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Clinical history for diagnosis of dementia in men:

Caerphilly Prospective Study

Abstract

Background
Diagnosis of dementia often requires specialist referral and detailed, time-consuming assessments.

Aim
To investigate the utility of simple clinical items that non-specialist clinicians could use, in addition to routine practice, to diagnose all-cause dementia syndrome.

Design and setting
Cross-sectional diagnostic test accuracy study. Participants were identified from the electoral roll and general practice lists in Caerphilly and adjoining villages in South Wales, UK.

Method
Participants (1225 men aged 45–59 years) were screened for cognitive impairment using the Cambridge Cognitive Examination, CAMCOG, at phase 5 of the Caerphilly Prospective Study (CaPS). Index tests were a standardised clinical evaluation, neurological examination, and individual items on the Informant Questionnaire for Cognitive Disorders in the Elderly (IQCODE).

Results
Two-hundred and five men who screened positive (68%) and 45 (4.8%) who screened negative were seen, with 59 diagnosed with dementia. The model comprising problems with personal finance and planning had an area under the curve (AUC) of 0.92 (95% confidence interval [CI] = 0.86 to 0.97), positive likelihood ratio (LR+) of 23.7 (95% CI = 5.88 to 95.6), negative likelihood ratio (LR–) of 0.41 (95% CI = 0.27 to 0.62). The best single item for ruling out was no problems learning to use new gadgets (LR– of 0.22, 95% CI = 0.11 to 0.43).

Conclusion
This study found that three simple questions have high utility for diagnosing dementia in men who are cognitively screened. If confirmed, this could lead to less burdensome assessment where clinical assessment suggests possible dementia.

Keywords
cohort studies; dementia; diagnostic tests; general practice; sensitivity and specificity.

INTRODUCTION

The diagnostic pathway for dementia, particularly in the UK, is changing. Case-finding seeks to identify people with possible dementia who have not been formally diagnosed, and has been a source of particular debate.[1–4] In contrast, a formal diagnosis aims to be as definitive as possible about the presence or absence of dementia, but the process of getting a diagnosis is often not patient-centred.[5] In the general population there are often multiple contributing pathologies to dementia syndrome,[6,7] with the association between Alzheimer's pathology and dementia weakening with age.[8] Recent innovations in UK clinical practice have expanded the role of primary care in the diagnosis of dementia, such as GPs diagnosing patients without referral,[9] or arranging for a specialist to visit primary care.[10] In the UK, GPs are being encouraged to diagnose dementia independently,[11] at least in people with moderately advanced disease.[12]

Few studies exist to provide an evidence-based approach to the diagnosis of dementia by GPs. The World Health Organization recommends that dementia is diagnosed by non-specialists in routine cases in low and middle income countries[13]; indeed the global clinical judgement of repeated GP consultations (three or four 10-minute-consultations) has moderate utility for the diagnosis of dementia with an area under the curve (AUC) of 0.74.[14] An AUC of 0.5 indicates a test no better than chance, such as coin-tossing, whereas an AUC of 1 indicates no diagnostic errors. In community-dwelling older people, a combination of functional activities questionnaire score[15] with Mini Mental State Examination (MMSE) score[16] and age had an AUC of 0.95.[17] However, the MMSE is relatively time-consuming (between 7 and 18 minutes)[18] and copyright-protected. GPs commonly report lack of time as a barrier to diagnosing dementia.[19] It is desirable to identify the utility of simple clinical items that could be used easily by clinicians, as has been shown for the diagnosis of major depression in which two simple items have an AUC of 0.93.[20]

The present study used data from the Caerphilly Prospective Study (CaPS) to examine the utility of a variety of simple questions around everyday function, as well as conventional clinical assessment, for diagnosing dementia in older men. It aimed at identifying a quick and simple combination of questions that could be used by a GP as a further diagnostic test, in a person whom they suspected of having dementia after the usual clinical evaluation.

METHOD

Participants

CaPS is a cohort study of men that was established to investigate cardiovascular

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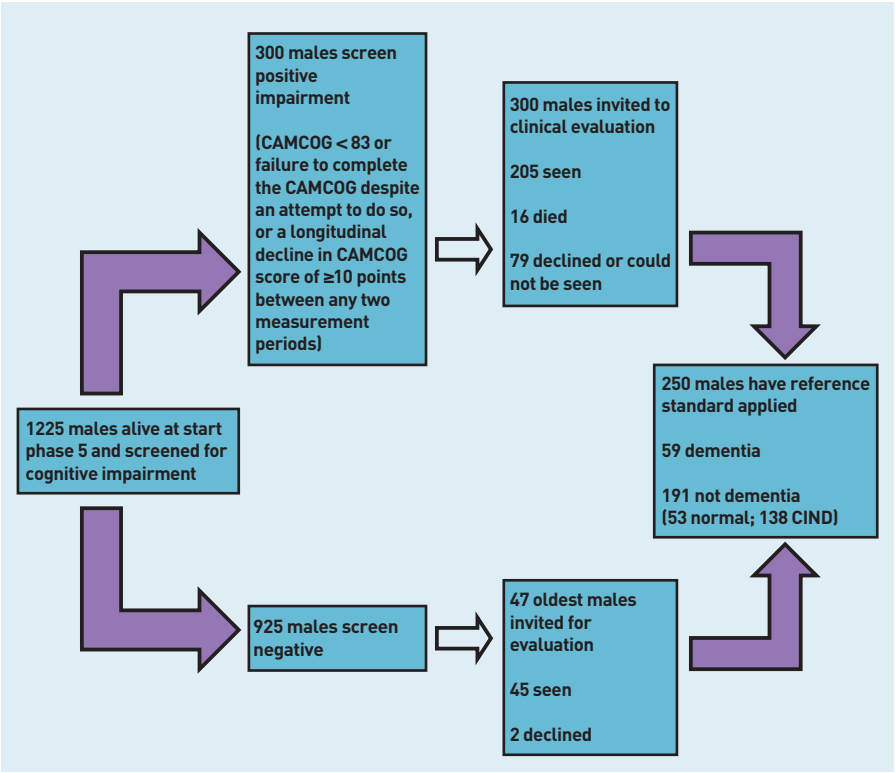
How this fits in

Commissioners are interested in expanding the role of primary care in diagnosing some people with dementia without referral. However, GPs report lack of time as a barrier to this. The present study identifies three simple questions about functioning that had greater specificity than the composite MMSE (Mini Mental State Examination) for diagnosing dementia. These can be used easily by GPs as part of their assessment of a patient whom they believe may have a diagnosis of dementia.

disease.[21] Men aged 45–59 years were identified from the electoral roll and general practice lists in Caerphilly and adjoining villages in South Wales, UK. Initial participation rate was 89% and 2512 men were examined in phase 1 (July 1979 to September 1983) and then followed-up at regular intervals. Cognition was assessed at phases 3 (November 1989 to September 1993), 4 (October 1993 to February 1997), and 5 (September 2002 to June 2004) using tests including the MMSE.[16] At phase 5 all men who met screening criteria,[22] as well as a sample of those who screened negative, were invited for a clinical evaluation in their home or research clinic by a neurologist. Figure 1 shows the selection of participants and provides the screening criteria.

Figure 1. Flow of participation in the study.



Index test and reference standard

The reference standard was a consensus diagnosis of dementia made by two clinicians with specialist training in memory disorders using the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV),[23] after reviewing all relevant information including medical records (including investigations where available) and the clinical assessment.[22]

The index tests were items from the clinical assessment, incorporating a structured history and neurological examination (Cardiff modified CAMDEX[24] and Frontal Assessment Battery[25]) and an informant interview (IQCODE[26]). Clinical assessment was conducted without prior knowledge of the patient and the informant questionnaire was conducted at the end of the evaluation. Individual items evaluated physical functioning (for example, incontinence), symptom patterns (for example, variability), personality (for example, aggression), and social functioning (for example, ability to plan), and were assessed either directly by the clinician or from the participant and informant (see Appendix 1 for detailed list of items).

Statistical methods

The diagnostic utility of each index item was assessed by calculating standard diagnostic measures, positive and negative predictive values (PPV, NPV), sensitivity, specificity, positive and negative likelihood ratio (LR+, LR–), diagnostic odds ratio (DOR), and AUC with 95% confidence intervals (CIs). As a result of small cell counts, any variable that had more than two categories (for example, normal versus abnormal) was dichotomised. Equivocal physical examination findings were analysed initially as present.

As it was desired to combine index items, only items that met conventional statistical significance ($P<0.05$) were modelled, and where there were at least 20 subjects in each cell so diagnostic but infrequent items (for example, pout reflex) were excluded. Logistic regression models were used with dementia as the outcome and the index items as diagnostic predictors.[27] First, backward stepwise logistic regression models were used with all items meeting the above criteria. Second, this was repeated but using only the five items with the greatest DOR and backwards and forwards stepwise models were run. This was also repeated using the Youden Index,[28] as standard stepwise approaches maximise the AUC but not necessarily the diagnostic utility.[28]

For each model, the model probability of dementia was examined, and only models

Table 1. Cross-tabulation of cognitive impairment screen against reference standard

			Dementia (DSM-IV)		
			Yes	No	Total
Cognitive impairment screen[a]	Positive	58	147	205	
		Negative	1	44	45
		Total	59	191	250

[a] Cambridge Cognitive Examination (CAMCOG) <83 or failure to complete the CAMCOG despite an attempt to do so, or a longitudinal decline in CAMCOG score of ≥10 points between any two measurement periods.

in which the highest risk was at least 90% were selected, then goodness of fit statistics were calculated to choose between these models.[29]

In addition the following supplementary analyses were made: any subjects with a prior diagnosis of dementia were excluded; analyses were repeated but recoding equivocal clinical items as absent; imputation was used for missing item data using chained equations and creating seven simulated datasets.[30] All analyses were conducted in Stata (version 13).

RESULTS

At the start of phase 5, 1225 men were alive and 300 were screen positive. Of those who were screen positive 205 (68%) attended clinical assessment. In addition, 47 of the 925 men who screened negative were invited for clinical assessment,[22] with 45 (95.7%) of these subsequently assessed (see Figure 1 for details for non-response). Seven had already been given a diagnosis of dementia. The cognitive screening procedures were 98% sensitive for identifying men with dementia (Table 1).

Fifty-nine men (24%; 95% CI = 19% to 29%) were diagnosed as having dementia (median age 77.8 years; interquartile range [IQR] 74.9–80.0) and 191 (76%; 95% CI = 71% to 81%) did not have dementia (median age 75.7 years; IQR 71.8–79.3). The median (IQR) MMSE score in men with dementia was 20 (16–23) compared with 25 (22–29) in those without dementia. One-hundred and thirty-eight men were identified as having cognitive impairment not dementia (CIND), and they were included in the no-dementia group for analysis.

Table 2 presents the sensitivity and specificity for the individual clinical items that were examined in combinations. The most sensitive items were participant report of any memory difficulty (91.1%; 95% CI = 80.4% to 97.0%) or forgetting where things were left (91.1%, 95% CI = 80.4% to 97.0%), but specificity was only 19.8% and 31.9%, respectively. Highly specific items were: informant report of problems with reasoning (95.1%; 95% CI = 90.6% to 97.9%); hygiene (95.3%; 95% CI = 90.9% to 98.0%); and disinhibited behaviour (94.7%; 95% CI = 89.9% to 97.7%). A list of diagnostic utility of all single items, regardless of cell counts, is available from the authors on request; the diagnostic accuracy for some items could not be calculated because they were not identified in any men (details in Appendix 1).

The best performing individual items for LR–, LR+, and AUC were as follows: problems with 'learn new gadget' (LR– 0.22; 95% CI = 0.11 to 0.43), problems with 'reasoning' (LR+ 10.4; 95% CI = 5.06 to 21.5), and problems with 'personal finance' (AUC 0.80; 95% CI = 0.72 to 0.88) (Table 3). The optimal cut-point for diagnosis of dementia using age alone was 75.8 years (LR– 0.61; LR+ 1.40; AUC 0.60). In contrast the utility of the MMSE at a traditional cut-point of ≥24 indicating normality was LR– 0.28; LR+ 2.14; AUC 0.72, and the utility of memory problem noted by informant or participant was LR– 0.45; LR+ 1.10; AUC 0.55 suggesting this alone is not a useful diagnostic feature in this population.

The results from the stepwise procedures using all or selected index items can be found in Table 4. There were 10 models meeting the criteria of predictive value and goodness of fit. All were better in terms of specificity than sensitivity and all but one had an AUC value ≥0.90. It was judged that the best overall model comprised problems with personal finance and planning (AUC 0.92, 95% CI = 0.86 to 0.97), but the model comprising personal finance and reasoning (AUC 0.86, 95% CI = 0.80 to 0.93) had almost as good a performance profile based on a larger sample size.

Supplementary analyses when excluding the seven men who had an existing diagnosis of dementia, produced similar results for specificity, but sensitivity was lower (up to 20 percentage points). When analysing equivocal findings as normal the results were almost identical (to two decimal places) to the main analysis. Multiple imputation also resulted in similar results to the main analysis with specificity within 10% of the main estimates, but sensitivity often lower (up to 20 percentage points, details available from the authors). The AUC was consistent between imputed analyses and main.

DISCUSSION

Summary

This study found that combinations of

Table 2. Sensitivity and specificity for most useful individual clinical items

	Number with data (% missing)			
	No dementia (n = 191)	Dementia (n = 59)	Sensitivity (95% CI)	Specificity (95% CI)
Any memory difficulty (subject)	187 (0.02)	56 (0.05)	91.1 (80.4 to 97.0)	19.8 (14.3 to 26.2)
Any memory difficulty (informant)	157 (0.18)	53 (0.10)	83.0 (70.2 to 91.9)	31.2 (24.1 to 39.1)
Forget where left things (subject)	188 (0.02)	56 (0.05)	91.1 (80.4 to 97.0)	31.9 (25.3 to 39.1)
Forget where left things (informant)	159 (0.17)	53 (0.10)	81.1 (68.0 to 90.6)	40.9 (33.2 to 49.0)
Forget what going to do (informant)	148 (0.23)	51 (0.14)	66.7 (52.1 to 79.2)	56.8 (48.4 to 64.9)
Forget names (subject)	189 (0.01)	56 (0.05)	62.5 (48.6 to 75.1)	66.7 (59.5 to 73.3)
Forget names (informant)	161 (0.16)	53 (0.10)	62.3 (47.9 to 75.2)	65.2 (57.3 to 72.5)
Repeat question (subject)	186 (0.03)	55 (0.07)	65.5 (51.4 to 77.8)	63.3 (56.0 to 70.2)
Repeat question (informant)	159 (0.17)	53 (0.10)	66.0 (51.7 to 78.5)	63.5 (55.5 to 71.0)
Wrong word (subject)	189 (0.01)	56 (0.05)	51.8 (38.0 to 65.3)	68.3 (61.1 to 74.8)
Wrong word (informant)	161 (0.16)	53 (0.10)	50.9 (36.8 to 64.9)	70.8 (63.1 to 77.7)
Examination findings				
Any gait disturbance	184 (0.04)	56 (0.05)	42.9 (29.7 to 56.8)	91.3 (86.3 to 95.0)
Any primitive reflexes	166 (0.13)	46 (0.22)	45.7 (30.9 to 61.0)	77.1 (70.0 to 83.3)
Pout	183 (0.04)	51 (0.14)	21.6 (11.3 to 35.3)	93.4 (88.8 to 96.6)
IQCODE (informant). Compared with 10 years ago, how is this person at:				
Family and friends	133 (0.30)	44 (0.25)	75.0 (59.7 to 86.8)	70.7 (62.2 to 78.3)
Recall recent events	163 (0.15)	54 (0.08)	79.6 (66.5 to 89.4)	65.6 (57.8 to 72.9)
Recall conversations	164 (0.14)	55 (0.07)	78.2 (65.0 to 88.2)	53.7 (45.7 to 61.5)
Recall own address	161 (0.16)	52 (0.12)	50.0 (35.8 to 64.2)	91.3 (85.8 to 95.2)
Recall day	162 (0.15)	55 (0.07)	69.1 (55.2 to 80.9)	78.4 (71.3 to 84.5)
Recall where kept	159 (0.17)	52 (0.12)	73.1 (59.0 to 84.4)	77.4 (70.1 to 83.6)
Recall different place	161 (0.16)	51 (0.14)	86.3 (73.7 to 94.3)	50.9 (42.9 to 58.9)
Work appliances	156 (0.18)	49 (0.17)	53.1 (38.3 to 67.5)	91.0 (85.4 to 95.0)
Learn new gadget	157 (0.18)	52 (0.12)	86.5 (74.2 to 94.4)	62.4 (54.4 to 70.0)
Learn in general	162 (0.15)	55 (0.07)	81.8 (69.1 to 90.9)	68.5 (60.8 to 75.6)
Follow story	159 (0.17)	52 (0.12)	65.4 (50.9 to 78.0)	79.3 (72.1 to 85.3)
Decisions	157 (0.18)	48 (0.19)	60.4 (45.3 to 74.2)	89.2 (83.2 to 93.6)
Shopping money	156 (0.18)	48 (0.19)	50.0 (35.2 to 64.8)	94.2 (89.3 to 97.3)
Personal finance	135 (0.29)	42 (0.29)	66.7 (50.5 to 80.4)	93.3 (87.7 to 96.9)
Everyday maths	130 (0.32)	43 (0.27)	65.1 (49.1 to 79.0)	90.8 (84.4 to 95.1)
Reasoning	164 (0.14)	55 (0.07)	50.9 (37.1 to 64.7)	95.1 (90.6 to 97.9)
Everyday activities (asked of subject and informant, present if either identified)				
Any problems with daily activities	184 (0.04)	55 (0.07)	54.6 (40.6 to 68.0)	75.5 (68.7 to 81.6)
Dressing	172 (0.10)	54 (0.08)	31.5 (19.5 to 45.6)	90.1 (84.7 to 94.1)
Toileting	172 (0.10)	55 (0.07)	29.1 (17.6 to 42.9)	91.9 (86.7 to 95.5)
Hygiene	170 (0.11)	55 (0.07)	32.7 (20.7 to 46.7)	95.3 (90.9 to 98.0)
Physical symptoms (informant)				
Any physical symptoms	181 (0.05)	52 (0.12)	63.5 (49.0 to 76.4)	75.7 (68.8 to 81.8)
Urinary incontinence	184 (0.04)	55 (0.07)	47.3 (33.7 to 61.2)	92.9 (88.2 to 96.2)
Falls	186 (0.03)	55 (0.07)	49.1 (35.4 to 62.9)	79.6 (73.1 to 85.1)
General functioning report (informant)				
Often muddled	104 (0.46)	49 (0.17)	53.1 (38.3 to 67.5)	94.2 (87.9 to 97.9)
Sometimes muddled	102 (0.47)	50 (0.15)	66.0 (51.2 to 78.8)	78.4 (69.2 to 86.0)
Planning	103 (0.46)	46 (0.22)	76.1 (61.2 to 87.4)	82.5 (73.8 to 89.3)
Concentrating	103 (0.46)	47 (0.20)	80.9 (66.7 to 90.9)	57.3 (47.2 to 67.0)

... continued

Table 2 continued. Sensitivity and specificity for most useful individual clinical items

	Number with data (% missing)			
	No dementia (*n* = 191)	Dementia (*n* = 59)	Sensitivity (95% CI)	Specificity (95% CI)
Talk less	103 (0.46)	49 (0.17)	55.1 (40.2 to 69.3)	78.6 (69.5 to 86.1)
Repeat words	102 (0.47)	50 (0.15)	48.0 (33.7 to 62.6)	81.4 (72.5 to 88.4)
No insight	101 (0.47)	47 (0.20)	61.7 (46.4 to 75.5)	82.2 (73.3 to 89.1)
Personality/emotion/behaviour (informant)				
Any personality change	164 (0.14)	52 (0.12)	71.2 (56.9 to 82.9)	56.7 (48.8 to 64.4)
Labile	155 (0.19)	50 (0.15)	42.0 (28.2 to 56.8)	87.1 (80.8 to 91.9)
Unmotivated	152 (0.20)	48 (0.19)	37.5 (24.0 to 52.7)	83.6 (76.7 to 89.1)
Disinhibited	152 (0.20)	48 (0.19)	27.1 (15.3 to 41.9)	94.7 (89.9 to 97.7)
Sleep disturbed	152 (0.20)	48 (0.19)	45.8 (31.4 to 60.8)	79.0 (71.6 to 85.1)
Aggressive	153 (0.20)	49 (0.17)	40.8 (27.0 to 55.8)	89.5 (83.6 to 93.9)
Narrowed preoccupations	152 (0.20)	48 (0.19)	37.5 (24.0 to 52.7)	92.8 (87.4 to 96.3)
Mental rigidity	145 (0.24)	49 (0.17)	24.5 (13.3 to 38.9)	92.4 (86.8 to 96.2)
Any functioning problems	164 (0.14)	53 (0.10)	88.7 (77.0 to 95.7)	40.2 (32.7 to 48.2)
Symptom fluctuation (any)	146 (0.24)	49 (0.17)	42.9 (28.8 to 57.8)	78.1 (70.5 to 84.5)
Day to day	140 (0.27)	49 (0.17)	42.9 (28.8 to 57.8)	82.9 (75.6 to 88.7)
Age >75 years	191 (0.00)	59 (0.00)	72.9 (59.7 to 83.6)	45.6 (38.3 to 52.9)

simple questions had comparable or better diagnostic utility than the MMSE, with high utility for ruling-in a diagnosis, in men who were cognitively screened. Abnormal gait and primitive reflexes were the most useful physical findings. Some individual items were highly specific (for example, reasoning), whereas others were very sensitive (any memory difficulty reported by subject), but a combined approach enhanced their value.

Strengths and limitations

CaPS was not designed as a diagnostic test accuracy study, but, for the present study, a sample was selected with a high prior probability of some cognitive impairment from a larger population-based sample, with a broad spectrum of disease. A recognised reference standard was used, applied in consensus by experienced clinicians and a wide range of questionnaire items as well as neurological assessment were examined. Several models were tested that combined the best items. The reference standard was subject to incorporation bias (or circularity[31]) as results of the index tests could have been used in reaching a final diagnosis, but this is a common problem with clinical definitions

Table 3. Diagnostic utility of the best performing individual clinical items

Clinical item[a]	*N*	LR+ (95% CI)	LR– (95% CI)	DOR (95% CI)	AUC (95% CI)	Youden (95% CI)
Reasoning	219	10.4 (5.06 to 21.5)	0.52 (0.39 to 0.68)	20.2 (8.45 to 48.2)	0.73 (0.66 to 0.80)	0.46 (0.31 to 0.59)
Personal finance	177	10.0 (5.14 to 19.5)	0.36 (0.23 to 0.55)	28.0 (11.1 to 70.3)	0.80 (0.72 to 0.88)	0.60 (0.43 to 0.73)
Often muddled	153	9.20 (4.05 to 20.9)	0.50 (0.37 to 0.67)	18.5 (6.95 to 48.8)	0.74 (0.66 to 0.81)	0.47 (0.31 to 0.61)
Shopping money	204	8.67 (4.33 to 17.4)	0.53 (0.40 to 0.71)	16.3 (6.86 to 38.8)	0.72 (0.65 to 0.79)	0.44 (0.28 to 0.58)
Everyday maths	173	7.05 (3.94 to 12.6)	0.38 (0.25 to 0.58)	18.4 (7.80 to 43.2)	0.78 (0.70 to 0.86)	0.56 (0.39 to 0.69)
Learn new gadget	209	2.30 (1.83 to 2.89)	0.22 (0.11 to 0.43)	10.7 (4.60 to 24.7)	0.74 (0.68 to 0.81)	0.49 (0.36 to 0.60)
Learn in general	217	2.60 (2.01 to 3.37)	0.27 (0.15 to 0.47)	9.79 (4.62 to 20.7)	0.75 (0.69 to 0.81)	0.50 (0.37 to 0.62)
Recall difference place	212	1.76 (1.45 to 2.13)	0.27 (0.13 to 0.55)	6.52 (2.87 to 15.0)	0.69 (0.62 to 0.75)	0.37 (0.24 to 0.49)
Forget where left things	244	1.34 (1.18 to 1.52)	0.28 (0.12 to 0.66)	4.78 (1.87 to 12.2)	0.61 (0.56 to 0.67)	0.23 (0.13 to 0.33)
Any functioning problems	217	1.48 (1.27 to 1.74)	0.28 (0.13 to 0.61)	5.28 (2.18 to 12.7)	0.64 (0.59 to 0.70)	0.39 (0.24 to 0.53)
Planning	149	4.35 (2.78 to 6.83)	0.29 (0.17 to 0.49)	15.0 (6.49 to 34.8)	0.79 (0.72 to 0.87)	0.59 (0.42 to 0.71)
Recall where kept	211	3.23 (2.32 to 4.50)	0.35 (0.22 to 0.55)	9.27 (4.56 to 18.9)	0.75 (0.68 to 0.82)	0.50 (0.35 to 0.63)

AUC = area under receiver-operating characteristic (ROC) curve. DOR = diagnostic odds ratio. LR– = negative likelihood ratio. LR+ = positive likelihood ratio. [a]*For details of clinical items see Appendix 1.*

Table 4. Diagnostic utility of the best models

Model[a]	*n*	GOF[b]	LR+ (95% CI)	LR– (95% CI)	DOR (95% CI)	AUC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Finance + Planning	114	0.95	23.7 (5.88 to 95.6)	0.41 (0.27 to 0.62)	57.8 (13.3 to -)	0.92 (0.86 to 0.97)	60.0 (42.1 to 76.1)	97.5 (91.2 to 99.7)
Finance + Reasoning + Muddled + Money	110	0.89	∞	0.74 (0.61 to 0.90)	∞ (6.48 to ∞)	0.92 (0.86 to 0.98)	25.7 (12.5 to 43.3)	100 (95.2 to 100)
Finance + Reasoning + Muddled + Maths + Money	100	0.74	∞	0.73 (0.59 to 0.90)	∞ (6.25 to ∞)	0.93 (0.87 to 0.99)	27.3 (13.3 to 45.5)	100 (94.6 to 100)
Urinary incontinence + Planning + Maths	106	0.66	∞	0.63 (0.48 to 0.82)	∞ (11.0 to ∞)	0.95 (0.91 to 1.00)	37.5 (21.1 to 56.3)	100 (95.1 to 100)
Finance + Reasoning + Muddled + Maths	102	0.65	∞	0.61 (0.46 to 0.80)	∞ (11.1 to ∞)	0.92 (0.85 to 0.98)	39.4 (22.9 to 57.9)	100 (94.8 to 100)
Finance + Reasoning	176	0.65	∞	0.55 (0.42 to 0.72)	∞ (27.9 to ∞)	0.86 (0.80 to 0.93)	45.2 (29.9 to 61.3)	100 (97.3 to 100)
Finance + Planning + Maths	100	0.57	38.3 (5.34 to 274)	0.44 (0.30 to 0.66)	86.1 (13.2 to ∞)	0.93 (0.88 to 0.99)	56.3 (37.7 to 73.6)	98.5 (92.1 to 100)
Finance + Planning + Maths + Kept + Learn	97	0.55	31.9 (4.41 to 231)	0.52 (0.37 to 0.74)	∞ 60.9 (9.35 to ∞)	0.95 (0.89 to 1.00)	48.4 (30.2 to 66.9)	98.5 (91.8 to 100)
Finance + Reasoning + Muddled	116	0.54	∞	0.64 (0.50 to 0.82)	∞ (11.3 to ∞)	0.91 (0.84 to 0.97)	36.1 (20.8 to 53.8)	100 (95.5 to 100)
Finance + Planning + Maths + Recall	97	0.40	31.9 (4.41 to 231)	0.52 (0.37 to 0.74)	60.9 (9.35 to ∞)	0.95 (0.89 to 1.00)	48.4 (30.2 to 66.9)	98.5 (91.8 to 100)

AUC = area under receiver-operating characteristic (ROC) curve. DOR = diagnostic odds ratio. LR– = negative likelihood ratio. LR+ = positive likelihood ratio. ∞ = infinity. [a]IQCODE items Question 'Compared with 10 years ago how is this person at' Finances = personal finance; Muddled = often muddled; Money = shopping money; Maths = everyday maths; Kept = recall where kept; Learn = learn in general. See also Appendix 1. [b]Goodness of fit (GOF) assessed using Hosmer-Lemeshow statistic where a higher P-value indicates a better goodness of fit.

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Ethical approval

Ethical approval for phase 5 was provided by Gwent Research Ethics Committee (01/69).

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Competing interests

The authors have declared no competing interests.

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of dementia. The estimates for diagnostic utility require validation in further studies, although the index test items were generally derived from well-validated instruments or standard clinical practice. When multiple-imputation was used to deal with the issue of missing data, there was minimal change in the specificity, but the sensitivity of the clinical items was, in general, lower. One limitation is that the study findings cannot be generalised to women, and there may be sex-related and socially-determined patterns in the performance of some index tests. Although the authors examined for interactions, they were underpowered to detect them.

The estimates of diagnostic utility may not generalise to other populations, with different prevalence of disease, as sampling was done on the basis of cognitive testing. The overall utility (AUC) of 'any memory difficulty' reported by either subject or informant was close to chance, suggesting that the sampling strategy oversampled men with cognitive impairment and hence would overestimate the PPV but would have underestimated the specificity.[32] Other investigators have found that subjective memory problems are inconsistently associated with dementia.[33] The estimates for diagnostic utility are likely to be overoptimistic as they result from stepwise selection procedures; some items may have been identified as being diagnostically useful by chance.

Comparison with existing literature

To the authors knowledge, this is the first study that has investigated the utility of such a broad range of clinical items for diagnosing dementia in a community-based sample. The results are supported by findings from other investigators who demonstrated that most diagnostic information in primary care was gained from age, functional assessment,[34] and the clock drawing test (AUC 0.92).[35] The diagnostic utility of an abnormal neurological examination[36] and urinary incontinence[37] were examined, which have been shown previously to be associated with dementia. Items on everyday maths, personal finances, and reasoning were all derived from IQCODE,[26] and were previously found to have modest utility (AUC 0.85, 0.82, 0.82, respectively) in a case–control study in secondary care.[38] As a whole, the IQCODE is sensitive (0.80) and specific (0.84) for diagnosing dementia,[39] and functioning items have been found to be more discriminatory than memory items,[40] which is in keeping with the present results.

Implications for research and practice

The current policy in the UK is to encourage GPs to diagnose dementia in typical elderly cases without referral[11] unless there are

specific reasons (for example, young age) that require a specialist opinion. Avoiding overdiagnosis (high specificity) may be more important than finding all possible cases (high sensitivity), as currently there are no drugs that modify the natural history of dementia[41] and there are potential disadvantages from overdiagnosis.[1,11,42]

In this study, simple questions had high post-test probability of unspecified dementia. In principle, this raises the possibility that GPs who are considering dementia after evaluating a person with symptoms might be able to make the diagnosis, without specialist input, using relatively simple adjunct questions. GPs who are being asked to diagnose dementia in primary care might find measures of functional performance more useful than standard tests of cognition.

These findings, if replicated in other settings, would potentially be of clinical value in the assessment of patients who are frail and older, a group in whom post-mortem studies indicate a weaker association between neuropathology and clinical presentation.[7] It is not the intention that these questions should be used in isolation to diagnose dementia, but rather that they have added value after routine clinical assessment. This should not preclude the consideration of reversible causes of cognitive impairment (for example, infection or depression), the use of further investigations to exclude pathologies (for example, space-occupying-lesion) that mimic dementia, or specialist referral for dementia subtype diagnosis. Such a two-pronged approach would enable GP diagnosis for some patients, with advanced work-up and referral being reserved for scenarios where diagnostic uncertainty persists.[43] The utility of the observations in routine clinical settings requires further research. A prospective diagnostic test accuracy study is being conducted to validate these preliminary findings in men and women, and to quantify the incremental value of tests in the context of GP clinical suspicion of possible dementia.

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Appendix 1. Details of items in index test evaluation

Item (full details)	Referred to in manuscript as
Initial questions: asked of both subject and informant	
Have any difficulty with your memory?	Any memory difficulty
Forget where you left things more than you used to?	Forget where left things
Forget what you were going to do, on the way to doing it?	Forget what going to do
Forget names of close friends or relatives?	Forget names
Ever forgotten your way or got lost in own neighbourhood?	Get lost
Forget what said & ask same question over & over?	Repeat question
Aware of memory problem	Aware of problem
Difficulty finding word you want to say?	Word finding difficulty
Sometimes say the wrong word?	Wrong word
Interviewer observations	
Self-neglect	Interviewer: Self-neglect
Uncooperative behaviour	Interviewer: Uncooperative
Suspiciousness	Interviewer: Suspiciousness[a]
Hostile/irritable	Interviewer: Hostile[a]
Incongruent/bizarre	Interviewer: Bizarre[a]
Slow/underactive	Interviewer: Slow
Restless	Interviewer: Restless
Anxious out of proportion to situation	Interviewer: Anxious
Looks depressed	Interviewer: depressed
Emotional lability	Interviewer: Labile[a]
Flat affect	Interviewer: Flat
Appears to be hallucinating	Interviewer: Hallucinating[a]
Rapid speech	Interviewer: Rapid speech
Slow speech	Interviewer: Slow speech
No spontaneous speech, restricted in quantity	Interviewer: limited speech
Speech rambling, incoherent, irrelevant	Interviewer: Speech rambling
Speech slurred	Interviewer: Speech slurred
Perseverating	Interviewer: Perseverating[a]
No insight	Interviewer: No insight
Clouding of consciousness	Interviewer: Clouding of consciousness[a]
Peculiar use of terms	Interviewer: Peculiar terms
Speaking to self	Interviewer: Speaking to self
Impaired ability to focus, shift or sustain attention	Interviewer: Impaired focus
Impaired judgement of situations or persons	Interviewer: Impaired judgement
Hypochondriacal preoccupations with somatic discomfort	Interviewer: Hypochondriacal[a]
Repetitive conversation	Interviewer: Repetitive
Spontaneously talking about distant past	Interviewer: Distant past
Examination Findings	
Other significant findings	Other significant findings
Cranial Nerve abnormality	Cranial nerve defect
Field defect	Field defect
Horner Syndrome	Horner's
Acuity	Acuity
Ophthalmoplegia	Ophthalmoplegia
VII cranial nerve deficit	Facial nerve palsy
Hearing difficulty	Hearing difficulty

... continued

Appendix 1 continued. Details of items in index test evaluation

Pseudo-bulbar palsy	Pseudo-bulbar palsy
Bulbar palsy	Bulbar palsy
Speech disturbance: Dysarthria	Dysarthria
Gait disturbance any	Any Gait disturbance
Gait disturbance: Parkinsonian/Apraxic	Parkinsonian gait
Gait disturbance: Spastic	Spastic gait
Gait disturbance: Ataxic	Ataxic gait
Gait disturbance: Antalgic	Antalgic gait
Pyramidal Signs (not clinically due to myelopathy): on right, left or absent	Significant pyramidal signs
Drift	Drift
Weakness	Weakness
Hypertonia	Hypertonia
Hyperreflexia	Hyperreflexia
Babinski	Babinski
Extrapyramidal Signs	Significant Extrapyramidal Signs
Rigidity	Rigidity
Bradykinesia	Bradykinesia
Tremor	Tremor
Postural instability	Postural instability
Asymmetric deficit	Asymmetric deficit
Central Sensory disturbance (not peripheral nerve)	Sensory disturbance
Cerebellar signs	Cerebellar signs
Other localising signs	Other localising signs
Primitive reflexes	Any primitive reflexes
Palmomental	Palmomental
Pout	Pout
Grasp	Grasp
IQCode. Compared with 10 years ago how is this person at:	
Remembering things about family and friends (for example, birthdays, occupations, addresses)	Family and friends
Remembering things that have happened recently	Recall recent events
Recalling conversations a few days later	Recall conversations
Remembering own address and telephone number	Recall own address
Remembering what day and month it is	Recall day
Remembering where things are usually kept	Recall where kept
Remembering where to find things put in a different place from usual	Recall difference place
Working familiar household appliances	Work appliances
Learning to use new gadget or appliance around the house	Learn new gadget
Learning new things in general	Learn in general
Following a story in a book or on TV	Follow story
Making decisions on everyday matters	Decisions
Handling money for shopping	Shopping money
Handling personal finance (for example, pension, bank)	Personal finance
Handling everyday arithmetic (for example, how much food to buy, time between visits from friends/family	Everyday maths
Using intelligence to understand what's going on and to reason things through	Reasoning

... continued

Appendix 1 continued. Details of items in index test evaluation

Everyday Activities (asked of both subject and informant)	
Any problems with daily activities	Any ADL problems
Difficulty feeding self	Feeding
Change in eating habit	Appetite
Difficulty dressing	Dressing
Needing assistance with bathing/washing/toileting	Toileting
Decreased attention to personal hygiene	Hygiene
Physical Symptoms (informant)	
Physical symptoms (any)	Any physical symptoms
Urinary	Urinary incontinence
Faecal	Faecal incontinence
Tendency to fall	Falls
Syncope/unexplained loss of consciousness	Syncope
General Functioning report (informant)	
General functioning any problems	Any functioning problems
Tends to talk about distant past rather than present	Distant past
Loss of special skill or hobby	Hobby
Thinking often muddled	Often muddled
Greater difficulty thinking and planning ahead	Planning
Difficulty concentrating, more distractible	Concentrating
Talking more than previously	Talk more
Talking less than previously	Talk less
Repeating words or phrases	Repeat words
Fails to realise extent of any problems	No insight
Personality/emotion/behaviour (informant)	
Any personality change	Any personality change
Emotional lability	Labile
Emotional blunting	Blunting
Lack of motivation and spontaneous behaviour	Unmotivated
Breaches of social etiquette/disinhibited behaviour	Disinhibited
Perservative/stereotyped behaviour	Perseveration
Sleep pattern disturbance	Sleep disturbed
Aggression	Aggressive
Narrowed preoccupations	Narrowed preoccupations
Mental rigidity	Mental rigidity
Hyperorality (increased oral behaviours)	Hyperorality
Auditory hallucinations	Auditory hallucinations
Visual hallucinations	Visual hallucinations
Would (Has) subject cope (d) alone without partner/cohabitee?	Unable cope alone
Symptom onset and progression	
Onset	Months since onset: more than 12
Course of symptoms	Course not improving
Symptom fluctuation	Symptom fluctuation (any)
Hour to hour	Hour to hour
Day to night	Day to night
Day to day	Day to day
Week to week	Week to week[a]
Accommodation not own home	Accommodation not own home

[a]*Indicates features which were not identified in any men and so diagnostic utility could not be calculated.*
ADL = activities of daily living.