Mackowiak-Cordoliani MA, Pasquier F. Poststroke dementia. *Lancet Neurol*. 2005;4:752–759. doi: 10.1016/S1474-4422(05)70221-0
36. Deschaintre Y, Richard F, Leys D, Pasquier F. Treatment of vascular risk factors is associated with slower decline in Alzheimer disease. *Neurology*. 2009;73:674–680. doi: 10.1212/WNL.0b013e3181b59b3f