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An Investigation of the Utility of the Mini Addenbrooke's
Cognitive Examination (M-ACE) for the Early Detection of
Dementia and Mild Cognitive Impairment in People aged 75
and Over.

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Submitted in partial fulfilment of the requirements for the
degree of

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Chapter 1: Systematic Literature Review

Effort testing in dementia assessment: A systematic review.

Key Words

Dementia · Mild cognitive impairment · Effort · Malingering · Symptom validity · Performance validity · Systematic review

Abstract

Background/Aims: Data from cognitive assessment are examined alongside existing published normative data which assumes that the examinee has put forth optimal effort. Research however suggests that neuropsychologists do not always formally test for effort and that this may especially be the case in the context of dementia assessment. This review systematically explores the literature which has investigated the use of both purpose-built and embedded effort-sensitive indices in dementia, mild cognitive impairment (MCI) and healthy control samples. In particular this review seeks to determine which tests of effort (also known as Symptom Validity Tests or SVTs) are most sensitive to sub-optimal effort and least sensitive to the type of cognitive impairment seen in dementia. **Methods:** A systematic search of databases was conducted to April 2016. There was no start date. Reference lists were hand searched. Twenty studies were included for review. The studies were divided into two categories according to methodology. One category of studies (n=5) was reviewed using a tailored methodological quality rating checklist whilst the remaining studies (n=15) were reviewed using the Crowe Critical Appraisal Tool (CCAT). **Results:** The systematic search process identified 20 studies for review. **Conclusions:** The results of this review suggest that SVTs which take a hierarchical approach to effort testing such as the WMT, MSVT and NV-MSVT are preferable for use with older adults who are under investigation for possible dementia. These tests go above and beyond the traditional pass/fail approach of more traditional tests of effort since they allow the examiner to analyse the examinee's profile of scores. The methodological limitations and challenges involved in this field of research are discussed.

Introduction

Cognitive testing is used in many clinical settings, alongside information gathered from other sources, to develop a comprehensive understanding of a person's difficulties. Scores on cognitive tests are usually interpreted alongside published normative data which assume that the examinee has put forth good effort. The value and accuracy of an assessment therefore relies on the quality of the data to be interpreted and, as such, it is of great importance that the clinician has evaluated the examinee's level of effort and motivation during the assessment process.

This has led to the creation of both purpose-built tests designed to detect suboptimal effort such as the Test of Memory Malingering (TOMM) [1], the Word Memory Test (WMT) [2] and the Rey 15-Item Test (RFIT) [3] and those which have been developed from existing neuropsychological test batteries such as the Effort Index (IE) [24] and the Effort Scale (ES) [25] derived from the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) [4]. Effort tests are also known as symptom validity tests (SVTs). Both terms (effort test and SVT) will be used in this review.

It is a recommended practice of contemporary neuropsychology, that tests of effort be included as a routine component of neuropsychological assessment [5]. The British Psychological Society also holds this stance, as guidance regarding the assessment of effort in cognitive functioning in adults issued in 2009, states: 'cognitive test results are not valid if the examinee does not try hard on the tests and effort tests should be given routinely as part of clinical assessment of cognitive function' [6] (p.1).

There also exist published criteria which can aid clinicians in making a judgement about an examinee's level of effort or motivation. One such set of criteria was published in 1999 by Slick and colleagues [7] in a landmark paper which encouraged clinicians to apply a 'discrepancy method' to their judgement of poor effort (e.g. attending to inconsistencies between test scores and observed behaviours from the same domain).

Despite these recommendations, however, it appears that effort tests are not always routinely administered as part of cognitive assessment. A study carried out in 2009 surveyed

130 UK neuropsychologists about their practices and beliefs regarding tests of effort and found that whilst 59% of respondents working in forensic settings said that they always used a test of effort, only 15% of respondents working in other clinical settings said the same. One third of the respondents in this study said that there was no need to use a dedicated test of effort because non-credible symptoms were evident from the results of other tests and from the client's general presentation during assessment [8]. Research has found, however, that clinicians' subjective evaluation of test validity is often highly inaccurate [9 - 11] and that analysing performance on traditional neuropsychological measures alone is an unreliable method of detecting invalid or malingered performance [12].

It may be that clinicians consider effort tests to only be of relevance when there is suspicion that an individual is deliberately feigning symptoms and indeed the majority of the literature on effort testing focuses on populations in which the deliberate feigning of symptoms is thought to be most prevalent, e.g. medico-legal settings and disability payment assessments. Nevertheless, literature does exist which examines the validity and reliability of effort testing in various clinical groups such as brain injury [13, 14], depression [15], chronic fatigue syndrome [16] and conversion and somatoform disorders [17].

There is, however, a lack of information on how people with varying degrees of mild cognitive impairment (MCI) or dementia would be expected to perform on tests of effort as individuals with dementia are often excluded from samples used for effort test validation [18]. The BPS guidance states that in certain situations 'careful consideration of the usefulness of effort tests is needed' (including with subjects with possible dementia) [6] (p.8).

It may be that tests of effort are not routinely validated in samples of older adults who are under investigation for memory problems because it is thought that they are unlikely to be feigning symptoms. Indeed, a study found that as few as 2% of litigants and those seeking other forms of compensation alleged dementia [19]. However, effort can be defined as an '*investment in performing at capacity levels*' [5] (p.420) which is a broader view than malingering which refers to the deliberate production of false or exaggerated symptoms motivated by external incentives. Although deliberately feigning symptoms may be uncommon in older people who present at memory clinics, poor effort can nonetheless impact neuropsychological data for

many reasons: depression, medication side effects, stress, lack of interest, fatigue, lack of comprehension of the utility of the tests or motivation to be in a ‘sick role’ [20].

In order for clinicians to be able to adequately assess the reliability of data resulting from cognitive assessment in older adults presenting with memory problems, they must know which effort tests are the most suitable for use with this population.

To date there is no systematic review which examines the literature on the use of effort testing in dementia assessment.

Systematic review objectives

This review evaluates the literature on effort testing in dementia assessment with the following objectives:

1. Review which effort tests provide the lowest rate of false-positive error in people with MCI and dementia.
2. Examine the relationship between dementia severity and false-positive rates.

Methods

Search Strategy

The following electronic bibliographic databases were searched: PsycINFO, Cinahl, EMBASE, Medline and Psychology and Behavioural Sciences Collection. The search did not have a start date limit. The end date was April 2016. The databases were searched using various search terms such as “symptom validity test*”, “test* of effort”, “performance validity test*” and “dementia” (see Appendix 1.1 for full strategy). Titles and abstracts of studies identified were examined to identify those pertaining to effort testing in dementia assessment. Reference lists of all included papers were also examined to identify any further relevant studies.

All the titles and abstracts of identified papers featuring the use of effort testing in dementia assessment were screened against the following criteria:

Inclusion criteria:

- Studies investigating the performance of dementia and/or MCI samples on tests of effort.

Exclusion Criteria:

- Studies which did not use an MCI or dementia sample as their *primary sample* of interest (i.e. a dementia or MCI sample was included but was compared against various other clinical groups).
- Studies which solely used a sample of participants asked to simulate MCI or dementia.
- Single case studies.

Methodological quality

In order to rate the methodological quality of the studies included in this review, the studies were separated into two different categories based on their methodology. The first category pertained to papers where a reference standard is used to establish if a diagnosis is present or absent in the participants (in this case the diagnosis would be optimal or sub-optimal effort) and then results on the index test (the effort test(s) of interest) are compared between the two groups. A reference standard is the best available method for establishing the presence or absence of a particular diagnosis. To rate the papers included in this first category (n=5), a checklist was developed based on the SIGN Methodology Checklist 5 for Studies of Diagnostic Accuracy [21] and the Standards for the Reporting of Diagnostic accuracy studies (STARD) statement [22]. The quality rating checklist had a maximum score of 28 points (see Appendix 1.2 for a copy of the checklist).

The second category covers the majority of the papers included in this review (n=15) where the researchers have recruited a sample of participants whom they consider not to meet the diagnosis (of sub-optimal effort). In these studies the researchers have either excluded participants who may have motivation to feign impairment (involvement in litigation/in receipt of disability payments) or they have assumed that their sample will exert optimal effort by virtue of having a diagnosis of dementia/MCI. To rate the methodological quality of these papers, the Crowe Critical Appraisal Tool (CCAT) was used [23]. The CCAT contains 54

reporting items in 8 categories and has a maximum score of 40 points (see Appendix 1.3 for a copy of the checklist).

All papers were rated by the author. A second rater assessed 50% of the papers to examine the inter-rater reliability of the checklists. Across all the checklist items in the quality rating tools, there was 86% agreement between raters. Where discrepancies occurred, these were resolved through discussion.

Outcome of search process

A total of 20 papers met the inclusion criteria and are included in this review. Figure 1 is a flow diagram illustrating the systematic process of identifying the 20 papers included.

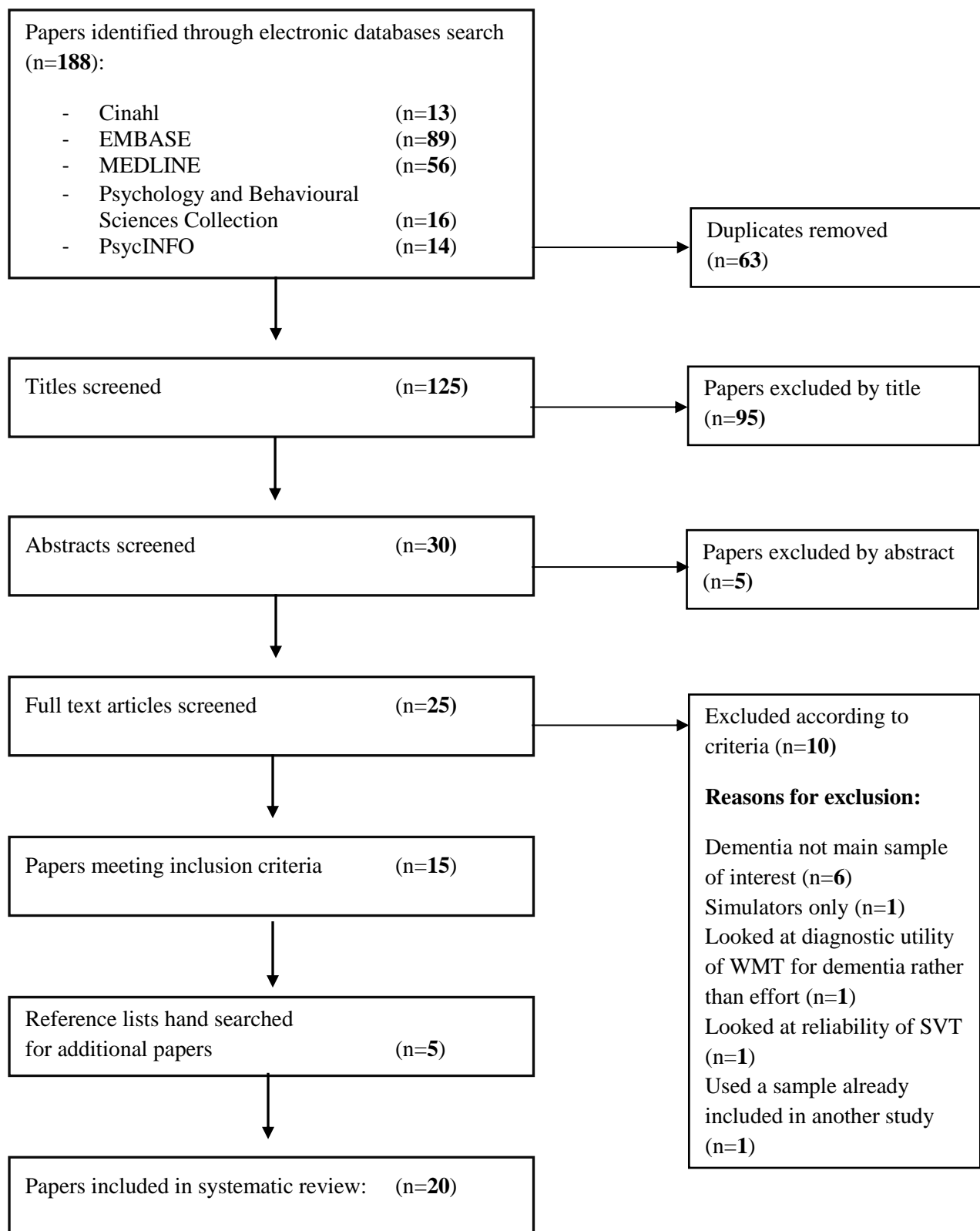


Figure 1. Flowchart illustrating the search process.

Results

In the review, sensitivity (also called the true positive rate) refers to the ability of the tests to identify suboptimal effort when suboptimal effort is present. Specificity (also called the true negative rate) refers to the ability of the tests to identify optimal effort when optimal effort is present. The majority of the studies included in this review involved participants who were deemed to be exerting adequate effort due to not being involved in litigation or by virtue of having an established diagnosis of MCI or dementia and therefore having little to no reason to feign impairment (n=15). This means that the methodology involved administering tests of effort to participants who were already deemed to be exerting optimal effort. These studies cannot possibly investigate the sensitivity levels of the effort test(s) in question (there are no true positives present in their samples). They report specificity levels only.

The studies (n=5) which include both participants who are and are not exerting adequate effort are able to report both sensitivity and specificity levels with the exception of Schroeder et al. [46] who used the RBANS Effort Scale as a reference standard but who deemed all of their participants to be exerting optimal effort therefore they report specificity levels only. See Table 1 for the data extraction table which includes demographic information and sensitivity and specificity levels where appropriate. This information is listed per SVT.

The majority of the studies included in this review therefore report specificity levels but not sensitivity levels.

The results of the studies included in this review will be reported by effort test:

1. Test of Memory Malingering (TOMM) [1].
2. Repeatable Battery for the Assessment of Neurological Status:
 - a. Effort Index (EI) [24].
 - b. Effort Scale (ES) [25].
 - c. Two novel indices (PVI and CRIER) [26].
3. Effort tests using *profile analysis*:
 - a. Word Memory Test (WMT) [2, 14].
 - b. Medical Symptom Validity Test ((MSVT) [27].
 - c. Non-Verbal Symptom Validity Test (NV-MSVT) [28].

4. Rey 15 Item Test (RFIT) [3, 29].
5. The Coin in the Hand (CIH) [30].
6. Reliable Digit Span (RDS) [31].
7. Amsterdam Short Memory Test (AMST) [32].
8. Dot Counting Test (DCT) [33].

Please note that the study by Dean et al. [18] included in this review investigated a total of 18 stand-alone and embedded effort tests. It was out with the scope of this review to include all of these SVTs however those which have also been investigated by other studies have been included. These are: TOMM, RFIT, DCT and RDS.

Table 1. Data extraction table per effort test for studies which investigated the diagnostic utility of effort tests in dementia and/or MCI samples.

1. Test of Memory Malinger (TOMM) [1] – all results refer to a TOMM cut-off of <45/50 on Trial 2.

Study	Sample (n)	Age (SD)	Education (SD)	Impairment measure	Impairment level	±Sensitivity (%)	*Specificity (%)	Quality Rating score
Walter et al., (2014) [34]	Dementia (mod/sev) (31)	69.48 (7.86)	15.63 (2.92)	RBANS total score	60.7 (7.48)	n/a	79	31/40 (78%)
	MCI (28)	66.02 (8.02)	14.68 (2.09)		80.72 (4.47)	n/a	91	
	Controls (30)	71.43 (8.99)	16.33 (3.19)		96.73 (8.61)	n/a	100	
Bortnik et al., (2013) [35]	Good effort (119)	77 (7)	11.42 (4)	MMSE	20.8 (5)	n/a	78	20/28 (71%)
	Suspect effort (9)	72 (8.13)	10.44 (2.3)		17.9 (4.5)	100	n/a	
Rudman et al., (2011) [36]	Dementia (mild) (20)	58.3	Not reported	CAMCOG	88.60 (5.03)	n/a	95	28/40 (70%)
	Dementia (mod/sev) (22)				62.45 (16.21)	n/a	36	
Dean et al., (2009) [18]	Dementia (20)	Not reported	Not reported	MMSE	19.2 (4.4)	n/a	45	30/40 (75%)
Merten et al., (2007) [37]	AD dementia (20)	73.5 (4.8)	11.7 (3.3)	MMSE	22.2 (2.9)	n/a	70	30/40 (75%)
	Controls (14)	76.6 (6.7)	11.3 (3.7)		28.9 (1.0)	n/a	100	

Teichner & Wagner., (2004) [38]	Dementia (21)	75.3 (6.1)	13.6 (3.3)	MMSE WAIS FSIQ	19.9 (2.8) MMSE	n/a	24	27/40 (68%)	
						80.6 (12) WAIS			
	MCI (36)	70.6 (8.1)	14.2 (3.2)			25.6 (2.5) MMSE	n/a		91.7
	Controls (21)	65.6 (8.6)	14.2 (3.6)		28.3 (1.7) MMSE	n/a	100		
Tombaugh et al., (1997) [1]	Dementia (37)	69.48 (7.86)	72.1 (7.6)	MMSE	Not reported	n/a	72.9	30/40 (75%)	
	Controls (13)	66.02 (8.02)	45.9 (15)						

*Specificity means that the test correctly identified optimal effort (i.e. the proportion of true negatives).
±Sensitivity means that the test correctly identified sub-optimal effort (i.e. the proportion of true positives).

RBANS = Repeatable Battery for the Assessment of Neuropsychological Status
MMSE = Mini-Mental State Examination
CAMCOG = Cambridge Cognitive Examination
WAIS FSIQ = Wechsler Adult Intelligence Scale, Full Scale Intelligence Quotient

2a. RBANS Effort Index (EI) [24] – all results refer to a cut-off of >3.

Study	Sample (n)	Age (SD)	Education (SD)	Impairment measure	Impairment level (mean)	±Sensitivity (%)	*Specificity (%)	Quality Rating score
Paulson et al., (2015) [26]	Valid responding (189)	69.2 (9.4)	12.9 (3.2)	MMSE RBANS Total scores	27.5 (2.2) MMSE 85 (12.2) RBANS	n/a	63	27/28 (96%)
	Invalid responding (45)	64.2 (10.9)	12.3 (2.9)		23.1 (4.9) MMSE 59.9 (10.7) RBANS	93	n/a	
Burton et al., (2015) [39]	AD dementia (90)	Not reported	Not reported	CDR	Not reported	n/a	51	27/40 (68%)
	Non-AD dementia (55)					n/a	54	
Dunham et al., (2014) [40]	Memory impairment (dementias) (46)	76.44 (10.49)	11.17 (2.82)	RBANS Total scores	57.48 (11.70)	n/a	41	20/28 (71%)
	^a Simulators (44)	27.82 (9.01)	16.41 (0.82)		48.52 (8.66)	89	n/a	
Bortnik et al., (2013) [35]	Good effort (119)	77 (7)	11.42 (4)	MMSE	20.8 (5)	n/a	69.6	20/28 (71%)
	Suspect effort (9)	72 (8.13)	10.44 (2.3)		17.9 (4.5)	50	n/a	
Novitski et al., (2012) [25]	aMCI (15)	80.61 (6.33)	Not reported	RBANS total scores	64.58 (12.89)	n/a	Not reported (AUC 0.608)	21/40 (53%)
	probable AD (54)					n/a	Not reported	
	Controls (540)					n/a	Not reported	
Duff et al., (2011) [41]	AD (126)	76.7 (6.8)	<9yrs=12 9-11yrs=14	RBANS Total scores	65.9 (5.9)	n/a	67.1	31/40 (78%)

			12yrs= 38 13-15yrs=10 >15yrs=26					
	aMCI (72)	72 (82.1)	<9yrs=0 9-11yrs=3 12yrs=17 13-15yrs=23 >15yrs=57		92.3 (9.1)	n/a	100	
	Controls (796)	73.4 (5.9)	<9yrs=5 9-11yrs=11 12yrs=26 13-15yrs=30 >15yrs=28		95.7 (13.3)	n/a	97.1	
Barker et al. (2010) [20]	Suspect effort (45)	67.1 (10.3)	12 (3)	RBANS total index scores	IM 57 (16.4) DM 51.6 (14.7) A 60.7 (15.6) L 72 (20.6) VS 70.7 (20.9)	n/a	42.2	22/28 (79%)
	Probable good effort (258)	72.5 (8.8)	12.5 (3.5)		IM 75.1 (15.8) DM 76 (19.9) A 81.9 (16.1) L 88.3 (10.6) VS 84.3 (17.7)	95.3	n/a	

*Specificity means that the test correctly identified optimal effort (i.e. the proportion of true negatives).

±Sensitivity means that the test correctly identified sub-optimal effort (i.e. the proportion of true positives).

MMSE = Mini-Mental State Examination RBANS = Repeatable Battery for the Assessment of Neuropsychological Status CDR = Clinical Dementia Rating

aMCI = amnesic MCI IM = Immediate Memory DM = Delayed Memory A = Attention L = Language VS = Visuospatial

b. RBANS Effort Scale (ES) [25] – all results refer to a cut-off of <12.

Study	Sample (n)	Age	Education	Impairment measure	Impairment level (mean)	±Sensitivity (%)	*Specificity (%)	Quality Rating score
Paulson et al., (2015) [26]	Valid responding (189)	69.2 (9.4)	12.9 (3.2)	MMSE RBANS Total scores	27.5 (2.2) MMSE 85 (12.2) RBANS	n/a	42	27/28 (96%)
	Invalid responding (45)	64.2 (10.9)	12.3 (2.9)		23.1 (4.9) MMSE 59.9 (10.7) RBANS	71	n/a	
Burton et al., (2015) [39]	AD dementia (53)	Not reported	Not reported	CDR	Not reported	n/a	96	27/40 (68%)
	Non-AD dementia (36)					n/a	69	
Dunham et al., (2014) [40]	Memory impairment (dementias) (46)	76.44 (10.49)	11.17 (2.82)	RBANS Total scores	57.48 (11.70)	n/a	81	20/28 (71%)
	^a Simulators (44)	27.82 (9.01)	16.41 (0.82)		48.52 (8.66)	88	n/a	
Novitski et al., (2012) [25]	aMCI (15)	80.61 (6.33)	Not reported	RBANS total scores	64.58 (12.89)	n/a	Not reported (AUC 0.908)	21/40 (53%)
	probable AD (54)						Not reported	
	Controls (540)						84.9	
<p><i>*Specificity means that the test correctly identified optimal effort (i.e. the proportion of true negatives). MMSE = Mini-Mental State Examination CDR = Clinical Dementia Rating ±Sensitivity means that the test correctly identified sub-optimal effort (i.e. the proportion of true positives). RBANS = Repeatable Battery for the Assessment of Neuropsychological Status</i></p>								

3a. Word Memory Test (WMT) [2, 48].

Study	Sample (n)	Age (SD)	Education (SD)	Impairment measure	Impairment level	%Failed easy subtests (met Criterion A)	% Produced dementia profile (met Criterion A not Criterion B)	*Specificity (%)	Quality Rating score
Green et al., (2011) [42]	Dementia group 1 (42)	70.9 (8)	Not reported	CDR	1.05 (0.6)	71	100	100	28/40 (70%)
	Dementia group 2 (23)	65.2 (8)			0.83 (0.35)	48	100	100	
	MCI (60)	68.8 (8.9)			0.5 single domain (29) 0.5 multi domain (31)	21.6	96.7	96.7	
	Controls (19)	55.8 (7.5)			0	0	n/a	100	
**Merten et al., (2007) [37]	AD dementia (20)	73.5 (4.8)	11.7 (3.3)	MMSE	22.2 (2.9)	**50	n/a	**50	30/40 (75%)
	Controls (14)	76.6 (6.7)	11.3 (3.7)		28.9 (1.0)	**100		**0	
<p><i>*Specificity means that the test correctly identified optimal effort (i.e. the proportion of true negatives). **Based on subtests passed/failed – profile analysis not used.</i></p> <p><i>CDR = Clinical Dementia Rating MMSE = Mini-Mental State Examination</i></p>									

b. Medical Symptom Validity Test (MSVT) [27].

Study	Sample (n)	Age (SD)	Education (SD)	Impairment measure	Impairment level	%Failed easy subtests (met Criterion A)	% Produce dementia profile (met Criterion A not Criterion B)	±Sensitivity (%)	*Specificity (%)	Quality Rating score
Green et al., (2011) [42]	Dementia group 1 (42)	70.9 (8)	Not reported	CDR	1.05 (0.6)	Not reported	Not reported	Not reported	Not reported	28/40 (70%)
	Dementia group 2 (23)	65.2 (8)			0.83 (0.35)	44	100	n/a	100	
	MCI (60)	68.8 (8.9)			0.5 single domain (29) 0.5 multi domain (31)	Not reported	Not reported	n/a	Not reported	
	Controls (19)	55.8 (7.5)			0	Not reported	Not reported	n/a	Not reported	
**Rudman et al., (2011) [36]	Dementia (mild) (20)	58.3	Not reported	CAMCOG	88.60 (5.03)	35	Not analysed	n/a	*65	28/40 (70%)
	Dementia (mod/sev) (22)				62.45 (16.21)	72		n/a	*28	
Singhal et al., (2009) [43]	Institutionalised dementia patients (10)	81.7 (4.6)	10 (2.9)	MMSE	15.5 (5.3)	100	100	n/a	100	31/40 (78%)
	^a Simulators (10)	36 (10)	17 (2)		n/a	100	40	60	n/a	

Howe et al., (2007) [44]	Disability:			WAIS-III FSIQ	FSIQ					35/40 (88%)
	Dementia (5)	56.60 (4.95)	11.60 (2.30)		82.20 (5.63)	60	100	n/a	100	
	MCI (3)	44.33 (19.50)	13.33 (2.31)		89.33 (5.63)	66.7	0	100	n/a	
	Controls (1)	58	13		102	0	n/a	n/a	n/a	
	No Disability				FSIQ					
	Dementia early (13)	73.54 (9.03)	12 (2.42)		89.27 (14.54)	38.46	80	n/a	80	
	Dementia advanced (18)	76.39 (6.89)	13.83 (2.92)		86.77 (13.45)	83.33	86	n/a	86	
	MCI (16)	69.50 (9.60)	15.75 (2.93)		100.94 (10.34)	12.5	100	n/a	100	
	Controls (5)	57.20 (17.33)	15.40 (1.67)		107.80 (10.26)	0	n/a	n/a	n/a	

*Specificity means that the test correctly identified optimal effort (i.e. the proportion of true negatives).

±Sensitivity means that the test correctly identified sub-optimal effort (i.e. the proportion of true positives).

**Based on subtests passed/failed – profile analysis not used.

CDR = Clinical Dementia Rating CAMCOG = Cambridge Cognitive Examination MMSE = Mini-Mental State Examination WAIS FSIQ = Wechsler Adult Intelligence Scale, Full Scale Intelligence Quotient

c. Non-verbal Medical Symptom Validity Test (NV-MSVT) [28].

Study	Sample (n)	Age (SD)	Education (SD)	Impairment measure	Impairment level	%Failed easy subtests (met Criterion A)	% Produced dementia profile (met Criterion A not Criterion B)	±Sensitivity (%)	*Specificity (%)	Quality Rating score
**Rudman et al., (2011) [36]	Dementia (mild) (20)	58.3	Not reported	CAMCOG	88.60 (5.03)	35	Not analysed	n/a	**65	28/40 (70%)
	Dementia (mod/sev) (22)				62.45 (16.21)	72		n/a	**28	
Henry et al., (2010) [45]	Dementia (21) Without dementia (n=44)	59.1 (16.1)	13.1 (3.4)	MMSE	25.7 (3.9)	61 15	61 15	n/a	100 97.7	28/40 (70%)
	Healthy controls (50)	62.8 (7.1)	15.8 (3)		28.7 (1.1)	2			2	
Singhal et al., (2009) [43]	Institutionalised dementia patients (10)	81.7 (4.6)	10 (2.9)	MMSE	15.5 (5.3)	100	100	n/a	100	31/40 (78%)
	^a Simulators (10)	36 (10)	17 (2)		n/a	90	40		60	

*Specificity means that the test correctly identified optimal effort (i.e. the proportion of true negatives).

±Sensitivity means that the test correctly identified sub-optimal effort (i.e. the proportion of true positives).

**Based on subtests passed/failed – profile analysis not used.

^a Asked to simulate memory impairment.

CAMCOG = Cambridge Cognitive Examination MMSE = Mini-Mental State Examination

4. Rey 15 Item Test (RFIT) [3, 29] – Bortnik et al. [35] use a cut-off of <9, Rudman et al. [36] use a cut-off of <8.

Study	Sample (n)	Age (SD)	Education (SD)	Impairment measure	Impairment level	±Sensitivity (%)	*Specificity (%)	Quality Rating score
Bortnik et al., (2013) [35]	Good effort (119)	77 (7)	11.42 (4)	MMSE	20.8 (5)	n/a	28	20/28 (71%)
	Suspect effort (9)	72 (8.13)	10.44 (2.3)		17.9 (4.5)	100	n/a	
Rudman et al., (2011) [36]	Dementia (mild) (20)	58.3	Not reported	CAMCOG	Not reported	n/a	85	28/40 (70%)
	Dementia (mod/sev) (22)					n/a	27	

**Specificity means that the test correctly identified optimal effort (i.e. the proportion of true negatives).
±Sensitivity means that the test correctly identified sub-optimal effort (i.e. the proportion of true positives).*

MMSE = Mini-Mental State Examination CAMCOG = Cambridge Cognitive Examination

5. Coin in the Hand (CIH) [30] – all studies used a cut-off of $\leq 7/10$.

Study	Sample (n)	Age (SD)	Education (SD)	Impairment measure	Impairment level	*Specificity (%)	Quality Rating score (CCAT)
Schroeder et al., (2012) [46]	Dementia (45)	77.98 (7.05)	12.76 (3.02)	MMSE	21.47 (5.71)	98	31/40 (78%)
Rudman et al., (2011) [36]	Dementia (mild) (20)	58.3	Not reported	CAMCOG	88.60 (5.03)	100	28/40 (70%)
	Dementia (mod/sev) (22)				62.45 (16.21)	77	
<p><i>*Specificity means that the test correctly identified optimal effort (i.e. the proportion of true negatives).</i></p> <p><i>MMSE = Mini-Mental State Examination CAMCOG = Cambridge Cognitive Examination</i></p>							

6. Reliable Digit Span (RDS) [31] – all results refer to a cut-off of ≤6.

Study	Sample (n)	Age (SD)	Education (SD)	Impairment measure	Impairment level	*Specificity (%)	Quality Rating score (CCAT)
Loring et al., (2015) [47]	AD (178)	75.7 (7.5)	Not reported	MMSE	23.3 (2)	87	31/40 (78%)
	aMCI (365)	74.9 (7.2)			27 (1.8)	96	
	Controls (206)	76 (5)			29.1 (1)	97	
Kiewel et al., (2012) [48]	Dementia (mild)	74.6 (8.8)	14.5 (2.7)	MMSE	23.4 (3.1)	89	30/40 (75%)
	Dementia (mod)	76.5 (9.4)	14.2 (2.7)		16.8 (2.9)	76	
	Dementia (sev)	71.2 (10.6)	13.5 (2.7)		7.7 (3.4)	17	
Dean et al., (2009) [18]	Dementia (172)	Not reported	Not reported	MMSE	19.2 (4.4)	70	30/40 (75%)
*Specificity means that the test correctly identified optimal effort (i.e. the proportion of true negatives). MMSE = Mini-Mental State Examination aMCI = amnesic MCI							

7. Amsterdam Short-Term Memory Test (ASTM) [32] – results based on cut-off of 84/85.

Study	Sample (n)	Age (SD)	Education (SD)	Impairment measure	Impairment level	*Specificity (%)	Quality Rating score (CCAT)
Merten et al. (2007)	AD dementia (20)	73.5 (4.8)	11.7 (3.3)	MMSE	22.2 (2.9)	10	30/40 (75%)

	Controls (14)	76.6 (6.7)	11.3 (3.7)		28.9 (1.0)	100	
<p><i>*Specificity means that the test correctly identified optimal effort (i.e. the proportion of true negatives).</i> <i>MMSE = Mini-Mental State Examination</i></p>							

8. Dot Counting Test (DCT) [33] – results based on ‘total ungrouped time<total grouped time’.

Study	Sample (n)	Age (SD)	Education (SD)	Impairment measure	Impairment level	*Specificity (%)	Quality Rating score (CCAT)
Rudman et al., (2011) [36]	Dementia (mild) (20)	58.3	Not reported	CAMCOG	88.60 (5.03)	90	28/40 (70%)
	Dementia (mod/sev) (22)				62.45 (16.21)	68	
Dean et al., (2009) [18]	Dementia (80)	Not reported	Not reported	MMSE	18.8 (5)	50	30/40 (75%)
<p><i>*Specificity means that the test correctly identified optimal effort (i.e. the proportion of true negatives).</i> <i>CAMCOG = Cambridge Cognitive Examination MMSE = Mini-Mental State Examination</i></p>							

1. **Test of Memory Malingering (TOMM) [1].**

Seven of the 20 papers included in this review investigated the use of the TOMM, one of the most widely used SVTs. The TOMM is a picture-recognition, forced-choice, purpose-designed effort test created by Tombaugh (1996). It consists of two learning trials and an optional retention trial. Tombaugh provides a cut-off of <45 for Trial 2 and suggests that a score lower than this is indicative of poor effort.

Across the seven studies, pass rates for the dementia groups (Trial 2 <45) ranged from a low of 24% [38] to a high of 95% [36]. Only two of the seven studies investigated the utility of the TOMM in MCI samples [38, 34]. Both studies found similar pass rates for these samples (91.7% and 90.3% respectively).

Drawing comparisons between the results of these studies is compromised to an extent, because they use different criteria for diagnosing dementia (DSM-III, DSM-IV and the ADRDA-NINDS) and they also assess cognitive function using different tools (five report MMSE scores, one uses the RBANS and one the CAMCOG). This is important because one reason for the discrepancy in results across studies might be that the samples include individuals with significantly different levels of cognitive function. The difference in results reported by Tombaugh [1] and Teichner and Wagner [38] may be explained by dementia severity. Tombaugh states that 4/37 dementia participants (i.e. 10% of their dementia sample) who scored below 40 on the TOMM, had MMSE scores of 7, 15, 16 and 19. The paper does not, however, give any detail about the MMSE scores of the rest of the sample (presumably the remaining participants all of whom scored > 45 in this sample had MMSE scores of >19). In Teichner and Wagner's [38] sample however, 9/21 (i.e. 42.9% of their dementia sample), had MMSE scores lower than 19. It may therefore be that Teichner and Wagner's [38] sample was more cognitively impaired than that of Tombaugh's [1]. Rudman and colleagues found a specificity of 95% for the TOMM, however this was in a sample of mildly impaired dementia participants. Specificity dropped to 36% in their moderate to severely impaired sample.

There are also some flaws in the reporting of results across studies. Tombaugh [1] which received a score of 30/40 on the CCAT, states that 'a cutting score of 45 on Trial 2 produced a high level of specificity. It correctly classified 95% of all non-demented patients (91% of all

patients) as non-malingering' (p.265). When consulting information presented in a table however, 89.1% of Tombaugh's [1] dementia sample passed the TOMM but only when a cut-off score of <40 was used. This drops to 72.9% with the recommended cut-off of <45, meaning that approximately one in four of their dementia patients were incorrectly classified as putting forth sub-optimal effort.

Additionally, with the exception of Bortnik et al. [35] sample sizes across studies were small.

2. The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) [4].

The RBANS is a widely used neurocognitive battery commonly used in the assessment of dementia. Two RBANS embedded measures of effort have been developed: the Effort Index (EI) [24] and the Effort Scale (ES) [25]. Seven of the eight studies which investigated these embedded indices, examined the utility of the EI, four examined the utility of the ES and one paper compared both the EI and the ES against two novel RBANS embedded indices.

a. RBANS Effort Index (EI) [24].

The EI combines performance on two subtests (Digit Span and List Recognition) to produce an 'effort index'. A score of greater than 3 is suggestive of suboptimal effort. In the development of the EI, it was found that very poor performance on both these subtests was extremely rare in a mixed clinical sample of patients with neurological disorders.

All 4 of the studies which use a reference standard in order to divide participants into optimal and sub-optimal effort groups, investigated the use of the EI. Sensitivity levels for the EI were 0.50, 0.89, 0.93 and 0.95. Unlike the TOMM studies, dementia severity does not appear to explain the differing sensitivity levels found for the EI. Bortnik et al. [35] who report a sensitivity level of only 0.50 in their 'suspect effort' dementia sample also report that this group had a mean MMSE score of 17.9. Compare this to Paulson et al. [26] who found a sensitivity level of 0.93 in a dementia sample with a mean MMSE score of 23.1. It should be noted however that the Bortnik study included a very small sample (n=9) and scored relatively poorly on the STARD (20/28) due to inadequate reporting.

Specificity levels were reported by all 6 papers and range from a low of 0.41[40] to a relative high of 0.69 [35]. Only controls and MCI samples produced acceptable levels of specificity on the EI.

b. RBANS Effort Scale (ES) [25].

The RBANS Effort Scale was devised by Novitski and colleagues and is based on the premise that when an individual has genuine memory impairment, their performance on free recall tasks (List Recall, Story Recall and Figure Recall subtests) will decline to close to zero before decline in List Recognition is seen. The authors of the ES propose a cut-off of <12 as being suggestive of sub-optimal effort (the ES calculation is: List Recognition – (List Recall + Story Recall + Figure Recall)) + Digit Span).

The studies investigating the ES scored relatively poorly on the quality checklists due to inadequate and/or missing information making it difficult to examine the results across studies. In the original validation study, Novitski et al. [25] compared dementia and MCI participants with a poor effort group of mild head injury participants, they report an impressive area under the curve (AUC) of 0.908. The paper scored poorly however on the CCAT (21/40) due to inadequate information given regarding data collection, inclusion and exclusion criteria and participant demographic information.

Burton et al. [39] compared the ES in AD and non-AD dementias. They found an impressively high specificity level of 0.96 in their AD sample, however this fell to 0.69 in their non-AD sample. The authors conclude that the ES may be an appropriate effort index to use when assessing effort level in people with a dementia of the Alzheimer's type, however in clinician practice, effort tests are most likely to be given during the diagnostic process when a person's diagnosis is as yet unknown. It does raise the issue that the ES is based on the premise that a person's performance on tests of free recall will decline before their performance on tests of recognition. This profile of impairment is more likely to be seen in AD, which is characterised by a deficit in episodic memory, than in non-AD dementias.

Paulson et al. [26] and Dunham et al. [40] investigated the ES in both good and suspect effort groups. They found sensitivity of 0.71 and 0.88 and specificity levels of 0.42 and 0.81

respectively. It is not clear why the studies found very different specificity levels and due to inadequate reporting by the studies it was impossible to investigate whether type of dementia had a bearing on the discrepancy in the results found (i.e. if the reason for the high failure rate in Paulson's good effort group was due to the majority having a non-AD dementia).

c. Performance Validity Index (PVI) [26] and Charleston Revised Index of Effort for RBANS (CRIER) [26]

Paulson and colleagues evaluated the EI and ES against two novel RBANS embedded indices of effort, the PVI and the CRIER. The PVI cut-off for detecting invalid responding is <42 and is calculated as follows:

RBANS PVI: List recall + story recall + figure recall + digit span + list recognition

The CRIER cut-off for detecting invalid responding is <24 and is calculated as follows:

RBANS CRIER: list recall + story recall + figure recall + digit span + list recognition – GDS

The PVI was found to have sensitivity of 0.82, specificity of 0.77 and AUC of 0.90 whilst the CRIER had sensitivity of 0.84, specificity of 0.90 and AUC of 0.94. These are promising results and warrant further research.

3. Effort tests using *profile analysis*:

The WMT, MSVT and NV-MSVT, all devised by Green and colleagues, are SVTs which are a departure from the traditional pass/fail effort tests in that they use profile analysis to determine an individual's level of effort. They are based on a hierarchical approach in line with the criteria devised by Slick et al. [7]. On these SVTSs, a participant's score is firstly compared against a cut-off (a pass/fail approach) and then for those participants who fail, their profile of scores over several subtests is analysed. These tests are unique in that they allow the examiner to distinguish between failure due to poor effort and failure due to cognitive impairment. Green and colleagues state that on the WMT, MSVT and NV-MSVT, people with genuine cognitive impairment produce a specific profile of results, different from the pattern of results produced by those exerting sub-optimal effort. To differentiate between the two, the difference between

the mean scores on the easy and hard subtests is calculated. Individuals with a diagnosis of dementia invariably show easy-hard differences of at least 20 points on these subtests, whereas such significant differences are rarely present in people asked to feign impairment. This pattern of results is known as the ‘dementia profile’. These three effort tests are described and the literature evaluated in turn.

a. Word Memory Test (WMT) [2, 49].

The WMT is a word-list learning task that involves learning a list of 20 word pairs which are presented twice, either on a computer screen or spoken aloud by the examiner (as in the original oral version of the test). It contains multiple subtests of which the first two are specifically designed to measure effort (Immediate and Delayed Recognition), the remaining subtests are conventional memory subtests. As stated above, the profile of scores on the WMT subtests (particularly the difference between the effort subtests and the conventional memory subtests) can indicate whether individuals fail the test due to insufficient effort or to the severity of their cognitive impairment.

Merten et al. [37] found that whilst all their controls passed the WMT effort subtests, almost all of the AD participants failed it (90% failed both the Immediate and Delayed Recognition trials). It is important to note however, that the authors were not able to analyse the profile of scores on the two effort subtests against those of the conventional memory tests because normative data for a Dutch population were not available at the time of the study. This is a significant limitation of the Merten et al. [37] study since the researchers were only able to look at whether participants passed or failed the effort subtests and were not able to look at the profile of their scores to investigate whether they indicated a ‘dementia profile’.

A study in 2011 by Green et al. [42] found that 41/65 (63%) of their dementia sample and 13/60 (21.6%) of their MCI sample failed the easy subtests of the WMT. Using profile analysis however they found that every participant with dementia exhibited a ‘dementia profile’ meaning there were no false positives. Regarding the MCI sample, only 2 of the 11 participants who failed the easy subtests of the WMT, indicated a profile suggestive of poor effort, which represents a false-positive rate of 3.3%. The study however scored 28/40 on the CCAT due to inadequate reporting such as missing demographic data. It should perhaps also be noted that

the participants were not screened for potential financial incentives, meaning that it cannot be concluded that the 2 participants who generated a poor effort profile were real false-positives.

b. Medical Symptom Validity Test (MSVT) [27].

The MSVT is a shorter, modified and easier version of the WMT.

Four of the papers in this review examined the utility of the MSVT in people with dementia, MCI, cognitively intact controls and volunteers asked to simulate dementia. Two of the papers were able to report sensitivity levels of 60% (simulators) and 100% (suspect effort MCI sample). Specificity levels for the MSVT across the 4 studies ranged from 80 -100% with the exception of Rudman et al. [36] who calculated effort based on whether participants had passed or failed the effort subtests. They did not use profile analysis. Although these results are promising, they should be treated as preliminary as the studies involved very small sample sizes.

c. Non-Verbal Medical Symptom Validity Test (NV-MSVT) [28].

The NV-MSVT is the non-verbal equivalent of the MSVT. Three studies were found to investigate the diagnostic accuracy of this SVT in dementia and healthy controls.

As noted with the MSVT, Rudman et al. [36] found low specificity of the NV-MSVT (33% in their overall dementia sample), however they did not use profile analysis therefore their results are not complete or accurate. Henry et al. [45] found specificity of 100% in their controls and dementia sample and 97.7% in their non-dementia (neurological) sample whilst Singhal et al. [43] found 100% specificity for their institutionalised dementia patients. Interestingly, Singhal's entire dementia sample failed the effort subtests of the NV-MSVT however they all showed a 'dementia profile' therefore they were not misclassified as malingering. They were also a particularly impaired sample (average MMSE of 15.5).

4. Rey 15 Item Test (RFIT) [3, 29].

Alongside the TOMM, the RFIT is one of the most widely used effort tests in clinical practice [50]. The task consists of studying a card for 10 seconds which has five rows of three characters. The test consists of a free-recall and an optional combination equation. A score lower than 9 on the free-recall trial and a score lower than 20 on the combination equation are said to be indicative of suboptimal effort [29].

Bortnik et al. [35] reported a high sensitivity to sub-optimal effort in their ‘suspect effort’ group (100%) but a very low specificity (28%) in their good effort group. Rudman et al. [36] found a similar specificity level (27%) for their moderate/severe dementia group. The studies use different tools to assess cognitive impairment (MMSE and CAMCOG) however research suggests these screens are highly correlated [50] therefore it was possible to note that both Rudman and Bortnik’s dementia samples were equally impaired (mean CAMCOG 62.45, mean MMSE 20.8). Rudman found far better specificity in their mildly impaired sample (85% specificity, mean MMSE 20.8). Both studies performed similarly on the quality rating checklists (70%).

5. The Coin in the Hand (CIH) [30].

The Coin in the Hand Test was developed by Kapur (1994) [30] to be a ‘simple, brief test designed to detect the presence of malingering in patients who are suspected of simulating poor memory performance’ (p.385). It is a stand-alone, forced-choice test where the clinician holds a coin in their right or left hand in front of the examinee who then closes their eyes and counts backwards from 10 before opening their eyes to report which hand the coin is in. A score of 7 or less out of 10 trials is used as the cut-off for this test.

Two of the papers included in this review examined the utility of the CIH. Schroeder et al. [46] used a sample of 45 inpatients with a diagnosis of dementia. The Schroeder study performed fairly well on the CCAT (31/40). In order to ensure that their sample would put forth adequate effort on the CIH, Schroeder excluded participants involved in litigation or who were collecting disability payments and they also excluded any participant failing the RBANS Effort Scale. Using a cut-off score of ≤ 7 , resulted in a specificity of 98% in the Schroeder sample. Using the same cut-off, Rudman found specificity of 100% in their mild dementia sample

compared to 77% in the moderate/severe sample. Specificity therefore is high with a CIH cut-off of ≤ 7 as long as the examinee is not too cognitively impaired.

6. Reliable Digit Span (RDS) [31].

Greiffenstein, Baker, and Gola [52] originally derived the RDS from the Digit Span subtest of the Wechsler Adult Intelligence Scale–Revised (Wechsler, 1981) by ‘summing the longest string of digits repeated without error over two trials under both forward and backward conditions’ (pp. 219-220).

RDS specificity was found to be greatly impacted by severity of cognitive impairment. It had high specificity for Loring’s dementia (87%), MCI (96%) and control samples (97%) whilst Kiewel found high specificity for their mild dementia sample (89%). All of these samples had MMSE scores of 23 or more. In contrast, with Kiewel’s more impaired groups, the RDS yielded an unacceptable level of false positives similar to those in the equally impaired Dean study.

7. Amsterdam Short Memory Test (AMST) [32].

The AMST is a forced-choice test where five examples from a category (e.g. animals, colours etc.) are read aloud by the examinee. A relatively simple mathematical problem is then presented to the examinee after which time another five words from the same category are presented. The examinee’s task is to recognise which three words are identical to those in the first list. The test maximum score is 90 and the cut-off is 84/85. Merten et al. [37] found that all of their controls passed the ASTM however only 10% of their Alzheimer’s dementia participants passed the test (i.e. specificity, 10%). Given that 70% of the same AD sample passed the TOMM, it would appear that the ASTM is unlikely to be an appropriate choice of SVT for individuals with cognitive impairment due to a possible dementia because the false-positive rate is likely to be high.

8. Dot Counting Test (DCT) [33].

The DCT was originally devised by Rey in 1941 and is a task where the examinee is presented with twelve cards containing different numbers of dots. The first six cards contain

dots arranged in a random order and the following six cards contain grouped dots. Examinees are asked to count the dots as quickly as possible. Suspect effort is considered if the time taken to count the grouped dots is equal to or more than the time required to count the ungrouped dots [53].

Similar to the results found for the RFIT, Rudman and Dean found low specificity (50% and 68% respectively) in their more impaired samples whereas Rudman found relatively high specificity in their mild dementia sample (90%).

Discussion

This review included 20 papers examining the diagnostic accuracy of 12 embedded and stand-alone tests of effort in dementia and MCI samples. In particular this review sought to establish which SVTs were most sensitive to sub-optimal effort whilst being insensitive to the cognitive impairment seen in individuals who meet criteria for these diagnoses. The effort tests which were found to be most sensitive to sub-optimal effort whilst being least sensitive to dementia-related cognitive impairment were the three SVTs devised by Green et al [2, 27, 28]. The WMT, MSVT and NV-MSVT go beyond the pass/fail approach of traditional effort tests and instead use profile analysis to determine if the pattern of results which an examinee produces are indicative of poor effort or if they show a 'dementia profile'. The vast majority of the studies which investigated these tests found 100% specificity. The only studies which found low levels of specificity for these SVTs were those which calculated Criterion A only and did not use profile analysis to determine effort level (i.e. determined effort level on whether the participants scored below cut-off on the effort tests but did not determine whether a dementia profile was present). The WMT, MSVT and NV-MSVT therefore appear to be the most appropriate effort tests for use in cognitive assessment when a dementia is queried. These results should be taken as provisional however since, although the evidence is promising there is not a wealth of literature to draw from. Future research may also seek to further evaluate the use of the two new RBANS embedded indices (PVI and CRIER) created by Paulson and colleagues as these showed good potential and the RBANS is a commonly used tool in older adult memory clinics in the UK.

Methodological limitations of effort testing literature

Compared to other areas of research in clinical neuropsychology, effort testing research faces significant methodological challenges since no ‘gold-standard’ exists with which to reliably determine performance validity. Five of the 19 papers included in this review attempted to independently assess effort by use of a reference standard (three used the TOMM, one used the MSVT and one used the RBANS Effort Scale). The remaining 14 papers either excluded participants who may have had an incentive to feign impairment or they assumed good effort by virtue of the participants having a diagnosis of dementia. This makes it difficult to know what the true false-positive rate actually is.

Diagnostic tests should be evaluated in samples that are representative of those with whom the test will be used in practice. The majority of the studies included in this review use a methodology whereby participants with an established dementia are compared to healthy controls. This is likely to lead to bias since the participants included have a more advanced stage of the disease (in this case dementia) than studies using a clinical sample of consecutive referrals to memory clinics. Indeed there appears to be a positive correlation between SVT specificity and severity of cognitive impairment, such that as scores on cognitive tests decrease, so too does the specificity level of an SVT.

Also, very few of the studies included samples with a diagnosis of MCI, a population of importance when evaluating the diagnostic accuracy of effort tests in older adults presenting with memory difficulties. Additionally, very few of the studies included in this review were able to assess sensitivity levels because they only included participants who were deemed to exert optimal effort from the outset, either due to not being involved in litigation/claiming disability benefits or simply by virtue of having a diagnosis of dementia.

Finally, the studies included in this review largely approach the subject of effort in its ‘malingering’ definition whereby examinees are deemed to be feigning impairment. As discussed previously, indications of poor or atypical motivation are not always the result of deliberate malingering, rather there are many reasons for an individual to put forth less than optimal effort such as low mood, stress, conversion disorder, medication side effects and fatigue amongst others. The majority of the studies in this review did not assess for these factors

Methodological limitations of the current review

This systematic review faced some methodological limitations. Firstly, it was out with the scope of the review to include every study which has investigated the diagnostic utility of SVTs in dementia samples. The current study focused on papers which included dementia/MCI samples as their primary interest. There are, however, other studies which include a dementia sample alongside other clinical samples. Additionally, as previously mentioned, it was also out with the scope of the current review to examine every SVT investigated by the papers included therefore only the SVTs which are known to be most used in clinical practice were reviewed.

Finally, some of the studies examined the performance of the SVTs across different cut-offs. It was not possible to review each of these cut-offs therefore those most used in clinical practice were evaluated.

Conclusions

Future research on the diagnostic accuracy of SVTs in older adults should aim to focus on the recruitment of consecutive referrals to memory clinics and should employ a multi-method approach such as that proposed by Slick et al. [7]. As part of the cognitive test battery, the participants should receive a reference standard (such as the MSVT or NV-MSVT) and the SVT of interest (the index test). The index test should only be calculated once the final diagnosis is known. This method would allow for both sensitivity and specificity of the SVT in question to be investigated since both good effort and suspect effort participants would be included. Future research should also seek to review the diagnostic utility of SVTs across various cut-offs in MCI/dementia samples.

Following evaluation of the studies in this review, tests which take a hierarchical approach to effort testing such as the WMT, MSVT and the NV-MSVT may be the best SVTs to use in clinical practice given that these tests have been found to be particularly robust in dementia samples (i.e. they have very low false-positive rates).

Finally it must be stressed that determining an individual's level of effort should not be judged on the basis of scores on an effort test alone. It should also be noted that the vast majority

of older people referred for memory assessment will have no incentive to purposefully feign impairment.

References

1. Tombaugh TN. The Test of Memory Malingering (TOMM): Normative data from cognitively intact and cognitively impaired individuals. *Psychol Assess* 1997 September 1997;9(3):260-268.
2. Green, P. Manual for the Word Memory Test. Edmonton, Alberta, Canada: Green's publishing; 2003.
3. Rey, A. L'examen clinique en psychologie. Paris: Presses Universitaires de France; 1964.
4. Randolph C, Tierney MC, Mohr E, Chase TN. The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS): preliminary clinical validity. *Journal of Clinical & Experimental Neuropsychology: Official Journal of the International Neuropsychological Society* 1998 Jun;20(3):310-319.
5. Bush SS, Ruff RM, Tröster A,I., Barth JT, Koffler SP, Pliskin NH, et al. Symptom validity assessment: practice issues and medical necessity NAN policy & planning committee. *Arch Clin Neuropsychol* 2005 06;20(4):419-426.
6. McMillan, T, Anderson, S, Baker, G, Berger, M, Powell, G.E., Knight, R. Assessment of effort in clinical testing of cognitive functioning for adults. :British Psychological Society; 2009.
7. Slick DJ, Sherman EM, Iverson GL. Diagnostic criteria for malingered neurocognitive dysfunction: proposed standards for clinical practice and research. *Clin Neuropsychol* 1999 Nov;13(4):545-561.
8. McCarter RJ, Walton NH, Brooks DN, Powell GE. Effort testing in contemporary UK neuropsychological practice. *Clin Neuropsychol* 2009 08;23(6):1050-1066.

9. Faust D, Hart K, Guilmette TJ. Pediatric malingering: the capacity of children to fake believable deficits on neuropsychological testing. *J Consult Clin Psychol* 1988 08;56(4):578-582.
10. Faust D. The detection of deception. *Neurol Clin* 1995 05;13(2):255-265.
11. Heaton RK, Smith HHJ, Lehman RA, Vogt AT. Prospects for faking believable deficits on neuropsychological testing. *Journal of Consulting & Clinical Psychology* 1978 Oct;46(5):892-900.
12. van Gorp WG, Humphrey LA, Kalechstein A, Brumm VL, McMullen WJ, Stoddard M, et al. How well do standard clinical neuropsychological tests identify malingering? A preliminary analysis. *Journal of Clinical and Experimental Neuropsychology* 1999 04;21(2):245-250.
13. Hampson NE, Kemp S, Coughlan AK, Moulin CJA, Bhakta BB. Effort Test Performance in Clinical Acute Brain Injury, Community Brain Injury, and Epilepsy Populations. *Applied Neuropsychology: Adult* 2014 09;21(3):183-194.
14. Green P, Rohling ML, Lees-Haley P, Allen LMI,II. Effort has a greater effect on test scores than severe brain injury in compensation claimants. *Brain Injury* 2001 12;15(12):1045-1060.
15. Ashendorf L, Constantinou M, McCaffrey RJ. The effect of depression and anxiety on the TOMM in community-dwelling older adults. *Archives of Clinical Neuropsychology* 2004 01;19(1):125-130.
16. Van dW, Prins JB, Jongen PJH, van dM, Bleijenberg G. Abnormal neuropsychological findings are not necessarily a sign of cerebral impairment: A matched comparison between chronic fatigue syndrome and multiple sclerosis. *Neuropsychiatry, Neuropsychology, & Behavioral Neurology* 2000 07;13(3):199-203.
17. Boone KB, Lu PH. Impact of somatoform symptomatology on credibility of cognitive performance. *Clin Neuropsychol* 1999 11;13(4):414-419.

18. Dean A.C., Victor T.L., Boone K.B., Philpott L.M., Hess RA. Dementia and effort test performance. *Clin Neuropsychol* 2009 January 2009;23(1):133-152.
19. Mittenberg W., Patton C., Canyock E.M., Condit DC. Base rates of malingering and symptom exaggeration. *Journal of Clinical and Experimental Neuropsychology* 2002 December 2002;24(8):1094-1102.
20. Barker MD, Horner MD, Bachman DL. Embedded indices of effort in the repeatable battery for the assessment of neuropsychological status (RBANS) in a geriatric sample. *Clin Neuropsychol* 2010 08;24(6):1064-1077.
21. Scottish Intercollegiate Guidelines Network. Methodology checklist 5. Studies of diagnostic accuracy: A guidelines developers handbook. Edinburgh: SIGN; 2007.
22. Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig L, et al. STARD 2015: An Updated List of Essential Items for Reporting Diagnostic Accuracy Studies. *Radiology* 2015 12;277(3):826-832.
23. Crowe M, Sheppard L. A general critical appraisal tool: An evaluation of construct validity. *Int J Nurs Stud* 2011 12;48(12):1505-1516.
24. Silverberg ND, Wertheimer JC, Fichtenberg NL. An effort index for the Repeatable Battery For The Assessment Of Neuropsychological Status (RBANS). *Clin Neuropsychol* 2007 09;21(5):841-854
25. Novitski J, Steele S, Karantzoulis S, Randolph C. The Repeatable Battery for the Assessment of Neuropsychological Status effort scale. *Arch Clin Neuropsychol* 2012 03;27(2):190-195.
26. Paulson D, Horner MD, Bachman D. A comparison of four embedded validity indices for the RBANS in a memory disorders clinic. *Arch Clin Neuropsychol* 2015 05;30(3):207-216.
27. Green, P. Test manual for the Medical Symptom Validity Test. Edmonton: Green's Publishing; 2004.

28. Green, P. Test manual for the Nonverbal Symptom Validity Test. Edmonton: Green's Publishing; 2008.
29. Boone KB, Salazar X, Lu P, Warner-Chacon K, Razani J. The Rey 15-item recognition trial: a technique to enhance sensitivity of the Rey 15-item memorization test. *J Clin Exp Neuropsychol* 2002 08;24(5):561-573.
30. Kapur N. The coin-in-the-hand test: a new "bed-side" test for the detection of malingering in patients with suspected memory disorder. *J Neurol Neurosurg Psychiatry* 1994 03;57(3):385-386.
31. Boone, K.B. Assessment of feigned cognitive impairment: A neuropsychological perspective. New York: Guilford Press; 2007.
32. Schmand, B, Lindeboom, J. Amsterdam Short Term Memory Test Manual. The Netherlands: PITS Test Publisher; 1998.
33. Rey A. L'examen psychologique dans les cas d'encéphalopathie traumatique. (Les problems.). The psychological examination in cases of traumatic encephalopathy. Problems. *Archives de Psychologie* 1941;28:215-285.
34. Walter J., Morris J., SwierVosnos A., Pliskin N. Effects of severity of dementia on a symptom validity measure. *Clin Neuropsychol* 2014 2014;28(7):1197-1208.
35. Bortnik KE, Horner MD, Bachman DL. Performance on Standard Indexes of Effort Among Patients with Dementia. *Applied Neuropsychology: Adult* 2013 10;20(4):233-242.
36. Rudman N., Oyebode J.R., Jones C.A., Bentham P. An investigation into the validity of effort tests in a working age dementia population. *Aging & mental health* 2011 Jan 2011;15(1):47-57.
37. Merten T., Bossink L., Schmand B. On the limits of effort testing: Symptom validity tests and severity of neurocognitive symptoms in nonlitigant patients. *Journal of Clinical and Experimental Neuropsychology* 2007 April 2007;29(3):308-318.

38. Teichner G, Wagner MT. The Test of Memory Malingering (TOMM): normative data from cognitively intact, cognitively impaired, and elderly patients with dementia. *Arch Clin Neuropsychol* 2004 04;19(3):455-464.
39. Burton RL, Enright J, O'Connell M,E., Lanting S, Morgan D. RBANS embedded measures of suboptimal effort in dementia: effort scale has a lower failure rate than the effort index. *Arch Clin Neuropsychol* 2015 02;30(1):1-6.
40. Dunham KJ, Shadi S, Sofko CA, Denney RL, Calloway J. Comparison of the repeatable battery for the assessment of neuropsychological status effort scale and effort index in a dementia sample. *Arch Clin Neuropsychol* 2014 11;29(7):633-641.
41. Duff K, Spring CC, O'Bryant SE, Beglinger LJ, Moser DJ, Bayless JD, et al. The RBANS Effort Index: Base Rates in Geriatric Samples. *Appl Neuropsychol* 2011 01;18(1):11-17.
42. Green P., Montijo J., Brockhaus R. High specificity of the word memory test and medical symptom validity test in groups with severe verbal memory impairment. *Appl Neuropsychol* 2011 April 2011;18(2):86-94.
43. Singhal A., Green P., Ashaye K., Shankar K., Gill D. High specificity of the medical symptom validity test in patients with very severe memory impairment. *Archives of Clinical Neuropsychology* 2009 December 2009;24(8):721-728.
44. Howe L.L.S., Anderson A.M., Kaufman D.A.S., Sachs B.C., Loring DW. Characterization of the Medical Symptom Validity Test in evaluation of clinically referred memory disorders clinic patients. *Archives of Clinical Neuropsychology* 2007 August 2007;22(6):753-761.
45. Henry M., Merten T., Wolf S.A., Harth S. Nonverbal Medical Symptom Validity Test performance of elderly healthy adults and clinical neurology patients. *Journal of Clinical and Experimental Neuropsychology* 2010 January 2010;32(1):19-27.

46. Schroeder R.W., Peck C.P., Buddin W.H., Heinrichs R.J., Baade LE. The coin-in-the-hand test and dementia: More evidence for a screening test for neurocognitive symptom exaggeration. *Cognitive and Behavioral Neurology* 2012 September 2012;25(3):139-143.
47. Loring DW, Goldstein FC, Chen C, Drane DL, Lah JJ, Zhao L, et al. False-Positive Error Rates for Reliable Digit Span and Auditory Verbal Learning Test Performance Validity Measures in Amnesic Mild Cognitive Impairment and Early Alzheimer Disease. *Arch Clin Neuropsychol* 2016 06;31(4):313-331.
48. Kiewel NA, Wisdom NM, Bradshaw MR, Pastorek NJ, Strutt AM. A retrospective review of digit span-related effort indicators in probable Alzheimer's disease patients. *Clin Neuropsychol* 2012;26(6):965-974.
49. Green, P, Allen, L, Astner, K. Manual for Computerised Word Memory Test, US. (1 ed.). Durham, NC: Cognycist; 1996.
50. Slick DJ, Tan JE, Strauss EH, Hultsch DF. Detecting malingering: a survey of experts' practices. *Arch Clin Neuropsychol* 2004 06;19(4):465-473.
51. Heinik J, Solomesh I, Berkman P. Correlation between the CAMCOG, the MMSE, and three clock drawing tests in a specialized outpatient psychogeriatric service. *Arch Gerontol Geriatr* 2004 01/20;38(1):77-84.
52. Greiffenstein MF, Baker WJ, Gola T. Validation of malingered amnesia measures with a large clinical sample. *Psychol Assess* 1994 09;6(3):218-224.
53. Lezak, M.D. *Neuropsychological assessment*. (3rd ed.). New York: Oxford University Press; 1995.
54. Lezak, M.D, Howieson, D.B, Loring, D.W. *Neuropsychological assessment*. (4th ed.). New York: Oxford University Press; 2004.

Chapter 2: Major Research Project

An Investigation of the Utility of the Mini Addenbrooke's Cognitive Examination (M-ACE) for the Early Detection of Dementia and Mild Cognitive Impairment in People Aged 75 and Over

(Prepared in accordance with Dementia and Geriatric Cognitive Disorders guidelines)

Plain English Summary

Title: An Investigation of the Utility of the Mini Addenbrooke's Cognitive Examination (M-ACE) for the Early Detection of Dementia and Mild Cognitive Impairment in People Aged 75 and Over.

Background: Cognitive screening tools are crucial for the accurate detection and differential diagnosis of dementias. The Mini Mental State Examination (MMSE) [1] is the most popular short screen used in clinical UK settings and is recommended by both the Scottish Intercollegiate Guidelines Network (SIGN) and the National Institute for Clinical Excellence (NICE). The MMSE has however been found to have several drawbacks such that it is less sensitive to mild cognitive impairments (MCI) and is prone to ceiling and floor effects [2]. An alternative resource is the Mini-Addenbrooke's Cognitive Examination (M-ACE) [3] which is a shortened version of the widely used Addenbrooke's Cognitive Examination III (ACE-III). The current study investigated the utility of the M-ACE at detecting dementia in people aged 75. The study focused on over 75s as this is the fastest growing section of our population, projected to increase by 75% by 2031 [4].

Aims: This study aimed to investigate if the M-ACE can be used with people aged 75 and over to distinguish between those who do and do not have a diagnosis of dementia. It also aimed to investigate whether the cut-off scores recommended by Hsieh et al. (2014) [3] in the original validation study for the M-ACE are optimal for an older population.

Participants: Participants were people aged 75 and over who were referred to Community Mental Health Teams (CMHTs) in Glasgow. There was also a group of participants who did not have memory problems, all of whom were the spouses/carers of patients receiving care from a CMHT.

Recruitment: Participants were given information about the study on their first contact with the CMHT. If they gave consent to take part they were contacted again by telephone to arrange a home visit.

Consent: Informed consent was given by participants via a signature on a consent form.

Study Design: There were three groups of participants: a dementia group, a group with mild cognitive impairment (MCI) and a control group (who do not have memory problems). All participants had their cognitive function assessed using the M-ACE.

Data Collection: Participants referred to the CMHT for memory problems were introduced to the project by a member of staff involved in their care. They were provided with an information sheet and if they gave verbal consent to be contacted with regards the study, the primary researcher arranged a home visit to carry out the M-ACE.

Ethical Issues: Participants were fully briefed on the implications of having their cognition assessed.

Main Findings and Conclusions: The optimal cut-off for detecting dementia was $\leq 21/30$, lower than the original published cut-off of $\leq 25/30$ by Hsieh et al. [3]. The M-ACE has excellent diagnostic accuracy for the detection of dementia in a UK clinical sample.

References:

1. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975 11;12(3):189-198.
2. Newman JC. Copyright and Bedside Cognitive Testing: Why We Need Alternatives to the Mini-Mental State Examination. JAMA Intern Med 2015 09;175(9):1459-1460.
3. Hsieh S, McGrory S, Leslie F, Dawson K, Ahmed S, Butler CR, et al. The Mini-Addenbrooke's Cognitive Examination: a new assessment tool for dementia. Dement Geriatr Cogn Disord 2015;39(1-2):1-11.
4. All Our Futures, Planning for a Scotland with an Ageing Population, Scottish Executive: Edinburgh 2007 <http://www.scotland.gov.uk/Topics/People/OlderPeople> [Accessed 15th February 2015].

Word Count: 590.

Key Words

Mini Addenbrooke's Cognitive Examination · Cognitive assessment · Diagnosis · Dementia · Mild cognitive impairment

Abstract

Background/Aims: The Mini Addenbrooke's Cognitive Examination (M-ACE) is the abbreviated version of the widely-used Addenbrooke's Cognitive Examination (ACE-III), a cognitive screening tool that is used internationally in the assessment of mild cognitive impairment (MCI) and dementia. The objectives of this study were to investigate the diagnostic accuracy of the M-ACE with individuals aged 75 and over to distinguish between those who do and do not have a dementia or MCI, and also to establish whether the cut-off scores recommended by Hsieh et al. (2014) [9] in the original validation study for the M-ACE are optimal for this age group. **Methods:** The M-ACE was administered to 58 participants (24 with a diagnosis of dementia, 17 with a diagnosis of MCI and 17 healthy controls). The extent to which scores distinguished between groups (dementia, MCI or no diagnosis) was explored using receiver operating characteristic curve analysis. **Results:** The optimal cut-off for detecting dementia was $\leq 21/30$ (score $\leq 21/30$ indicating dementia with a sensitivity of 0.95, a specificity of 1 and a positive predictive value of 1) compared to the original higher published cut-off of $\leq 25/30$ (sensitivity of 0.95, specificity of 0.70 and a positive predictive value of 0.82 in this sample). **Conclusions:** The M-ACE has excellent diagnostic accuracy for the detection of dementia in a UK clinical sample. It may be necessary to consider lower cut-offs than those given in the original validation study.

Introduction

Dementia describes a set of symptoms that may include memory loss and difficulties with thinking, problem-solving or language [1]. As of 2015, there were an estimated 46.8 million people living with dementia throughout the world, with this number expected to double every 20 years, reaching an estimated 74.7 million by 2030 [2]. Although diagnosis rates have improved in recent years, it is estimated that there are still approximately a third of those with dementia who do not have a diagnosis. It has been recognised that although dementia has a profound impact on the individual and their family, a timely and accurate diagnosis can lead to better support, can enable people to maintain a good quality of life at home for as long as possible and can also empower them to make their own choices about their future care [3].

The use of cognitive screening tools in dementia assessment

In order to provide appropriate support to individuals with dementia, it is first necessary to be able to make an accurate diagnosis. Cognitive screening tools are an important part of dementia assessment. These tools indicate whether an individual's cognitive difficulties fall within an expected range for their age or whether there is a need for further investigation such as neuroimaging or neuropsychological assessment. Cognitive screening tools can also inform differential diagnosis between different types of dementia or other conditions which can cause cognitive impairment.

One of the most popular cognitive screening tools is the Mini Mental State Examination (MMSE) [4] which has been used worldwide to detect dementia for the past three decades. The MMSE is a 30-point questionnaire that takes 5-10 minutes to administer. It is often used to track changes in a person's cognitive function which helps to either aid a diagnosis of dementia, or if already diagnosed, to determine what stage the person is at. However, despite its popularity the MMSE has been found to have several weaknesses, including poor sensitivity to mild cognitive impairment and it is also prone to ceiling and floor effects [5]. The test also relies heavily on verbal items which is problematic when using the test with individuals with poor language skills and/or low education [6]. A further disadvantage to using the MMSE is a

financial one: the test has been placed under copyright since 2001, incurring a cost of 80p every time it is used [7]. This clearly has financial implications for healthcare providers who face either continuing to pay for continued access to the MMSE or finding an alternative resource.

Due to an increasing awareness of the insufficient assessment provided by the MMSE, other cognitive tests have been developed which aim to examine cognitive domains not assessed by the MMSE whilst remaining relatively brief. One of the most popular of these extended tests is the Addenbrooke's Cognitive Examination (ACE) which was introduced in 2000 as a brief cognitive screening tool which incorporated the MMSE but also explored important areas not covered by it, such as visuospatial skills, frontal-executive function and more complex language assessment. The ACE is a 100-point test battery which takes approximately 15-20 minutes to administer. The validation study of the first version of the ACE showed that it was superior to the MMSE in both detecting dementia and differentiating between Alzheimer's disease and fronto-temporal dementia [8]. The ACE, which is now in its third version (the ACE-III, Neuroscience Research Australia, 2012), is recommended by both National Institute of Clinical Excellence (NICE) and the Scottish Intercollegiate Guidelines Network (SIGN) as an extended screening to be used when clinicians require a more detailed picture of a patient's cognitive function. Despite the ACE-III being a robust screening tool, the time taken to complete it means that it is not always a viable option in busy clinics. Whilst clinicians should aim to complete as comprehensive an initial cognitive screen as possible, in practice this is not always viable, meaning that clinicians need to have the option of a very brief measure for such occasions.

The M-ACE as a cognitive screening tool and its adjusted cut-offs

The focus of the current study concerns one such new brief screening tool: the Mini Addenbrooke's Cognitive Examination (M-ACE) [9] which is a shortened version of the ACE. The M-ACE takes under 5 minutes to administer and contains 5 items assessing orientation, memory, category fluency and clock drawing. It is scored out of 30 with two cut-offs recommended: (1) 25/30 and (2) 21/30. The higher cut-off of 25/30 has both high sensitivity

and specificity and is at least 5 times more likely to have come from a patient with dementia than without. The lower cut-off of 21/30, by contrast, is almost certainly diagnostic of a dementia syndrome regardless of the prevalence rate. This is important because a test's diagnostic accuracy will vary with disease prevalence [10]. The M-ACE validation study showed that the M-ACE is more sensitive than the MMSE and is less likely to have ceiling effects. There is a need to further explore the M-ACE and its potential as a brief screening tool which is the purpose of the current study.

The current study

The initial validation study for the M-ACE was conducted in Australia therefore there is a requirement for the utility of the M-ACE to be investigated in a UK clinical setting. The focus of the current study was on individuals aged 75 and over who are referred to a Community Mental Health Team (CMHT) for memory problems. A control group of healthy individuals with no history of memory problems were also aged 75+. There are several reasons for focusing on this age group. One reason is that age is a key risk factor for developing a dementia. The prevalence of dementia in people aged 70-74 is 3% which rises to 6% for 75-79 olds and 11.1% for 80-84 year olds [11].

Further, with increased improvements in healthcare there is going to be a significant increase in the proportion of people aged 75+ in the population. By 2031 the number of people aged 75+ is projected to increase by 75% [12]. In Scotland alone this figure is projected to increase to 94,000 by 2017 and 108,000 by 2022; with incidence of 9,400 and 10,800 respectively. This represents a 12% increase by 2017 and a 29% increase by 2022. [13]. This creates a challenge for our health and social care services that will increasingly be called on to meet the needs of this population.

A third reason for this focus comes from a limitation of the original M-ACE validation study by Hsieh et al. [9]. This study was limited to comparing patients with controls in the age

range 61-74 therefore the validity of the tool has not been demonstrated in the age range of people most likely to present to memory clinics. As people get older, they may be more suited to a shorter cognitive test as they may have more visual, auditory or concentration difficulties than younger patients.

There is also a need to investigate the optimal cut-offs for the M-ACE for discriminating between those who have a diagnosis of dementia in people aged 75+. A recent study found that the optimal cut-offs for the ACE-III for people over the age of 75 in a UK clinical sample were lower than those recommended in the ACE-III validation study [14]. This is also the case for other brief cognitive screens. Oren et al. [15] found that 42% of their cognitively-intact sample who were aged 80 and over scored below the recommended cut-offs proposed by the authors of the Montreal Cognitive Examination (MoCA).

Objectives

The primary objective of this study was to investigate the diagnostic accuracy of the M-ACE in people aged 75 and over to distinguish between those who do and do not have a diagnosis of dementia and those who have a diagnosis of MCI. The secondary objective was to investigate whether the cut-off scores recommended by Hsieh et al. [9] in the original validation study for the M-ACE are optimal for this older age group.

Primary hypothesis

It was hypothesized that there would be a significant difference in the M-ACE scores for the three groups of participants i.e. those who have a diagnosis of dementia, MCI or no diagnosis. Furthermore it was predicted that the score on the M-ACE would accurately discriminate between those who have a diagnosis of dementia, MCI and those who have no diagnosis in those aged 75 and over. It was predicted that the minimum level of sensitivity/specificity would be at least as good as those found for the original M-ACE study

(i.e. $\leq 25/30$, sensitivity of 0.85, specificity of 0.87 and $\leq 21/30$, sensitivity of 0.61, specificity of 1).

Secondary hypothesis

It was also hypothesized that the optimal cut-off for discriminating between those who have a diagnosis of dementia would be lower in this sample of participants aged 75 and over than those suggested in the Hsieh et al. [9] original validation study. This is because previous research investigating the diagnostic accuracy of cognitive screens in older populations found that the optimal cut-offs were lower than those reported in the original validation studies [14, 15]. It is also expected that cognitive ability will naturally decline with age.

Methods

Participants - Clinical samples (MCI and dementia)

Participants with a diagnosis of MCI and dementia were recruited from five Older Adult Community Mental Health Teams (CMHTs) across NHS Greater Glasgow and Clyde.

Inclusion criteria. All participants:

1. Were aged 75 and over.
2. Had previously completed the ACE-III as part of routine clinical care.
3. Were able to give informed consent.
4. Spoke English as their first language.

Exclusion criteria

There was minimal exclusion criteria for the MCI and dementia groups since the study aimed to use a sample of all patients referred to CMHTs for memory problems over the time period of the study. However patients in the dementia and MCI groups were not recruited to the study if they:

1. Were experiencing cognitive impairment due to another neurological condition (e.g. due to head injury, alcohol-related damage, epilepsy).
2. Had significant hearing or vision problems which would prevent their completion of the M-ACE.
3. Had a learning disability (meaning that no participant had a significantly reduced ability to understand new or complex information or to learn new skills; a reduced ability to cope independently or an impairment that started before adulthood, with a lasting effect on development.).

Participants - Control group

Inclusion criteria

All participants were aged 75 and over and spoke English as their first language.

Exclusion criteria

Control participants were not recruited to the study if they:

1. Had a significant hearing or vision problems which would prevent their completion of the M-ACE.
2. Had a neurological condition.
3. Had a learning disability.
4. Had prior history of memory problems.

Justification of sample size

The sample size required was based on a power calculation for a one-way ANOVA as this was the planned method for statistical analysis. The original validation study of the M-ACE (Hsieh et al., [9]) does not report an effect size, therefore the validation study for the ACE-R informs the likely effect size for the current study [16]. In Mioshi et al., [16] Cohen's *d* for the difference between controls and those with Alzheimer's dementia was 1.84, which is a large effect size. GPower (v 3.1.9.2) [17] was used to calculate sample size. In order to detect a large

effect size (Cohen's $f = .40$) with $\alpha = 0.05$, on a one-way ANOVA, 66 participants would be required across the three groups (22 participants in each group).

Measures

The Mini Addenbrooke's Cognitive Examination (M-ACE) was the primary outcome measure and is available free of charge at: <https://www.neura.edu.au/frontier/research/test-downloads/>.

Recruitment Procedure

All participants in the dementia and MCI groups were patients referred to the CMHT for assessment of cognitive difficulties. All of the participants in the control group were the spouses/carers of patients receiving input from the CMHTs for MCI/dementia.

Research Procedure

Dementia and MCI group participants

Patients with a diagnosis of dementia or MCI who met the inclusion criteria were approached to take part by members of the clinical team. Staff members introduced the current study to patients who had a diagnosis of either dementia or MCI during routine home or clinic appointments by providing them with an information sheet and a letter of invitation (See Appendices 2.5 and 2.6). If the patient expressed an interest in taking part, the member of staff passed their details (name, address and telephone number) to the primary researcher in order for them to arrange a home visit. The primary researcher then carried out a home visit to further explain the study, answer any questions the participant may have had and gain written consent (see Appendix 2.7). The primary researcher then carried out the M-ACE.

During the course of the study, it became clear that there were fewer participants with MCI being recruited to the study than dementia or control participants. This is because, at present, clients who are given a diagnosis of MCI are usually discharged back to the care of their GP within a short timeframe. A new procedure was developed which involved members of the clinical team posting out information sheets (see Appendices 2.11 and 2.12) to clients with a diagnosis of MCI who had received input from the CMHT within the last two months. After a period of one week, the clinician who had provided their care telephoned the participant to enquire if they wished to take part in the current study. If so, the primary researcher visited the client at home to further explain the study, gain written consent and complete the M-ACE.

Control group participants

If there was a carer or relative present on the clinical team member's home visit who was aged 75+ and did not meet exclusion criteria (see above), they were approached to take part in the study. If the carer/relative wished to take part, they were provided with an information sheet (Appendices 2.8 and 2.9) and the member of staff passed on their details to the primary researcher who contacted the carer/relative by telephone in order to arrange a home visit. The primary researcher then carried out a home visit to further explain the study, gain written consent (see Appendix 2.10) and carry out the M-ACE. Some control participants were also recruited from carers' groups held at the various CMHTs involved in the study.

Ethical approval

Ethical approval was gained from the West of Scotland Research Ethics Committee 3 (15/WS/0279) and practice was informed by the British Psychological Society Code of Ethics and Conduct (2009) [18].

Statistical analysis

Statistical analyses were performed using either SPSS (Version 24) [19] or Medcalc (Version 16.4.3) [20]. Preliminary analyses included testing the data for normality (Shapiro-Wilks). Some of the variables were normally distributed and some were not, therefore both parametric and non-parametric statistical tests were used. A one-way ANOVA was used to examine if there were significant differences between the three groups with regards M-ACE score. The non-normally distributed variables of age, years of education and M-ACE subscales were examined using the Kruskal Wallis. The relationship between the participants' years of education and M-ACE scores and their age and M-ACE scores was calculated using Spearman's rank-order correlation coefficient. Analysis of the M-ACE diagnostic accuracy was explored using receiver operating characteristic (ROC) curves. This provided sensitivity and specificity values for a range of M-ACE scores and the area under the curve (AUC) which is an overall measure of discriminative power. Additional statistics were calculated, namely, positive and negative likelihood ratios (LR+, LR-), Youden index and positive and negative predictive values (PPV, NPV). The impact of disease prevalence on the performance of the M-ACE for various cut-offs was also explored by calculating PPV and NPV for various prevalence levels.

It had been intended to examine the relationship between a participant's score on the M-ACE and their score on the ACE-III. Unfortunately most of the participants in this study had completed the ACE-III more than 6 months before administration of the M-ACE meaning that it was inappropriate to compare these scores.

Results

Preliminary Analyses

In total, 58 participants were recruited to the study: 24 participants in the dementia group, 17 in the MCI group and 17 in the control group.

Initial analysis was undertaken to determine whether the data set was normally distributed. The Shapiro-Wilks test was undertaken for M-ACE scores, age, years of education and the 5

subscales of the M-ACE (Attention, Immediate Memory, Fluency, Visuospatial and Delayed Memory). The null hypothesis of the Shapiro-Wilks test is that the data are normally distributed.

The null hypothesis was retained for the M-ACE scores suggesting that the data for this variable were normally distributed. This means that the M-ACE scores for the dementia group ($W = 0.975$, $p = .796$, n.s), the MCI group ($W = 0.952$, $p = .481$, n.s) or the control group ($W = 0.963$, $p = .688$, n.s) did not deviate significantly from normal.

The null hypothesis was rejected however for age and years of education. Age was normally distributed in both the dementia ($W = 0.954$, $p = .323$, n.s) and MCI groups ($W = 0.919$, $p = .142$, n.s) however it deviated significantly from normal for the control group ($W = 0.830$, $p < .005$). Years of education for the dementia group ($W = 0.831$, $p < .001$), MCI ($W = 0.616$, $p < .001$) and control group ($W = 0.828$, $p < .005$) all deviated significantly from normal.

None of the 5 M-ACE subscales were normally distributed (Attention, $W = 0.774$, $p < .001$, Immediate Memory, $W = 0.845$, $p < .001$, Fluency, $W = 0.924$, $p = .001$, Visuospatial, $W = 0.797$, $p < .001$, Delayed Memory, $W = 0.899$, $p < .001$).

Therefore, subsequent analysis for M-ACE scores used parametric tests whilst for the non-normally distributed variables (age, years of education and M-ACE subscales) non-parametric tests were used.

Demographic details for the three groups of participants were analysed and are presented in Table 1 below.

Table 1. Demographic details of participants by group.

	Dementia (n=24)	MCI (n=17)	Controls (n=17)
Gender			
Male (%)	9 (37.5)	4 (23.5)	6 (35.3)
Female (%)	15 (62.5)	13 (76.5)	11 (64.7)
Age, years	80 (7)	79 (7)	78 (6)
Education, years	11 (2)	10 (2)	11 (4)
M-ACE score (max score 30) (mean and SD)	14.8 (4.9)	20.9 (3.8)	26.5 (2.2)
<i>*Figures are median values with interquartile range in parentheses unless otherwise stated.</i>			

In the overall sample, there were 19 (32%) males and 39 (68%) females with ages ranging from 75 to 89. Of the dementia group, 13 (54.2%) had Alzheimer's dementia, 8 (33.3%) had vascular dementia, 1 (4.2%) had Lewy body dementia and 2 (8.3%) had a mixed type dementia. Fourteen participants in the dementia group (58.3%) were taking a cognitive enhancer at the time of testing.

Primary hypothesis

It was hypothesized that there would be a significant difference in the M-ACE scores for the three groups of participants, i.e. those who have a diagnosis of dementia, MCI or no diagnosis.

A significant difference was found between the groups for M-ACE score ($F(2, 55) = 43.5, p < .001$) and a Tukey post-hoc test revealed that all the groups differed significantly

from each other with regards M-ACE score. Unsurprisingly, the control group performed significantly better on the M-ACE (26.5 ± 2.2) than the MCI group who in turn performed significantly better (21 ± 3.8) than the dementia group (14.8 ± 4.9).

A Kruskal-Wallis test showed that there was no significant difference between the groups concerning age ($X^2(2) = 3.242, p = .198, n.s$) but that there was a significant difference for years of education ($X^2(2) = 7.206, p = .027$). The effect size for years of education was 0.14. Further analysis using Kruskal-Wallis found a significant difference between the MCI and dementia ($X^2(1) = 5.299, p = .021$) and the MCI and controls ($X^2(1) = 5.473, p = .019$) regarding years of education. The MCI group had significantly less years of education (9.82 ± 2.19) than either the dementia (11.5 ± 2) or control groups (12 ± 2.38). The dementia and control groups did not differ significantly ($X^2(1) = .317, p = .573$) on this variable.

A Spearman's correlation was run to determine if there existed a significant relationship between M-ACE score and years of education and M-ACE score and age for each of the groups. There was no significant relationship found between M-ACE score and years of education for any of the groups (dementia, $r_s(24) = .125, p = n.s$, MCI, $r_s(17) = -.320, p = n.s$, control, $r_s(17) = .066, p = n.s$). There was no significant relationship between M-ACE score and age for any of the groups (dementia, $r_s(24) = -.064, p = n.s$, MCI, $r_s(17) = -.058, p = n.s$, control, $r_s(17) = -.243, p = n.s$).

A Kruskal-Wallis was also carried out to determine if there was a statistically significant difference between the groups with regards the different subscales which make up the M-ACE (Attention, Immediate Memory, Language, Visuospatial and Delayed Memory). It was revealed that the groups differed significantly regarding performance on all domains (Attention, $X^2(2) = 22.874, p = .000$, Immediate Memory, $X^2(2) = 23.185, p = .000$, Fluency, $X^2(2) = 31.475, p = .000$, Delayed Memory, $X^2(2) = 26.221, p = .000$) with the exception of visuospatial (Visuospatial, $X^2(2) = 4.580, p = .101, n.s$).

The results of further analysis for the subscales can be found in Table 2.

Table 2. Significance levels for subscales by group.

Attention		Asymp. Sig
Dementia	MCI	.020
	Control	.000
MCI	Control	.006
Immediate Memory		
Dementia	MCI	.003
	Control	.000
MCI	Control	.078
Fluency		
Dementia	MCI	.004
	Control	.000
MCI	Control	.000
Visuospatial		
Dementia	MCI	.259
	Control	.034
MCI	Control	.377
Delayed Memory		
Dementia	MCI	.007
	Control	.000
MCI	Control	.001

Secondary hypothesis

It was also hypothesized that the optimal cut-off for discriminating between those who have a diagnosis of dementia will be lower in this sample of participants aged 75 and over than those suggested in the Hsieh et al. [9] original validation study.

Diagnostic interpretation

Dementia vs controls

Figure 1 shows the ROC curve for M-ACE total score differentiating dementia from healthy controls. The AUC of 0.975 (95% CI 0.871 – 0.999) indicates excellent diagnostic accuracy. The optimal cut-off score was defined as that with the maximal classification accuracy. See Table 3 for sensitivity, specificity, PPV, NPV, Youden index and likelihood ratios for all potential cut-offs.

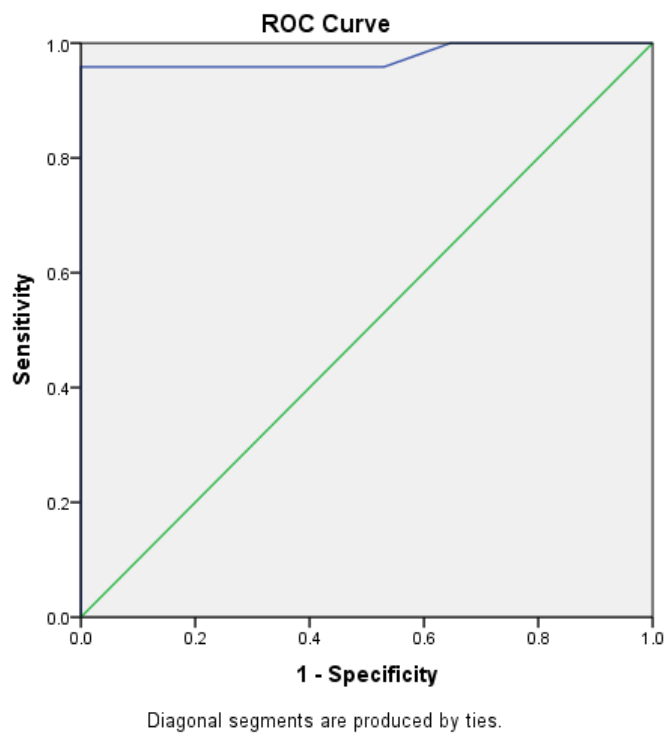


Figure 1. ROC curve of the M-ACE detecting dementia (dementia vs controls)

Table 3. Sensitivity, specificity, positive and negative predictive values (PPV, NPV), Youden index and likelihood ratios (LR) for the M-ACE at different cut-offs for dementia.

Cut-off	Sensitivity	Specificity	PPV(NPV)	Youden Index	LR+	LR-
≤29	100	0.11	17.65 (0)	0.11	1.13	0
≤28	100	0.17	0.63 (100)	0.17	1.21	0
≤27	100	0.35	0.68 (100)	0.35	1.55	0
≤26	0.95	0.47	0.71 (0.88)	0.42	1.81	0.09
≤25	0.95	0.70	0.82 (0.92)	0.65	3.26	0.06
≤24	0.95	0.76	0.85 (0.92)	0.71	4.07	0.05
≤23	0.95	0.94	0.95 (0.94)	0.89	16.29	0.04
≤22	0.95	0.94	0.95 (0.94)	0.89	16.29	0.04
≤21	0.95	1	100 (0.94)	0.95	Infinity	0.04
≤20	0.95	1	100 (0.94)	0.95	Infinity	0.04
≤19	0.83	1	100 (0.80)	0.75	Infinity	0.17

Statistics characterising the diagnostic performance for the existing M-ACE cut-offs and an optimal alternative cut-off are presented in Table 3. For the higher published cut-off (≤25/30), sensitivity was excellent (0.95) however specificity was much poorer (.70). The lower published cut-off (≤21/30) demonstrated excellent sensitivity (0.95) and specificity (1) and is the optimal cut-off from the data in the current study as it also had the equal highest Youden index (published and proposed cut-offs are highlighted in bold). ≤20/30 had an equally high Youden index however ≤21/30 has been chosen here as the maximum cut-off as it is preferred to err on the side of capturing impairment where it is potentially present. It should be noted that one participant in the dementia group scored 27/30 whilst the remaining participants all had scores of ≤20/30. The participant who scored 27/30 had the highest years of education of any of the dementia group (17 years). Data in Table 4 illustrate how disease prevalence level impacts the diagnostic performance of the lower cut-off of ≤21/30.

Table 4. PPV and NPV for different prevalence rates for a lower potential cut-off score

M-ACE cut-off	PPV/NPV at specified prevalence					
	5%	10%	20%	40%	50%	60%
≤21 PPV	1	1	1	1	1	1
NPV	0.99	0.99	0.99	0.97	0.95	0.93

Dementia & MCI vs controls

The data were also analysed to examine the diagnostic performance of the M-ACE in distinguishing between all impaired participants (dementia and MCI) and healthy controls. Figure 2 shows the ROC curve for M-ACE total score differentiating all impaired participants (dementia and MCI) from healthy controls. The AUC of 0.941 (95% CI 0.886 – 0.997) indicates excellent diagnostic accuracy. Again, the optimal cut-off score was defined as that with the maximal classification accuracy.

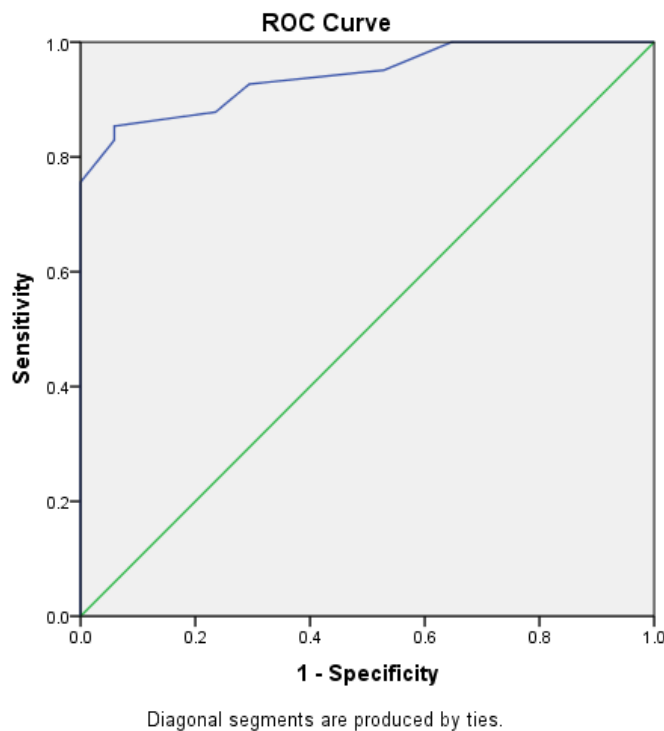


Figure 2. ROC curve of the M-ACE detecting dementia and MCI (dementia & MCI vs controls).

For the higher published cut-off ($\leq 25/30$), sensitivity was high (0.92) however specificity was poorer, (0.70). The lower published cut-off ($\leq 21/30$) demonstrated poor sensitivity (0.78) but excellent specificity (1). The optimal cut-off for distinguishing between the impaired participants (dementia and MCI) and the healthy controls in this sample was $\leq 23/30$ as this had the highest sensitivity, specificity and the highest Youden index (published and proposed cut-offs highlighted in bold). See Table 5 for sensitivity, specificity, Youden index, PPV, NPV, LR+ and LR- for all potential cut-offs.

Table 5. Sensitivity, specificity, positive and negative predictive values (PPV, NPV) and likelihood ratios (LR) for the M-ACE at different cut-offs for dementia.

Cut-off	Sensitivity	Specificity	PPV(NPV)	Youden Index	LR+	LR-
≤ 29	1	0.11	0.61 (1)	0.11	1.13	0.00
≤ 28	1	0.17	0.63 (1)	0.17	1.21	0.00
≤ 27	1	0.35	0.68 (1)	0.35	1.55	0.00
≤ 26	0.95	0.46	0.81 (0.80)	0.41	1.80	0.10
≤ 25	0.92	0.70	0.88 (0.80)	0.62	3.15	0.10
≤ 24	0.87	0.76	0.90 (0.72)	0.63	3.73	0.16
≤ 23	0.85	0.94	0.97 (0.72)	0.79	14.10	0.18
≤ 22	0.82	0.94	0.97 (0.69)	0.76	14.10	0.18
≤ 21	0.78	1	1 (0.65)	0.78	Infinity	0.22
≤ 20	0.73	1	1 (0.60)	0.73	Infinity	0.27

Table 6 highlights how disease prevalence impacts the diagnostic accuracy of the alternative cut-off. As disease prevalence increases, the NPV decreases gradually whilst the PPV only falls below chance levels when prevalence reaches 5%.

Table 6. PPV and NPV for different prevalence rates for a potential alternative cut-off score.

M-ACE cut-off	PPV/NPV at specified prevalence					
	5%	10%	20%	40%	50%	60%
≤ 23 PPV	0.43	0.61	0.78	0.90	0.93	0.95
NPV	0.99	0.98	0.96	0.90	0.86	0.81

Dementia vs MCI

The data were also analysed to examine the diagnostic performance of the M-ACE in distinguishing between the dementia and MCI groups. Figure 3 shows the ROC curve for M-ACE total score differentiating dementia participants from those with a diagnosis of MCI. The AUC of 0.849 (95% CI 0.731 – 0.967) indicates excellent diagnostic accuracy. The optimal cut-off score was defined as that with the maximal classification accuracy.

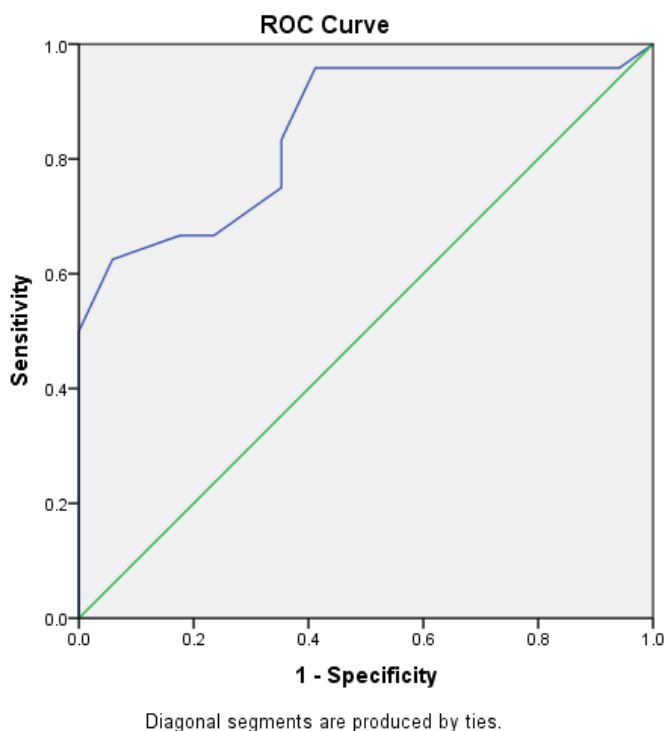


Figure 3. ROC curve of the M-ACE detecting dementia (dementia vs MCI)

For the higher published cut-off ($\leq 25/30$), sensitivity was high (0.95) however specificity was poor (0.11). The lower published cut-off ($\leq 21/30$) demonstrated poor sensitivity (0.47) but excellent specificity (0.95). The optimal cut-off for distinguishing between the participants with a dementia and those with an MCI in this sample was $\leq 15/30$ as this had the highest sensitivity, specificity and the highest Youden index. It should be noted however that the sensitivity for $\leq 15/30$ was poor (0.62), therefore the test is not particularly good at distinguishing between MCI and dementia. (See Table 7 for sensitivity, specificity, PPV, NPV,

Youden index LR+ and LR- for all potential cut-offs (with published and proposed cut-offs highlighted in bold).

Table 7. Sensitivity, specificity, positive and negative predictive values (PPV, NPV) and likelihood ratios (LR) for the M-ACE at different cut-offs for dementia.

Cut-off	Sensitivity	Specificity	PPV(NPV)	Youden Index	LR+	LR-
≤25	0.95	0.11	0.60 (0.66)	0.06	1.09	0.35
≤24	0.95	0.23	0.63 (0.80)	0.18	1.25	0.18
≤23	0.95	0.29	0.65 (0.83)	0.24	1.36	0.14
≤22	0.95	0.35	0.67 (0.85)	0.30	1.48	0.12
≤21	0.95	0.47	0.71 (0.88)	0.42	1.81	0.089
≤20	0.95	0.58	0.76 (0.90)	0.53	2.33	0.071
≤19	0.83	0.64	0.76 (0.73)	0.47	2.36	0.26
≤18	0.75	0.64	0.75 (0.64)	0.39	2.12	0.39
≤17	0.66	0.76	0.80 (0.61)	0.42	2.83	0.44
≤16	0.66	0.82	0.84 (0.63)	0.48	3.78	0.40
≤15	0.62	0.94	0.93 (0.64)	0.56	10.62	0.40
≤14	0.50	1	1 (0.58)	0.50	Infinity	0.50

Table 8 shows how disease prevalence impacts the diagnostic accuracy of the M-ACE using the proposed alternative cut-off. As disease prevalence increases, NPV decreases. PPV falls to almost chance levels when it reaches 10% prevalence.

Table 8. PPV and NPV for different prevalence rates for a lower potential cut-off score.

M-ACE cut-off	PPV/NPV at specified prevalence					
	5%	10%	20%	40%	50%	60%
≤15 PPV	0.35	0.54	0.72	0.87	0.91	0.94
NPV	0.97	0.95	0.90	0.79	0.71	0.62

Discussion

This study adds to the literature regarding the diagnostic utility of the Mini-Addenbrooke's Cognitive Examination. In particular, it extends our knowledge of how we should expect over 75s with dementia, MCI or no cognitive impairment in a UK population to perform on this cognitive screen. This study shows that the M-ACE can accurately distinguish between patients with dementia and controls. For the diagnosis of dementia in a UK sample of 75-89 year olds, the results of the study also suggest that the higher published cut-off of $\leq 25/30$ has unacceptably low specificity (0.70). The lower published cut-off (21/30) performs much better at differentiating dementia from controls (sensitivity 0.95, specificity 1). To distinguish between all impaired participants (those with dementia and MCI) and healthy controls, the maximal cut-off was found to be $\leq 23/30$, with a sensitivity of 0.85 and specificity of 0.94. When differentiating between dementia and MCI, a potential cut-off of $\leq 15/30$ was revealed to yield poor sensitivity (0.62) but excellent specificity (0.94).

Although the planned sample size was not achieved, the study had a high level of statistical power. Large effect sizes were found for all groups (1.4 for dementia/MCI, 1.9 for MCI/control and 3.3 for dementia/control.)

Additionally it should be noted that one dementia participant with 17 years education, achieved an unusually high score on the M-ACE (27/30). It is a reminder that clinicians must bear in mind a participant's education level when evaluating the results of any cognitive screen.

Implications for Clinical Practice

The results of the current study show that the M-ACE has excellent diagnostic accuracy in distinguishing between dementia and healthy controls however a lower cut-off of $\leq 21/30$ may have greater accuracy with those in the 75+ age group. The M-ACE also showed good ability to distinguish between participants with any cognitive impairment (MCI/dementia) from healthy controls however as one might expect there was far more overlap between scores for these groups highlighting the importance of not relying on

cognitive test scores from a brief screening tool but rather to use scores as a guide when deciding on whether to carry out more detailed neuropsychological assessment.

Limitations of the study

This study has some limitations. The key limitation of this study is that the procedure involved comparing clearly defined patients with healthy controls which does not reflect the challenge facing clinicians in clinical practice. The ideal method, such as that employed in Jubb & Evans (2015) [14], would be to test consecutive referrals to a memory clinic. This would ensure that the researcher is truly blind to the participant's condition (given that it would be unknown at this point) and it would also reflect the population seen in memory clinics. The current study included many more female than male participants and not every participant was recruited with an age-matched control. This proved difficult mainly because the current study sought to recruit older adults in an age range where many were widowed.

Another limitation of this study is that whilst dementia and MCI participant's ACE-III scores were collected, the majority of them had been carried out more than six months before data collection. This means that it was not possible to explore the relationship between M-ACE and ACE-III score.

Research which seeks to recruit older adults also faces challenges such as older people being less mobile and therefore less likely to be able to attend clinic visits. This study involved visiting the majority of participants at their homes which placed significant time constraints on data collection for the current study. Participants with a diagnosis of MCI are particularly difficult to recruit. The principal reason for this is that patients diagnosed with MCI are often discharged back to the care of their GP. Previous research has noted the challenges of recruiting for studies which involve participants with MCI and dementia [21].

Implications for Further Research

Future research should seek to further validate the M-ACE in a UK sample by recruiting a larger sample with an extended age range. It will also be necessary to explore the relationship

between M-ACE and ACE-III scores. To do this, it would be ideal to recruit consecutive referrals from a UK memory clinic such as the procedure used in Jubb & Evans (2015) [14]. This would allow for better recruitment of dementia, MCI and age/education-matched controls and would be highly representative of the population seen in clinical practice.

Conclusions

This study further validated the M-ACE in a UK sample of older adults aged 75-89. It confirmed that the M-ACE has excellent diagnostic accuracy in detecting dementia and mild cognitive impairment in clinical practice. As with the ACE-R and ACE-III, it may be necessary to consider cut-offs lower than those specified in the original M-ACE validation paper.

References

1. Alzheimer's society. 1. Alzheimers.org.uk. [Online]. Available from: https://www.alzheimers.org.uk/site/scripts/documents_info.php?documentID=106 [Accessed 9 June 2016].
2. Alzheimer's society. 1. Alzheimers.org.uk. [Online]. Available from: https://www.alzheimers.org.uk/site/scripts/documents_info.php?documentID=412 [Accessed 16th June 2016].
3. Govscot. 1. Govscot. [Online]. Available from: <http://www.gov.scot/Topics/Health/Services/Mental-Health/Dementia/DementiaStrategy1316> [Accessed 2 June 2016].
4. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975 11;12(3):189-198.
5. Mitchell AJ. A meta-analysis of the accuracy of the mini-mental state examination in the detection of dementia and mild cognitive impairment. *J Psychiatr Res* 2009 01;43(4):411-431.
6. Lopez MN, Charter RA, Mostafavi B, Nibut LP, Smith WE. Psychometric properties of the Folstein Mini-Mental State Examination. *Assessment* 2005 06;12(2):137-144.
7. Newman JC. Copyright and Bedside Cognitive Testing: Why We Need Alternatives to the Mini-Mental State Examination. *JAMA Intern Med* 2015 09;175(9):1459-1460.
8. Mathuranath PS, Nestor PJ, Berrios GE, Rakowicz W, Hodges JR. A brief cognitive test battery to differentiate Alzheimer's disease and frontotemporal dementia. *Neurology* 2000 12/12;55(11):1613-1620.

9. Hsieh S, McGrory S, Leslie F, Dawson K, Ahmed S, Butler CR, et al. The Mini-Addenbrooke's Cognitive Examination: a new assessment tool for dementia. *Dement Geriatr Cogn Disord* 2015;39(1-2):1-11.
10. Flicker L, Logiudice D, Carlin JB, Ames D. The predictive value of dementia screening instruments in clinical populations. *Int J Geriatr Psychiatry* 1997 02;12(2):203-209.
11. Alzheimer's society. 1. Alzheimersorguk. [Online]. Available from: https://www.alzheimers.org.uk/site/scripts/download_info.php?fileID=2323 [Accessed 2 June 2016].
12. Govscot. 1. Govscot. [Online]. Available from: <http://www.gov.scot/Topics/People/OlderPeople> [Accessed 15 February 2016].
13. Alzscotorg. 1. Alzscotorg. [Online]. Available from: http://www.alzscot.org/campaigning/eight_pillars_model_of_community_support [Accessed 20th February 2016].
14. Jubb MT, Evans JJ. An Investigation of the Utility of the Addenbrooke's Cognitive Examination III in the Early Detection of Dementia in Memory Clinic Patients Aged over 75 Years. *Dement Geriatr Cogn Disord* 2015;40(3-4):222-232.
15. Oren N, Yogev-Seligmann G, Ash E, Hendler T, Giladi N, Lerner Y. The Montreal Cognitive Assessment in cognitively-intact elderly: a case for age-adjusted cut-offs. *J Alzheimers Dis* 2015;43(1):19-22.
16. Mioshi E, Dawson K, Mitchell J, Arnold R, Hodges JR. The Addenbrooke's Cognitive Examination Revised (ACE-R): a brief cognitive test battery for dementia screening. *Int J Geriatr Psychiatry* 2006 11;21(11):1078-1085.
17. Faul, F, Erdfelder, E, Lang, A-G, Buchner, A. G*Power 3: A flexible statistical power analysis program for the social, behavioural and biomedical sciences. *Behavior Research Methods* 2007 39: 175-191.

18. Bpsorguk. 1. Bpsorguk. [Online]. Available from:
http://www.bps.org.uk/system/files/documents/code_of_ethics_and_conduct.pdf [Accessed 15th February 2016].
19. IBM Corp. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY 2016.
20. Mecal Statistical Software, Version 16.4.3. Ostend, Belgium.
21. Grill JD, Galvin JE. Facilitating Alzheimer disease research recruitment. *Alzheimer Dis Assoc Disord* 2014 01/20;28(1):1-8.

Systematic Review Appendices

Appendix 1.1: Search terms.

Mesh term (“malingering”)

OR

Keywords (“test* of effort” OR “symptom validity test*” OR “symptom validity” OR “effort test*” OR “validity test*” OR “performance validity”)

AND

Mesh term (dementia)

OR

Mesh term (MCI) OR (mild cognitive impairment)

Appendix 1.2: Quality Rating Checklist.

Quality Rating Checklist

Study Reference: _____

- 2 Information well-presented and in detail.
- 1 Information presented but not in adequate detail.
- 0 Information not present.

Items	Score
Abstract and Introduction	
Abstract provides a structured summary of study design, methods, results, and conclusions.	
Introduction clearly states the scientific and clinical background, including intended use and clinical role of index test and clearly states the research objectives and hypotheses.	
Total for abstract and introduction	/4
Methodology	
On what basis potentially eligible participants were identified (such as symptoms, results from previous tests, inclusion in registry)	
Selection criteria are clearly described (inclusion and exclusion)	
Describes the number, training and expertise of the persons executing and reading the index tests and the reference standard	
Whether data collection was planned before the index test and reference standard were performed (prospective study) or after (retrospective study)	
Index test, in sufficient detail to allow replication	
Reference standard in sufficient detail to allow replication	
Is the reference standard likely to classify the condition correctly	
The reference standard was independent of the index test (i.e. the index test did not form part of the reference standard).	
Reference standard results are interpreted without knowledge of the results of the index test	
Total for methodology	/18
Results and Discussion	

An explanation is provided for withdrawals from the study	
Methods for estimating or comparing measures of diagnostic accuracy seem reasonable	
Discussion: Study limitations, including sources of potential bias, statistical uncertainty, and generalizability	
Total for results and discussion	/6
Score overall	/28

Appendix 1.3: Crowe Critical Appraisal Tool (CCAT) Version 1.4 (2013).

Crowe Critical Appraisal Tool (CCAT) Form (v1.4)

Reference

Reviewer

This form must be used in conjunction with the CCAT User Guide (v1.4); otherwise validity and reliability may be severely compromised.

Citation	
	Year

Research design (add if not listed)

<input type="checkbox"/> Not research	Article Editorial Report Opinion Guideline Pamphlet ...
<input type="checkbox"/> Historical	...
<input type="checkbox"/> Qualitative	Narrative Phenomenology Ethnography Grounded theory Narrative case study ...
<input type="checkbox"/> Descriptive, Exploratory, Observational	A. Cross-sectional Longitudinal Retrospective Prospective Correlational Predictive ...
	B. Cohort Case-control Survey Developmental Normative Case study ...
Experimental	<input type="checkbox"/> True experiment Pre-test/post-test control group Solomon four-group Post-test only control group Randomised two-factor Placebo controlled trial ...
	<input type="checkbox"/> Quasi-experiment Post-test only Non-equivalent control group Counter balanced (<i>cross-over</i>) Multiple time series Separate sample pre-test post-test [no Control] [Control] ...
	<input type="checkbox"/> Single system One-shot experimental (<i>case study</i>) Simple time series One group pre-test/post-test Interactive Multiple baseline Within subjects (<i>Equivalent time, repeated measures, multiple treatment</i>) ...
<input type="checkbox"/> Mixed Methods	Action research Sequential Concurrent Transformative ...
<input type="checkbox"/> Synthesis	Systematic review Critical review Thematic synthesis Meta-ethnography Narrative synthesis ...
<input type="checkbox"/> Other	...

Variables and analysis

Intervention(s), Treatment(s), Exposure(s)	Outcome(s), Output(s), Predictor(s), Measure(s)	Data analysis method(s)

Sampling

Total size	Group 1	Group 2	Group 3	Group 4	Control
Population, sample, setting					

Data collection (add if not listed)

Audit/Review	a) Primary Secondary ... b) Authoritative Partisan Antagonist ... c) Literature Systematic ...	Interview a) Formal Informal ... b) Structured Semi-structured Unstructured ... c) One-on-one Group Multiple Self-administered ...
	Observation a) Participant Non-participant ... b) Structured Semi-structured Unstructured ... c) Covert Candid ...	

Scores

Preliminaries	Design	Data Collection	Results	Total [/40]
Introduction	Sampling	Ethical Matters	Discussion	Total [%]

General notes



Crowe Critical Appraisal Tool (CCAT) :: Version 1.4 [19 November 2013] :: Michael Crowe (michael.crowe@my.jcu.edu.au)
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Page 1 of 2

Appraise research on the merits of the research design used, not against other research designs.

Category Item	Item descriptors [<input type="checkbox"/> Present; <input type="checkbox"/> Absent; <input type="checkbox"/> Not applicable]	Description [Important information for each item]	Score [0-5]
1. Preliminaries			
Title	1. Includes study aims <input type="checkbox"/> and design <input type="checkbox"/>		
Abstract (assess last)	1. Key information <input type="checkbox"/> 2. Balanced <input type="checkbox"/> and informative <input type="checkbox"/>		
Text (assess last)	1. Sufficient detail others could reproduce <input type="checkbox"/> 2. Clear/concise writing <input type="checkbox"/> , table(s) <input type="checkbox"/> , diagram(s) <input type="checkbox"/> , figure(s) <input type="checkbox"/>		
			Preliminaries [/5]
2. Introduction			
Background	1. Summary of current knowledge <input type="checkbox"/> 2. Specific problem(s) addressed <input type="checkbox"/> and reason(s) for addressing <input type="checkbox"/>		
Objective	1. Primary objective(s), hypothesis(es), or aim(s) <input type="checkbox"/> 2. Secondary question(s) <input type="checkbox"/>		
Is it worth continuing?			Introduction [/5]
3. Design			
Research design	1. Research design(s) chosen <input type="checkbox"/> and why <input type="checkbox"/> 2. Suitability of research design(s) <input type="checkbox"/>		
Intervention, Treatment, Exposure	1. Intervention(s)/treatment(s)/exposure(s) chosen <input type="checkbox"/> and why <input type="checkbox"/> 2. Precise details of the intervention(s)/treatment(s)/exposure(s) <input type="checkbox"/> for each group <input type="checkbox"/> 3. Intervention(s)/treatment(s)/exposure(s) valid <input type="checkbox"/> and reliable <input type="checkbox"/>		
Outcome, Output, Predictor, Measure	1. Outcome(s)/output(s)/predictor(s)/measure(s) chosen <input type="checkbox"/> and why <input type="checkbox"/> 2. Clearly define outcome(s)/output(s)/predictor(s)/measure(s) <input type="checkbox"/> 3. Outcome(s)/output(s)/predictor(s)/measure(s) valid <input type="checkbox"/> and reliable <input type="checkbox"/>		
Bias, etc	1. Potential bias <input type="checkbox"/> , confounding variables <input type="checkbox"/> , effect modifiers <input type="checkbox"/> , interactions <input type="checkbox"/> 2. Sequence generation <input type="checkbox"/> , group allocation <input type="checkbox"/> , group balance <input type="checkbox"/> , and by whom <input type="checkbox"/> 3. Equivalent treatment of participants/cases/groups <input type="checkbox"/>		
Is it worth continuing?			Design [/5]
4. Sampling			
Sampling method	1. Sampling method(s) chosen <input type="checkbox"/> and why <input type="checkbox"/> 2. Suitability of sampling method <input type="checkbox"/>		
Sample size	1. Sample size <input type="checkbox"/> , how chosen <input type="checkbox"/> , and why <input type="checkbox"/> 2. Suitability of sample size <input type="checkbox"/>		
Sampling protocol	1. Target/actual/sample population(s): description <input type="checkbox"/> and suitability <input type="checkbox"/> 2. Participants/cases/groups: inclusion <input type="checkbox"/> and exclusion <input type="checkbox"/> criteria 3. Recruitment of participants/cases/groups <input type="checkbox"/>		
Is it worth continuing?			Sampling [/5]
5. Data collection			
Collection method	1. Collection method(s) chosen <input type="checkbox"/> and why <input type="checkbox"/> 2. Suitability of collection method(s) <input type="checkbox"/>		
Collection protocol	1. Include date(s) <input type="checkbox"/> , location(s) <input type="checkbox"/> , setting(s) <input type="checkbox"/> , personnel <input type="checkbox"/> , materials <input type="checkbox"/> , processes <input type="checkbox"/> 2. Method(s) to ensure/enhance quality of measurement/instrumentation <input type="checkbox"/> 3. Manage non-participation <input type="checkbox"/> , withdrawal <input type="checkbox"/> , incomplete/lost data <input type="checkbox"/>		
Is it worth continuing?			Data collection [/5]
6. Ethical matters			
Participant ethics	1. Informed consent <input type="checkbox"/> , equity <input type="checkbox"/> 2. Privacy <input type="checkbox"/> , confidentiality/anonymity <input type="checkbox"/>		
Researcher ethics	1. Ethical approval <input type="checkbox"/> , funding <input type="checkbox"/> , conflict(s) of interest <input type="checkbox"/> 2. Subjectivities <input type="checkbox"/> , relationship(s) with participants/cases <input type="checkbox"/>		
Is it worth continuing?			Ethical matters [/5]
7. Results			
Analysis, Integration, Interpretation method	1. A.I.I. method(s) for primary outcome(s)/output(s)/predictor(s) chosen <input type="checkbox"/> and why <input type="checkbox"/> 2. Additional A.I.I. methods (e.g. subgroup analysis) chosen <input type="checkbox"/> and why <input type="checkbox"/> 3. Suitability of analysis/integration/interpretation method(s) <input type="checkbox"/>		
Essential analysis	1. Flow of participants/cases/groups through each stage of research <input type="checkbox"/> 2. Demographic and other characteristics of participants/cases/groups <input type="checkbox"/> 3. Analyse raw data <input type="checkbox"/> , response rate <input type="checkbox"/> , non-participation/withdrawal/incomplete/lost data <input type="checkbox"/>		
Outcome, Output, Predictor analysis	1. Summary of results <input type="checkbox"/> and precision <input type="checkbox"/> for each outcome/output/predictor/measure 2. Consideration of benefits/harms <input type="checkbox"/> , unexpected results <input type="checkbox"/> , problems/failures <input type="checkbox"/> 3. Description of outlying data (e.g. diverse cases, adverse effects, minor themes) <input type="checkbox"/>		
			Results [/5]
8. Discussion			
Interpretation	1. Interpretation of results in the context of current evidence <input type="checkbox"/> and objectives <input type="checkbox"/> 2. Draw inferences consistent with the strength of the data <input type="checkbox"/> 3. Consideration of alternative explanations for observed results <input type="checkbox"/> 4. Account for bias <input type="checkbox"/> , confounding/effect modifiers/interactions/imprecision <input type="checkbox"/>		
Generalisation	1. Consideration of overall practical usefulness of the study <input type="checkbox"/> 2. Description of generalisability (external validity) of the study <input type="checkbox"/>		
Concluding remarks	1. Highlight study's particular strengths <input type="checkbox"/> 2. Suggest steps that may improve future results (e.g. limitations) <input type="checkbox"/> 3. Suggest further studies <input type="checkbox"/>		
			Discussion [/5]
9. Total			
Total score	1. Add all scores for categories 1-8		
			Total [/40]

Major Research Project Appendices

Appendix 2.1: Author Guidelines

Dementia and Geriatric Cognitive Disorders

Guidelines for Authors

www.karger.com/dem_guidelines

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- ▼ Self-Archiving/Green Open Access, *Author's Choice*[™],
Funding Organizations (NIH etc.)
- ▼ Page Charges
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Should you experience any problems with your submission, please contact:

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Authors are required to disclose any sponsorship or funding arrangements relating to

their research and all authors should disclose any possible conflicts of interest. Conflict of interest statements will be published at the end of the article.

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Background/Aims: What is the major problem that prompted the study?

Methods: How was the study carried out?

Results: Most important findings?

Conclusion: Most important conclusion?

Footnotes: Avoid footnotes.

Abbreviations: Abbreviations should not be used excessively in the text. Only standard abbreviations should be used. Nonstandard abbreviations of terms that are used frequently in the text should be explained by the term written out completely and followed immediately by the abbreviation in parentheses, for example: 'increase in norepinephrine (NE) content ...'.

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In the text identify references by Arabic numerals [in square brackets]. Material submitted for publication but not yet accepted should be noted as 'unpublished data' and not be included in the reference list. The list of references should include only those publications which are cited in the text. Do not alphabetize; number references in the order in which they are first mentioned in the text. The surnames of the authors followed by initials should be given. There should be no punctuation other than a comma to separate the authors. Preferably, please cite all authors. Abbreviate journal names according to the Index Medicus system. Also see International Committee of Medical Journal Editors: Uniform requirements for manuscripts submitted to biomedical journals (www.icmje.org).

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Allain H, Bentue-Ferrer D, Tribut O, Pinel J-F: Drugs and vascular dementia. *Dement Geriatr Cogn Disord* 2003;16:1–6.

(b) Papers published only with DOI numbers:

Theoharides TC, Boucher W, Spear K: Serum interleukin-6 reflects disease severity and osteoporosis in mastocytosis patients. *Int Arch Allergy Immunol* DOI: 10.1159/000063858.

(c) Monographs:

Matthews DE, Farewell VT: *Using and Understanding Medical Statistics,*

ed 3, revised. Basel, Karger, 1996.

(d) Edited books:

Tarou LR, Bloomsmith MA, Hoff MP, Erwin JM, Maple TL: The behavior of aged great apes; in Erwin JM, Hof PR (eds): Aging in Nonhuman Primates. Interdiscipl Top Gerontol. Basel, Karger, 2002, vol 31, pp 209–231.

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Appendix 2.2: Major Research Project proposal

Major Research Project Proposal

An investigation of the utility of the Mini Addenbrooke's Cognitive Examination (M-ACE) for the early detection of dementia and mild cognitive impairment in people aged 75 and over.

Matriculation number: 2109099

Version number: 3

Word count: 4054

Abstract

Background: Cognitive screening tools are crucial for the accurate detection and differential diagnosis of dementias. Accurate and timely assessment is important for accessing appropriate support and treatment options and for estimating the likely course of the disease. There are a range of screening tools available to clinicians however shorter cognitive tools are particularly useful in busy clinical settings. The Mini Mental State Examination (MMSE; Folstein et al, 1975) is one the most widely used screens. Despite being recommended by national guidelines SIGN and NICE, the MMSE has several shortcomings. In 2014, Hsieh et al introduced the Mini Addenbrooke's Cognitive Examination (M-ACE, a shortened version of the widely used Addenbrooke's Cognitive Examination III - ACE III), a possible alternative to the MMSE. The current study aims to further the validation of the M-ACE by exploring its use in a UK clinical setting with individuals aged 75 and over.

Aims: The primary aim of this study is to investigate if the M-ACE can be used with people aged 75 and over to distinguish between those who do and do not have a diagnosis of dementia.

The secondary aim is to investigate whether the cut-off scores recommended by Hsieh et al (2014) in the original validation study for the M-ACE are optimal.

Methods: Participants will be approximately 66 individuals aged 75 and over who will have their cognitive function assessed using the M-ACE. There will be approximately 44 participants who will be patients referred to Community Mental Health Teams (CMHTs) (22 with a diagnosis of dementia, 22 with mild cognitive impairment (MCI)) for investigation of memory problems whilst 22 individuals will be healthy controls (the spouses/relatives/carers of the referred patients).

Applications: This study will examine if the M-ACE is sensitive and specific to dementia and MCI in people aged 75 and over. It also aims to investigate if the existing published cut-off scores are accurate for use in people aged 75+ in a UK sample. This study is intended to be of use to health care professionals as they are increasingly called on to investigate memory problems in those aged 75+ and as there is more demand for shorter cognitive screens in busy clinical settings.

Background Information and Rationale:

Background:

Dementia describes a set of symptoms that may include memory loss and difficulties with thinking, problem-solving or language. In 2013, there were an estimated 44.4 million people with dementia making it one of the foremost public health challenges of our time (Alzheimer's disease International). As of 2015, there are an estimated 850,000 people living with dementia in the UK. Although diagnosis rates have improved in recent years, it is estimated that there are still approximately a third of those with dementia in Scotland who do not have a diagnosis (Scotland's National Dementia Strategy, 2013-2016). It has been recognised that although dementia has a profound impact on the individual and their family, a timely and accurate diagnosis can lead to better support, can enable people to maintain a good quality of life at home for as long as possible and can also empower them to make their own choices about their future care (World Alzheimer Report, 2011).

In order to provide appropriate support to individuals with dementia, it is first necessary to be able to make an accurate diagnosis. Cognitive screening tools are an important part of dementia assessment. These tools inform whether an individual's cognitive difficulties fall within an expected range for their age or whether there is a need for further investigation such as neuroimaging or neuropsychological assessment. Cognitive screening tools can also inform differential diagnosis between different types of dementia or other conditions which can cause cognitive impairment.

One of the most popular cognitive screening tools is the Mini Mental State Examination (MMSE; Folstein et al, 1975) which has been used worldwide to detect for dementia for the past three decades. The MMSE is a 30-point questionnaire that takes around 5-10 minutes to administer and is recommended by national guidelines (SIGN 86 and NICE). It is often used to track changes in a person's cognitive function which helps to either aid a diagnosis of dementia, or if already diagnosed, helps to determine what stage the person is at. However, despite its popularity the MMSE has been found to have several weaknesses including poor sensitivity to mild cognitive impairment and it is also prone to ceiling and floor effects (Mitchell, 2009). The test also relies heavily on verbal items which is problematic when using the test with individuals with poor language skills and/ or low education (Lopez et al, 2005). A further key disadvantage to using the MMSE is a financial one: the test has been placed under copyright since 2001, incurring a cost of 80p every time it is used. This clearly has huge financial implications for healthcare providers such as the National Health Service who face either continuing to pay thousands of pounds for continued access to the MMSE or finding an alternative resource.

Due to an increasing awareness of the insufficient assessment provided by the MMSE, other cognitive tests have been developed which aim to be extended versions of the test. One of the most popular of these extended tests is the Addenbrooke's Cognitive Assessment (ACE) which was introduced in 2000 as a brief cognitive screening tool which incorporated the MMSE but which also explored important areas not covered by it, such as visuospatial skills, frontal-executive function and more complex language assessment. The ACE is a 100-point test battery which takes approximately 15-20 minutes to administer. The validation study of the first version of the ACE indeed showed that it was superior to the MMSE in both detecting dementia and differentiating between Alzheimer's disease and fronto-temporal dementia (Mathuranath et al, 2000). The ACE which is now in its third version (the ACE-III) is recommended by both NICE and SIGN guidelines as an extended screening to be used when clinicians require a more detailed picture of a patient's cognitive function. Despite the ACE-III being a robust screening tool, the time that it takes to complete it means that it is not

always a viable option in busy clinics. Whilst clinicians should aim to complete as comprehensive an initial cognitive screen as possible, in practice this is not always viable meaning that clinicians need to have the option of a very brief measure for such occasions.

The focus of the current study concerns one such new brief screening tool: the Mini Addenbrooke's Cognitive Examination (M-ACE) which is a shortened version of the ACE. The M-ACE was devised and validated by Hsieh et al in 2014 as it was felt that the ACE-III which takes 15-20 minutes to administer is 'outwith the scope of many clinical settings'. (Hsieh et al, 2014). The M-ACE takes under 5 minutes to administer and contains 5 items assessing orientation, memory, animal fluency and clock drawing. It is scored out of 30 with two cut-offs recommended: (1) 25/30 and (2) 21/30. First, the higher cut-off of 25/30 has both high sensitivity and specificity and is at least 5 times more likely to have come from a patient with dementia than without. A lower cut-off of 21/30, by contrast, is almost certainly diagnostic of a dementia syndrome regardless of the prevalence rate. The M-ACE validation study showed that the M-ACE is more sensitive than the MMSE and is less likely to have ceiling effects. There is a need to further explore the M-ACE and its potential as a brief screening tool which is the purpose of the current study.

The initial validation study for the M-ACE was conducted in Australia, therefore there is a requirement for the utility of the M-ACE to be investigated in a UK clinical setting. The focus of the current study will be on individuals aged 75 and over who are referred to a CMHT for memory problems. A control group of healthy individuals with no history of memory problems will also be aged 75+. There are several reasons for focusing on this age group. One reason is that age is a key risk factor for developing a dementia. The prevalence of dementia in people aged 70-74 is 3% which rises to 6% for 75-79 olds and 11.1% for 80-84 year olds (Dementia UK Update, Alzheimer's Society, 2014).

Further, with increased improvements in healthcare there is going to be a significant increase in the proportion of people aged 75+ in the population. By 2031 the number of people aged

75+ is projected to increase by 75% (All Our Futures, Planning for Scotland with an Ageing Population, Scottish Executive, 2007). In Scotland alone this figure is projected to increase to 94,000 by 2017 and 108,000 by 2022; with incidence of 9,400 and 10,800 respectively. This represents a 12% increase by 2017 and a 29% increase by 2022. (Delivering Integrated Dementia Care: The 8 Pillars Model of Community Support, Alzheimer's Scotland). This creates a challenge for our health and social care services that will increasingly be called on to meet the needs of this population.

A third reason for this focus comes from a limitation of the original M-ACE validation study by Hsieh et al (2014). This study was limited to comparing patients with controls in the age range 61-74.

Furthermore, as people get older, they may be more suited to a shorter cognitive test as they may have more visual, auditory or concentration difficulties than younger patients.

There is also a need to investigate the optimal cut-offs for the M-ACE for discriminating between those who have a diagnosis of dementia in people aged 75+. A recent study found that the optimal cut-offs for the ACE-III for people over the age of 75 in a UK clinical sample were lower than those recommended in the ACE-III validation study (Jubb et al, 2015).

Aims:

1. The primary aim of this study is to investigate if the M-ACE can be used with people aged 75+ to distinguish between those who do and do not have a diagnosis of dementia and those who have a diagnosis of MCI.
2. The secondary aim is to investigate whether the cut-off scores recommended by Hsieh et al (2014) in the original validation study for the M-ACE are optimal.

Hypotheses:

Primary hypothesis:

1. There will be a significant difference between the means of the M-ACE scores for the three groups of participants i.e. those who have a diagnosis of dementia, MCI or no diagnosis. The score on the M-ACE will enable accurate discrimination between those who have a diagnosis of dementia, MCI and those who have no diagnosis in those aged 75+.

Secondary hypothesis:

1. The optimal cut-off for discriminating between those who have a diagnosis of dementia will be lower in this sample of participants aged 75+ than those suggested in the Hsieh et al (2014) original validation study.

Methodology:

Participants:

Participants will be recruited from Older Adult CMHTs in Glasgow. Participants will be patients aged 75+ who have been referred to the CMHT for memory problems.

Service users:

Inclusion criteria:

5. All participants must be aged 75 and over.
6. All participants must be able to give informed consent.
7. Have English as their first language.

Exclusion criteria: there will be minimal patient exclusion criteria since the study aims to use a sample of all patients referred to CMHTs for memory problems over the time period of the study. However patients in the dementia and MCI groups should:

4. Not be experiencing cognitive impairment due to a neurological condition (e.g. due to head injury, alcohol-related damage, epilepsy).
5. Have no significant hearing or vision problems which would prevent their completion of the M-ACE.
6. Not have a learning disability.

Control group:

Inclusion criteria:

1. 1. All participants must be aged 75 and over and have English as their first language.

Exclusion criteria: similar exclusion criteria will exist for control group participants.

Therefore participants in the control group should:

2. Not have significant hearing or vision problems which would prevent their completion of the M-ACE.
3. Not have a neurological condition.
4. Not have a learning disability.
5. Have no prior history of memory problems.

Recruitment Procedure: All participants in the dementia and MCI groups will be patients who have been referred to the CMHT. All participants in the no diagnosis group will be spouses/carers of people referred to the CMHT (not just those patients who are included in the study).

Measures:

- The Mini Addenbrooke's Cognitive Examination (M-ACE) is the primary outcome measure and is free of charge to download (<https://www.neura.edu.au/frontier/research/test-downloads/>).
- Information sheet and consent form (to be drawn up by primary researcher).
- Access to ACE-III scores from patient case files.
- Demographic sheet to record demographic details of each participant. In order to know about years of education, exact age.

Research Procedure:**Dementia and MCI group participants:**

All patients referred to the CMHT for investigation of memory problems who meet the inclusion criteria will be approached to take part in the study. As part of usual procedure, patients will be visited at home and have their cognitive function assessed using the ACE-III by a member of the team (usually a Community Psychiatric Nurse - CPN). The CPN will give the patient an information sheet about the study and if they agree to take part then they will allow the CPN to pass on their contact details to the primary researcher. The CPN will make it explicit that the patient can withdraw their participation in the study at any time and that they will not be required to give a reason for doing so.

In order to access potential participants who have a diagnosis of MCI, staff will contact clients who have been recently discharged from their caseload (within the past 2 months) and who have been given a diagnosis of MCI. The staff member who provided input to the client with MCI will telephone the client to ask if they are interested in participating. At present, clients who are given a diagnosis of MCI, are usually discharged back to the care of their GP within a short timeframe.

The primary researcher will telephone the patient to arrange a home visit. At the home visit the primary researcher will explain the purpose of the study, answer any questions the patient may have about participation in the study and they will sign a consent form. The patient will also be asked to complete a brief information sheet asking about age, gender and years of education (Appendix). The researcher will then administer the M-ACE.

The scores from the ACE-III will fall into one of three possible groups: 1) the patient scores above the cut-off and no further investigation is necessary (unlikely outcome given that they have been referred for memory problems), 2) the patient scores in a borderline range (MCI), 3) the patient scores below cut-off and is given a diagnosis of dementia. The primary researcher will not know the result of the ACE-III until the end of data collection.

Control group participants:

If there is a carer or relative present on the home visit and if they are aged 75+ and they do not meet exclusion criteria (see above), the CPN will ask if they would be interested in taking part in the study and will provide them with an information sheet. If the carer/relative wishes to take part, the CPN will pass on the contact details to the primary researcher who will contact the carer/relative by telephone in order to arrange a home visit to carry out the M-ACE. At the visit the patient will fill out a brief information sheet and sign a consent form.

Data Analysis and Justification of Sample Size:

There will be two approaches to data analysis, the first being to examine group differences and the second is to investigate the diagnostic utility of the M-ACE.

The original validation study of the M-ACE (Hsieh et al, 2014) does not report an effect size therefore the validation study for the ACE-R informs the likely effect size for the current study. In the Hsieh et al (2014) study, Cohen's d for the difference between controls and those with Alzheimer's dementia was 1.84 which is a large effect size. GPower (v 3.1.9.2) (Faul et al, 2009) was used to calculate sample size. In order to detect a large effect size (Cohen's $f = .40$) with $\alpha = 0.05$, on a one-way ANOVA, 66 participants would be required across the three groups (22 in each group).

Data regarding referrals to one of the CMHTs shows that they receive on average 35 new referrals each per month. Approximately 70% of these referrals are for memory problems therefore we could expect around 70 patients in a three month period from each CMHT which suggests the target of 66 participants (22 with dementia diagnosis, 22 with MCI and 22 healthy controls) is feasible.

Furthermore, for a test to be useful in a diagnostic sense, it needs to show good separation of groups (the M-ACE scores from the control, MCI and dementia groups should be as separate as possible).

The primary hypothesis will be analysed using a one-way ANOVA to compare the means of the three groups. The data will be tested to check it is normally distributed. If it is found not to be normally distributed, the non-parametric equivalent of the one-way ANOVA, the Kruskal Wallis, will be used.

Subsequent analysis of the diagnostic accuracy of the M-ACE scores will be operated using Receiver Operating Characteristic (ROC) analysis which will allow for examination of the sensitivity and specificity of different cut-off scores. In addition, positive predictive values and negative predictive values (PPV, NPV) will be calculated.

Demographic data (age and years of education) will be analysed across the three groups to examine if the groups differ significantly on these variables. If so, subsequent analysis will control for this effect.

Settings and Equipment:

The study will be conducted in participants' homes. Print outs of the M-ACE will be required however there is no cost involved as the tool is free of charge to download.

Health and Safety Issues

Researcher Safety Issues:

Due to the population being studied, mobility and transport difficulties are common and standard clinical practice involves staff conducting home visits in order to provide an equitable service. Therefore, permission has been granted to conduct home visits as necessary in order to allow people with such difficulties to still participate. All participants requiring a home visit will have been thoroughly risk assessed by trained staff in the community mental health teams. Local and national policy guidelines on health and safety and emergency procedures (e.g. lone working policy, fire safety) will be sought. A health and safety assessment form is included in Appendix 1. The researcher will use Guardian 24 when conducting home visits and all visits will be carried out during office working hours. Guardian 24 is a lone worker service which the researcher can call to record the time and duration of their visit. The researcher then calls this number again to record that they have safely left the visit. If the researcher fails to call this number they will be contacted by Guardian 24 to check their location. If there is still no response the system will contact the researcher's clinical supervisor.

Participant Safety Issues:

Risks to participants include the stress of having cognitive function assessed. There is also the risk that being assessed will uncover a problem with a participant's cognitive function that they were not previously aware of. Making sure participants are fully informed and that pre-diagnostic counselling is given should limit these risks to the participant.

Ethical Issues:

Ethical permission will need to be sought and granted from Local Research Ethics Committee as the project involves accessing ACE-III scores from patient case files. Management approval will be sought from NHS Greater Glasgow and Clyde Research and Development. There are also ethical implications for administering the M-ACE to individuals who do not have a diagnosis. This will be made clear to participants through the information sheet and pre-diagnostic counselling.

Financial Issues:

Researcher will incur costs for travel to home visits. Participants are not remunerated for their participation. The study will be submitted to R&D NHS Greater Glasgow and Clyde for sponsorship. The project will be funded by the University of Glasgow. A total of £153.50 has been secured to cover the cost of photocopies and researcher travel expenses.

Amendments:

Following advice from the Sponsor, NHS R&D and the ethics board, amendments will be discussed by the research team and implemented accordingly. Any amendments to the study will be submitted to R&D and ethics for further ethical consideration.

The researcher will aim to present the findings of the current study at relevant conferences and to publish the study in relevant journals. Participants will also be informed of the study results by a letter which will be drafted, summarising the main findings.

Timetable

April 2015	Submit research proposal to University Complete Ethics and R&D forms and submit
May - August 2015	Making practical arrangements with local services. Processing of ethics and R&D
	Processing of ethics and R&D proposals with any corrections
September 2015– April 2016	Data collection
May 2016	Data analysis
June and July 2016	Write up
July 2016	Submit for examination

Practical Applications

This study aims to determine if the Mini Addenbrooke’s Cognitive Examination (M-ACE) can be used with people aged 75+ to distinguish between those who do and do not have a diagnosis of dementia or MCI in a UK clinical population. The study also aims to provide guidance to clinicians about the appropriate cut-offs to be used in this context.

Word count: 4054

References:

All Our Futures, Planning for a Scotland with an Ageing Population, Scottish Executive: Edinburgh 2007 <http://www.scotland.gov.uk/Topics/People/OlderPeople> [Accessed 15th February 2015]

Alzheimer Scotland, Action on Dementia, http://www.alzscot.org/campaigning/eight_pillars_model_of_community_support [Accessed 15th February 2015]

Alzheimer's Society. Increase in number of people diagnosed with dementia: over 400 000 remain undiagnosed, according to Alzheimer's Society. 2012. http://alzheimers.org.uk/site/scripts/news_article.php?newsID=1164. [Accessed 15th February 2015]

Alzheimer's Disease International <http://www.alz.co.uk/research/statistics> [Accessed 15th February 2015]

Folstein MF, Folstein SE, McHugh PR. "Mini-mental state." A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* 1975;12(3):189-198

Hsieh, McGrory, Leslie, Dawson, Ahmed, Butler, Rowe, Mioshi & Hodges 2014. The Mini-Addenbrooke's Cognitive Examination: A New Assessment Tool for Dementia. *Dement Geriatr Cogn Disord* 2014;39:1-11.

Hsieh, Schubert, Hoon, Mioshi & Hodges 2013. Validation of the Addenbrooke's Cognitive Examination III in Frontotemporal Dementia and Alzheimer's Disease, *Dement Geriatr Cogn Disord* 2013;36:242–250.

Jubb, M (2015) An Investigation of the utility of the Addenbrooke's Cognitive Examination – III for the Early Detection of Dementia in People Over the Age of 75 years.

Lopez MN, Charter RA, Mostafavi B, Nibut LP, Smith WE. Psychometric properties of the Folstein Mini-Mental State Examination. *Assessment*. 2005;12(2):137-144.

Mathuranath PS, Nestor PJ, Berrios GE, et al (2000). A brief cognitive test battery to differentiate Alzheimer's disease and frontotemporal dementia. *Neurology* 55 (11): 1613–1620.

Mitchell AJ (2009). A meta-analysis of the accuracy of the mini-mental state examination in the detection of dementia and mild cognitive impairment. *J Psychiatr Res*. 2009;43(4):411-431

National Institute for Health and Clinical Excellence (NICE). 2006. Clinical Guideline 42, Dementia: Supporting people with dementia and their carers in health and social care.

[Internet] NICE: London. Available at:

<http://www.nice.org.uk/nicemedia/pdf/CG042NICEGuideline.pdf><http://www.nice.org.uk/nicemedia/pdf/CG042NICEGuideline.pdf> [Accessed 15th February 2015]

Prince M, Bryce R, Ferri C. World Alzheimer report 2011: the benefits of early diagnosis and intervention. London (UK): Alzheimer's Disease International (ADI); 2011 Sep. 68 p. [Accessed 26th February 2015].

Scotland's National Dementia Strategy 2013-2016, Scottish Intercollegiate Guidelines Network (SIGN). 2006. Management of patients with dementia, a National Clinical Guideline, (SIGN publication 86). [Internet] SIGN: Edinburgh. Available at: <http://www.sign.ac.uk/pdf/sign86.pdf> [Accessed 15th February 2015].

Appendix 2.3: Letter of ethical approval (original)

WoSRES
West of Scotland Research Ethics Service



West of Scotland REC 3
West of Scotland Research Ethics Service
West Glasgow Ambulatory Care Hospital
(former Royal Hospital for Sick Children Yorkhill)
Dalnair Street
Glasgow G3 8SW
www.nhsggc.org.uk

Professor Jonathan Evans
Professor of Applied Neuropsychology
NHS Greater Glasgow and Clyde
1055 Great Western Road
Glasgow
G12 0XH

Date 10th December 2015
Your Ref
Our Ref
Direct line 0141 232 1805
E-mail WOSREC3@ggc.scot.nhs.uk

Dear Professor Evans

Study title:	An Investigation of the Utility of the Mini-Addenbrooke's Cognitive Examination (M-ACE) for the Early Detection of Dementia and Mild Cognitive Impairment in People Aged 75 and over.
REC reference:	15/WS/0279
IRAS project ID:	183123

Thank you for responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to make a request to postpone publication, please contact the REC Manager, Mrs Liz Jamieson, wosrec3@ggc.scot.nhs.uk.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for NHS permission for research is available in the Integrated Research Application System, www.hra.nhs.uk or at <http://www.rdforum.nhs.uk>.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

<i>Document</i>	<i>Version</i>	<i>Date</i>
GP/consultant information sheets or letters [GP Letter for Patients]	1	30 October 2015
Letters of invitation to participant [Letter of invitation]	3	13 November 2015
Other [Demographic Information]	1	30 October 2015
Other [Addenbrooke's Cognitive Examination - ACE-III]		02 November 2015
Other [Peer Review]		30 March 2015
Other [No Opinion Letter]		11 November 2015
Other [Participant information sheet (partner)]	3	13 November 2015
Other [Participant consent form (partner)]	3	13 November 2015
Other [Letter of invitation (partner)]	3	13 November 2015
Other [Response to REC]	1	09 December 2015
Participant consent form [Participant consent form]	3	13 November 2015
Participant information sheet (PIS) [Participant information sheet]	3	13 November 2015
REC Application Form [REC Form 02112015]		02 November 2015
Research protocol or project proposal	2	09 August 2015
Summary CV for Chief Investigator (CI) [Jon Evans]		07 September 2015
Summary CV for student [Claire McGuire]		04 August 2015
Summary CV for supervisor (student research) [Stephanie Crawford]		10 February 2014
Validated questionnaire [Mini Addenbrooke's Cognitive Examination]	A	25 May 2014

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document "*After ethical review – guidance for researchers*" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website:

<http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/>

HRA Training

We are pleased to welcome researchers and R&D staff at our training days – see details at <http://www.hra.nhs.uk/hra-training/>

15/WS/0279

Please quote this number on all correspondence

With the Committee's best wishes for the success of this project.

Yours sincerely



Liz Jamieson
REC Manager
On behalf of Dr Adam Burnel, Chair

Enclosures: "After ethical review – guidance for researchers"
Copy to: Miss Emma Jane Gault
Ms Lorraine Reid, NHS Greater Glasgow and Clyde

Appendix 2.4: Letter of ethical approval (substantial amendment)

WoSRES
West of Scotland Research Ethics Service



West of Scotland REC 3
West of Scotland Research Ethics Service
West Glasgow Ambulatory Care Hospital
(former Royal Hospital for Sick Children Yorkhill)
Dalnair Street
Glasgow G3 8SW
www.nhsggc.org.uk

Professor Jonathan Evans
1055 Great Western Road
Glasgow
G12 0XH

Date 1st June 2016
Your Ref
Our Ref
Direct line 0141 232 1805
E-mail WOSREC3@ggc.scot.nhs.uk

Dear Professor Evans

Study title:	An Investigation of the Utility of the Mini-Addenbrooke's Cognitive Examination (M-ACE) for the Early Detection of Dementia and Mild Cognitive Impairment in People Aged 75 and over.
REC reference:	15/WS/0279
Amendment number:	AM01
Amendment date:	20 May 2016
IRAS project ID:	183123

The above amendment was reviewed by the Sub-Committee in correspondence.

Summary of Amendment

The amendment to the existing protocol is to increase access to potential participants who have a diagnosis of mild cognitive impairment (MCI). In the existing procedure staff have been approaching existing clients on their caseload to ask them if they wish to take part in the study. However clients who receive a diagnosis of MCI are typically discharged back to the care of their GP shortly after diagnosis therefore this has presented a challenge for the recruitment of MCI participants to the project. In the new procedure participants who have recently (within the past 2 months) been a client of one of the recruitment sites, but who have recently been discharged, would be contacted by telephone (by the healthcare professional who provided their care) to ask if they wish to take part in the current study. It is hoped that this will increase the number of participants who have a diagnosis of MCI.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation based on the following:

The Sub-Committee discussed the content of the amendment and had some concerns about 'unannounced' telephone calls and asked that a Participant Information Sheet together with a covering letter of invitation and opt-in/opt-out form be sent to potential

participants who could if they wish send back the opt-in/opt-out form indicating their willingness or otherwise to receive a telephone call. After one week the Investigator would then telephone those patients who had not chosen to send back the opt-in/opt-out form to ask them if they would be willing to take part.

The REC Manager contacted the Investigator who accepted the Sub-Committee's recommendations and submitted an appropriate Participant Information Sheet and Letter of Invitation with an opt-in/opt-out slip for approval by the Sub-Committee.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Letters of invitation to participant [Including Opt-In/Out form]	1	31 May 2016
Notice of Substantial Amendment (non-CTIMP)	AM01	20 May 2016
Other [Email submitting Amendment]		23 May 2016
Participant information sheet (PIS)	4	31 May 2016
Research protocol or project proposal	3.0	12 April 2016

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at <http://www.hra.nhs.uk/hra-training/>

15/WS/0279: Please quote this number on all correspondence

Yours sincerely



Liz Jamieson, REC Manager
On behalf of Dr Adam Burnel, Chair

Enclosures: *List of names and professions of members who took part in the review*

Copy to: *Emma-Jane Gault, NHS Greater Glasgow and Clyde*

West of Scotland REC 3

Sub-Committee of the REC meeting held in Correspondence between 16th May and 27th May 2016

Committee Members involved in the Review:

<i>Name</i>	<i>Profession</i>	<i>Present</i>	<i>Notes</i>
Dr Adam Burnel	Consultant Psychiatrist - Chair	Yes	
Dr Anne-Louise Cunnington	Consultant Geriatrician	Yes	
Mrs Monica Dickson	Retired – Lay Plus Member	Yes	

Also in attendance:

<i>Name</i>	<i>Position (or reason for attending)</i>
Mrs Liz Jamieson	REC Manager

Appendix 2.5: Participant information sheet – for people with a dementia or mild cognitive impairment.



Mental Health & Wellbeing

Gartnavel Royal Hospital

1055 Great Western Road

Glasgow

An Investigation of the Utility of the Mini Addenbrooke's Cognitive Examination (M-ACE) for the Early Detection of Dementia and Mild Cognitive Impairment in People Aged 75 and Over

Information Sheet

[Version 3: 13/11/2015]

I would like to invite you to take part in a research study. Before you decide you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully. If there is anything that is not clear or if you would like more information please contact me. All relevant contact details are at the bottom of this leaflet.

Who is conducting the research?

The research is being carried out by Claire McGuire (Trainee Clinical Psychologist) from the Institute of Mental Health and Wellbeing. I am a postgraduate student at the University of Glasgow and this research is being conducted as part of a Doctorate in Clinical Psychology.

What is the purpose of the study?

The study aims to explore whether the Mini Addenbrooke's Cognitive Examination (M-ACE), a short test of mental ability, is useful in detecting dementia in people aged 75 and over.

Why have I been invited?

You have been invited to take part in this study because you have been given a diagnosis of dementia or mild cognitive impairment and you are aged 75 or over. The study aims to explore the test with people who have a dementia and with people who do not have a dementia and who are aged 75 or over.

Do I have to take part?

No. It is up to you to decide. You will be asked to sign a consent form to show you have agreed to take part. You are free to withdraw at any time, without giving reason. If you do decide to withdraw from the study, this would not affect any care you are receiving. If you do decide to take part, we will, with your permission, let your G.P. know of your test results. This is standard practice in research and will not affect any care you receive from the NHS or your G.P. We will inform your G.P. of test results so that if you require any further assessment of your memory, these results can help inform the assessment.

What does taking part involve?

You will be invited to your nearest clinic or, if appropriate, the researcher can (with your permission) visit you at home. You will only need to attend the clinic (or receive a home visit) once. We are unfortunately unable to pay travel expenses.

Taking part involves one short test which will assess your mental ability. You will also be asked for information about your age, gender, postcode and the number of years of education you have. The amount of time you can expect all this to take is approximately 15 minutes.

The researcher will also require access to previous ACE-III scores held within your medical records.

What happens to the information?

Your identity and personal information will be completely confidential and known only to the researcher, her academic supervisor (Professor Jonathan Evans) and representatives of the study Sponsor, NHS Greater Glasgow & Clyde, who may look at it to make sure the study is being conducted correctly. The information obtained will remain confidential and stored within a locked filing cabinet and on a password protected computer. The data are held in accordance with the Data Protection Act, which means they are kept safely and cannot be revealed to other people, without your permission.

What are the possible benefits of taking part?

Many people find completing these sorts of tests interesting. It is hoped that by taking part you will be providing valuable information regarding how individuals aged 75 and over who are experiencing memory problems should score on the M-ACE. It is hoped that this information will influence further research into the use of short screening tools for detecting dementia.

What are the possible disadvantages and risks of taking part?

Your test results could indicate that your difficulties such as memory have become worse over time. In this instance, additional support can be provided by contacting your healthcare provider who may arrange a review or additional support measures for you. The researcher will be happy to help you with this if required. It will be helpful for your GP to be aware of the results of the tests and therefore if you give your permission we will inform your GP of your test results.

If during the study, the researcher becomes aware that there are any risks of harm to yourself or other people, she will be duty-bound to pass this information on to relevant services, such as social work who may wish to speak with you further about this. Such risks include things like physical abuse and neglect. The researcher would, wherever possible, discuss this with you first, however would still need to pass the information on. This is standard practice and is designed to ensure that you and others are safe and are receiving the right amount of support and care.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by the NHS West of Scotland Research Ethics Committee, Greater Glasgow and Clyde Research and Development Department and the University of Glasgow.

What will happen to the results of the study?

If you would like to know of the overall results and conclusions of the study, the researcher can provide this information to you upon completion of the study.

If you have any further questions?

You will have a copy of the information sheet and signed consent form to keep.

If you would like any general information about participating in research within the NHS, please contact:

Professor Tom McMillan

Director of Research and Professor of Clinical Neuropsychology

Room 213 Level 2

Mental Health and Wellbeing

Gartnaval Royal Hospital

Glasgow G12 0XH

Telephone: 0141 211 0354

If you would like further information about this particular research project please contact Claire McGuire, her academic supervisor Professor Jonathan Evans or her clinical supervisor Dr Stephanie Crawford:

Contacts:

Miss. Claire McGuire

Trainee Clinical Psychologist

Gartnavel Royal Hospital

1055 Great Western Road

G12 0XH

Tel: 0141 211 3920

Professor Jonathan Evans

Professor of Applied Neuropsychology

Gartnavel Royal Hospital

1055 Great Western Road

G12 0XH

Tel: 0141 211 3978

Dr Stephanie Crawford

Clinical Psychologist

Belmont Centre

Stobhill Hospital

300 Balgrayhill Road

[G21 3UR](#)

Tel: [0141 232 6660](tel:01412326660)

If you have a complaint about any aspect of the study?

If you are unhappy about any aspect of the study and wish to make a complaint, please contact the researcher in the first instance. The normal NHS complaint mechanisms are also available to you. For information on our complaints procedures or advice on how to make a complaint:

- phone: 0141 201 4500 (for complaints only)
- email: complaints@ggc.scot.nhs.uk

Thank you for your time

Appendix 2.6: Letter of invitation – for people with a dementia or mild cognitive impairment.



An Investigation of the Utility of the Mini Addenbrooke’s Cognitive Examination (M-ACE) for the Early Detection of Dementia and Mild Cognitive Impairment in People Aged 75 and Over

My name is Claire McGuire and I am a trainee Clinical Psychologist. I would like to invite you to take part in a research study which is exploring whether a short test is able to accurately predict if a person is experiencing problems with their mental ability which may be associated with the early stages of dementia.

The study aims to explore these tests with **people who have a dementia or mild cognitive impairment and with people who do not. All participants will be adults aged 75+.**

Taking part involves short tests of attention, memory and language which will take approximately 5-10 minutes in total. You will be invited to your nearest clinic or, if appropriate, the researcher can (with your permission) visit you at home. You will only need to attend the clinic (or receive a home visit) once.

It is hoped that this information will influence how NHS staff use different tests and information to predict a person’s general functioning when assessing someone who has concerns about their memory.

If you would like further information about this study, please complete the slip below and hand it to your health care worker. The researcher will then be in touch to provide more information to help you decide if you would like to participate.

An Investigation of the Utility of the Mini Addenbrooke’s Cognitive Examination (M-ACE) for the Early Detection of Dementia and Mild Cognitive Impairment in People Aged 75 and Over

I would like to find out more about this study and I can be contacted on the details below by the researcher:

Name: _____

Address: _____

Telephone number: _____

Appendix 2.7: Consent form – for people with a dementia or mild cognitive impairment



Mental Health & Wellbeing

Gartnavel Royal Hospital

1055 Great Western Road

Glasgow

Participant number:

An Investigation of the Utility of the Mini Addenbrooke’s Cognitive Examination (M-ACE) for the Early Detection of Dementia and Mild Cognitive Impairment in People Aged 75 and Over

Consent Form

Please initial box

- | | |
|---|--------------------------|
| I confirm that I have read and understand the information sheet (a) [Version 3: 13/11/2015] for the above study and have had the opportunity to ask questions. | <input type="checkbox"/> |
| I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason. | <input type="checkbox"/> |
| I agree for my G.P. to be informed of my test results. | <input type="checkbox"/> |
| I consent for my G.P. and any other relevant health and social care professionals to be contacted in the event of any concerns raised about risk of harm to myself or others. | <input type="checkbox"/> |
| I agree that representatives of the study Sponsor, NHS Greater Glasgow and Clyde, may look at my information for audit purposes. | <input type="checkbox"/> |
| If I have completed the ACE-III test (Addenbrooke’s Cognitive Examination III) in the last 6 months, I give permission for this result to be released and used in this study. | <input type="checkbox"/> |

I agree to take part in the above study.



Name of participant: _____ Date: _____

Signature: _____

Name of person taking consent: _____ Date: _____

Signature: _____

1 copy to the participant, 1 copy to the researcher

Appendix 2.8: Participant information sheet – for controls.



Mental Health & Wellbeing

Gartnavel Royal Hospital

1055 Great Western Road

Glasgow

An Investigation of the Utility of the Mini Addenbrooke's Cognitive Examination (M-ACE) for the Early Detection of Dementia and Mild Cognitive Impairment in People Aged 75 and Over

Information Sheet

[Version 3: 13/11/2015]

I would like to invite you to take part in a research study. Before you decide you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully. If there is anything that is not clear or if you would like more information please contact me. All relevant contact details are at the bottom of this leaflet.

Who is conducting the research?

The research is being carried out by Claire McGuire (Trainee Clinical Psychologist) from the Institute of Mental Health and Wellbeing. I am a postgraduate student at the University of Glasgow and this research is being conducted as part of a Doctorate in Clinical Psychology.

What is the purpose of the study?

The study aims to explore whether the Mini Addenbrooke's Cognitive Examination (M-ACE), a short test of mental ability, is useful in detecting dementia in people aged 75 and over.

Why have I been invited?

You have been invited to take part in this study because you are an adult aged 75+ who does not have a diagnosis of dementia. The study aims to explore these tests with people who have a dementia and with people who do not have a dementia and who are aged 75 and over.

Do I have to take part?

No. It is up to you to decide. You will be asked to sign a consent form to show you have agreed to take part. You are free to withdraw at any time, without giving reason. If you do decide to withdraw from the study, this would not affect any care you receive. If you do decide to take part, we will, with your permission, let your G.P. know of your test results. This is standard practice in research and will not affect any care you receive from the NHS or your G.P. We will inform your G.P. of test results so that if you require any future assessment of your memory, these results can help inform the assessment.

What does taking part involve?

You will be invited to your nearest clinic or, if appropriate, the researcher can (with your permission) visit you at home. You will only need to attend the clinic (or receive a home visit) once. We are unfortunately unable to pay travel expenses.

Taking part involves one short test which will assess your mental ability. You will also be asked for information about your age, gender, postcode and the number of years of education you have. The amount of time you can expect all this to take is approximately 15 minutes.

What happens to the information?

Your identity and personal information will be completely confidential and known only to the researcher, her academic supervisor (Professor Jonathan Evans) and representatives of the study Sponsor, NHS Greater Glasgow & Clyde, who may look at it to make sure the study is being conducted correctly. The information obtained will remain confidential and stored within a locked filing cabinet and on a password protected computer. The data are held in accordance with the Data Protection Act, which means they are kept safely and cannot be revealed to other people, without your permission.

What are the possible benefits of taking part?

Many people find completing these sorts of tests interesting. It is hoped that by taking part you will be providing valuable information regarding how individuals aged 75 should score on the M-ACE. It is hoped that this information will influence further research into the use of short screening tools for detecting dementia.

What are the possible disadvantages and risks of taking part?

There is the possibility that completing these tests might raise concerns for you about some of your abilities, such as memory. Whilst this test does not diagnose dementia, it can indicate areas which are becoming problematic. If your score on the test is lower than expected, with your permission we can inform your GP and you would then be able to discuss options for further assessment.

If during the study, the researcher becomes aware that there are any risks of harm to yourself or other people, she will be duty-bound to pass this information on to relevant services, such as social work who may wish to speak with you further about this. Such risks include things like physical abuse and neglect. The researcher would, wherever possible, discuss this with you first, however would still need to pass the information on. This is standard practice and is designed to ensure that you and others are safe and are receiving the right amount of support and care.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by the NHS West of Scotland Research Ethics Committee, Greater Glasgow and Clyde Research and Development Department and the University of Glasgow.

What will happen to the results of the study?

If you would like to know of the overall results and conclusions of the study, the researcher can provide this information to you upon completion of the study.

If you have any further questions?

You will have a copy of the information sheet and signed consent form to keep. If you would like any general information about participating in research within the NHS, please contact:

Professor Tom McMillan

Director of Research and Professor of Clinical Neuropsychology

Room 213 Level 2

Mental Health and Wellbeing

Gartnaval Royal Hospital

Glasgow G12 0XH

Telephone: 0141 211 0354

If you would like further information about this particular research project please contact Claire McGuire or her clinical supervisor Dr Stephanie Crawford:

Contacts:

Miss Claire McGuire

Trainee Clinical Psychologist

Gartnavel Royal Hospital

1055 Great Western Road

G12 0XH

Tel: 0141 211 3920

Professor Jonathan Evans

Professor of Applied Neuropsychology

Gartnavel Royal Hospital

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Dr Stephanie Crawford

Clinical Psychologist

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300 Balgrayhill Road

[G21 3UR](#)

Tel: [0141 232 6660](tel:01412326660)

If you have a complaint about any aspect of the study?

If you are unhappy about any aspect of the study and wish to make a complaint, please contact the researcher in the first instance. The normal NHS complaint mechanisms are also available to you. For information on our complaints procedures or advice on how to make a complaint:

- phone: 0141 201 4500 (for complaints only)
- email: complaints@ggc.scot.nhs.uk

Thank you for your time

Appendix 2.9: Letter of invitation – for control participants.



An Investigation of the Utility of the Mini Addenbrooke’s Cognitive Examination (M-ACE) for the Early Detection of Dementia and Mild Cognitive Impairment in People Aged 75 and Over

My name is Claire McGuire and I am a trainee Clinical Psychologist. I would like to invite you to take part in a research study which is exploring whether a short test is able to accurately predict if a person is experiencing problems with their mental ability which may be associated with the early stages of dementia

The study aims to explore these tests with **people who have a dementia or mild cognitive impairment and with people who do not. All participants will be adults aged 75+.**

Taking part involves short tests of attention, memory and language which will take approximately 5-10 minutes in total. You will be invited to your nearest clinic or, if appropriate, the researcher can (with your permission) visit you at home. You will only need to attend the clinic (or receive a home visit) once.

It is hoped that this information will influence how NHS staff use different tests and information to predict a person’s general functioning when assessing someone who has concerns about their memory.

If you would like further information about this study, please complete the slip below and hand it to your health care worker. The researcher will then be in touch to provide more information to help you decide if you would like to participate.

An Investigation of the Utility of the Mini Addenbrooke’s Cognitive Examination (M-ACE) for the Early Detection of Dementia and Mild Cognitive Impairment in People Aged 75 and Over

I would like to find out more about this study and I can be contacted on the details below by the researcher:

Name: _____

Address: _____

Telephone number: _____

Appendix 2.10: Consent form – for control participants



Mental Health & Wellbeing

Gartnavel Royal Hospital

1055 Great Western Road

Glasgow

An Investigation of the Utility of the Mini Addenbrooke's Cognitive Examination (M-ACE) for the Early Detection of Dementia and Mild Cognitive Impairment in People Aged 75 and Over

Consent Form

Participant number:

Please initial box

I confirm that I have read and understand the information sheet (b) [Version 3: 13/11/2015] for the above study and have had the opportunity to ask questions.

I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason.

I agree for my G.P. to be informed of my test results.

I consent for my G.P. and any other relevant health and social care professionals to be contacted in the event of any concerns raised about risk of harm to myself or others.

I agree that representatives of the study Sponsor, NHS Greater Glasgow and Clyde, may look at my information for audit purposes.

I agree to take part in the above study.

Name of participant: _____ Date: _____

Signature: _____

Name of person taking consent: _____ Date: _____

Signature: _____

1 copy to the participant, 1 copy to the researcher

Appendix 2.11: Information sheet for people with an MCI



Mental Health & Wellbeing

Gartnavel Royal Hospital

1055 Great Western Road

Glasgow

An Investigation of the Utility of the Mini Addenbrooke's Cognitive Examination (M-ACE) for the Early Detection of Dementia and Mild Cognitive Impairment in People Aged 75 and Over

Information Sheet

[Version 4: 31/05/2016]

I would like to invite you to take part in a research study. Before you decide you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully. If there is anything that is not clear or if you would like more information please contact me. All relevant contact details are at the bottom of this leaflet.

Who is conducting the research?

The research is being carried out by Claire McGuire (Trainee Clinical Psychologist) from the Institute of Mental Health and Wellbeing. I am a postgraduate student at the University of Glasgow and this research is being conducted as part of a Doctorate in Clinical Psychology.

What is the purpose of the study?

The study aims to explore whether the Mini Addenbrooke's Cognitive Examination (M-ACE), a short test of mental ability, is useful in detecting dementia and mild cognitive impairment in people aged 75 and over.

Why have I been invited?

You are being invited to take part in this study because you have been given a diagnosis of mild cognitive impairment and you are aged 75 or over. The study aims to explore the test with people who have a dementia or mild cognitive impairment and with people who do not have either of these diagnoses and who are aged 75 or over.

Do I have to take part?

No. It is up to you to decide. **The clinician who provides your care will contact you within the next few days to further discuss the project with you. There is also an opt-in/opt-out sheet included with this information sheet which you can post to your clinician indicating if you wish to be contacted about the study.** You will be asked to sign a consent form to show you have agreed to take part. You are free to withdraw at any time, without giving reason. If you do decide to withdraw from the study, this would not affect any care you are receiving. If you do decide to take part, we will, with your permission, let your G.P. know of your test results. This is standard practice in research and will not affect any care you receive from the NHS or your G.P. We will inform your G.P. of test results so that if you require any further assessment of your memory, these results can help inform the assessment.

What does taking part involve?

You will be invited to your nearest clinic or, if appropriate, the researcher can (with your permission) visit you at home. You will only need to attend the clinic (or receive a home visit) once. We are unfortunately unable to pay travel expenses.

Taking part involves one short test which will assess your mental ability. You will also be asked for information about your age, gender, postcode and the number of years of education you have. The amount of time you can expect all this to take is approximately 15 minutes.

The researcher will also require access to previous ACE-III scores held within your medical records.

What happens to the information?

Your identity and personal information will be completely confidential and known only to the researcher, her academic supervisor (Professor Jonathan Evans) and representatives of the

study Sponsor, NHS Greater Glasgow & Clyde, who may look at it to make sure the study is being conducted correctly. The information obtained will remain confidential and stored within a locked filing cabinet and on a password protected computer. The data are held in accordance with the Data Protection Act, which means they are kept safely and cannot be revealed to other people, without your permission.

What are the possible benefits of taking part?

Many people find completing these sorts of tests interesting. It is hoped that by taking part you will be providing valuable information regarding how individuals aged 75 and over who are experiencing memory problems should score on the M-ACE. It is hoped that this information will influence further research into the use of short screening tools for detecting dementia.

What are the possible disadvantages and risks of taking part?

Your test results could indicate that your difficulties such as memory have become worse over time. In this instance, additional support can be provided by contacting your healthcare provider who may arrange a review or additional support measures for you. The researcher will be happy to help you with this if required. It will be helpful for your GP to be aware of the results of the tests and therefore if you give your permission we will inform your GP of your test results.

If during the study, the researcher becomes aware that there are any risks of harm to yourself or other people, she will be duty-bound to pass this information on to relevant services, such as social work who may wish to speak with you further about this. Such risks include things like physical abuse and neglect. The researcher would, wherever possible, discuss this with you first, however would still need to pass the information on. This is standard practice and is designed to ensure that you and others are safe and are receiving the right amount of support and care.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by the NHS West of Scotland Research Ethics Committee, Greater Glasgow and Clyde Research and Development Department and the University of Glasgow.

What will happen to the results of the study?

If you would like to know of the overall results and conclusions of the study, the researcher can provide this information to you upon completion of the study.

If you have any further questions?

You will have a copy of the information sheet and signed consent form to keep.

If you would like any general information about participating in research within the NHS, please contact:

Professor Tom McMillan

Director of Research and Professor of Clinical Neuropsychology

Room 213 Level 2

Mental Health and Wellbeing

Gartnavel Royal Hospital

Glasgow G12 0XH

Telephone: 0141 211 0354

If you would like further information about this particular research project please contact Claire McGuire, her academic supervisor Professor Jonathan Evans or her clinical supervisor Dr Stephanie Crawford:

Contacts:

Miss. Claire McGuire

Trainee Clinical Psychologist

Gartnavel Royal Hospital

1055 Great Western Road

G12 0XH

Tel: 0141 211 3920

Professor Jonathan Evans

Professor of Applied Neuropsychology
Gartnavel Royal Hospital
1055 Great Western Road
G12 0XH
Tel: 0141 211 3978

Dr Stephanie Crawford

Clinical Psychologist
Belmont Centre
Stobhill Hospital
300 Balgrayhill Road
[G21 3UR](#)
Tel: [0141 232 6660](tel:01412326660)

If you have a complaint about any aspect of the study?

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- phone: 0141 201 4500 (for complaints only)
- email: [**complaints@ggc.scot.nhs.uk**](mailto:complaints@ggc.scot.nhs.uk)

Thank you for your time

Appendix 2.12: Opt-in/Opt-out letter for people with an MCI



An Investigation of the Utility of the Mini Addenbrooke's Cognitive Examination (M-ACE) for the Early Detection of Dementia and Mild Cognitive Impairment in People Aged 75 and Over

My name is Claire McGuire and I am a trainee Clinical Psychologist. I would like to invite you to take part in a research study which is exploring whether a short test is able to accurately predict if a person is experiencing problems with their mental ability which may be associated with the early stages of dementia.

The study aims to explore these tests with **people who have a dementia or mild cognitive impairment and with people who do not. All participants will be adults aged 75+.**

Taking part involves short tests of attention, memory and language which will take approximately 5-10 minutes in total. You will be invited to your nearest clinic or, if appropriate, the researcher can (with your permission) visit you at home. You will only need to attend the clinic (or receive a home visit) once.

It is hoped that this information will influence how NHS staff use different tests and information to predict a person's general functioning when assessing someone who has concerns about their memory.

Your clinician will contact you about this study within the next few days. If you would like to indicate that you wish to take part or that you do not wish to take part please complete the opt-in/opt-out slip below and send to your clinician.

An Investigation of the Utility of the Mini Addenbrooke's Cognitive Examination (M-ACE) for the Early Detection of Dementia and Mild Cognitive Impairment in People Aged 75 and Over

I wish/do not wish to be contacted regarding the above named study.

Name: _____

Address: _____

Telephone number: _____