Copyright is owned by the Author of the thesis. Permission is given for a copy to be downloaded by an individual for the purpose of research and private study only. The thesis may not be reproduced elsewhere without the permission of the Author.

# Brief Cognitive Screening Instruments and the Clinical Utility of Three Screens in a New Zealand Clinical Geriatric Setting

A thesis presented in partial fulfilment of the requirements for the degree of

Doctorate in

Clinical Psychology

at Massey University, Wellington, New Zealand.

Heide-Marie Strauss 2012

### **Abstract**

Cognitive impairment (CI) is a serious concern for an aging global population, and its impact is not only felt within the family unit but also society at large.

The current thesis involved two studies – an online survey about the use and role of screening instruments in New Zealand, and an evaluation of the clinical utility of three screens used in a clinical geriatric setting.

The survey found that the Mini Mental Status Examination (MMSE) was the most frequently used screen, followed by the Clock Drawing Test (CDT), Addenbrooke's Cognitive Examination-Revised (ACE-R), Verbal Fluency (FAS), Three Word Recall (3WR), and Trail-making Test (TMT). The opinions of the survey respondents confirmed international publications suggesting that the MMSE does not fulfil the requirements of current assessment and/or screening practices. The survey further suggested that the ACE-R showed promise as an appropriate alternative to the MMSE due to its continuity from the MMSE, and because it appears to meet clinician requirements for brief screening instruments.

The second study evaluated the clinical utility of the ACE-R, MMSE and the Modified Mini Mental State (3MS) within a larger assessment approach. It found that all three screens successfully differentiated between milder forms of CI and dementia; however, predictive ability for milder CI could not be determined. The ACE-R outperformed both the 3MS and MMSE in terms of predictive ability for dementia, with the 3MS showing marginally higher predictive ability than the MMSE. The study suggested that the 3MS's incremental validity did not justify its inclusion in a routine assessment process.

Optimal sensitivity and specificity ratios – providing the best balance between sensitivity and specificity – were obtained with different cut-off scores than those recommended by the screens' original publications. This may have been due to the screens' authors seeking ratios that favoured sensitivity at the cost of specificity. However, in the data set from a clinical geriatric setting, used for this current study, the focus was on limiting both false-negatives and false-positives. While the MMSE

showed adequate sensitivity and specificity, its known cultural and socio-economic bias makes it inappropriate for widespread use.

The predictive ability (and incremental validity) of the ACE-R, coupled with the fact that it is cost-effective, relatively brief and covers all the recommended cognitive domains suggest that it is a suitable substitute for the MMSE in clinical geriatric service settings. Further research is however required to assess any potential biases inherent in the ACE-R. It is recommended that all initial assessments with CI patients include a mood screen due to their high comorbidity and the increased scope of treatment options available when a mood component underlies cognitive complaints.

## Acknowledgements

First and foremost, I would like to thank my primary supervisor, Professor Janet Leathem for her guidance and unwavering support throughout the research process. Our numerous brainstorming sessions, your continuous encouragement, and the tissues and hugs you so readily offered during times of struggle were invaluable and very much appreciated. Your patience, good humour, and caring certainly made all the difference in facilitating the completion of this project.

Thank you to Dr Steve Humphries, who provided guidance with questionnaire design, statistical analyses and interpretation. I appreciate your help with the SPSS software and the often step-by-step guidance in performing analyses.

I am very grateful to Dr Crawford Duncan (Psycho-geriatrician) who provided not only expert advice, but granted me access to his clinical database containing test scores of patients spanning at least 7 years. Thank you so much for all the help you provided and the work you put in to transform the data of thousands of people into a user-friendly format that helped me focus on the research questions at hand.

I also want to thank the anonymous patients in the database. While I never met you, your scores formed the basis of the second study, and in my mind, the core of the project as a whole. Likewise, a big thank you to the geriatricians, neurologists, geriatric psychiatrists, and psychologists who participated in the first study. Thank you for your honest comments and ratings in the survey.

To my family, my heartfelt thanks and appreciation for your love, understanding, and support. This thesis was very much a team effort with my parents' constant support and encouragement, and the chats and beers with my brother Werner. Thanks team.

I dedicate this to my parents, Dawie and Annette Strauss.

The Massey University Human Ethics Committee (MUHEC) granted approval to conduct the survey nationwide, and the Health and Disability Ethics Committees (HDEC), and Central Regional Ethics Committee granted ethical approval for the second (ACE-R) study.

# **Table of Contents**

Abstract	1
Acknowledgements	3
Table of Contents	5
List of Tables and Figures	7
Chapter: 1 Overview	9
Chapter 2: Age-related cognitive impairment and dementia	
2.1 Defining dementia	12
2.1.1 The shifting view of dementia	16
2.1.2 Mild cognitive impairment (MCI)	18
2.2.1 Prevalence, societal cost and effects of cognitive impairment	19
2.2.2 Effects of dementia – quality of life, impact on families & society	21
2.2.3 Increased need for services	22
2.3. The neuropsychology of cognitive impairment	23
2.3.1 Cognitive changes associated with normal aging	23
2.3.2 Alzheimer's disease	23
2.3.3 Vascular dementia	24
2.3.4 Fronto-temporal dementia	25
2.3.5 MCI	25
2.4 Summary	26
Chapter 3: Assessment and Screening in Cognitive Impairment	27
3.1. Introduction	27
3.2. The assessment and screening of CI	27
3.2.1. Cultural issues	30
3.2.2. Validity & reliability issues	31
3.3. An overview of CI screening instruments	33
3.4. Conclusion	41
Chapter 4: The use of brief cognitive screening instruments in New Zealand	
Preface	
Abstract	11

Introduction	45
Method	47
Participant recruitment	47
The questionnaire	48
Results	49
Participant characteristics	49
Cognitive screens	50
Discussion	57
References	61
Chapter 5: The clinical utility of the ACE-R, 3MS, and MMSE in Zealand geriatric clinical setting	
Preface	
Abstract	
Introduction	
Method	76
Screen description	76
Participants	77
Statistical analysis	79
Results	79
ACE-R, 3MS, and MMSE total scores	79
ACE-R subdomain scores	82
ROC analyses	85
Discussion	88
References	92
Chapter 6: Conclusion	97
6.1 Overall summary	
6.2 Implications	
6.3 Future research	101
6.4 Concluding comments and recommendations	101
References	103

# **List of Tables and Figures**

Chapter 2: A	Age-related cognitive impairment and dementia	
Table 2.1:	DSM-IV-TR diagnostic criteria for dementia of Alzheimer's	
	type1	4
Table 2.2:	Vascular dementia (formerly multi-infarct dementia)	.5
Table 2.3:	The original 1999 Petersen criteria for MCI1	8
Table 2.4:	Updated Mayo Clinic criteria for MCI	8
Figure 2.1:	MCI types and subtypes	19
Table 2.5:	Prevalence of dementia in New Zealand in 1983	:1
Chapter 3: A	Assessment and Screening in CI	
Table 3.1:	Overview of brief cognitive impairment screens32	1
Chapter 4:	The use of brief cognitive screening instruments in New Zealand	
Table 1:	Participant characteristics and response rate according to	
	professional discipline (N=82)	50
Table 2:	Screening instruments most frequently used for cognitive	
	impairment	52
Figure 1:	Frequency of use for screening measures	6
Chapter 5:	The Clinical Utility of the ACE-R versus the MMSE and 3MS: A	
retrospectiv	e New Zealand study	
Table 1:	Research studies examining the clinical utility of the ACE,	
	ACE-R, MMSE and 3MS for detecting dementia7	4
Table 2:	Clinical comparison of the ACE-R, 3MS, and MMSE total	
	scores for the three diagnostic groups	31
Table 3:	Clinical comparison of the ACE-R subdomain scores for the	
	three diagnostic groups	84
Figure 1:	Receiver Operating Characteristic Curve of the ACE-R, 3MS,	
	and MMSE as a function of sensitivity and specificity at identifyin	g
	dementia (N = 196)	86
Table 4:	Area Under the Curve statistics for the ACE-R, 3MS, and MMSE	
	(N=196)	37

Table 5:	Optimal cut-off scores and associated sensitivity and specificity	
	for the ACE-R, 3MS, and MMSE.	88
Appendices		
APPENDIX I	: Survey Information Sheet	
APPENDIX I	I: Survey Questionnaire	

## Chapter 1

#### Overview

The topic of the present study grew out of an interest in neuropsychology, cognitive psychology, and the psychological wellbeing of older adults, and, most importantly, an expressed need for research in the area of cognitive screening.

More specifically, the Psychology Clinic, Massey University Wellington, had received requests for research from clinicians in psychiatry and neurology who questioned the validity of the Mini-Mental State Exam (MMSE) – a widely used screening instrument for cognitive function. They had noted a gap in New Zealand-based research regarding appropriate and robust screens for the New Zealand context that could replace the MMSE as the industry standard.

Initial ideas for research involved the use of screens with a number of populations, namely Electroconvulsive Therapy patients, dementia patients, and other neurological disorders. However, as the study evolved it was decided to narrow the scope to focus on cognitive screening with older adults who presented to geriatric services with cognitive impairment (CI) complaints.

An initial literature review confirmed the need for research in the field of age-related cognitive decline and dementia, as the ratio of older people, and incidence of dementia-related disorders, were increasing without a corresponding increase in clinical services (including assessment) and support provision.

The first step in investigating CI screens in the New Zealand context was to determine the current status quo and role of screening measures in clinical assessment, how they were used, and what clinicians required of screens in clinical practice, by means of a survey. This first step further provided guidance in choosing which screens to assess in terms of psychometric properties and clinical utility.

As expected, the survey indicated that the MMSE was the most frequently used screen, despite a significant number of participants commenting that it was

inadequate. Their sentiments were echoed in a large body of research literature that found the MMSE to be biased according to gender, culture, and other sociodemographic variables.

An extensive literature review further suggested that the continued use of the MMSE was not in keeping with a global shift towards viewing dementia as part of a continuum, and an increased emphasis on milder forms of impairment. The shift of focus from dementia to mild cognitive impairment (MCI) also reflected a worldwide move to reduce the rate of dementia onset by addressing MCI. The MMSE, not being sensitive to MCI, was therefore deemed inadequate when measured against current requirements.

The next step involved selecting appropriate screens for evaluation and comparison against the MMSE. The first measure chosen was the Addenbrooke's Cognitive Examination-Revised (ACE-R), as it was well-known according to the survey respondents. It includes the top five most frequently used screens (including the MMSE) and according to the survey, it met clinicians' criteria for an ideal screen. Moreover, a significant number of clinicians had received training in its administration. Despite it being frequently used, the ACE-R had not been studied in a New Zealand clinical setting, and it would therefore be of benefit to New Zealand clinicians and their patients to examine its clinical utility.

We were fortunate in gaining access to an existing clinical database, created and maintained by Dr Crawford Duncan, psychogeriatrician at Te Whare Ra Uta, Inpatient Psychogeriatric assessment unit at Kenepuru Hospital, Wellington, New Zealand, which provided test score data of patients spanning a number of years. In addition to the ACE-R and MMSE, the available data also included test scores on another measure, the Modified Mini Mental State Exam (3MS), and the study design was adapted to include the 3MS in the analyses.

The aim of the second study was amended to evaluate the clinical utility of the ACE-R, 3MS, and the MMSE as part of a wider, comprehensive assessment approach in initial assessments with individuals presenting with cognitive complaints.

#### Thesis outline

The thesis comprises two studies, a survey investigating the use and role of screening measures for CI in New Zealand, and a retrospective study examining the clinical utility of the ACE-R, the 3MS, and the MMSE. These two studies are presented as journal article manuscripts that have been submitted for consideration for publication.

The two studies are preceded by introductory chapters, the first (Chapter 2) covers the conceptualisation, prevalence, societal impact, and neuropsychology of CI. The second (Chapter 3), provides an overview of issues in assessment and screening of CI and includes a discussion of pertinent ethical concerns, cultural issues, validity and reliability, and an overview of published screening measures.

The thesis is concluded with an overall discussion chapter, and followed by the reference list and appendices including the web-based survey questionnaire, and copies of the ACE-R, 3MS, and MMSE questionnaires.

## Chapter 2

# Age-related cognitive impairment and dementia

### 2.1 Defining dementia

Dementia generally refers to the deterioration of mental function that is beyond that which would be expected during the course of normal aging. It is mostly used as an umbrella term for the syndrome of cognitive symptoms associated with a variety of disorders, including Alzheimer's disease, Korsakoff's syndrome, and HIV/AIDS-related cognitive impairment.

Dementia traditionally suggested a general mental deterioration (Davidoff, 1986), which reflected the long-established understanding of dementia as a unitary syndrome irrespective of the particular brain pathology involved (Bak & Mioshi, 2007). However, published clinical observations and research over time revealed variable rates of deterioration in specific cognitive domains such as memory, language, visuospatial ability and executive function, depending on the particular disorder (Lezak, Howieson, & Loring, 2004). In most cases, the causal factors in dementia also vary according to the particular underlying disorder. For example in vascular dementia (VaD), lifestyle factors such as high cholesterol diets and smoking are risk factors associated with hypertension, which in turn increases the risk of developing vascular dementia (Whitmer, Sidney, Selby, et al., 2005). In contrast, having a parent with late-onset Alzheimer's disease (AD) significantly increases one's risk of developing this particular disorder (Berti, Mosconi, Glodzik, et al., 2011).

The complexity of AD causality is compounded by the fact that neocortical or senile plaques, one of the traditional hallmarks of AD, have been found in cognitively intact individuals (Crystal, Dickson, Fuld, et al., 1988; Katzman, Terry, DeTeresa, et al., 1988). This suggests that these neurological phenomena are not as necessary and/or sufficient criteria for AD as previously believed (Morris, Storandt, McKeel, et al., 1996). Added to the confusion of what dementia involves and how it is caused, the term dementia refers to both stable (such as caused by anoxia) and progressive disorders (such as AD) (Davidoff, 1986), and while there is a strong correlation

between age and progressive dementias (Gao et al., 1998; Kukull & Ganguli, 2000), age does not necessarily cause dementia.

Yet a further complication arises due to the overlap of affected areas and associated cognitive difficulties in normal aging, cognitive impairment, and dementia. Certain brain areas atrophy at different rates and stages and this provides a very useful diagnostic tool for the differentiation between normal and abnormal function. For example, the entorhinal cortex and hippocampus are the first areas to show impairment indicative of AD (Atriya, et al., 2003). However, the strong correlation between AD and normal aging means that individuals diagnosed with AD would most likely have undergone the characteristic brain changes associated with normal aging as well.

Furthering the debate as to what constitutes dementia, a number of problems arise with the diagnostic criteria for the disorder. First, the DSM-IV-TR definition (see Tables 1 & 2) involves significant impairment in social and occupational functioning regardless of the level of cognitive function, and this ignores those who were functioning at a higher level previously, and have suffered functional impairment despite their current function being at comparably average levels (Knopman & Selnes, 2003). A related problem involves the subjective clinical judgement required in differentiating 'significant' from subclinical impairment of function. Third, the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) and National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria are somewhat Alzheimer-centric in their requirement of memory impairment for diagnosis (Knopman & Selnes, 2003).

As dementia involves multiple domains, a more general definition of dementia may be more appropriate, such as that suggested by Cummings and Benson (1992), whose criteria requires impairment in 3 of 5 major domains (namely memory, language, executive, visuospatial, and affective-personality) (Knopman & Selnes, 2003). The lack of widely accepted, objective and quantifiable diagnostic criteria may have, in part, contributed to the development of a number of assessment tools (reviewed in Ch. 3).

- A. The development of multiple cognitive deficits manifested by both
  - 1. Memory impairment (impaired ability to learn new information or to recall previously learned information)
  - 2. One (or more) of the following cognitive disturbances:
    - a. Aphasia (language disorder)
    - Apraxia (impaired ability to carry out motor activities despite intact motor function)
    - c. Agnosia (failure to recognise or identify objects despite intact sensory function)
    - d. Disturbance in executive functioning (i.e. planning, organising, sequencing, abstracting)
- B. The cognitive deficits in Criteria A1 and A2 each cause significant impairment in social or occupational functioning and represent a significant decline from a previous level of functioning.
- C. The course is characterised by gradual onset and continuing cognitive decline.
- D. The cognitive deficits in Criteria A1 and A2 are not due to any of the following:
  - Other central nervous system conditions that cause progressive deficits in memory and cognition (e.g., cerebrovascular disease, Parkinson's disease, Huntington's disease, subdural hematoma, normal-pressure hydrocephalus, brain tumour).
  - Systemic conditions that are known to cause dementia (e.g. hypothyroidism, vitamin B12 or folic acid deficiency, niacin deficiency, hypercalcemia, neurosyphilis, HIV infection)
  - 3. Substance-induced conditions.
- E. The deficits do not occur exclusively during the course of a delirium.
- F. The disturbance is not better accounted for by another Axis I disorder (i.e. Major Depressive Disorder, Schizophrenia.

(American Psychiatric Association, 2000)

- A. The development of multiple cognitive deficits manifested by both
  - 1. Memory impairment (impaired ability to learn new information or to recall previously learned information)
  - 2. One (or more) of the following cognitive disturbances:
    - a. Aphasia (language disorder)
    - b. Apraxia (impaired ability to carry out motor activities despite intact motor function)
    - c. Agnosia (failure to recognise or identify objects despite intact sensory function)
    - d. Disturbance in executive functioning (i.e. planning, organising, sequencing, abstracting)
- B. The cognitive deficits in Criteria A1 and A2 each cause significant impairment in social or occupational functioning and represent a significant decline from a previous level of functioning.
- C. Focal neurological signs and symptoms (e.g. exaggeration of deep tendon reflexes, extensor plantar response, pseudobulbar palsy, gait abnormalities, weakness of an extremity) or laboratory evidence of cerebrovascular disease (e.g. multiple infarctions involving cortex and underlying white matter) that are judged to be etiologically related to the disturbance.
- D. The deficits do not occur exclusively during a course of a delirium.

(American Psychiatric Association, 2000)

One difficulty with dementia as it is currently conceptualised, is that the diagnosis constitutes 'the end of the road' with no chance of recovery. Once symptoms are 'significant' enough to warrant a dementia diagnosis, little can be done aside from providing appropriate supports and environmental adaptations. A diagnosis of mild cognitive impairment (MCI) on the other hand, while requiring a significant level of cognitive impairment from a patient's subjective perspective, does not require significant impairment in activities of daily living. It therefore constitutes a diagnosis that holds potential for treatment options, and allows for some hope tempered with realistic information regarding risk of conversion to dementia. MCI as a clinical

diagnostic entity has grown over time (Roberts, Karlawish, Uhlmann, et al., 2010) and has been further validated in a number of studies (Peterson, 2004; Snyder, Jackson, Petersen, et al., 2011).

The National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (now known as the Alzheimer's Association) (NINCDS-ADRDA) criteria were recently reviewed by McKhann, Knopman, Chertkow, et al. (2011) in an effort to address the complexities of AD dementia criteria; they proposed new classification criteria for "all-cause dementia" (McKhann, Knopman, Chertkow, et al., 2011, p 3), AD dementia, probable AD dementia, possible AD dementia, probable and possible AD dementia with evidence of the AD pathophysiological process, pathophysiologically proved AD dementia, and dementia unlikely to be due to AD (McKhann, Knopman, Chertkow, et al., 2011). The current change in defining dementia types, criteria and diagnoses continues with the proposed DSM-IV diagnostic criteria.

There are no DSM-IV-TR diagnostic criteria for MCI; however, it is proposed to be encapsulated in the forthcoming DSM-V's Mild Neurocognitive Disorder. The Dementia category is also to be renamed Neurocognitive disorders, which will include Delirium, Mild Neurocognitive Disorders, and Major Neurocognitive Disorders. Mild and major neurocognitive disorders will in turn consist of the specific neurocognitive disorders associated with AD, vascular disease, frontotemporal lobar degeneration, traumatic brain injury, Lewy body disease, Parkinson's disease, HIV infection, substance use, Huntington's disease, and Prion disease (www.dsm5.org, 2011).

#### 2.1.1 The shifting view of dementia

Hachinski (2008) questioned the validity of the concept of dementia, stating that the dichotomy between dementia and non-dementia fails to capture the spectrum of cognitive function and impairment as it presents in the real world. *Dementia* as a concept has evolved over hundreds of years, ranging from being viewed as a normal side-effect of aging in the Classical era, denoting demonic possession during the Middle Ages, and more recently, being viewed through the lens of Alzheimer's disease and its traditionally associated amyloid plaques (Bak & Mioshi, 2007).

While lay people tend to equate dementia with AD and the work of Alois Alzheimer, cognitive impairment, dementia, or 'senility' is a much wider phenomenon. Until recently, most cases of dementia were viewed as either vascular or AD, however new studies show that most cases of late-onset dementia involve a mixture of cerebrovascular and AD-type brain lesions (Fotuhi, Hachinski, & Whitehouse, 2009). Cognitive impairment affects different cognitive domains, at widely varying rates, and with heterogenous causal factors. Current definitions of dementia do not account for this variability.

The formulation of a clinical stage between 'non-demented' and 'demented' represents a shift from viewing cognitive function in dichotomous terms towards a continuum of cognitive function/impairment. Similar to the "aging-disease continuum", which proposed that differences between normal aging and dementia are quantitative rather than qualitative (Morris et al., 1996; Von Dras & Blumenthal, 1992), the emerging continuum model of cognitive impairment proposes subclinical cognitive impairment related to normal aging processes at one end, dementia at the other, and mild cognitive impairment towards the middle (Hachinski, 2008). While being more conceptually valid, the continuum model poses further difficulties for diagnoses and research that remain based on distinct categories like dementia versus healthy, and MCI versus AD. For example, screening tools traditionally provided a yes/no result for the possible presence of dementia. Clinicians who work from a continuum perspective would require more from screens, such as norms and appropriate cut-off scores for each "pit stop" on the continuum. These pit stops should reflect normal aging, MCI, and dementia, and possibly another significant cause of cognitive impairment, namely mood disorders (Schatzberg, 2002). The relationship between depressive disorders and cognitive impairment is however complex and controversial, with heterogenous findings across studies suggesting a correlation that is not necessarily causative (McClintock, Husain, Greer, & Cullum, 2010).

There are a number of advantages in the shift towards a continuum view of cognitive impairment (CI). An increased rate of detecting early stages of impairment would enhance clinical intervention and greatly improve quality of living and health outcomes (Hachinski, 2008; Alzheimers New Zealand, 2008). Specifically, a

diagnosis of MCI for example, may facilitate patients' motivation to minimise risk factors of developing dementia, and would facilitate therapeutic intervention (including memory training strategies) rather than purely management strategies when treatment is too late.

### 2.1.2 Mild cognitive impairment (MCI)

The original conceptualisation of MCI, as proposed by Petersen and colleagues from the Mayo Clinic, emphasised MCI as a prodromal condition for AD (Petersen, Roberts, Knopman et al., 2009), with their original diagnostic criteria focusing on memory impairment (Table 3). However, not all cases of MCI developed into AD, and the criteria were updated to reflect this (see Table 4). Two types of MCI were subsequently delineated, namely amnestic (referring to a presentation of memory impairment) and nonamnestic (referring to no memory impairment). These types are further categorised according to whether single or multiple cognitive domains are impaired (Figure 1) (Petersen, Roberts, Knopman et al., 2009).

Table 2.3

The original 1999 Petersen criteria for MCI

- 1. Memory complaint, preferably corroborated by an informant
- 2. Memory impairment documented according to appropriate reference values
- 3. Essentially normal performance in nonmemory cognitive domains
- 4. Generally preserved activities of daily living
- 5. Not demented

(Petersen, Roberts, Knopman et al., 2009)

Table 2.4

### Updated Mayo Clinic criteria for MCI

- 1. Cognitive function not normal for age
- 2. Not demented
- 3. Cognitive decline
- 4. Essentially normal functional activities

(Petersen, Roberts, Knopman et al., 2009)

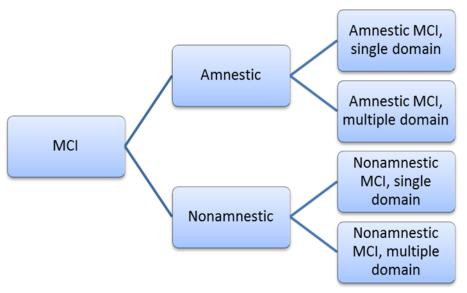


Figure 2.1. MCI types and subtypes

(Adapted from Petersen, Roberts, Knopman et al., 2009)

A number of studies have produced estimates of conversion rates from MCI to dementia, ranging between 2% and 31% (Bruscoli & Lovestone, 2004). A more recent study estimated an annual conversion rate of between 8% and 15% (Devanand, Liu, Tabert, et al., 2008); however, another study by Ishikawa and Ikeda (2007) found that approximately 40% of their research participants returned to 'normal' function at 5-year follow-up. This may provide an indication that MCI is an unstable diagnostic construct, but may also indicate inadequate accuracy of screening instruments used – in this case, the Mini-Mental State Examination (Folstein, Folstein, & McHugh, 1975).

#### 2.2.1 Prevalence, societal cost and effects of cognitive impairment

Prevalence and societal cost of cognitive impairment dementia has become a significant health concern in recent years due to the aging of the world population (Fotuhi, Hachinski, & Whitehouse, 2009) and its high correlation with advancing age (Gao, Hendrie, Hall, & Hui, 1998). In New Zealand, it is estimated that the ratio of older people in relation to the general population will increase to 25.5% over the next 44 years (Statistics New Zealand, 2000) and that this in turn will lead to an increase in age-related health concerns, including dementia. It has been estimated that between 24.3 million (Ferri et al., 2005) and 29.3 million (Wimo et al., 2010) people worldwide had dementia in 2005, with 4.6 million new cases every year, thereby doubling the number of those with dementia every 20 years (Ferri et al.,

2005). The most current estimate for the global prevalence of dementia is 34.37 million people (Wimo et al., 2010), the same number as the estimated population size of Canada (Statistics Canada, 2011), and approximately eight times the size of the New Zealand population (Statistics New Zealand, 2002).

Prevalence estimates vary widely according to country and sample population. For example, studies suggest American base rates ranging between 5% to 37.4% according to advancing age (Plassman et al., 2007), while age-standardised estimates include 5.8% in Spain (Bermejo-Pareja et al., 2009), 1.26% in Singapore (Sahadevan et al, 2008), and 8,2% in Korea (Lee et al, 2002). When it comes to specific types of population samples, 43.2% of individuals aged over 70 in UK acute hospital settings had dementia (Sampson et al., 2009). While the prevalence rates of dementia within developed countries are mostly consistent (compare European with American for example), estimates vary widely within developing countries (Kalaria et al., 2008).

Direct comparisons of studies are difficult however, due to different study designs employed, the use of different age groups across studies, different settings of sampled populations (such as community versus clinical samples), and different diagnostic criteria used. The lack of operationalised diagnostic criteria underlies much of the variability in epidemiological findings, and the measures used to diagnose dementia are prone to cultural bias (Mayeux, Reitz, Brickman, et al., 2011).

To date, a single dementia prevalence study has been conducted in New Zealand (Campbell, McCosh, Reinken, et al., 1983) producing an age-standardised prevalence of 7.7% (Table 5). Considering that these figures are almost 30 years old, the current prevalence is likely to be higher due to increased life expectancy and improved health care (Alzheimers New Zealand, 2008).

Table 2.5

Prevalence of dementia in New Zealand in 1983

Age	Prevalence
All people over 65 years	7.7%
65 – 74 years	3.8%
80 – 84 years	11%
85 – 89 years	23.6%
90+ years	40.4%

Prevalence estimates of MCI, like those of dementia, vary according to the country and population studied (Busse, Hensel, Guhne, et al., 2006; Das, Bose, Biswas, et al., 2007; Palmer, Backman, Winblad, et al., 2008), with estimates ranging from 3.2% to 24.3% (Petersen, Roberts, Knopman et al., 2009). A recent study by the Mayo Clinic (Petersen, Roberts, Knopman, et al., 2010) estimated a prevalence of MCI in the community of 16%. This result was based on 1969 participants aged 70 to 89 without dementia, and findings indicated that prevalence was higher in men, and lower with higher levels of education. Amnestic MCI (a-MCI) (considered a precursor to AD) was 2.3 times more common than nonamnestic MCI (na-MCI). Further, a population-based German study based on 4145 participants aged 50–80 years suggested MCI prevalence of 7.8% when based on the original Petersen criteria, and 12.1% based on the modified criteria (Dlugaj, Wimar, Wege, et al., 2010). The prevalence of dementia and MCI combined has been estimated at 24% (Peterson, 2010).

## 2.2.2 Effects of dementia – quality of life, impact on families & society

The effects of dementia are insidious and pervasive in the lives of those who have it and the people who love and care for them. The ripple effect of dementia touches immediate families, social and work contexts, and has broader effects on economic productivity and the loss of valuable expertise.

From a micro-level perspective, cognitive impairment affects activities of daily living (ADL's), which leads to reduced levels of personal independence and the necessity of having to rely on others for adaptive tasks, ranging from financial

management, household maintenance, shopping, and towards the severe end of the spectrum, personal cares. People with dementia have to rely more on the help of others, and in some cases are entirely dependent on the goodwill of family and/or friends and neighbours for meeting the demands of everyday life. The burden of dementia on caregivers can be immense, and often leads to emotional fatigue, burnout, and has flow-on effects on carers' personal lives and their ability to fulfil their responsibilities in their own work and family lives (Arai & Zarit, 2011).

It may be argued that carer burden is a part of family life and a socialised norm in most cultures; however, as the population ages as a whole, carer burden may have increasingly significant negative impacts on families and communities beyond that which is deemed adaptive and cohesive to family culture and society (Schulz & Martire, 2004). Moreover, the costs of caring for aging individuals who lack the cognitive capacity to care for themselves in the context of ever expanding life expectancy are enormous and often carried (at least in part) by the families themselves, whether by actual expenditures or by reduced income due to a family member staying home as a full-time, unpaid, caregiver. More often than not, the children in affected families suffer as well, due to resources being spread more thinly and less time and energy available for nurturing and assisting children (Setia, Islam, Thompson, & Matchar, 2011).

#### 2.2.3 Increased need for services

A recent study estimated that the worldwide cost of dementia has increased by 34% since 2005 (Wimo et al., 2010) and that dementia-related costs amounted to US\$422 billion in 2009. In the Oceania region, dementia-related costs increased from US\$ 4.5 billion in 2005 to US\$6.4 billion in 2009 (Wimo et al, 2010).

Updated New Zealand-based studies on the prevalence of dementia and cognitive impairment are required in order to facilitate accurate planning of services. There is an imperative need to determine the number of dementia and cognitive impairment cases among Maori, as there are no estimates at this time, and New Zealand's Maori population is aging faster than the population as a whole (Statistics New Zealand, 1995).

#### 2.3. The neuropsychology of cognitive impairment

#### 2.3.1 Cognitive changes associated with normal aging

Changes in cognitive function are a natural part of aging, with most people noticing changes in their memory abilities first and foremost, and research studies agree that the domains of learning and memory undergo the greatest rate of change with normal aging (Knopman & Selnes, 2003). While there is no uniform deterioration of memory ability, memory for recent information tends to become less efficient after the age of 67 (Sbordone, Saul, & Purisch, 2007). Procedural and semantic memory tends to be less affected than working memory and episodic memory, while recognition memory typically remains unaffected. Information retrieval and processing becomes slower with age and forgetting becomes more rapid. Autobiographical memories also tend to become less detailed with advancing age (Sbordone, Saul, & Purisch, 2007).

Language abilities tend to remain stable throughout one's lifetime, with vocabulary, naming, and comprehension abilities changing very little. Even on tasks involving verbal fluency, it is the influence of slower processing speed that causes most day-to-day difficulties (Knopman & Selnes, 2003). Age-related language differences have also been attributed to deficits in working memory and visual perceptual skills (Dennis & Cabeza, 2008). Abstract reasoning abilities are likewise negatively affected by slower processing speed (Knopman & Selnes, 2003).

#### 2.3.2 Alzheimer's disease

While Alzheimer's disease (AD) involves multiple changes across a person's cognitive, behavioural, and emotional abilities, the memory domain is the first and most prominently affected area (Knopman & Selnes, 2003). Memory impairments typically involve learning, recall and recognition, specifically observed as flat learning curves across trials, poor delayed recall, impaired recognition memory, frequent intrusions, and positive response bias (Lezak, Howieson, & Loring, 2004). Storage (consolidation) of new information is impaired, compounded by impaired encoding and retrieval, and rapid forgetting (Sbordone & Purisch, 2007). Anterograde amnesia is pronounced and both anterograde and retrograde amnesia are evident in the early stages of disease progression (Knopman & Selnes, 2003).

Episodic memory (verbal and visual) is severely affected, with impairment present also in semantic and implicit memory, and temporal orientation, while procedural memory remains relatively intact (Lezak, Howieson, & Loring, 2004).

Besides memory impairment, AD affects a variety of other cognitive domains such as language, number processing, and higher executive functions such as abstract reasoning. The language domain, like memory, is affected early in the disease course, and is characterised by the deterioration of semantic relationships and understandings, which appears to follow the sequence of language development in reverse (Lezak, Howieson, & Loring, 2004; Emery, 2000). Arithmetic, mathematical, and number processing abilities are also affected, and reasoning abilities become impaired to the extent that thinking becomes vague and overgeneralised, and may result in incompetent decision-making and an inability to manage one's affairs (Lezak, Howieson, & Loring, 2004).

Social competence is likewise compromised due to impairment in higher executive functions, often early in the disease course. Specific executive impairments involve impaired self-awareness, perseverations, and intrusions in speech. Social function is further impaired by changes in personality, most notably increased apathy, and increased anxiety and depression, sleep disorders, incontinence, impaired self-care, increased agitation, and restlessness (Sbordone & Selnes, 2007).

#### 2.3.3 Vascular dementia

Vascular dementia (VaD) is caused by vascular disease (Lezak, Howieson, & Loring, 2004), and in contrast to AD, may or may not involve memory impairment, and symptoms vary according to the location and size of affected neuroanatomical areas (Haaland & Swanda, 2008). The heterogeneity of VaD has led to classification subtypes, based predominantly on neuroimaging test results. Subtypes include single infarcts in strategic regions, multi-infarct dementia, and the presence of lacunar states (Haaland & Swanda, 2008), all of which may involve impairment of varying cognitive domains depending on the site/s of the lesion/s. The differential diagnosis between AD and VaD relies on the most distinguishing differences between the disorders, which are stepwise progressive deterioration, fluctuating course, hypertension, history of stroke, and focal neurologic symptoms (Haaland & Swanda,

2008). Nevertheless, the diagnosis of VaD is difficult due to the lack of widely accepted diagnostic criteria and uniform clinical presentation (Lezak, Howieson, & Loring, 2004).

## 2.3.4 Fronto-temporal dementia

Fronto-temporal dementia (FTD) is characterised by insidious onset and slow progression of impairment involving the frontal and temporal lobes (Lezak, Howieson, & Loring, 2004). Distinguishing features involve impaired personal and social awareness, disinhibition, poor insight, impulsivity and hyperorality (Kaye, Petrovic-Poljak, Verhoeff, Freedman, 2010). An inability to recognise emotion, especially anger and disgust, inability to empathise with others, and impaired moral reasoning are also observed in FTD patients (Lough, Kipps, Treise, et al., 2006), and cases of psychosis, increased risk-taking behaviour, compulsions and apathy have also been observed (Kaye, Petrovic-Poljak, Verhoeff, Freedman, 2010).

In contrast to AD, cognitive impairment in FTD presents after personality changes, which mostly involve impairments in higher executive functions (Mathuranath et al., 2000). Other neuropsychological difficulties are verbal fluency, and difficulties with speech, specifically pressure of speech, echolalia, perseveration, and poverty of speech (Lezak, Howieson, & Loring, 2004). Visuospatial orientation, praxis, and arithmetic abilities remain unaffected (Lezak, Howieson, & Loring, 2004).

#### 2.3.5 MCI

Neuropsychological impairments associated with MCI vary according to type (a-MCI versus na-MCI) and can involve impairment across multiple domains. Overall impairments are less than those observed in dementia; however, changes in cognition are still more than would be expected for unimpaired age-matched peers. Further, the nature of MCI-related cognitive impairment does not affect a person's ability to fulfil everyday tasks and adaptive functions. On neuropsychological testing, people with MCI generally score 1 to 1.5 standard deviations below the mean for age and education matched peers (Albert, DeKosky, Dickson, et al., 2011). Studies further indicate that amnestic mild cognitive impairment involves not only anterograde memory impairment, but autobiographical episodic memory as well (Murphy, Troyer, Levine, & Moskovitch, 2008; Nordlund et al., 2008).

A recent longitudinal study (Saunders & Summers, 2011) involved neuropsychological assessment of 52 a-MCI, 29 na-MCI, and 25 age-and education matched healthy controls at 10 month intervals. The study found that both MCI groups showed a stable pattern of decline in attention, working memory, and executive function. The a-MCI group showed a significant decline in especially divided attention, and visual and verbal memory (Saunders & Summers, 2011).

#### 2.4 Summary

In summary, age-related cognitive impairment is a complex condition characterised by a continuum of cognitive decline that ranges from age-appropriate function, to MCI, and dementia. Not everyone follows the same course of progression – between 2% and 31% of those with MCI convert to dementia, while some (one study suggesting up to 40%) may revert back to age-appropriate function. Given the aging global population and the associated costs of providing health and support services for those most at risk, cognitive impairment is a growing concern that affects families, communities, and societies at large. Further, the heterogenous nature of cognitive impairment, the lack of clear boundaries between conditions, and the lack of operationalised criteria for diagnosing disorders create challenges for accurate diagnosis, particularly in the detection and treatment of the milder expressions of cognitive impairment. However, updated criteria were recently published, and steps taken to address these issues.

A large number of screening tools have emerged in the last decade in response to the challenges of efficient assessment, which further include the importance of brevity, comprehensiveness, psychometric validity and reliability, and cost-effectiveness.

## **Chapter 3**

# **Assessment and Screening in Cognitive Impairment**

#### 3.1. Introduction

Despite great advances in the understanding of cognitive impairment and increasing complexity of assessment procedures such as neuroimaging and expanded screening tools, clinical assessment is always accompanied by important ethical considerations, such as the validity and efficiency of assessment methods, cross cultural sensitivity, and accuracy of diagnostic outcomes. In addition, the expected societal impact of age-related cognitive impairment requires efforts to prevent onset, and to minimise the burden on families, health care systems, and governments.

This chapter discusses the various approaches to cognitive impairment (CI) including, assessment and screening, current clinical guidelines, and comorbid factors that influence CI assessment and diagnosis. Further, cultural and psychometric validity factors are considered, which is followed by an overview of a number of screening measures.

#### 3.2. The assessment and screening of CI

The National Institute for Health and Clinical Excellence (NICE, 2006) recommended early detection of pathological cognitive impairment – specifically, that primary health staff should be vigilant for MCI symptoms in their older patients, and refer them for further assessment at a memory clinic when these are observed. Likewise, the New Zealand 2008 Dementia Manifesto (Alzheimer's NZ, 2008) emphasised the need for early diagnosis in addition to dementia-specific training for primary health staff. This is because dementia is often only diagnosed at a late stage, as primary care settings are not geared to routinely screen for CI (Grober et al, 2008).

The NICE (2006) guidelines recommended that a dementia diagnosis be made following a comprehensive assessment involving history taking, cognitive and

mental state examination, physical examination and neuroimaging (where appropriate), and a review of medications (prescribed and over-the-counter). The cognitive assessment should include attention and concentration, short and long term memory, praxis, language, and executive functioning. Comprehensive assessment of these areas is more often conducted as part of research studies. In day-to-day primary care screening it is an initial step in cognitive assessment, while in clinical geriatric settings, cognitive screening tools are used as part of an overall assessment process. (Cognitive screens are also used in epidemiological research to measure cognitive function in the general, unimpaired population [Ismail, Rajji, Shulman, 2010]).

There are generally four, not mutually exclusive, approaches to using screening in assessment and diagnosis. The traditional approach is to use tests of global cognitive function such as the MMSE. The second approach involves an emphasis on memory testing, using for example, the Hopkins Verbal Learning Test, East Boston Memory Test, and the Memory Impairment Screen (referred to in Table 3.1 as test numbers 9, 13, and 24 respectively) and further testing that controls for attention and concentration difficulties. A third approach involves measuring several specific cognitive domains, for example the Cognitive Abilities Screening Test, Repeatable Battery for the Assessment of Neuropsychological Status, Addenbrooke's Cognitive Examination, Montreal Cognitive Assessment, and Addenbrooke's Cognitive Examination-Revised (referred to in Table 3.1 numbers 11, 18, 21, 27, and 29 respectively). The fourth approach focuses on interviewing reliable informant/s by, for example, using the Informant Questionnaire on Cognitive Decline in the Elderly (referred to in Table 3.1, number 12) (Grober et al., 2008).

Regardless of the strategy used, it is widely agreed that screening strategies should be accurate (having adequate sensitivity and specificity), and efficient (Grober et al., 2008). Two-stage screening models have been proposed where a brief and highly sensitive screen is administered with eligible patients, possibly in primary care settings, which is then followed, if indicated, by a second stage involving in-depth assessment (Grober et al., 2008).

There are a number of factors that may complicate the assessment and accurate diagnosis of dementia, such as the overlap of the biological processes in dementia

and normal aging, and testing issues such as validity, true score and testing error, and confounding variables that may disguise true cognitive function.

Cognitive changes associated with the healthy aging process (as discussed in Chapter 1) often prompt individuals and families to seek assessment for CI; however, what is 'normal' for some individuals may not always be 'normal' for others, and the line between normal and impaired becomes blurred in relation to an individual's premorbid function (for example a person with previously above average cognitive abilities may be more sensitive to noticing cognitive change even when their current functioning is in the average range), and in relation to the person's level of function required to meet daily environmental demands.

Alexander and Geschwind (1984) drew attention to the tendency for older people to be more cautious in taking risks, more rigid in their thinking and problem solving (such as rejecting an old hypothesis in the face of disconfirming evidence and changing long-held attitudes), and to have fewer social interactions. These may contribute to apathy, abulia, and a narrowed range of behaviours that not only may resemble cognitive deterioration, but also quicken the clinical appearance of cognitive impairment.

The process of growing older may (but not always) involve a range of experiential losses, which may lead to social isolation (losing loved ones and peers through death), financial isolation (through loss of employment or reduced income), and physical isolation (due to reduced physical abilities or through illness) (Davidoff, 1986). These types of isolation often lead to reduced mental activity, reduced opportunities for positive reinforcement, and reduced self-care, which in turn contribute to an increased vulnerability to depression and a dampening of cognition.

The prevalence of depression among older adults is high – estimated at approximately 11% (Steffens, Fisher, Langa, et al., 2009) – and is often misdiagnosed as dementia due to the clinical presentation of the so-called pseudodementia of depression, which involves psychomotor retardation, abulia, reduced attention and memory abilities, and increased apathy (Davidoff, 1986). In cases where depression is not ruled out, the clinical presentation may resemble MCI, AD (in the case of predominantly memory impairment), or fronto-temporal dementia,

when in fact the individual is severely depressed. Depression may also be comorbid with an organic cognitive impairment process, the challenge then being to accurately determine the level of severity of impairment without the confounding effect of depression. The differential diagnosis of depression is therefore "not only the most difficult to make, but also perhaps, the most important, because a pseudodementia of depression is potentially reversible" (Davidoff, 1986, p.12).

A further factor that may confound accurate cognitive assessment, especially in the case of Lewy-body dementia, involves fluctuation in cognitive performance ranging from impaired to unimpaired. The presence of cognitive fluctuations in themselves increases the risk of dementia eightfold (Escandon et al., 2010).

#### 3.2.1. Cultural issues

The need for culturally appropriate assessment measures and procedures is an international imperative as countries across the world become increasingly multicultural and cosmopolitan. The bicultural nature of New Zealand society is especially important, as enshrined by the Treaty of Waitangi. Further, the New Zealand Psychologists' Code of Ethics makes clear reference to the need for services to be culturally sensitive and appropriate. To this end, diagnosing clinicians should be culturally competent (Shepherd & Leathem, 1999) and use psychometric tools that have proven cross-cultural validity. While some may argue that the cost of validating tools for specific countries outweigh the expected small differences in norms across populations, cross-cultural validation is nevertheless essential in order to fulfil the requirement for evidence-based practice.

In New Zealand, it was found that the norms for standard cognitive measures were different for Maori and Pakeha children (McGregor, 1988). This finding was unsurprising, given that standard measures are based on Western schooling traditions and assumptions that favour individuals from "Western" backgrounds. Given that Maori cultural values and assumptions of epistemology are very different to that of Western cultures, this study emphasised the need for New Zealand based norms in order to ensure valid assessment and accurate diagnosis of children, and this should also be extended to CI assessment with older people.

For example, some cognitive and screening tests rely on reading ability, such as the MMSE, the Modified Mini Mental State, and the Middlesex Assessment of Mental State (referred to in Table 3.1 as test numbers 2, 6, and 7 respectively), which each includes items requiring reading ability, and uses English words of phenomena that may not have the same significance across cultures. It is furthermore based on a Western cultural value of individual achievement, which is not held to the same extent in Maori culture. Using a Western-based test across cultures does therefore not meet the requirement for a standardised assessment for everyone, and those of other cultures would be unfairly disadvantaged and over-diagnosed (false-positives). This obstacle may be overcome to an extent by having different sets of norms for different cultural groups, as in the case of having age-based norms and controlling for age without having to resort to using a different test altogether.

According to the 2008 Dementia Manifesto (Alzheimer's New Zealand, 2008), ongoing collection of population-based data is required in order to maximise crosscultural validity. When considering the impact of a diagnosis of CI on an individual's life and future, and the potential loss of independence, as a result of such a diagnosis, it is important to ensure that the norms against which a person's function is compared is valid and appropriate.

#### 3.2.2. Validity & reliability issues

The general definition of validity refers to whether an instrument measures what it is intended to measure (Tabachnick & Fidell, 2007). Various types of validity exist in order to capture the different aspects involved in assessing accuracy, for example construct validity (does the instrument measure the target construct and not another related construct), and concurrent validity (does the instrument measure the target construct as well as other instruments) (Tabachnick & Fidell, 2007).

Different types of study design exist in order to investigate the various aspects of validity of assessment instruments; for example, in a concurrent validity study, the performance of the instrument would be measured against the performance of another instrument or method of assessment – the 'gold standard' commonly used for the same construct. This design requires the instrument under scrutiny to be administered independently of the gold standard assessment process (Wright, 1997).

This type of study often involves quasi-experimental or experimental techniques, as the testing situation is manipulated in some way in order to control for confounding variables or bias (Wright, 1997).

In order to test the validity of an instrument in this way, it is standard practice to limit potentially confounding variables by using certain exclusion criteria. For example, when examining the validity of a screening instrument for cognitive impairment, the population sample may be simplified by removing individuals who have comorbid difficulties such as depression or psychosis. Also, when comparing the performance of an instrument with another, any supplementary instruments normally used in assessment may be removed. It makes sense to manipulate variables in this way because it increases the scientific rigour and robustness of the study and allows for increased certainty that one's findings are indeed as a result of known variables, rather than unknown and uncontrolled influences. This does not, however, reflect the real-life situation in clinical practice.

In the clinical setting, it is standard practice to use a number of instruments and methods in assessment, the assumption being that cross-method agreement increases the validity of the overall conclusion, decision, or prediction, and that this will lead to improved outcomes via related clinical intervention (Hunsley, 2003; Meyer, Finn, Eyde, Kay, Moreland, et al., 2001). The extra time and resources required to use multiple methods further necessitate scientific justification and empirical support for each method.

This leads to the determination of incremental validity, which investigates whether an instrument adds to the prediction of a certain criterion beyond that of other methods (Hunsley & Meyer, 2003). Incremental validity can add to the validation of newly created stand-alone measures, cost-benefit analyses, technical aspects of behavioural observations (such as adding more time-sampling intervals), and assessing the validity of adding an instrument to an existing assessment battery or assessing the relative clinical utility of one measure within a multi-method assessment approach (Haynes & Lench, 2003).

While not as well-known as the traditional types of validity, incremental validity has been discussed in studies dating back to 1929 (Sangren, 1929). Despite it being advocated and recommended for all new clinical assessment measures since at least 1963 (Sechrest, 1963), relatively little attention has been given to incremental validity. A 2003 study found that only 11% of manuscripts submitted to the Psychological Assessment journal over the course of four years addressed incremental or relative validity of a new instrument or scale (Haynes & Lench, 2003). None of the studies reviewed in Table 3.1 assessed incremental validity.

In contrast to other types of validity, study designs that assess incremental validity do not assume that the target construct (in this case the particular screening tool) is independent of the gold standard against which it is compared. Rather, statistical procedures such as logistic regression and discriminant analysis can estimate the weight of the screening tool in predicting the final diagnostic outcome.

#### 3.3. An overview of CI screening instruments

A large number of screening instruments has been published in recent years in response to the increasing prevalence of dementia, the increasing focus on early detection of cognitive impairment and MCI, and the growing discontent with the MMSE. Whereas the MMSE enabled a quick snapshot of global cognitive function with an emphasis on memory, more recent instruments, such as the Addenbrooke's Cognitive Examination-Revised (see table 3.1, number 29) and the Montreal Cognitive Assessment (see table 3.1, number 27) include items that assess higher executive function (Ismail, et al., 2010). Table 3.1 provides an overview of the more well-known screens in chronological order, and illustrates how the newer screens (table 3.1, numbers 26 to 29) tend toward higher degrees of sensitivity, with an increased coverage of the various cognitive domains.

Table 3.1

Overview of brief cognitive impairment screens

Author/s	Year of publication	Screen name	Abbre- viation	Admin time	<b>Domains covered</b>	Sensitivity	Specifi city	PPV @ 20% BS
1. Reitan	1958	Trail-making Test	TMT	5-10 min	executive function praxis	*	*	*
2. Folstein	1975	Mini-Mental State Examination	MMSE	5-10 min	attention / working memory, verbal recall, expressive language, visual construction	61-91%	87-99%	*
3. Mohs	1983	Alzheimer's Disease Assessment Scale	ADAS	*	*	*	*	*
4. Wilson	1985	The Rivermead Behavioural Memory Test	RBMT	30 min	everyday memory tasks, orientation, attention, verbal & non-verbal memory, comprehension, prospective memory	67-93%	79- 100%	*

5. Kiernan	1987	Neurobehavioral Cognitive Status Examination	NCSE	5-20 min	language constructions memory calculation reasoning orientation attention	*	*	*
6. Teng et al.	1987	Modified Mini Mental State	3MS	10-15 min	orientation, registration, immediate & delayed verbal recall, working memory, language, writing, visuospatial	91%	97%	*
7. Golding	1989	Middlesex Assessment of Mental State	MEAMS	*	orientation, verbal learning & memory, visual memory, working memory, visuospatial, language, executive function	*	*	*
8. Sunderland	1989	Clock drawing test	CDT	*	comprehension, visuospatial, executive function	*	72-94%	65-98%
9. Brandt	1991	Hopkins Verbal Learning Test	HVLT	<10 min	verbal learning, memory	94%	100%	*

10. Royall	1992	The Executive Interview	EXIT-25	*	executive function	*	*	*
11. Teng et al.	1994	Cognitive Abilities Screening Test	CASI	15-20 min	attention orientation short-term memory long- term memory language visual construction executive function	91-95%	91-94%	*
12. Jorm	1994	Informant Questionnaire on Cognitive Decline in the Elderly	IQCODE	*	single general factor of cognitive decline	*	*	*
13. Gfeller, Horn	1996	East Boston Memory Test	EBMT	5 min	verbal memory	78-97%	*	*
14. Drachman	1996	Cognitive Assessment Screening Test	CAST	*	*	88-95%	88- 100%	*
15. Leopold, Borson	1997	Modified WORLD test	WORLD	< 1 min	attention language	85%	88%	95%
16. Froelich	1998	Time and Chance Test	T&C			86%	71%	97%

17. Solomon	1998	7 minute screening battery	7MS	7 min	memory verbal fluency visuospatial visuoconstruction orientation for time	92%	96%	85%
18. Randolph	1998	Repeatable Battery for the Assessment of Neuropsychological Status	RBANS	< 30 min	orientation, attention, verbal & nonverbal immediate & delayed memory, language, visioconstruction	90%	90%	*
19. Borson	2000	Mini-cog	Mini-cog	3 min	memory (verbal recall), visuospatial, executive function	99%	93%	96%
20. Dubois	2000	Frontal Assessment Battery	FAB	*	*	*	*	*
21. Mathuranath	2000	Addenbrooke's Cognitive Examination	ACE	15-20 min	orientation attention memory verbal fluency language visuospatial ability	93%	71%	44%
22. De Koning	2000	Rotterdam CAMCOG	R- CAMCOG	< 15 min	orientation , memory (immediate & remote), executive function, perception	91%	90%	*

23. Jurica	2001	Dementia Rating Scale-2	DRS-2	*	*	*	*	*
24. Kuslansky, Buschke	2002	Memory Impairment Screen	MIS	4 min	attention verbal memory	86%	97%	80%
25. Storey	2004	Rowland Universal Dementia Assessment Scale	RUDAS	*	*	*	*	*
26. Kalbe	2004	DemTect	DemTect	8-10min	immediate & delayed verbal recall, working memory, language, number processing, executive functioning	85%	97%	89%
27. Nasreddine	2005	Montreal Cognitive Assessment	MoCA	10 min	short term memory visuospatial executive attention language orientation	MCI=90% AD=100%	87%	89%
28. Molloy	2005	ABCS	ABCS	3 min	orientation, attention, immediate & delayed verbal recall, word fluency, exec function	95%	*	*

29. Mioshi et al.	2006	Addenbrooke's Cognitive Examination- Revised	ACE-R	12-20 min	orientation/ attention, memory, verbal fluency, language, visuo- spatial, executive function	88: 94% 82: 84%	89% 100%	88: 68%, 82: 100%	
-------------------	------	---	-------	-----------	--	--------------------	-------------	----------------------	--

<sup>\*</sup> Information not available.

Inspection of the published studies cited in Table 3.1 reveals that a large number do not include recommended cut-offs or sensitivity/specificity ratios, making informed choices as to their suitability for use difficult. Screens offering excellent sensitivity *and* specificity were, in chronological order, the 3MS, HVLT, CASI, 7MS, RBANS, Mini-cog, R-CAMCOG, and MoCA (Table 3.1, 6, 9, 11, 17, 18, 19, 22, and 27 respectively). These screens were not necessarily longer than the others; for example, the 7MS was described as taking only seven minutes to administer when some longer tests such as the RBMT was cited as taking 30 minutes to administer while providing only good sensitivity or specificity depending on the balance chosen. Clinicians looking for the most appropriate screen to use in their particular settings may be hard-pressed to make an informed choice based on the relatively little information provided with their publications.

Further, the various validation studies compared test performance according to differing participant groups, for example in the MoCA study (Table 3.1, 27), participant groups consisted of patients with mild AD, MCI, and normal elderly controls, whereas the ACE-R study (Table 3.1, 29) compared a general dementia group, a MCI group, and a normal control group. The Mini-Cog study (Table 3.1, 19) compared only two groups, a dementia group and a normal control group, and the R-CAMCOG study (Table 3.1, 22) used a group of stroke patients only.

While some studies had adequate sample sizes, such as the MIS study (Table 3.1, 24) with a sample size of 240, the EBMT study (Table 3.1, 13) had only 23 participants. Age groups also differed across studies, for example the DemTect study (Table 3.1, 26) had two age groups, those younger than 60 and those 60 years and older, whereas the CASI study (Table 3.1, 11) had age groups ranging between 51 and 91 years old. The choice of which screen to use is therefore complicated by the necessity to investigate each study's scientific rigour, their comparability to each other, and their applicability to one's client group in terms of, for example clinical presentation and age groups,

An important consideration is also whether the screens are culturally appropriate to be used with populations other than those for which the screens were initially validated.

#### 3.4. Conclusion

The preceding table represents relatively few of the screening measures currently in publication. Most of them cover the same core set of cognitive domains, with emphasis on different types of memory, and orientation/attention. Many of the tests involve the same type of tasks, such as naming date, time and place, and immediate and delayed verbal recall, while those that include executive function assessment incorporate trail making and/or verbal fluency tasks.

Given the large number of validated and psychometrically adequate screens available, making an informed choice regarding which screen to use can be difficult in settings where time is limited and efficiency paramount. Screens may fulfil different purposes depending on the setting and the population it is used for, and these would in turn influence the choice of a particular screen over another.

Further research is required in order to investigate the use and role of brief cognitive screening in clinical practice, to determine which factors clinicians consider when selecting a particular screen, and in turn to evaluate the clinical utility of some commonly used screens in a New Zealand setting. An online survey was subsequently conducted with New Zealand clinicians to obtain cross-sectional data about which screens are commonly used, how they are used, and clinicians' attitudes towards various aspects of screening and assessment.

# **Chapter 4**

# The use of brief cognitive screening instruments in New Zealand

#### Preface

This chapter consists of a journal article that reports the results of an internet-based survey, conducted with geriatricians, psychiatrists, neurologists, and psychologists, on their use of brief cognitive screening instruments.

The article was accepted for publication in the *New Zealand Journal of Psychology*.

# The Use of Brief Screening Instruments for Age-Related Cognitive Impairment in New Zealand Heide-Marie Strauss, Janet Leathem, Steve Humphries, John Podd

### **Massey University**

#### **Author Note**

Heide-Marie Strauss, DClinPsych candidate, Massey University Wellington; Janet M Leathem, Professor of Neuropsychology, Massey University Wellington; Steven Humphries, Lecturer, Massey University, Wellington; John Podd, Associate Professor, Massey University, Palmerston North.

Correspondence concerning this article should be addressed to:

Professor Janet Leathem, School of Psychology, Massey University Wellington,
PO Box 756, Wellington, 6140, Tel: 04 801 5799 Ext: 62035, Fax: 04 801 0493,
Email: J.M.Leathem@massey.ac.nz

#### **Abstract**

This study aimed to determine which measures are most commonly used to screen for age-related cognitive impairment in New Zealand, to describe how and why they are used, determine the factors clinicians deem most important in the selection of a particular screen, and their levels of training and expertise in using particular screens. A web survey was completed by geriatricians, neurologists, psychiatrists, and psychologists (N=82). Cognitive screening measures were selected for the survey based on previous research. According to the sample, the most frequently used screen was the Mini-Mental State Exam (MMSE), followed by the Clock Drawing Test (CDT), and Addenbrooke's Cognitive Examination Revised (ACE-R). Cognitive screening fulfilled a variety of functions in clinical practice and was widely used, especially in services for older people; however, formal training was limited. Availability, reliability and validity, and brevity (respectively) were the most important factors clinicians considered when selecting a screening instrument. Respondent comments agreed with current literature that the MMSE is inadequate as a screening instrument for cognitive impairment, and this was reflected in the comments of respondents on the survey questionnaire, yet this was still the most commonly used measure in New Zealand.

Keywords: cognitive impairment, dementia, screen

#### Introduction

It is widely recognised that the ratio of older adults in the general population of Western societies is growing rapidly. This international trend is also seen in New Zealand, where the number of people aged 65 years and older has increased by 86.4% between 1971 and 2001 (Statistics New Zealand, 2002), and it is estimated that the rate of older people in the total population will grow to 25.5% over the next 44 years, up from 12% in 1999 (Statistics New Zealand, 2000). As cognitive impairment is highly correlated with age (Gao, Hendrie, Hall, & Hui, 1998), the absolute number of people presenting with cognitive complaints is therefore likely to increase exponentially within the next few years, with a corresponding increase in the need for assessment and management of these complaints.

Cognitive screening is typically conducted by general practitioners, neurologists, psychiatrists, geriatricians, and psychologists as a precursor to, or as part of, comprehensive clinical assessment of cognitive impairment (Cullen, O'Neill, Evans, Coen, et al., 2007). In addition, screening instruments monitor change over time and assists in ongoing clinical decision-making. Early detection of cognitive impairment maximises the opportunity to put in place compensatory strategies useful as cognitive status deteriorates (Hachinski, 2008).

Previous overseas surveys (Reilly, Challis, Burns, & Hughes, 2004; Shulman, Herrmann, Brodaty, Chiu, Lawlor, et al., 2006) found that the screening measure most commonly used internationally was the Mini-Mental State Exam (MMSE; Folstein, Folstein, & McHugh, 1975), followed by the Clock Drawing Test (CDT; Shulman, Shedletsky, & Silver, 1986), the Middlesex Examination of Mental State (MEAMS; Golding, 1989), Cambridge Mental Disorders of the Elderly Examination (CAMDEX; Roth, et al., 1986), CDT and Delayed Word Recall (Mini-Cog; Borson, Scanlan, Brush, Vitaliano, & Dokmak, 2000), Verbal Fluency Test (FAS; Bechtoldt, Benton, & Fogel, 1962), Similarities (Wechsler, 1997), and the Trail Making Test (Reitan, 1958). While Similarities is not a stand-alone screening instrument, the study by Shulman et al., (2006) included it as a task commonly used for screening purposes.

It is unclear which cognitive screening instruments are most frequently used in New Zealand, and clarification of this is one focus of the current study. Anecdotal reports from clinicians suggested that the MMSE was also used extensively in New Zealand, although there were concerns regarding its validity. These concerns were based on clinical observations of the MMSE's relative insensitivity to the milder forms of dementia and research literature examining the validity and utility of the MMSE in a variety of contexts (Anderson, Sachdev, Brodaty, et al., 2007; Bak & Mioshi, 2007; Cullen, O'Neill, Evans, Coen, et al., 2007).

The MMSE was developed in the 1970's and was based on a unitary, global understanding of dementia (Bak & Mioshi, 2007), a view that has radically changed over time. Whereas dementia was conceived of as a global deterioration of cognitive function, it is currently understood as encompassing a number of neurological conditions with divergent patterns of cognitive impairment (Lezak, Howieson, & Loring, 2004).

The MMSE, as a measure of global impairment, is therefore inadequate for detecting various disorders within the dementia spectrum. Moreover, it virtually ignores the frontal-executive, visuospatial, and semantic memory domains, which are affected in disorders such as fronto-temporal dementia, Parkinson's disease, progressive supranuclear palsy, cortico-basal deterioration, and right-hemispheric stroke (Bak & Mioshi, 2007). Further, a number of studies have shown the MMSE to be biased according to age, education, gender, socio-economic status, culture, language and ethnicity, test location, and test repetition (Anderson, Sachdev, Brodaty, et al., 2007; Black, Espino, Mahurin, et al., 1999; Riddha & Rossor, 2005).

The current study extends previous surveys (Reilly, et al., 2004; Shulman, et al., 2006) of the use of cognitive screening measures in geriatric settings by determining what clinicians looked for in a screen, the role of screens in clinical practice, clinicians' levels of competency and training, and their attitudes toward the current issues in cognitive screening. The objective of the current study was

to investigate the current use and role of cognitive screens in New Zealand geriatric services, the current needs and attitudes of New Zealand clinicians regarding the use of cognitive screens, and to compare practice in New Zealand with overseas.

#### Method

#### Participant recruitment

Potential participants were initially those working in all clinical areas involved in all adult cognitive screening such as dementia, electroconvulsive therapy, depression, brain injury, and other forms of brain damage. Participants were recruited via the professional bodies of the targeted occupational groups – the Royal Australian and New Zealand College of Psychiatrists (RANZCP), the Australian and New Zealand Society of Geriatric Medicine (ANZSGM), the Neurology Association of New Zealand (NANZ), and the New Zealand Psychology of Older People (NZPOPs) group.

The RANZCP consists of 610 New Zealand members, of whom 327 are active Fellow members, 143 are associate members (trainees) and 140 are Affiliate members (The Royal Australian and New Zealand College of Psychiatrists, 2011). The ANZSGM had 134 active NZ members, NANZ had 50 neurologist members, and NZPOPS had 59 full members at the time of the survey.

In consultation with executive members of the RANZCP, it was agreed to publish a research notification in their online bulletin, which invited psychiatrists to participate in the online survey, hosted by the Massey University website. Similar consultation with the ANZSGM and NANZ resulted in email invitations being sent to each of their individual New Zealand members that included the same live web-link to the online survey. Follow-up email reminders were sent out approximately three weeks later. The RANZCP did not agree to send individual email invitations as with ANZSGM and NANZ, and this may have biased the representativeness of the sample.

At this stage, the study design was adapted to focus on cognitive screening measures used with older adults, and further recruitment efforts targeted clinicians working with older adults. The researcher gained permission and access to the NZPOPs mailing list and sent a similar email invitation to each of their members. The email invitation to NZPOPs members was preceded by an introductory email by one of the heads of the NZPOPs group and a presentation of the research project at the NZPOPs annual conference by the first author. The email invitation followed soon after. A follow-up reminder email was sent out a week later to the POPs group as the survey was drawing to a close. In an effort to further increase the participation rate of geriatric psychiatrists, a clinician in the field re-invited psychiatrists on his mailing list, requesting their participation if they had not already done so.

#### The questionnaire

The list of screening measures to be rated was taken initially from the review by Cullen, O'Neill, Evans, Coen, et al. (2007). This study reviewed a number of screening instruments and included some neuropsychological tasks (such as FAS, TMT, and HVLT) that are often used in brief screening assessments. While not the specific focus of the current survey, these were included in order to maximise comprehensiveness and enable comparison with previous surveys (Reilly, et al., 2004; Shulman, et al., 2006). Before finalising the survey, separate discussions were held with a psycho-geriatrician and psychiatrist regarding their perspectives on cognitive screens from their work in District Health Board settings. They reviewed the list of measures included in the overseas surveys and added some that were not listed.

The final list of 23 screens was rated for frequency of use using a scale with five options (never, seldom, sometimes, often, and routinely), and rated for level of training and experience using a similar 5-point scale. In addition, respondents could add up to three screens not in the list and rate their frequency of use. A further question asked respondents to list the three screens they used most frequently in descending order (which could include listed and self-generated screens), and to rate their level of confidence in the psychometric properties of

the screen used most frequently. Rating options for training and experience were 1) No formal training of practical experience; 2) Some practical experience; 3) Some formal training and practical experience; 4) Extensive practical experience only; 5) Extensive training and practical experience.

Further questions explored respondents' views of the importance of test administration factors such as standardisation, proficiency and flexibility, the role and weight of cut-off scores in clinical decision-making, and the factors that determine the use of a particular screen. Three comment boxes were placed in the questionnaire for respondents to add any comments related to the relevant question, or make comments about screening or the study in general.

Completed questionnaires were submitted electronically through Massey University's Information Technology system. The responses were collated electronically and forwarded to the researcher in an Excel spreadsheet file. The captured data was imported into the SPSS statistical programme for statistical analysis. The statistical methods used involved calculating frequency distributions, means and standard deviations, and ANOVA calculations.

#### **Results**

#### **Participant characteristics**

The survey resulted in 82 response sets received, with most from geriatric medicine and geriatric psychiatry, followed by psychology and neurology (Table 1). It is uncertain whether the Geriatric Psychiatrists (n=15) were recruited from RANZCP or ANZSGM. No General Psychiatrists responded to the survey. Overall, 853 individuals were invited to participate in the survey, 243 of which received direct email invitations, while 610 (RANZCP members) were invited via an email newsletter.

Table 1: Participant numbers and response rates according to professional discipline (N=82)

N	%	Professional Discipline	Response Rate
44	53.7	Geriatric Medicine	32.8% of ANZSGM
			members
15	18.3	Geriatric Psychiatry	Unknown
14	17	Psychology	23.7% of NZPOPS
			members
8	9.8	Neurology	16% of NANZ
			Neurologists
1	1.2	Other (Nursing)	Unknown
0	0	General psychiatry	0% of RANZCP
			General psychiatrists

Of respondents, 36.6% were aged between 46 and 55, 34.1% between 35 and 45, and 13.4% respectively between 56 and 65 and 35 or younger, and 2.4% were over 65. Just over half (53.7%) were female. 34% Of respondents had more than 20 years clinical experience, 28% had 11 to 20 years' experience, and 18% 6-10 years and 0-5 years' experience respectively. This suggests representation from all levels of expertise, but with senior clinicians outnumbering their junior counterparts.

The majority of respondents used cognitive screening measures for queried dementia (99%), age-related cognitive decline (95%), and for differentiating between cognitive impairment and depression (72%). In addition, cognitive screening measures were used in alcohol and drug settings (33%), traumatic brain injury assessments (29%), and with electroconvulsive therapy (16%).

#### **Cognitive screens**

Most respondents (78%) reported routine and regular ("often") use of the Mini-Mental State Exam (MMSE), 74% the Clock Drawing Test (CDT), 43% the Addenbrooke's Cognitive Examination-Revised (ACE-R), 29% the Verbal Fluency Task (FAS), 32% the Three-word Recall (3WR), and 12% the Trail-

making Test (TMT). The screens used on a routine basis were the MMSE, CDT, ACE-R, and 3WR, in descending order. Table 2 lists all the screens listed in the questionnaire as well as those added by clinicians. As can be seen, a large number of screens were seldom or never used. Figure 1 depicts the frequency of use for all measures used sometimes, often, and routinely.

Table 2: Screening instruments most frequently used for cognitive impairment

		Routinely	Often	Sometimes	Seldom	Never
Screen	(N)	% (n)	% (n)	% (n)	% (n)	% (n)
Mini-Mental State Exam (MMSE; Folstein, 1975)	82	69.5 (57)	8.5 (7)	8.5 (7)	8.5 (7)	5 (4)
Clock Drawing Test (CDT; Sunderland, 1989)	82	44 (36)	30.5 (25)	16 (13)	2.4 (2)	7.3 (6)
Addenbrooke's Cognitive Examination-Revised (ACE-R; Mioshi, 2006)	79	26.6 (21)	16.5 (13)	20.3 (16)	3.8 (3)	32.9 (26)
Verbal Fluency (FAS; Bechtold, 1962)	76	10.5 (8)	21.1 (16)	11.8 (9)	11.8 (9)	44.7 (34)
Three-Word Recall (3WR; Kuslanski, 2002)	75	20 (15)	12 (9)	9.3 (7)	2.7 (2)	56 (42)
Trail-Making Test (TMT; Reitan, 1958)	74	4.1 (3)	8.1 (6)	10.8 (8)	25.7 (19)	51.4 (38)
Modified Mini-Mental State (3MS; Teng, 1987)	75	10.7 (8)	4 (3)	9.3 (7)	16 (12)	60 (45)
Abbreviated Mental Test (AMT;	76	6.6 (7)	5.3 (4)	7.9 (6)	14.5 (11)	65.8 (50)

Hodkinson 1072)						
Hodkinson, 1972)						
Neurobehavioral Cognitive Status Exam (NCSE; Kiernan, 1987)	75	1.3 (1)	4 (3)	10.7 (8)	8 (6)	76 (57)
Hopkins Verbal Learning Test (HVLT; Brandt, 1991)	74	1.4 (1)	2.7 (2)	1.4 (1)	1.4 (1)	93.2 (69)
Informant Questionnaire on Cognitive Decline in the Elderly (IQCode; Jorm, 1989)	75	1.3 (1)	0	1.3 (1)	4 (3)	93.3 (70)
Informant Questionnaire on Cognitive Decline in the Elderly- Short Form (IQCode-SF, Jorm, 1994)	73	0	0	4.1 (3)	2.7 (2)	93.2 (68)
MiniCog (Borson, 2000)	74	0	0	4.1 (1.3)	1.4 (1)	94.6 (70)
Time and Change (T&C Froelich, 1998)	74	0	0	2.7 (2)	1.4 (1)	95.9 (71)
Dementia Questionnaire (DQ; Silverman, 1986)	74	0	0	2.7 (2)	0	97.3 (72)
Cognitive Abilities Screening Inventory (CASI; Teng, 1994)	74	0	0	0	2.7 (2)	97.3 (72)
7-Minute Screen (7MS; Solomon, 1998)	74	0	0	0	2.7 (2)	97.3 (72)

Cognitive Assessment Screening Test (CAST; Drachman, 1996)	72	0	0	0	2.8 (2)	97.2 (70)
Middlesex Elderly Assessment of Mental State (MEAMS; Golding, 1989)	73	0	0	0	1.4 (1)	98.6 (72)
ABCS (Molloy, 2005)	73	0	0	0	1.4 (1)	98.6 (72)
Deterioration Cognitive Observee(DECO; Ritchie, 1996)	71	0	0	0	0	100 (71)
Memory Impairment Screen (MIS; Buschke, 1999)	73	0	0	0	0	100 (73)
Short Portable Mental State Questionnaire (SPMSQ; Pfeiffer, 1975)	73	0	0	0	0	100 (73)
Added:						
The Executive Interview (EXIT-25; Royall, 1992)	15	13.3 (2)	20 (3)	46.7 (7)	20 (3)	0
Montreal Cognitive Assessment (MoCA; Nasreddine, 2005)	11	27.3 (3)	27.3 (3)	36.4 (4)	9.1 (1)	0
CAMCOG(part of CAMDEX; Roth, 1986)	6	33.3 (2)	16.7 (1)	33.3 (2)	0	16.7 (1)
Frontal Assessment Battery	5	20 (1)	0	40 (2)	40 (2)	0

(FAB; Dubois, 2000)						
Rowland Universal Dementia Assessment Scale (RUDAS; Storey, 2004)	5	0	20 (1)	60 (3)	20 (1)	0
Repeatable Battery for the Assessment of Neuropsychological Status (RBANS; Randolph, 1998)	3	0	100 (3)	0	0	0
Rivermead Behavioral Memory Test (RBMT; Wilson, 1985)	2	0	100 (2)	0	0	0
Alzheimer's Disease Assessment Scale- Cognitive (ADAS-cog; Mohs, 1983)	2	0	50 (1)	50 (1)	0	0
Digit Span subtest of the WAIS (Wechsler, 1997)	1	0	100 (1)	0	0	0
Digit Symbol subtest of the WAIS (DS; Wechsler, 1997)	1	100 (1)	0	0	0	0
Dementia Rating Scale-II (DRS-II; Jurica, 2001)	1	0	0	0	0	100 (1)
DKEFS Category Switching (Delis, 2001)	1	0	100 (1)	0	0	0

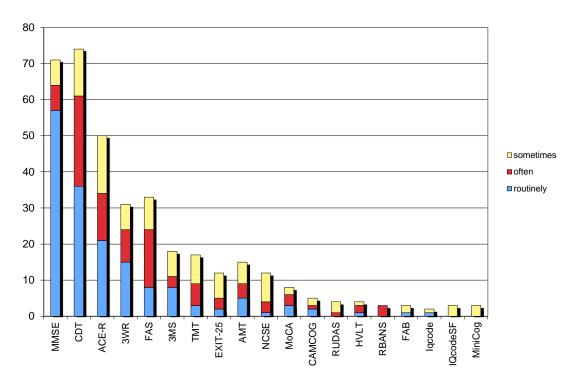


Figure 1: Frequency of use for screening measures

Measuring clinicians' levels of training quantitatively was difficult as there is no standardised training path across occupations when it comes to the use of screening instruments. The highest level of competence – formal training combined with practical experience – accounted for 36% of respondents administering the MMSE, 30% administering the CDT, and 16% and 14% for the FAS and ACE-R respectively. A large number of clinicians reported having extensive practical, supervised experience *without* formal training. Again, the MMSE had the highest frequency for this rating, (42%), followed by the CDT (28%), the ACE-R, (17.5%) and the FAS (16%). Of those screens with which clinicians have had *some* formal training and practical experience, the ACE-R had the highest percentage (24%), followed by the MMSE (21%), CDT (21%), and FAS (16%).

Regarding the importance of test administration factors such as standardised administration, formal training, supervised practical training, and flexible administration according to patient needs, all were rated as "important" and "very important", with the highest mean score obtained for standardised

administration (2.89), while flexible administration obtained a mean score of 2.42 (the maximum score possible being 4).

Regarding the role of cut-off scores in clinical decision-making, most respondents (73%) reported that it should inform diagnosis and supplement clinical interviews. Many (41%) reported that screening should often be used as a first step in assessment, indicating the need for more in-depth assessment, and a further 6% indicated that step-wise assessment should be routine practice. Two of the 65 responses (3%) indicated that screen cut-off scores alone determined diagnosis.

In determining which factors are most important when clinicians select a specific screen, 8 options were listed. These covered psychometric properties (validity and reliability statistics, research regarding usefulness in your setting, and comprehensive coverage of the cognitive domains), practical issues (time required to use and score, and cost), and familiarity (widespread use, known and trusted, and availability). Respondents were provided with 5 response options "not important", "somewhat important", "important", "very important", and "crucial". Availability was the most highly rated factor (mean score 3.31), followed by validity and reliability statistics (3.17), time to use and score (3.14), research regarding usefulness in your setting (2.92), known and trusted (2.92), widespread use (2.64), comprehensive coverage (2.47), and finally cost (2.24). The median scores for all the items except cost were 3.00, a rating indicating 'very important'.

#### **Discussion**

The survey indicated that the current sample used the MMSE, CDT, ACE-R, FAS, 3WR, and TMT most frequently. The MMSE consists of six tasks involving immediate and delayed verbal recall, learning ability, short-term memory, comprehension of instructions, naming objects, constructing and writing a sentence, and copying a design (Folstein et al., 1975). It covers

attention/orientation, memory, language, and visuoconstruction, and takes approximately 5-10 minutes to administer (Folstein et al., 1975). Numerous studies have investigated the psychometric properties of the MMSE, and findings are variable according to the study sample. For example, Tombaugh, McDowell, Kristjansson, and Hubley (1996) reported good sensitivity and specificity, while McDowell, Kristjansson, Hill, and Hebert (1997) reported inadequate to good sensitivity and adequate to excellent specificity depending on the cut-off score used.

The CDT is a simple and reliable measure of visuospatial ability, which requires the drawing of a clock face reading the time of 2:45 (Sunderland et al., 1989).

The ACE-R consists of a series of subtests covering 5 cognitive domains: attention/orientation, memory, verbal fluency (a measure of executive function), language, and visuospatial ability (Mioshi et al., 2006). It requires approximately 15 minutes of administration time, has alternate forms, and is accompanied by clear administration and scoring instructions (Mioshi et al., 2006).

The FAS is a time-limited verbal fluency task over three trials, which requires generating a list of words starting with F, A, and S respectively (Bechtold, 1962). The FAS task has been incorporated into a number of screens and assessment batteries, including the ACE-R, the MoCA, and the Delis-Kaplan Executive Function System (DKEFS). A recent study (Passos, Giatti, Barreto, Figueiredo, Caramelli, et al., 2011) confirmed the reliability and validity of verbal fluency tests.

The 3WR is another task that is incorporated into a number of screens including the MMSE (Kuslansky, Buschke, Katz, Sliwinski, & Lipton, 2002). As a stand-alone test the 3WR had inadequate sensitivity (0.65) and good specificity (0.85), however the associated positive predictive value was poor (0.37) (Kuslansky et al., 2002).

The TMT, originally published in 1958 (Reitan, 1958), is also incorporated in the DKEFS, and measures psychomotor speed and cognitive flexibility. Test-retest reliability was estimated as moderate to high (Matarazzon et al., 1974), and content validity as moderate (Heilbronner et al., 1991).

Consistent with the Reilly (2004) and Shulman (2006) surveys, a large majority of respondents reported frequent use of the MMSE and CDT, despite the varying degree of representation of the various professions.

A finding unique to the current study was that the ACE-R is third most commonly used in New Zealand. The ACE-R has been validated in various settings (Larner, 2007; Reyes, Lloret, & Gersovich, 2009), and has very good to excellent positive predictive values, sensitivity and specificity to both dementia and mild cognitive impairment. The screen includes the MMSE (exact items) and MMSE scores and can therefore be formally derived from performance with the ACE-R. In addition, the ACE-R contains a clock-drawing task, a 3-word recall task, an abstract reasoning task (Similarities) and a trail-making task (Mioshi, et al., 2006). The ACE-R therefore contains all the tests rated as most frequently used according to both the Shulman study and current survey. An interesting finding was that a relatively large number of clinicians have had training exposure to the ACE-R, and this may explain why it was used more frequently than others.

What do clinicians look for in a screen for cognitive impairment? As previously described, practical factors such as availability (ranked as most important) and time required to use and score (ranked third most important) were important factors for clinicians when they chose a particular screen. Validity and reliability was considered second most important. Surprisingly, comprehensive coverage of the cognitive domains was rated second *least* important. Clinicians may use the MMSE and CDT most frequently because they meet the requirements of availability and brevity; however, most qualitative comments expressed agreement that the MMSE is psychometrically inadequate and biased according to sociodemographic variables. While these factors indirectly suggest why clinicians used the

above screens, the survey did not investigate why such a relatively small group of screens were used when there are so many screens currently available. It is likely due to clinicians being familiar with the small number of commonly used screens, while there is little exposure to the less well-known screens.

The survey indicated that cognitive screens were mostly used in assessments of dementia and/or age-related cognitive decline. The current diagnostic shift from detecting severe dementia to milder and/or earlier signs of cognitive impairment (Diniz, Yassuda, Nunes, et al., 2007; Hachinski, 2008), add further weight to the argument that clinicians have come to expect more from cognitive screens, but that the practical issues of day to day work limits a shift to newer and better screens. In other words, there has been a shift in the requirements of screens, but this has not translated into practice. Clinicians continue to use the MMSE despite wide agreement that it is inadequate. This could be due to clinicians seeking continuity; for example, when the MMSE is used to monitor change over time, and when comparing scores across patients and research studies where the MMSE was used.

It is recommended that clinicians consider using a more robust screening measure than the MMSE in this patient population. As formal MMSE scores can be derived from the ACE-R, using this screen instead would enable consistency in initial and follow-up assessment and comparison over time despite a change of routine screen. In cases where time is crucial, the MoCA could be a compromise as it is shorter, very similar to the ACE-R, with clear cognitive domains and satisfactory psychometric properties. It too is freely available, but MMSE scores cannot be derived from the MoCA.

There are a number of limitations to the generalisability of the present study. While the sample at first glance appears to be representative of clinicians belonging to their respective pertinent organisations, it is not representative of those who are not involved with these groups or those who chose not to complete the questionnaire. In hindsight, sampling may have been more

representative had recruitment involved mental health services for older adults directly, which would have included Occupational Therapists as well – a group that was not included in the study.

Further, the use of a broad, all-inclusive conceptualisation of screening instruments allowed for the inclusion of single cognitive subtests extracted from larger batteries such as the WAIS. However, these are not generally considered screening measures, as they were not initially designed for screening purposes, and do not provide clear dichotomous cut-off scores, and often cover single domains of cognitive function only, even though they are often used for screening or quick assessment purposes.

The inclusive approach of the current study (also used in the previous surveys discussed; Reilly et al., 2004; Shulman et al., 2006), allowed for a more comprehensive investigation of clinicians' views on screening, and revealed that respondents often used single subtests, perhaps as part of their own routine testing batteries.

#### References

- Anderson, T. M., Sachdev, P. S., Brodaty, H., Trollor, J. N., & Andrews, G. (2007). Effects of sociodemographic and health variables on Mini-Mental State Exam scores in older Australians. *American Journal of Geriatric Psychiatry*, 15, 467-476.
- Bak, T. A., & Mioshi, E. (2007). A cognitive bedside assessment beyond the MMSE: the Addenbrooke's Cognitive Examination. *Practical Neurology*, 7, 245-249.
- Bechtoldt, H. P., Benton, A. L., & Fogel, M. L. (1962). An application of factor analysis in neuropsychology. *The Psychological Record*, 12, 147-56.
- Black, S. A., Espino, D. V., Mahurin, R., Lichtenstein, M. J., Hazuda, H.P., Fabrizio, D., Ray, L. A., & Markides, K. S. (1999). The influence of noncognitive factors on the Mini-Mental State Examination in

- older Mexican-Americans: Findings from the Hispanic EPESE. *Journal of Clinical Epidemiology*, *52*, 1095-102.
- Borson, S., Scanlan, J., Brush, M., Vitalliano, P., & Dokmak, A. (2000). The mini-cog: a cognitive vital signs' measure for dementia screening in multi-lingual elderly. *International Journal of Geriatric Psychiatry*, 15, 1021-1027.
- Brandt, J. (1991). The Hopkins Verbal Learning Test: Development of a new memory test with six equivalent forms. *Clinical Neuropsychology*, *5*, 125-142.
- Buschke, H., Kuslansky, G., Katz, M., Stewart, W. F., Sliwinski, M. J., Eckholdt, H. M., & Lipton, R. B. (1999). Screening for dementia with the memory impairment screen. *Neurology*, *52*, 231-238.
- Cullen, B., O'Neill, B., Evans, J. J., Coen, R. F., & Lawlor, B. A. (2007).
  A review of screening tests for cognitive impairment. *Journal of Neurology, Neurosurgery and Psychiatry*, 78, 790-799.
- Delis, D. C., Kaplan, E., Kramer, J. H. (2001). *Delis-Kaplan Executive Function System*. San Antonio, TX: Psychological Corporation.
- Diniz, B. S. O., Yassuda, M. S., Nunes, P. V., Radanovic, M., Forlenza, O. V. (2007). Mini-Mental State Examination performance in mild cognitive impairment subtypes. *International Psychogeriatrics*, 19, 647-656.
- Drachman, D. A. & Swearer, J. M. (1996). Screening for dementia:

  Cognitive assessment screening test (CAST). *American Family Physician*, *54*(6), 200-208.
- Dubois, B., Slachevsky, A., Litvan, I., & Pillon, B. (2000). The FAB: a frontal assessment battery at bedside. *Neurology*, 55, 1621-1626.
- Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). Mini-Mental State: A practical method for grading the state of patients for the clinician. *Journal of Psychiatric Research*, *12*, 189-198.
- Froehlich, T. E., Robison, J. T., & Inouye, S. K. (1998). Screening for dementia in the outpatient setting: the time and change test. *Journal of the American Geriatric Society*, 46, 1056-1011.
- Golding, E. (1989). *The Middlesex Assessment of Mental State*. Bury St Edmunds, UK: Thames Valley Test Company, 1989.

- Hachinski, V. (2008). Shifts in thinking about dementia. Journal of the American Medical Association, 300, 2172-2173.
- Heilbronner, R.L., Kinsella, G.J., Ong, B., & McGregor, J., (1991).

  Lateralized brain damage and performance on Trail Making A and B, Digit Span Forward and Backward, and TPT memory and location. *Archives of Clinical Neuropsychology*, 6, 251-258.
- Hodkinson, H. M. (1972). Evaluation of a mental test score for assessment of mental impairment in the elderly. *Age Ageing*, *1*, 233-238.
- Jorm, A. F. (1994). A short form of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE): development and cross-validation. *Psychological Medicine*, 24, 145-53.
- Jorm, A. F., & Jacomb, P. A. (1989). The Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE): socio-demographic correlates, reliability, validity and some norms. *Psychological Medicine*, 19, 1015-1022.
- Jurica, P. J., Leitten, C. L., & Mattis, S. (2001). *Dementia Rating Scale*–2. Lutz, FL: Psychological Assessment Resources.
- Kiernan, R. J., Mueller, J., Langston, J. W., & Van Dyke, C. (1987). The Neurobehavioral Cognitive Status Examination: a brief but quantitative approach to cognitive assessment. *Annals of Internal Medicine*, 107, 481-485.
- Kuslansky, G., Buschke, H., Katz, M., Sliwinsky, M., & Lipton, R. B.
  (2002). Screening for Alzheimer's disease: the Memory Impairment
  Screen versus the conventional Three-word Memory Test. *Journal of the American Geriatric Society*, 50, 1086-91.
- Larner, A. J. (2007). Addenbrooke's Cognitive Examination-Revised (ACE-R) in day-to-day clinical practice. *Age Ageing*, *36*, 685-686.
- Lezak, M. D., Howieson, D. B., & Loring, D. W. (2004).

  \*Neuropsychological Assessment (4<sup>th</sup> Ed). Oxford University Press:

  New York, NY.
- Matarazzo, J. D., Wiens, A. N., Matarazzo, R. G., & Goldstein, S. G. (1974). Psychometric and clinical test-retest reliability of the Halstead impairment index in a sample of healthy, young, normal men. *Journal of Nervous and Mental Disorders*, 158, 37-49.

- McDowell, I., Kristjansson, B., Hill, G. B., Hebert, R. (1997). Community screening for dementia: the Mini-Mental State Examination (MMSE) and Modified Mini-Mental State Exam (3MS) compared. *Journal of Clinical Epidemiology*, *50*(4), 377-383.
- Mioshi, E., Dawson, K., Mitchell, J., Arnold, R., & Hodges, J. R. (2006). The Addenbrooke's Cognitive Examination revised (ACE-R): A brief cognitive test battery for dementia screening. *International Journal of Geriatric Psychiatry*, 21(11), 1078-1085.
- Mohs, R. C., Rosen, W. G., & Davis, K. L. (1983). The Alzheimer's disease assessment scale: an instrument for assessing treatment efficacy. *Psychopharmacology Bulletin*, *19*, 448-450.
- Molloy, D. W., Standish, T. I., & Lewis, D. L. (2005). Screening for mild cognitive impairment: comparing the SMMSE and the ABCS.

  Canadian Journal of Psychiatry, 50, 52-58.
- Nasreddine, Z. S., Phillips, N. A., Bedirian, V., Charnonneau, S., Whitehead, V., Collin, I., ... Cherthow, H. (2005). The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. *Journal of the American Geriatric Society*, *53*, 695-99.
- Passos, V. M. A., Giatti, L., Barreto, S. M., Figueiredo, R. C., Caramelli, P.,
  Benseñor, I., da Fonseca, M. J. M., Cade, N. V., Goulart, A. C.,
  Nunes, M. A., Alves, M. G. M., da Trindade, A. A. M. (2012).
  Verbal fluency tests reliability in a Brazilian multicentric study,
  ELSA-Brasil. *Arquivos de Neuro-Psiquiatria*, 69(5), 814-816.
- Pfeiffer, E. (1975). A short portable mental status questionnaire for the assessment of organic brain deficit in elderly patients. *Journal of the American Geriatric Society*, 23, 433-441.
- Randolph, C., Tierney, M. C., Mohr, E., & Chase, T. N. (1998). The
  Repeatable Battery for the Assessment of Neuropsychological Status
  (RBANS): preliminary clinical validity. *Journal of Clinical & Experimental Neuropsychology*, 20, 310-319.
- Reilly S., Challis D., Burns A., & Hughes J. (2004). The use of assessment scales in Old Age Psychiatry services in England and Northern Ireland. *Aging & Mental Health*, 8, 249-55.

- Reitan, R. M. (1958). Validity of the trail-making test as an indicator of organic brain damage. *Perceptual Motor Skills*, 8, 271-6.
- Reyes, M. A., Lloret, S. P., Gerscovich, E. R. (2009). Addenbrooke's Cognitive Examination validation in Parkinson's disease. European Journal of Neurology, 16, 142-147.
- Riddha B, & Rossor M. (2005). The Mini Mental State Examination. *Practical Neurology*, *5*, 298-303.
- Ritchie, K., & Fuhrer, R. (1996). The validation of an informant screening test for irreversible cognitive decline in the elderly: performance characteristics within a general population sample. *International Journal of Geriatric Psychiatry*, 11, 149-56.
- Roth, M., Tym, E., Mountjoy, C., Huppert, F. A., Hendrie, H., Verma, S., & Goddard, R. (1986). CAMDEX. A standardised instrument for the diagnosis of mental disorder in the elderly with special reference to the early detection of dementia. *British Journal of Psychiatry*, 149, 698-709.
- Royall, D. R., Mahurin, R. K., & Gray, K. F. (1992). Bedside assessment of executive cognitive impairment: The Executive Interview. *Journal of American Geriatric Society*, 40, 1221-1226.
- Shulman, K. I., Herrmann, N., Brodaty, H., Chiu, H., Lawlor, B., Ritchie,K., & Scanlan, J. M. (2006). IPA survey of brief cognitive screening instruments. *International Psychogeriatrics*, 8, 281-94.
- Shulman, K., Shedletsky, R. and Silver, I. (1986). The challenge of time: clock- drawing and cognitive function in old age. International Journal of Geriatric Psychiatry, 1, 135–141.
- Silverman, J. M, Breitner, J. C., Mohs, R. C., Davis, K. L. (1986).

  Reliability of the family history method in genetic studies of
  Alzheimer's disease and related dementias. *American Journal of Psychiatry*, 143, 1279-1282.
- Solomon, P. R., Hirschoff, A., Kelly, B., Relin, M., Brush, M., DeVeaux, R. D., & Pendlebury, W. W. (1998). A 7 minute neurocognitive screening battery highly sensitive to Alzheimer's disease. *Archives of Neurology*, 55, 349-55.

- Statistics New Zealand. (2000). *Population Aging in New Zealand*. Wellington: Statistics New Zealand
- Statistics New Zealand (2002). *Population Structure and Internal Migration*. Wellington: Statistics New Zealand.
- Storey, J. E., Rowland, J. T. J., Conforti, D. A., & Dickson, H. G. (2004). The Rowland Universal Dementia Assessment Scale (RUDAS): a multicultural cognitive assessment scale. *International Psychogeriatrics*, 16, 13–31.
- Sunderland, T., Hill, J. L., Mellow, A. M., Lawlor, B. A., Gundersheimer, J., Newhouse, P. A., & Grafman, J. H. (1989). Clock drawing in Alzheimer's disease. A novel measure of dementia severity. *Journal of the American Geriatric Society*, 37, 725-729.
- Teng, E. L., Hasegawa, K., Homma, A., Imai, A., Larson, E., Graves, A.
  ... Chui, D. (1994). The Cognitive Abilities Screening Instrument
  (CASI): A practical test for cross-cultural epidemiological studies of dementia. *International Psychogeriatrics*, 6, 45-58.
- Teng, E. L., & Chui, H. C. (1987). The Modified Mini-Mental State (3MS) examination. *Journal of Clinical Psychiatry*, 48, 314-18.
- The Royal Australian and New Zealand College of Psychiatrists. (2011).

  \*\*RANZCP annual report and review 2011. Melbourne, Australia: Author.
- Tombaugh, T. N., McDowell, I., Kristjansson, B., & Hubley, A. M. (1996).

  Mini-Mental State Examination (MMSE) and the modified MMSE

  (3MS): A psychometric comparison and normative data.

  Psychological Assessment, 8(1), 48-59.
- Wechsler D. (1997). Wechsler Adult Intelligence Scale Third Edition (WAIS–III). San Antonio: Pearson Education.
- Wilson, B. A., Cockburn, J. M., & Baddeley, A. D. (1985). *The Rivermead Behavioural Memory Test*. Bury St Edmunds: Thames Valley Test Co.

## Chapter 5

# The clinical utility of the ACE-R, 3MS, and MMSE in a New Zealand geriatric clinical setting

#### **Preface**

The findings of the online survey (Chapter 4) suggested the ACE-R as an appropriate screen for further evaluation due to its relative common use and that it appeared to meet the practical requirements clinicians had in using a particular screen (availability, brevity, and psychometric robustness).

The 3MS was added to the analysis as patient scores for this measure were available in the dataset and because, like the ACE-R, it contains the formal MMSE and was published as an extended and improved version of the MMSE.

The study is presented as a journal article which is to be submitted to an appropriate journal for possible publication.

# The Clinical Utility of the ACE-R versus the MMSE and 3MS: A retrospective New Zealand study

Article keywords: dementia, cognitive impairment, ACE-R, 3MS, MMSE

#### **Key points:**

- The ACE-R, 3MS, and MMSE could all differentiate dementia and milder forms of cognitive impairment; however when using the recommended cut-off scores, only the ACE-R could.
- There was no significant difference across the screen scores between MCI and comorbid mood disorder-MCI.
- Of the three screens, the ACE-R carried the most weight in predicting dementia within the diagnostic process.
- Optimal cut-off scores (providing the best balance between sensitivity and specificity) for dementia were 76.5 for the ACE-R, 81.5 for the 3MS, and 25.5 for the MMSE.

#### **Authors:**

Strauss, Heide-Marie\*, Leathem, Janet\*, Duncan, Crawford†, Humphries, Steven\*

#### **Institutions:**

6140

#### **Corresponding author:**

Professor Janet Leathem
School of Psychology
Massey University Wellington
PO Box 756
Wellington

<sup>\*</sup> Massey University, Wellington, New Zealand

<sup>&</sup>lt;sup>†</sup>Te Whare Ra Uta, Inpatient Psychogeriatric assessment unit at Kenepuru Hospital, Wellington, New Zealand

New Zealand

Tel: +64 4 801 5799 Ext: 62035

Fax: +64 4 801 0493

Email: J.M.Leathem@massey.ac.nz

There are no conflicts of interest regarding this study or its authors.

The study was approved by the Health and Disability Ethics Committees, Central Regional Ethics Committee, Ministry of Health, New Zealand (Ref. CEN/11/04/020).

#### **Abstract**

Objective: The increased prevalence of cognitive impairment and dementia has been paralleled with the development of a wide range of brief cognitive screening instruments. While the Mini-Mental State Exam (MMSE) remains the most commonly used screen, it is considered inadequate in the assessment of milder forms of cognitive impairment. It has been proposed that Addenbrooke's Cognitive Assessment-Revised (ACE-R) and/or the Modified Mini Mental State (3MS) replace the MMSE as both include the formal MMSE and extend on it. The current study investigated and compared the diagnostic utility, as indicated by the relative diagnostic weight, of the ACE-R, 3MS, and MMSE as part of a multidimensional diagnostic process within a clinical geriatric setting.

**Method:** The sample (N=281) was analysed retrospectively, and consisted of patients presenting with cognitive impairment complaints, and who were subsequently diagnosed with dementia, mild cognitive impairment (MCI), or a comorbid mood-MCI disorder. The ACE-R, 3MS, and MMSE items were embedded within a larger cognitive test battery, the total scores of which were used in conjunction with extensive interview assessment involving the patient, significant others, home visit/s, and an adaptive functioning assessment by a multidisciplinary team.

**Results**: All three screens could differentiate between dementia and MCI, and between dementia and mood-MCI, but not between MCI and mood-MCI. Further, when using established cut-off scores, only the ACE-R could detect MCI and mood-MCI. The ACE-R outperformed both the 3MS and MMSE for relative predictive weight within the diagnostic process. For the current sample, optimal cut-off scores (providing the best balance between sensitivity and specificity) for dementia were 76.5 for the ACE-R, 81.5 for the 3MS, and 25.5 for the MMSE. Of the ACE-R subdomains, the Memory and Orientation/Attention domains carried the most weight in predicting dementia.

**Conclusion:** While the ACE-R outperformed the 3MS and MMSE in terms of diagnostic weight within the gold standard, its published recommended cut-off scores may not be appropriate for the New Zealand population,

specifically if an optimal balance between sensitivity and specificity is required. The MMSE had a marginally higher optimal sensitivity and specificity ratio for detecting dementia; however, this could not be determined for MCI. While the ACE-R shows promise as a replacement for the MMSE, further research is required to assess its predictive and ecological validity within the New Zealand context.

#### Introduction

In developed nations, people are living longer as result of improved living conditions, advances in medicine, and availability of appropriate health care (Robine & Michel, 2004). This has resulted in an ever-expanding cohort of people at risk for developing cognitive impairment (CI) (Gao, Hendrie, Hall, & Hui, 1998). The upsurge in people with dementia and milder forms of CI has been paralleled with a development of brief screening tools for the assessment and diagnosis of CI (Cullen, O'Neill, Evans, et al., 2007).

The Mini-Mental State Examination (MMSE) (Folstein & Folstein, 1975) is most commonly used (Reilly, Challis, Burns, & Hughes, 2004; Shulman, Hermann, Brodaty, et al., 2006). While useful in the detection and monitoring of advanced stages of dementia (Ridha & Rossor, 2005), the MMSE is less sensitive in the detection of mild cognitive impairment (MCI) (Bak & Mioshi, 2007). With the current diagnostic shift from a focus on dementia to milder forms and earlier stages of cognitive impairment (Hachinski, 2008), a more sensitive measure is needed. In response, a number of screens addressing the limitations of the MMSE were developed. The downside of the proliferation of new measures was that comparisons between studies became difficult as they each used different, new measures. Further, switching from the MMSE to a newer measure created difficulties in continuity in follow-up assessments.

The Addenbrooke's Cognitive Assessment (ACE) (Mathuranath, Nestor, Berrios, et al., 2000) and Modified Mini-Mental State (3MS) (Teng & Chui, 1987), were developed in part as screening tools addressing the shortcomings of the MMSE. While still integrating the MMSE, they thereby enabled comparisons over time, between patients, and between research studies.

Studies investigating the performance of the ACE found it to be superior to the MMSE in the detection of dementia, and able to differentiate between Alzheimer's disease and fronto-temporal dementia (Mathuranath et al., 2000), and other subtypes of dementia (Davies, Dawson, Mioshi, et al., 2008; Galton et al., 2005; Larner, 2007). Further, the ACE differentiates between patients with dementia and those with affective disorders (Dudas, Berrios, & Hodges, 2005), and has sensitivity comparable to the Dementia Rating Scale (Bak, Rogers, Crawford et al., 2005) (a functional rather than neuropsychological measure of dementia severity) (Bak & Mioshi, 2007; Mattis, 1976). However, a number of weaknesses have been linked with the ACE, including limited cross-cultural validity, ceiling effects for the naming component, a limited visuospatial component, and a lack of equivalent forms (Mioshi et al., 2006). In response to these limitations, the ACE was modified and published as the ACE-R in 2006 (Mioshi et al., 2006).

The ACE-R is reported to further differentiate between progressive and non-progressive fronto-temporal dementia (Hornberger et al., 2009), and like its predecessor, has consistently outperformed the MMSE (Bak & Mioshi, 2007). The ACE-R has been translated into at least 19 languages (Bak & Mioshi, 2007), and has been validated for the Japanese (Yoshida, Terada, Honda, et al., 2011), Greek (Konstantinopoulou, Kosmidis, Ioannidis, et al., 2011), Brazilian (Carvalho & Caramelli, 2007), Korean (Kwak, Yang, & Kim, 2010), Spanish (Garcia-Caballero, Garcia-Lado, Gonzalez-Hermida, et al., 2006), and German (Alexopoulos, Mioshi, Greim, et al., 2007) populations.

As shown in Table 1, numerous studies have investigated the clinical utility of the ACE and ACE-R in terms of sensitivity and specificity ratios. Likewise, as is also shown in Table 1, a number of studies have compared the clinical usefulness of the 3MS versus the MMSE in a variety of samples, and consistently reported that the 3MS exhibit greater reliability, validity, and sensitivity (Bland & Newman, 2001; Bravo & Hebert, 1997; Grace et al., 1995; McDowell et al., 1997; Nadler et al., 1995; Tombaugh et al., 1996; Jones et al., 2002).

Table 1
Research studies examining the clinical utility of the ACE, ACE-R, MMSE and 3MS for detecting dementia

Study	n	Cut-off score:	Sensitivity & specificity (%)	Diagnostic accuracy
ACE			<i>specially</i> (,0)	
Mathuranath et al.,	139	88*	93; 71	PPV 44%
2000		83**	82; 96	PPV 83%
				(based on 20% base
				rate)
Bier et al., 2005	158	88	97.9; 59	Not reported
		83	86.6; 70.5	
Garcia-Caballero et al.,	97	74	96; 85 <sup>†</sup>	Not reported
2006		68	96; 85 <sup>††</sup>	
Larner, 2007	285	88	100; 43	PPV 63%
		83	96; 63	PPV 71 %
		75	85; 83	PPV 83%
Alexopoulos et al., 2007	102	AD: 86	AD: 93; 86	Not reported
		VaD: 86	VaD: 93; 100	
Lloret et al., 2009	44	86	100; 77	0.67 Kappa
		83	92; 90	concordance
		82	85; 90	0.79
				0.73
Mathew et al., 2011	23	88	91.3; 93.6	43.48 (likelihood
		82	82.6; 100	ratio)
				likelihood ratio
				cannot be 1,
				specificity=0
Yoshida et al., 2011	201	80/81	98; 87	80/81: PPV 65%
		74/75	89; 99	74/75: PPV 94%
				(based on 20% base
				rate)
ACE-R				

Mioshi et al., 2006	241	88*	94; 89	69 %
		82**	84; 100	100%
				(based on 20% base
				rate)
Kwak et al., 2010	156	78	93; 95	78: 18.1:1 (likelihood
				ratio)
Konstantinopoulou et	95	85	97; 82	76 PPV
al., 2011		82	89; 88	82 PPV
		80	86; 92	86 PPV
MMSE				
Tombaugh et al., 1996	525	All AD:	81; 83	19: PPV 67-59
		Mild AD:	81; 77	19: PPV 79-93
				(age & educ.
				dependent)
McDowell et al., 1997	1166	16	20; 99	Not reported
		25	86; 77	
3MS				
McDowell et al., 1997	1166	61	41; 99	Not reported
		77	86; 87	
Bland & Newman,	1092	77	88: 90	PPV 29%
2001				

<sup>\*</sup>Cut-off maximising sensitivity; \*\*\* Cut-off maximising specificity

While studies show that the ACE and ACE-R can discriminate between various types of dementia, MCI, and other cognitive impairment disorders (Hornberger, Shelley, Kipps, Piquet, & Hodges, 2009; Kwak, Yand, & Kim, 2010; Larner, 2007; Mathew, Bak, & Hodges, 2011), only one study tested whether it (in this case the ACE) could differentiate between cognitive impairment due to mood difficulties and organically based dementia (Dudas, Berrios, & Hodges, 2005). While it is expected that the ACE-R should differentiate between mood disorders and dementia as well, this has to date not been formally researched. The 3MS and MMSE have likewise

<sup>&</sup>lt;sup>†</sup> Optimal cut-off for higher level of education group; <sup>††</sup> Optimal cut-off for lower level of education group.

not been assessed in this way. Further, no studies on the MMSE, 3MS, or ACE-R have to date been conducted in New Zealand.

Given the findings of previous research, it is hypothesised that the ACE-R would outperform the MMSE and 3MS in terms of differentiating between MCI and dementia, that it would carry the most diagnostic weight within the larger cognitive test battery, and that it would provide the most optimal sensitivity and specificity ratios for dementia. It is expected that the optimal cut-off scores in the current sample would be different to those proposed in the screens' original studies, as evidenced by other international studies where different cut-off scores were recommended for their specific sample populations. It is further hypothesised that, of the ACE-R subdomains, memory would be the strongest predictor of dementia.

#### Method

# **Screen description**

The ACE-R (Mioshi, et al., 2006) requires approximately 15 minutes of administration time, and consists of a series of subtests covering 5 cognitive domains: attention/orientation (constituting 18% of the overall score), memory (26%), verbal fluency (a measure of executive function) (14%), language (26%), and visuospatial (16%) (Mioshi et al., 2006). Clear scoring guidelines accompany the ACE-R, and are similar to those for the 3MS and MMSE. The Modified Mini-Mental State (3MS) (Teng & Chui, 1987) has, like the ACE-R, a scoring system from 0 to 100, takes approximately 15 minutes to administer, and covers attention/orientation, memory, language, and visuoconstruction (Teng & Chui, 1987). The 3MS consists of 15 tasks, while the ACE-R has 18. By contrast, the Mini-Mental State Exam (MMSE) (Folstein, Folstein, & McHugh, 1975), has six tasks, a scoring system of 0 to 30, and takes 5-10 minutes to administer (Folstein et al., 1975; Ridha & Rossor, 2005). Like the 3MS, it covers attention/orientation, memory, language, and visuoconstruction. Of the three screens, only the ACE-R has alternate, equivalent forms.

## **Participants**

Participants were those referred over the preceding four years to a Memory Clinic run by a mental health service for older adults in Wellington, New Zealand. Inclusion criteria were that they had been assessed according to a standard procedure in line with the National Institute for Health and Clinical Excellence (NICE) guidelines (2006) and the New Zealand Dementia Manifesto guidelines (2008). Specifically, assessments had to include a clinical interview with the patient and significant other/s, cognitive testing, an assessment of adaptive function and behaviour, and assessment of mental health, including mood.

For this Memory Clinic, all referrals involved older adults with memory complaints. Assessments routinely involved a clinical interview with the patient and significant other/s, with the psychogeriatrician, home visit/s by a nurse and/or occupational therapist who conducted an adaptive functioning assessment, and where considered appropriate cognitive testing by a clinical psychologist and neuroimaging, and. The administered cognitive test battery, known as the Extended Mental State (EMS), included the ACE-R, 3MS, MMSE, Frontal Assessment Battery (FAB) and Psychogeriatric Assessment Scale (PAS) items. The total score of the EMS provided the cognitive test performance quotient that informed final diagnoses in combination with the interview, adaptive functioning assessment, and neuroimaging sources of information.

Diagnoses followed a differential diagnosis process where all other possible causes of CI (physiological disorders, medication interactions, and mood disorder symptoms) were ruled out before a diagnosis of MCI or dementia was made. Diagnostic criteria followed ICD-10 criteria (World Health Organisation, 1992) and the Petersen criteria for MCI (Petersen, Roberts, Knopman, et al., 2009), and met the current Dementia Manifesto (2008) guidelines of assessment. Further, final diagnoses were made by a multidisciplinary team consisting of a psychogeriatrician, an occupational therapist, a nurse, and a psychologist.

In instances where a patient with CI had a mood disorder, the patient was classified as having a mood disorder regardless of potentially comorbid MCI or dementia. Those with a mood disorder diagnosis would be followed up on in the future to assess whether the remission of mood symptoms were correlated with an increase in cognitive abilities. The emphasis on ruling out depression as a cause of CI is important, as there are specific interventions available for mood difficulties. Nevertheless, close inspection of these patient scores indicated that they were most likely comorbid mood-MCI cases, and were subsequently treated as such in the statistical analyses. The diagnosis of MCI was made in cases where the patient had CI that was less severe than that typically found in dementia, did not present with significant functional impairments, and where underlying medical conditions or mood symptoms could not explain the impairment.

The overall sample consisted of 291 patients, all of whom presented with memory complaints. The mean age was 78.75 years, and females constituted 58% of the sample. Five people were Maori (1.7%), five Samoan (1.7%), and the remainder (96.8%) were 'New Zealand European' and 'Other European'. This suggests that, while our sample was consistent with the wider population<sup>1</sup> in terms of gender and Pacific Island ethnicity, Maori were underrepresented.

The selected sample for analysis constituted 208 patients who were grouped according to their final diagnostic outcome, namely comorbid mood-MCI, MCI (no mood component), and dementia, while those with other diagnoses (n=11), such as psychosis, delusional disorder, and intellectual disability, were not included in the analyses. The mood group constituted those diagnosed with major depressive episodes, depressive disorder, dysthymia, and adjustment disorder with depressive features, while also meeting criteria for MCI.

-

<sup>&</sup>lt;sup>1</sup> It is estimated that there were 40 746 New Zealanders with dementia in 2008, of which 60.2% were female and 39.8% male. Those of Maori and Pacific Island descent constituted 3% and 1.7% respectively (Alzheimer's New Zealand, 2008).

## Statistical analysis

The statistical analysis was conducted using the SPSS software package, version 19. Screen total score means and ACE-R subdomain score means were compared using one-way Analysis of Variance (ANOVA), or Welch and Brown-Forsyth tests if the data violated the assumption of homogeneity of variances, as indicated by a significant Levene test (Tabacknick & Fidell, 2007). Where Welch and Brown-Forsyth tests replaced ANOVA, the corresponding post-hoc multiple comparisons used Dunnet C and Games-Howell tests instead of Tukey-HSD and Bonferonni.

Due to the multivariate non-normality encountered in the dataset, logistic regression was chosen over discriminant analysis to test the ability of each of the screens, and the ACE-R subdomain scores to predict diagnostic group membership. As the ACE-R, 3MS, and MMSE items were embedded in the EMS, which, in turn, was part of the gold standard for overall assessment, logistic regression could only provide an indication of each screen's relative contribution to the final diagnosis, and could not assess predictive validity. Finally, optimal sensitivity and specificity for dementia for each screen was determined by ROC analyses.

# Results

## ACE-R, 3MS, and MMSE total scores

Comparisons of mean scores for the ACE-R, 3MS, and MMSE according to diagnostic group are shown in Table 2 below. It shows that the Mood-MCI and MCI groups were significantly different from the dementia group on all three screens, while there were no significant differences between the Mood-MCI and MCI groups across the screens.

A comparison between group means and the recommended cut-off scores for the screens indicate that for the ACE-R, the MCI and dementia groups scored below the recommended 88 and 82 cut-offs (Mioshi, et al., 2006),

while the mood group did not. For the 3MS, only the dementia group scored below the recommended cut-off of 77 (Bland & Newman, 2001). Similarly for the MMSE, only the dementia group scored below the recommended cut-off of 25 (McDowell et al., 1997

Table 2

Clinical comparison of the ACE-R, 3MS, and MMSE total scores for the three diagnostic groups<sup>†</sup>

Screen	Diagnostic gro	oups		Welch	Brown-Forsyth	Post-hoc comparisons*
	Mood	MCI	Dementia			
ACE-R	85.35 (9.14)	81.26	64.09 (12.17)	F(2, 36.471)=81.237,	F(2, 59.104)=90.501,	Mood = MCI >
	n = 14	(8.60)	n = 165	p=.000	p=.000	Dementia
		n = 57				
3MS	87.0 (17.487)	87.27	69.059 (13.269)	F(2, 27.872)=70.846,	F(2, 18.609)=36.118,	Mood = MCI >
	n = 12	(7.45)	n = 169	p=.000	p=.000	Dementia
		n = 43				
MMSE	26.73 (4.11)	26.91	21.05 (4.44)	F(2, 37.222)=93.247,	F(2, 34.203)=71.784,	Mood = MCI >
	n = 15	(2.25)	n = 208	p=.000	p=.000	Dementia
		n = 58				

 $<sup>^{\</sup>dagger}$ Values are mean  $SD^*p < 0.05$  for Dunnet C post hoc test

The lack of significant differences found between the Mood-MCI and MCI groups confirmed that the Mood-MCI group were likely a subset of MCI diagnoses, and showed that the presence of a mood disorder did not significantly affect MCI-related cognitive function. Accordingly, the Mood-MCI and MCI groups were collapsed into one for the purposes of the logistic regression, which left two diagnostic groups for analysis, a CI group, which combined the Mood-MCI and MCI groups and the original dementia group.

A binary logistic regression analysis was performed with the dichotomous diagnostic group variable (CI and Dementia) as the dependent variables and the ACE-R, 3MS, and MMSE total scores as predictor variables. Of the 208 patients, 12 cases were removed due to missing variables required in this analysis. A total of 196 cases were included in the analysis. Other sources of diagnostic information (the FAB and PAS items in the EMS, interview, adaptive functioning assessment, and neuroimaging results) were not included in the analysis.

The full model significantly predicted diagnostic outcomes (omnibus chi-square = 114.645, df = 3, p=.000; Hosmer and Lemeshow chi-square = 5.408, df = 8, p=.713). The model accounted for 64.0% of the variance in diagnostic status, with 66.7% of those without dementia successfully predicted, and 90.1% of those with dementia correctly predicted. Overall, 83.7% of predictions were accurate. The logistic regression showed that only the ACE-R reliably predicted dementia or non-dementia. The values of the coefficients revealed that an increase of one point on the ACE-R was associated with a decrease in the odds of dementia by a factor of 0.87.

## **ACE-R** subdomain scores

As with the comparisons of the screens' total score means, a series of oneway between-groups comparisons with post-hoc tests were conducted using the ACE-R subdomain scores. The analysis similarly used the three diagnostic groups, and where the assumption of homogeneity of variances was violated, the Walch and Brown-Forsyth tests replaced ANOVA.

Clinical comparisons between the ACE-R subdomain scores are presented in Table 3 below, and show that the MCI group scored significantly higher than the dementia group on all domains, while the Mood-MCI group scored significantly higher than the dementia groups on all domains except Visuospatial. There were no significant differences between the Mood-MCI and MCI groups in any domain.

Table 3

Clinical comparison of the ACE-R subdomain scores for the three diagnostic groups<sup>†</sup>

ACE-R subdomain	Diagnost	tic groups		ANOVA / Walch	Brown-Forsyth	Post-hoc comparisons
	Mood	MCI	Dementia			
Orientation/Attention	16.4	16.87	13.08	F(2, 38.957)=77.325,	F(2, 50.200)=75.941,	$Mood = MCI > Dementia^*$
	(2.29)	(1.511)	(3.29)	p=.000	p=.000	
	n = 15	n = 58	n = 201			
Memory	20.57	18.07	11.80	F(2, 233)=49.35, p=.000	Not applicable	Mood = MCI > Dementia**
	(6.11)	(4.37)	(4.91)			
	n = 14	n = 57	n = 165			
Verbal Fluency	9.42	8.45	5.84	F(2, 233)=30.940, p=.000	Not applicable	$Mood = MCI > Dementia^{**}$
	(2.24)	(2.59)	(2.54)			
	n = 14	n = 57	n = 165			
Language	24.14	23.05	20.62	Walch: F(2,	F(2, 72,68)=23.427,	$Mood = MCI > Dementia^*$
	(2.50)	(2.55)	(3.85)	38.03)=20.000, p=.000	p=.000	
	n = 14	n = 57	n = 164			
Visuospatial	14.14	14.77	12.54	Walch: F(2,	F(2, 59.411)=20.91,	Mood = MCI; Mood =
	(2.24)	(1.85)	(3.33)	37.21)=19.30, p=.000	p=.000	Dementia; MCI > Dementia*
	n = 14	n = 57	n = 165			

 $<sup>^{\</sup>dagger}$ Values are mean SD  $^{*}$ p < 0.05 for Games-Howell post hoc test;  $^{**}$ p < 0.05 for Tukey HSD post hoc test

As there were again no significant differences between the Mood-MCI and MCI groups on the ACE-R subdomains, a binary logistic regression analysis was performed with the dichotomous diagnostic group variable (CI and Dementia) as dependent variable, and the Memory, Orientation/Attention, Verbal Fluency, Language, and Visuospatial subdomains of the ACE-R as predictor variables. The full model significantly predicted diagnostic outcomes (omnibus chi-square = 126.008, df = 5, p=.000; Hosmer and Lemeshow chi-square = 8.960, df = 8, p=.346). The model accounted for 58.8% of the variance in diagnostic status, with 67.6% of those without dementia successfully predicted. 88.4% Of predictions for the dementia group were accurate. Overall, 82.1% of predictions were accurate.

The regression analysis indicated that the Memory, Orientation/Attention, Verbal Fluency, and Visuospatial subdomains reliably predicted diagnostic status, while the Language subdomain did not. The values of the coefficients revealed that an increase of one point in these subdomains is associated with a decrease in the odds of dementia by a factor of 0.84 for Memory, 0.63 for Orientation/Attention, 0.81 for Verbal Fluency, and 0.82 for Visuospatial.

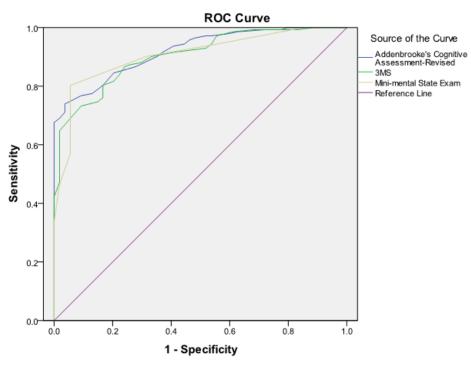
## **ROC** analyses

Receiver operating characteristic (ROC) analyses were conducted for each screen in order to determine the relative accuracy of the screen total score in predicting diagnostic outcome – CI and dementia. Areas under the curve (AUC) can range from 0 (perfect negative prediction) to .50 (chance) to 1.00 (perfect positive prediction). The AUC can be interpreted according to predictive ability or effect size, with an AUC above .65 indicating good predictive ability, while AUC of .56 indicates small effect, .64 indicates moderate effect, and .71 indicates large effect (Rice & Harris, 2005).

The ROC curve for the ACE-R, 3MS, and MMSE total scores is shown in Figure 1. The ACE-R had the largest AUC (.919), followed by the MMSE

(.906) and the 3MS (.903). This suggests that the probability of a randomly selected non-dementia patient scoring higher than a randomly selected dementia patient is 91.9% for the ACE-R, 90.6% for the MMSE, and 90.3% for the 3MS. The asymptomatic significance is less than .05 for all three screens, which means that using any of the measures offers superior predictive ability to guessing.

The AUC statistics for the three screens are provided in Table 4. Overall, the ACE-R had the most predictive power, followed closely by the MMSE and 3MS. Overall, the effect sizes for each ROC curve analysis were in the large range.



Diagonal segments are produced by ties.

**Figure 1.** Receiver Operating Characteristic Curve of the ACE-R, 3MS, and MMSE as a function of sensitivity and specificity at identifying dementia (N = 196).

Table 4

Area Under the Curve statistics for the ACE-R, 3MS, and MMSE (N=196)

				Asymptotic	2 95% Confidence
			Asymptotic	Interval	
Test Result Variable	Area	Std. Error <sup>a</sup>	Sig. <sup>b</sup>	Lower Bou	nd Upper Bound
ACE-R	.919	.018	.000	.883	.956
3MS	.903	.021	.000	.861	.945
MMSE	.906	.022	.000	.862	.949

- a. Under the nonparametric assumption
- b. Null hypothesis: true area = 0.5

Using the established cut-off scores for the ACE-R, 88 and 82 (Mioshi et al., 2006), as a guide, the present analysis found a sensitivity of 99.3% and specificity of 27.8% for the cut-off score 88.5 (specificity obtained by formula: 1-.722=.278). For the lower cut-off score 82, sensitivity was 95.8% and specificity 53.7%. For this sample, the optimal cut-off score (providing the best balance between sensitivity and specificity) was 76.5, which gave a sensitivity of 84.5% and a specificity of 79.6%. As expected, the sensitivity and specificity of this sample were lower than the original ACE-R study (Mioshi et al., 2006), as there was no healthy, unimpaired control group in our clinical sample.

The ROC analysis for the MMSE indicated that a total score of 25.5 out of a possible 30 provided a sensitivity of 84.5% and specificity of 83.3%. The ROC analysis for the 3MS indicated that the optimal cut-off score was 81.5, which produced a sensitivity of 81.7% and specificity of 79.6%. Optimal cut-off scores for the screens are provided in Table 5 below.

Table 5

Optimal cut-off scores for the current sample and associated sensitivity and specificity for the ACE-R, 3MS, and MMSE

Screen	Cut-off score	Sensitivity & specificity
		(%)
ACE-R	76.5	84.5 & 79.6
3MS	81.5	81.7 & 79.6
MMSE	25.5	84.5 & 83.3

#### **Discussion**

Results indicated that all three screens could differentiate between those with dementia and those with comorbid mood-MCI or MCI; however, when using the recommended cut-off score for each screen, only the ACE-R could detect milder forms of CI. As there were no significant differences in the cognitive scores between the mood-MCI and MCI group, the current study showed that none of the screens differentiated between comorbid mood-MCI and MCI, which suggests that MCI patients with mood disorders did not have significantly different cognitive profiles of function.

Research consistently indicates a strong association between depression and dementia, with depression often misdiagnosed as dementia in older people (up to 32% of cases). ,Depression is often a part of the early stages of dementia, and 30-40% of those with dementia experience depression at some stage during the course of illness (Pfennig, Littmann, & Bauer, 2007). A number of studies have suggested that depression may directly impair cognitive function (Schatzberg, 2002; Zakzanis, Leach, & Kaplan, 1999); however, newer studies (e.g., McClintock, Husain, Greer, & Cullum, 2010) have questioned the nature of the correlation, as some neuropsychological deficits continue after remission of clinical depression (Boeker, Schulze, Richter, et al., 2012), while depression severity and age

of onset further mediate the relationship between depression and cognitive impairment (McClintock, Husain, Greer, & Cullum, 2010).

The differential diagnosis approach used by the Memory Clinic in this study meant that patients who may have fulfilled criteria for MCI, but scored in the clinical range for mood disorders, were classified as mood disordered, the rationale being that only when mood symptoms are resolved, and CI remains, can MCI or dementia be more accurately diagnosed. As described, subsequent analysis of the Mood group test scores led to their reclassification as co-morbid mood-MCI for the purpose of analyses. The lack of difference between the MCI and mood-MCI groups may have reflected both groups' MCI profile of function rather than cognitive function impaired by mood versus MCI, and further underscored the lack of a purely linear relationship between mood problems and cognitive impairment.

The logistic regression comparing the dementia and CI groups revealed that, of the three screens, the ACE-R carried the most weight in reliably predicting dementia versus CI in a dataset where 90.1% of those with dementia were correctly classified. Given that these screens were a part of the wider gold standard assessment process, the regression provided an indication of the relative weight that each screen carried in making diagnoses where the respective screen items were embedded within the test battery, and where their scores added to the final, total cognitive testing score used in decision making. Again, this was from a sample where all patients had some degree of subjective memory complaint or CI (no healthy controls).

As with the screens' total scores, analysis of the ACE-R subdomain scores revealed significant differences between MCI and dementia, and no significant differences between mood and MCI on all the subdomains. However, while there were significant differences between MCI and dementia on the Visuospatial subdomain, there were, unexpectedly, no significant differences between mood and dementia. As visuospatial

abilities tend toward impairment in various types of dementia (Lezak, Howieson, & Loring, 2004), the impairment observed in the mood group may be due to anomalous visuospatial scores particular to this group. This finding should be interpreted with caution.

Of the ACE-R subdomains, Memory and Orientation/Attention, followed by Verbal Fluency (a measure of executive function), were the strongest predictors of dementia; while Visuospatial had less predictive ability, Language did not reliably predict dementia. This was consistent with the hypothesis that the Memory domain would carry the most weight in predicting diagnosis.

Consistent with the logistic regression, ROC analyses showed that the ACE-R had the best predictive ability, and, in this case, followed closely by the MMSE and 3MS. Areas Under the Curve for the screens indicated that all three screens had large effect sizes. Optimal cut-off scores for this sample, that is, scores which provided the highest sensitivity *and* specificity, were 76.5 for the ACE-R, 81.5 for the 3MS, and 25.5 for the MMSE.

For the ACE-R, the optimal cutoff score differed from those originally recommended (Mioshi et al., 2006). The Mioshi study recommended 88 for maximised sensitivity and 82 for maximised specificity, which implies that using 88 may be useful for detecting MCI, while 82 would be more appropriate for dementia. However, while the 88 cut-off produced excellent sensitivity and good specificity, it produced an inadequate positive predictive value (PPV); conversely, the 82 cut-off produced good sensitivity, excellent specificity, and excellent PPV (see Table 1). In contrast, the current recommended cut-off for the ACE-R (76.5) produced good sensitivity and adequate specificity for detecting dementia in a New Zealand clinical setting. This cut-off score is similar to that recommended by Kwak et al. (2010), but in the current sample this cut-off obtained lower sensitivity and specificity than in the Kwak sample.

The 3MS cutoff score recommended by Bland & Newman (2001), 77, which provided good sensitivity and excellent specificity, was lower than the optimal cut-off score for the current sample. The optimal cut-off score for the current sample (81.5) provided good sensitivity and adequate specificity, similar to that of the ACE-R. The optimal MMSE cut-off score for the New Zealand sample was 25.5, which provided good sensitivity and good specificity for detecting dementia. This was very similar to the MMSE cut-off score (25) recommended by McDowell et al. (1997), which in their sample provided good sensitivity and adequate specificity.

Overall, the MMSE provided the best balance between sensitivity and specificity for detecting dementia in the New Zealand sample. The MMSE is considered effective in detecting dementia and following disease progression on the severe end of the CI spectrum (Bak et al., 2005), and this was confirmed in the current study. While the MMSE's ability to detect MCI is questioned (Bak et al., 2005), it could not be determined with this sample.

#### Limitations

First, given that the ACE-R, 3MS, and MMSE items were embedded in the EMS, which, in turn, was part of a gold standard assessment for diagnosis of MCI or dementia, logistic regression could only provide an indication of each screen's relative contribution to the final diagnosis, and could not assess predictive validity. Second, the clinical utility of the ACE-R, 3MS, and MMSE could not be determined for detecting MCI. Third, given that both groups were cognitively impaired and separated only by degree, the sensitivity and specificity values obtained were lower than it would have been if there was an unimpaired group for comparison. A fourth limitation was that cases in the mood group could not be followed up to determine who had true mood-related CI and/or comorbid MCI.

## **Implications**

Findings suggest that the initial assessment process employed by the service, while very comprehensive, could be made more efficient by replacing the cognitive test battery (the EMS) with the ACE-R, and perhaps using the MMSE to follow disease progression where time is limited. Where time is not of the essence, the ACE-R is a useful follow-up measure as it has two alternate forms, thereby limiting potential retesting or learning effects.

The MMSE's optimal sensitivity and specificity ratio for dementia was surprisingly higher than that of the ACE-R and 3MS, albeit by a small margin. Further research is required to investigate its sensitivity and specificity for MCI. In addition, given that the MMSE has been shown to have a number of demographic biases, the ACE-R should be assessed for similar biases before it can be recommended to replace the widespread use of the MMSE.

#### References

- Alexopoulos, P., Mioshi, E., Greim, B., & Kurz, A. (2007). Brief assessment of cognitive mental status in German: The Addenbrooke's Cognitive Examination (ACE) and the Addenbrooke's Cognitive Examination Revised (ACE-R). *European Journal of Geriatrics*, *9*(4), 175-180.
- Alzheimers New Zealand. (2008). New Zealand 2008 Dementia Manifesto.
  Wellington, NZ: Alzheimers New Zealand.
- Bak, T. H, Mioshi E. (2007). A cognitive bedside assessment beyond the MMSE: the Addenbrooke's Cognitive Examination. *Practical Neurology*, 7, 245-249.
- Bak, T. H., Rogers, T. T., Crawford, L. M., Hearn, V. C., Mathuranath, P. S., & Hodges, J. R. (2005). Cognitive bedside assessment in atypical parkinsonian syndromes. *Journal of Neurology*, *Neurosurgery and Psychiatry*, 76(3), 420-422.

- Bland, R. C., & Newman, S. C. (2001). Mild dementia or cognitive impairment: The Modified Mini-Mental State Examination (3MS) as a screen for dementia. *Canadian Journal of Psychiatry*, 46(6), 506-510.
- Boeker, H., Schulze, J., Richter, A., Nikisch, G., Schuepbach, D., & Grimm, S. (2012). Sustained cognitive impairments after clinical recovery of severe depression. *Journal of Nervous and Mental Disease*, 200(9), 773-776.
- Bravo, G., & Hébert, R. (1997). Age-and education-specific reference values for the mini-mental and modified mini-mental state examinations derived from a non-demented elderly population.

  International Journal of Geriatric Psychiatry, 12(10), 1008-1018.
- Carvalho, V. A., & Caramelli, P. (2007). Brazilian adaptation of the Addenbrooke's Cognitive Examination-Revised (ACE-R).

  Dementia & Neuropsychologia, 2, 212-216.
- Cherie L. Marvel, C. L., & Paradiso, S. (2004). Cognitive and neurological impairment in mood disorders. *Psychiatric Clinics of North America*, 27(1), 19–36.
- Davies, R. R., Dawson, K., Mioshi, E., Erzinçlioğlu, S., & Hodges, J. R. (2008). Differentiation of semantic dementia and Alzheimer's disease using the Addenbrooke's Cognitive Examination (ACE).

  International Journal of Geriatric Psychiatry, 23(4), 370-375.
- Dudas, R. B., Berrios, G. E., & Hodges, J. R. (2005). The Addenbrooke's Cognitive Examination (ACE) in the differential diagnosis of early dementias versus affective disorder. *American Journal of Geriatric Psychiatry*, 13(3), 218-226.
- Folstein, M. F, Folstein, S. E, McHugh, P. R. "Mini-mental state". (1975). A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, 12, 189-98.
- Galton, C. J., Erzinçlioglu, S., Sahakian, B. J., Antoun, N., & Hodges, J.R. (2005). A comparison of the Addenbrooke's Cognitive Examination (ACE), conventional neuropsychological assessment, and simple MRI-based medial temporal lobe evaluation in the early

- diagnosis of Alzheimer's disease. *Cognitive and Behavioral Neurology*, 18(3), 144-150.
- Gao, S., Hendrie, H. S., Hall, H. S., & Hui, S. (1998). The relationship between age, sex, and the incidence of dementia and Alzheimer's disease: A meta-analysis. *Arch Gen Psychiatry*, 55, 809-15.
- García-Caballero, A., García-Lado, I., González-Hermida, J., Recimil, M. J., Area, R., Manes, F., ... Berrios, G. E. (2006). Validation of the Spanish version of the Addenbrooke's Cognitive Examination in a rural community in Spain. *International Journal of Geriatric Psychiatry*, 21, 239-245.
- Grace, J., Nadler, J. D., White, D. A., Guilmette, T. J., Giuliano, A. J., Monsch, A. U., Snow, & M. G. (1995). Folstein vs modified minimental state examination in geriatric stroke: Stability, validity, and screening utility. *Archives of Neurology*, 52(5), 477-484.
- Hachinski V. Shifts in thinking about dementia. (2008). *Journal of the American Medical Association*, 300, 2172-3.
- Hornberger, M., Shelley, B. P., Kipps, C. M., Piquet, O., & Hodges, J. R. (2009). Can progressive and non-progressive behavioural variant frontotemporal dementia be distinguished at presentation? *Journal of Neurology, Neurosurgery, and Psychiatry*, 80, 591-593.
- Jones, T. G., Schinka, J. A., Vanderploeg, R. D., Small, B. J., Graves, A.
  B., & Mortimer, J. A. (2002). 3MS normative data for the elderly.
  Archives of Clinical Neuropsychology, 17 (2), 171-177.
- Kwak, Y. T., Yang, Y., & Kim, G. W. (2010). Korean Addenbrooke's Cognitive Examination Revised (K-ACER) for differential diagnosis of Alzheimer's disease and subcortical ischemic vascular dementia. *Geriatrics and Gerontology International*, 10, 295-301.
- Konstantinopoulou, E., Kosmidis, M. H., Ioannidis, P., Kiosseoglou, G., Karacostas, D., & Taskos, N. (2011). Adaptation of Addenbrooke's Cognitive Examination-Revised for the Greek population. *European Journal of Neurology, 18*, 442-447.
- Mathuranath, P. S., Nestor, P. J., Berrios, G. E., Rakowicz, W., & Hodges,

- J. R. (2000). A brief cognitive test battery to differentiate Alzheimer's disease and frontotemporal dementia. *Neurology*, *55*, 1613-1620.
- Larner, A. J. (2007). Addenbrooke's Cognitive Examination (ACE) for the diagnosis and differential diagnosis of dementia. *Clinical Neurology and Neurosurgery*, 109, 491-494.
- Mathew, R., Bak, T. H., & Hodges, J. R. (2011). Screening for cognitive dysfunction in Corticobasal Syndrome: Utility of Addenbrooke's Cognitive Examination. *Dementia and Geriatric Cognitive Disorders*, 31, 254-258.
- McClintock, S. M., Husain, M. M., Greer, T. L., & Cullum, C. M. (2010). Association between depression severity and neurocognitive function in major depressive disorder: A review and synthesis. *Neuropsychology*, 24(1), 1-34.
- Mioshi, E., Dawson, K., Mitchell, J., Arnold, R., Hodges, J. R. (2006). The Addenbrooke's Cognitive Examination revised (ACE-R): A brief cognitive test battery for dementia screening. *International Journal of Geriatric Psychiatry*, 21(11), 1078-1085.
- McDowell, I., Kristjansson, B., Hill, G. B., & Hébert, R. (1997).

  Community screening for dementia: the Mini-Mental State

  Examination (MMSE) and Modified Mini-Mental State Exam

  (3MS) compared. *Journal of Clinical Epidemiology*, 50(4), 377-383.
- Nadler, J. D., Relkin, N. R., Cohen, M. S., Hodder, R. A., Reingold, J., Plum, F. (1995). Mental status testing in the elderly nursing home population. *Journal of Geriatric Psychiatry and Neurology*, 8(3), 177-183.
- National Institute for Health and Clinical Excellence. (2006). Dementia.

  Supporting People with Dementia and Their Carers in Health and
  Social Care (NICE Clinical Guideline 42). London: The National
  Institute for Health and Clinical Excellence.
- Petersen, R. C., Roberts, R. O., Knopman, D. S., Boeve, B. F., Geda, Y.

- E., Ivnik, R. J., Smith, G. E., & Jack Jr, C. R. (2009). Mild cognitive impairment: Ten years later. *Archives of Neurology*, 66(12), 1447-1455.
- Pfennig, A., Littmann, E., & Bauer, M. (2007). Neurocognitive Impairment and Dementia in Mood Disorders. *The Journal of Neuropsychiatry and Clinical Neurosciences*, 19, 373–382.
- Reilly S., Challis D., Burns A., & Hughes J. (2004). The use of assessment scales in Old Age Psychiatry services in England and Northern Ireland. *Aging & Mental Health*, 8, 249-55.
- Riddha B, & Rossor, M. (2005). The Mini Mental State Examination. *Practical Neurology*, 5, 298-303.
- Robine, J., & Michel, J. (2004). Looking forward to a general theory on population aging. *Journal of Gerontology*, *59A*(6), 590-597.
- Schatzberg, A. F. (2002). Major depression: Causes or effects? *American Journal of Psychiatry*, 159, 1077–1079.
- Shulman, K. I., Herrmann, N., Brodaty, H., Chiu, H., Lawlor, B., Ritchie,K., & Scanlan, J. M. (2006). IPA survey of brief cognitivescreening instruments. *International Psychogeriatrics*, 8, 281-94.
- Teng, E. L., & Chui, H. C. (1987). The Modified Mini-Mental State (3MS) examination. *Journal of Clinical Psychiatry*, 48, 314-18.
- Tombaugh, T. N., McDowell, I., Kristjansson, B., & Hubley, A. M. (1996).Mini-Mental State Examination (MMSE) and the modified MMSE (3MS): A psychometric comparison and normative data. *Psychological Assessment*, 8(1), 48-59.
- World Health Organisation. (1992). The ICD-10 classification of mental and behavioural disorders. Clinical descriptions and diagnostic guidelines. Geneva: World Health Organisation.
- Yoshida, H., Terada, S., Honda, H., Ata, T., Takeda, N. Kishimoto, Y., ... Kuroda, S. (2011). Validation of Addenbrooke's cognitive examination for detecting early dementia in a Japanese population. *Psychiatry Research*, 185, 211-214.
- Zakzanis, K. K., Leach, L., & Kaplan, E. (1999). *Neuropsychological differential diagnosis*. Netherlands: Krips, b. v. Meppel.

# Chapter 6

## **Conclusion**

### **6.1 Overall summary**

The current thesis involved two studies – the first, an online survey, informed the second, an evaluation of the clinical utility of three screens used in a clinical geriatric setting.

The initial literature review revealed that cognitive impairment (CI) is a serious concern for an aging global population and that its impact is not only felt within the family unit but also by society at large. While the prevalence of CI is expected to increase, clinical and social services are not geared to accommodate the expected surge in dementia cases worldwide. Further, the concept of CI and dementia has evolved over time and this, in turn, has influenced assessment and the requirements of screening instruments.

The diagnostic shift from dementia to the earlier stages of cognitive impairment was associated with the publication of new screens with increased coverage of the cognitive domains, and cut-off scores that maximised sensitivity to detect mild impairment. Making screens more comprehensive and robust unavoidably increases administration time; at the same time, it turns them into diagnostic tools instead of quick initial screens. Nevertheless, the attitudes and trends of cognitive screen use had to be determined first before a particular screen could be evaluated.

According to the subsequent online survey, the MMSE was the most frequently used screen, followed by the CDT, ACE-R, Verbal Fluency (FAS), Three Word Recall (3WR), and Trail-making (TMT). While the CDT, FAS, 3WR, and TMT are published stand-alone tools in their own

right, they are often included as tasks within broader assessment tools such as the ACE-R, 3MS, and MoCA.

The opinions of the survey respondents confirmed international publications that suggest the MMSE did not fulfil the requirements of current assessment and/or screening practices. As mentioned, these studies found that the MMSE was insensitive to the milder forms of CI, and that it was vulnerable to the effects of age, gender, education and ethnicity. The survey further suggested that the ACE-R showed promise as an appropriate alternative to the MMSE due to its continuity from the MMSE, and it meeting clinician requirements for brief screening instruments. The ACE-R was subsequently chosen for further evaluation, due to its high rate of use, and for including all five tests used most frequently by survey participants.

The second study (Chapter 5) evaluated the clinical utility of the ACE-R, MMSE and 3MS. It found that the MMSE successfully differentiated between milder forms of CI and dementia, as did the ACE-R and 3MS. While the MMSE's differentiating ability was in contrast with expectations and previous research, limitations inherent in the study could not explore this further, and this anomalous result may have been due to characteristics specific to the sample.

As expected, the MMSE showed comparable predictive ability for dementia (as viewed from its area under the curve in the ROC analysis); however, predictive ability, sensitivity, and specificity could not be calculated for MCI or comorbid mood-MCI. The study also did not investigate the MMSE's reported bias towards ethnicity due to the nature of the sample being overwhelmingly European, and other socio-economic variables not being available.

In terms of relative weight carried within the diagnostic process, the ACE-R outperformed both the 3MS and MMSE, with the 3MS carrying marginally higher diagnostic weight than the MMSE. Study 2 obtained no evidence that the 3MS added anything above and beyond the ACE-R (incremental validity).

Optimal sensitivity and specificity ratios – providing the best balance between sensitivity and specificity – were obtained with different cut-off scores than those recommended by the screens' original publications. This may have been due to the screens' authors seeking ratios that favoured sensitivity at the cost of specificity. In the Memory Clinic study however, the focus was on limiting both false-negatives and false-positives.

## **6.2 Implications**

With the reported shift in focus from dementia to milder forms of CI, clinicians screening for mild CI prefer highly sensitive screens. This has an unavoidable trade-off with specificity. For these clinicians the MMSE is, according to previous research, inadequate. However, the Memory Clinic service used screens for assessing the range of CI rather than purely screening for mild impairment. These types of services require an optimal balance between sensitivity and specificity to maximise accuracy.

If optimal sensitivity and specificity were the only requirements for assessment of specifically dementia, the MMSE would be adequate for initial and ongoing assessment of disease progression. However, while the MMSE meets the criteria of brevity, availability, and robustness in certain circumstances, it has limited coverage of the cognitive domains, and would therefore be blind to MCI and cognitive changes such as executive function in monitoring disease progression. Furthermore, its cultural and socioeconomic limitations make it inappropriate for widespread use.

As an extended and reportedly improved version of the MMSE, the 3MS fell short of expectations. Nevertheless, the 3MS discriminated mild CI from dementia, and showed adequate sensitivity and specificity similar to that of the ACE-R. The 3MS, however, was not frequently used according to the survey (Chapter 3), and is not as easily available as the ACE-R. It also did not add significantly to the assessment process in terms of incremental validity.

The ACE-R, well known and commonly used in New Zealand according to the survey findings and carrying the most weight of the three screens within the overall diagnostic process of the second study, appears to be the most appropriate screen to include in a comprehensive assessment process for age-related cognitive impairment. The test is available without charge and has two alternate forms, which facilitates retesting and patient followup. It covers the range of cognitive domains and provided a good, balanced sensitivity and specificity ratio within the studied sample. These are important aspects if a screen is to be used as part of an in-depth assessment process covering the range of cognitive impairment from MCI to dementia in its various presentations (such as fronto-temporal dementia, which is characterised by impairment in the executive domain), and which aims to limit both false-positives and false-negatives. Nevertheless, the ACE-R cannot be recommended based on the current studies alone, due to the limited generalsability of their findings, and the lack of New Zealandbased research findings regarding the ACE-R's predictive validity, reliability, and cross-cultural validity.

The findings of the current studies would be of use to other New Zealand-based Memory Clinics that have similar population demographics and follow similar assessment processes. For these clinics, the ACE-R may be an appropriate choice of screen, and if already in use, the recommended cut-off scores, associated sensitivity, and specificity ratios may further inform best evidenced-based practice.

#### 6.3 Future research

While Study 2 found the ACE-R to be an appropriate tool for assessing CI, there is a lack of research regarding its cross-cultural validity. While Mioshi et al. (2006) found no age-related bias, the ACE-R's potential bias towards other demographic variables is unknown, and further research is required in this area.

Future research is also required to assess the predictive validity of the ACE-R for dementia and MCI.

## **6.4 Concluding comments and recommendations**

Screening instruments are typically designed for screening purposes, that is, finding cases of impairment that require further in-depth assessment, and often occurs in a primary setting. However, results from the survey indicated that many secondary services use screens as complimentary diagnostic tools, as did the studied Memory Clinic service. Our study found that the ACE-R was adequate for use as a diagnostic tool, because it added valuable psychometric information similar to that which would have emerged from a neuropsychological assessment; in addition, its administration and scoring time is significantly shorter than a full neuropsychological assessment, and it was excellent at predicting final diagnostic outcome within the assessment process.

While screening in primary services requires screens with maximised sensitivity, such screens (like the ACE-R when using a higher cut-off score) often take longer to complete than the typical 15 minute GP appointment. It may be most prudent to refer any patients with subjective memory concerns that outweigh mood concerns for in-depth assessment with a specialised geriatric service (like a Memory Clinic). An initial, brief assessment at a memory clinic, using a measure like the ACE-R, and

administered by trained staff, may then determine whether a further, indepth assessment is required with a psychogeriatrician. Also, as the ACER contains the MMSE, scores can be readily compared with any previous assessments completed.

The excellent relative predictive ability (and incremental validity) of the ACE-R, makes for a cost-effective, relatively brief cognitive assessment which covers all the recommended cognitive domains. As such, the ACE-R total score indicates a 90.1% probability of genuine impairment.

It is further recommended that all initial assessments with CI patients include a valid and reliable mood screen due to the high comorbidity between mood difficulties and cognitive function, and the increased scope of treatment options available when a mood component confounds cognitive complaints.

#### References

- Albert, M. S., DeKosky, S. T., Dickson, D., Dubois, B., Feldman, H. H., Fox, N. C., ... Phelps, C. H. (2011). The diagnosis of mild cognitive impairment due to Alzheimer's disease:

  Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & Dementia*, 7, 270–279.
- Alexander, M. P., & Geschwind, N. (1984). Dementia in the elderly. In M. L. Albert (Ed.). Clinical Neurology of Aging. New York, Oxford University Press.
- Alexopoulos, P., Mioshi, E., Greim, B., & Kurz, A. (2007). Brief assessment of cognitive mental status in German: The Addenbrooke's Cognitive Examination (ACE) and the Addenbrooke's Cognitive Examination Revised (ACE-R). *European Journal of Geriatrics*, *9*(4), 175-180.
- Alzheimers New Zealand. (2008). New Zealand 2008 Dementia Manifesto. Wellington, NZ: Author.
- Alzheimers New Zealand. (2008). *Dementia Economic Impact Report*. Wellington, NZ: Author.
- American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders: DSM-IV-TR*. Washington, DC: Author.
- Anderson, T. M., Sachdev, P. S., Brodaty, H., Trollor, J. N., & Andrews,
  G. (2007). Effects of sociodemographic and health variables on
  Mini-Mental State Exam scores in older Australians. *American Journal of Geriatric Psychiatry*, 15, 467-476.
- Atiya, M., Hyman, B. T., Albert, M. S., & Killiany, R. (2003). Structural Magnetic Resonance Imaging in established and prodromal Alzheimer's disease: A review. *Alzheimer's Disease and Associated Disorders*, 17, 177-195.
- Arai, Y., & Zarit, S. H. (2011). Exploring strategies to alleviate caregiver

- burden: Effects of the National Long-Term Care insurance scheme in Japan. *Psychogeriatrics*, 11, 183-189.
- Bak, T. A., & Mioshi, E. (2007). A cognitive bedside assessment beyond the MMSE: the Addenbrooke's Cognitive Examination. *Practical Neurology*, 7, 245-249.
- Bak, T. H., Rogers, T. T., Crawford, L. M., Hearn, V. C., Mathuranath, P. S., & Hodges, J. R. (2005). Cognitive bedside assessment in atypical parkinsonian syndromes. *Journal of Neurology*, *Neurosurgery and Psychiatry*, 76(3), 420-422.
- Bechtoldt, H. P., Benton, A. L., & Fogel, M. L. (1962). An application of factor analysis in neuropsychology. *The Psychological Record*, 12, 147-56.
- Bermejo-Pareja, F., Benito-Leo´n, J., Vega, S., Olazara´n, J., de Toledo, M., Dı'az-Guzma'n, J., ... Roma'n, G. C. (2009). Consistency of clinical diagnosis of dementia in NEDICES: A population-based longitudinal study in Spain. *Journal of Geriatric Psychiatry and Neurology*, 22(4), 246-255.
- Berti, V., Mosconi, L., Glodzik, L., Li, Y., Murray, J., De Santi, S., Pupi, A., ... De Leon, M. J. (2011). Structural brain changes in normal individuals with a maternal history of Alzheimer's. *Neurobiology of Aging*, 32(12), 2325.e17-2325.e26.
- Black, S. A., Espino, D. V., Mahurin, R., Lichtenstein, M. J., Hazuda, H.
  P., Fabrizio, D., Ray, L. A., & Markides, K. S. (1999). The influence of noncognitive factors on the Mini-Mental State
  Examination in older Mexican-Americans: Findings from the
  Hispanic EPESE. *Journal of Clinical Epidemiology*, 52, 1095-102.
- Bland, R. C., & Newman, S. C. (2001). Mild dementia or cognitive impairment: The Modified Mini-Mental State Examination (3MS) as a screen for dementia. *Canadian Journal of Psychiatry*, 46(6), 506-510.
- Borson, S., Scanlan, J., Brush, M., Vitalliano, P., & Dokmak, A. (2000).

- The mini-cog: a cognitive vital signs' measure for dementia screening in multi-lingual elderly. *International Journal of Geriatric Psychiatry*, *15*, 1021-1027.
- Bravo, G., & Hébert, R. (1997). Age- and education-specific reference values for the mini-mental and modified mini-mental state examinations derived from a non-demented elderly population.

  International Journal of Geriatric Psychiatry, 12(10), 1008-1018.
- Brandt, J. (1991). The Hopkins Verbal Learning Test: Development of a new memory test with six equivalent forms. *Clinical Neuropsychology*, *5*, 125-142.
- Bruscoli, M., & Lovestone, S. (2004). Is MCI really just early dementia? A systematic review of conversion studies. *International Psychogeriatrics*, 16(2), 129-140.
- Buschke, H., Kuslansky, G., Katz, M., Stewart, W. F., Sliwinski, M. J., Eckholdt, H. M., & Lipton, R. B. (1999). Screening for dementia with the memory impairment screen. *Neurology*, *52*, 231-238.
- Busse, A., Hensel, A., Guhne, U., Angermeyer, M. C., & Riedel-Heller, S.
  G. (2006). Mild cognitive impairment: long-term course of four clinical subtypes. *Neurology*, 67, 2176 –2185.
- Campbell, A. J., McCosh, L. M., Reinken, J., & Allan, B. C. (1983).

  Dementia in old age and the need for services. *Age and Ageing*, *12*, 11–16.
- Carvalho, V. A., & Caramelli, P. (2007). Brazilian adaptation of the Addenbrooke's Cognitive Examination-Revised (ACE-R).

  Dementia & Neuropsychologia, 2, 212-216.
- Cherie L. Marvel, C. L., & Paradiso, S. (2004). Cognitive and neurological impairment in mood disorders. *Psychiatric Clinics of North America*, 27(1), 19–36.
- Cullen, B, O'Neill, B., Evans, J. J., Coen, R. F., & Lawlor, B. A. (2007).
  A review of screening tests for cognitive impairment. *Journal of Neurology, Neurosurgery and Psychiatry*, 78, 790-799.

- Crystal, H., Dickson, D., Fuld, P., Masur, D., Scott, R., Mehler, M., ... Wolfson, L. (1988). Clinico-pathologic studies in dementia: nondemented subjects with pathologically confirmed Alzheimer's disease. *Neurology*, *38*, 1682-1687.
- Das, S. K., Bose, P., Biswas, A., Dutt, A., Banerjee, T. K., Hazra, A., ... Roy, T. (2007). An epidemiologic study of mild cognitive impairment in Kolkata, India. *Neurology*, *68*, 2019 –2026.
- Davies, R. R., Dawson, K., Mioshi, E., Erzinçlioğlu, S., & Hodges, J. R. (2008). Differentiation of semantic dementia and Alzheimer's disease using the Addenbrooke's Cognitive Examination (ACE).

  International Journal of Geriatric Psychiatry, 23(4), 370-375.
- Davidoff, D. A. (1986). Issues in the clinical diagnosis of Alzheimer's disease. *American Journal of Alzheimer's Disease and Other Dementias*, 1(1), 9-15.
- Delis, D. C., Kaplan, E., Kramer, J. H. (2001). *Delis-Kaplan Executive Function System*. San Antonio, TX: Psychological Corporation, 2001.
- Del Ser, T., McKeith, I., Anand, R., Cicin-Sain, A., Ferrara, R., & Spiegel, R. (2000). The mini-cog: a cognitive 'vital signs' measure for dementia screening in multi-lingual elderly. *International Journal of Geriatric Psychiatry*, *15*, 1021-1027.
- Devanand, D. P., Liu, X., Tabert, M. H., Pradhaban, G., Cuasay, K., Bell, K., ... Pelton, G. H. (2008). Combining early markers strongly predicts conversion from mild cognitive impairment to Alzheimer's disease. *Biological Psychiatry*, 64(10), 871-879.
- Diniz, B. S. O., Yassuda, M. S., Nunes, P. V., Radanovic, M., Forlenza,
  O. V. (2007). Mini-Mental State Examination performance in mild cognitive impairment subtypes. *International Psychogeriatrics*, 19, 647-656.
- Dlugaj, M., Wimar, C., Wege, N., Verde, P. E., Gerwig, M., Dragano, N.,

- ... Siegrist, J. (2010). Prevalence of Mild cognitive impairment and its subtypes in the Heinz Nixdorf Recall Study Cohort.

  Dementia and Geriatric Cognitive Disorders, 30(4), 362-373.
- Drachman, D. A. & Swearer, J. M. (1996). Screening for dementia:

  Cognitive assessment screening test (CAST). *American Family Physician*, *54*(6), 200-208.
- Dubois, B., Slachevsky, A., Litvan, I., & Pillon, B. (2000). The FAB: a frontal assessment battery at bedside. *Neurology*, 55, 1621-1626.
- Dudas, R. B., Berrios, G. E., & Hodges, J. R. (2005). The Addenbrooke's Cognitive Examination (ACE) in the differential diagnosis of early dementias versus affective disorder. *American Journal of Geriatric Psychiatry*, 13(3), 218-226.
- Escandon, A., Al-Hammadi, N., & Galvin, J. E. (2010). Effect of cognitive fluctuation on neuropsychological performance in aging and dementia. *Neurology*, 74, 210–217.
- Ferri, C. P., Prince, M., Brayne, C., Brodaty, H., Fratiglioni, L., Ganguli,
  M., ... Scazufca, M. (2005). Global prevalence of dementia: A
  Delphi consensus study. *Lancet*, 366(9503), 17, 2112-2117.
- Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). Mini-Mental State: A practical method for grading the state of patients for the clinician. *Journal of Psychiatric Research*, *12*, 189-198.
- Fotuhi, M., Hachinski, V., & Whitehouse, P. J. (2009). Changing perspectives regarding late-life dementia. *Nature Reviews Neurology*, *5*, 649-658.
- Froehlich, T. E., Robison, J. T., & Inouye, S. K. (1998). Screening for dementia in the outpatient setting: the time and change test. *Journal of the American Geriatric Society*, 46, 1056-1011.
- Galton, C. J., Erzinçlioglu, S., Sahakian, B. J., Antoun, N., & Hodges, J.R. (2005). A comparison of the Addenbrooke's Cognitive Examination (ACE), conventional neuropsychological assessment, and simple MRI-based medial temporal lobe evaluation in the early

- diagnosis of Alzheimer's disease. *Cognitive and Behavioral Neurology*, 18(3), 144-150.
- Gao, S., Hendrie, H. S., Hall, H. S., & Hui, S. (1998). The relationship between age, sex, and the incidence of dementia and Alzheimer's disease: A meta-analysis. *Archives of General Psychiatry*, 55, 809-815.
- García-Caballero, A., García-Lado, I., González-Hermida, J., Recimil, M. J., Area, R., Manes, F., ... Berrios, G. E. (2006). Validation of the Spanish version of the Addenbrooke's Cognitive Examination in a rural community in Spain. *International Journal of Geriatric Psychiatry*, 21, 239-245.
- Golding, E. (1989). *The Middlesex Assessment of Mental State*. Bury St Edmunds, UK: Thames Valley Test Company, 1989.
- Grace, J., Nadler, J. D., White, D. A., Guilmette, T. J., Giuliano, A. J., Monsch, A. U., Snow, & M. G. (1995). Folstein vs. modified minimental state examination in geriatric stroke: Stability, validity, and screening utility. *Archives of Neurology*, *52*(5), 477-484.
- Grober, E., Hall, C., McGinn, M., Nicholls, T., Stanford, S., Ehrlich, A., ... Lipton, R. B. (2008). Neuropsychological strategies for detecting early dementia. *Journal of the International Neuropsychological Society*, 14, 130–142.
- Haaland, K. Y., & Swanda. R. M. (2008). Vascular dementia. In J. E.Morgan & J. H. Ricker (Eds.). *Textbook of ClinicalNeuropsychology*. New York: Taylor & Francis.
- Hachinski, V. (2008). Shifts in thinking about dementia. *Journal of the American Medical Association*, 300, 2172-2173.
- Haynes, S. N., & Lench, H. C. (2003). Incremental validity of new clinical assessment measures. *Psychological Assessment*, 15(4), 456-466.
- Hodkinson, H. M. (1972). Evaluation of a mental test score for assessment of mental impairment in the elderly. *Age Ageing*, *1*, 233-238.
- Hornberger, M., Shelley, B. P., Kipps, C. M., Piquet, O., & Hodges, J. R.

- (2009). Can progressive and non-progressive behavioural variant frontotemporal dementia be distinguished at presentation? *Journal of Neurology, Neurosurgery, and Psychiatry*, 80, 591-593.
- Hunsley, H. (2003). Introduction to the special section on incremental validity and utility in clinical assessment. *Psychological Assessment*, *15*(4), 443-445.
- Hunsley, J., & Meyer, G. J. (2003). The incremental validity of psychological testing and assessment: conceptual, methodological, and statistical issues. *Psychological Assessment*, 15(4), 446-455.
- Ishikawa, T., & Ikeda, M. (2007). Mild cognitive impairment in a population-based epidemiological study. *Psychogeriatrics*, 7, 104-108.
- Ismail, Z., Rajji, T. K., & Shulman, K. I. (2010). Brief cognitive screening instruments: an update. *International Journal of Geriatric Psychiatry*, 25, 111-120.
- Jorm, A. F. (1994). A short form of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE): development and cross-validation. *Psychological Medicine*, *24*, 145-53.
- Jorm, A. F., & Jacomb, P. A. (1989). The Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE): socio-demographic correlates, reliability, validity and some norms. *Psychological Medicine*, 19, 1015-1022.
- Jones, T. G., Schinka, J. A., Vanderploeg, R. D., Small, B. J., Graves, A. B., & Mortimer, J. A. (2002). 3MS normative data for the elderly. *Archives of Clinical Neuropsychology*, *17* (2), 171-177.
- Jurica, P. J., Leitten, C. L., & Mattis, S. (2001). *Dementia Rating Scale*–2. Lutz, FL: Psychological Assessment Resources.
- Kalaria, R. N., Maestre, G. E., Arizaga, R., Friedland, R. P., Galasko, D., Hall, K.,... Antuono, P. (2008). Alzheimer's disease and vascular dementia in developing countries: prevalence, management, and risk factors. *The Lancet Neurology*, 7(9), 812-826.

- Katzman, R., Terry, R., DeTeresa, R., Brown, T., Davies, P., Fuld, P., ... Peck, A. (1988). Clinical, pathological, and neurochemical changes in dementia: a subgroup with preserved mental status and numerous neocortical plaques. *Annals of Neurology*, *23*, 138-144.
- Kaye, E. D., Petrovic-Poljak, A., Nicolaas P. L. G. Verhoeff, N. P., & Freedman, M. (2010). Frontotemporal dementia and pharmacologic interventions. *Journal of Neuropsychiatry and Clinical Neuroscience*, 22, 19-29.
- Kiernan, R. J., Mueller, J., Langston, J. W., & Van Dyke, C. (1987). The Neurobehavioral Cognitive Status Examination: a brief but quantitative approach to cognitive assessment. *Annals of Internal Medicine*, 107, 481-485.
- Knopman, D., & Selnes, O. (2003). Neuropsychology of dementia. In K.
  M. Heilman & E. Valenstein (Eds.). *Clinical Neuropsychology* (4<sup>th</sup> *Ed.*). New York: Oxford University Press.
- Konstantinopoulou, E., Kosmidis, M. H., Ioannidis, P., Kiosseoglou, G., Karacostas, D., & Taskos, N. (2011). Adaptation of Addenbrooke's Cognitive Examination-Revised for the Greek population. European *Journal of Neurology*, *18*, 442-447.
- Kukull, W. A., & Ganguli, M. (2000). Epidemiology of dementia: concepts and overview. In S. DeKosky (Ed.), *Neurologic Clinics*. Philidelphia: W. B. Saunders.
- Kuslansky, G., Buschke, H., Katz, M., Sliwinsky, M., & Lipton, R. B. (2002). Screening for Alzheimer's disease: the Memory Impairment Screen versus the conventional Three-word Memory Test. *Journal* of the American Geriatric Society, 50, 1086-91.
- Kwak, Y. T., Yang, Y., & Kim, G. W. (2010). Korean Addenbrooke's Cognitive Examination Revised (K-ACER) for differential diagnosis of Alzheimer's disease and subcortical ischemic vascular dementia. *Geriatrics and Gerontology International*, 10, 295-301.
- Larner, A. J. (2007). Addenbrooke's Cognitive Examination-Revised (ACE-R) in day-to-day clinical practice. *Age Ageing*, *36*, 685-686.

- Lee, D. Y., Lee, J. H., Ju, Y., Lee, K. U., Kim, K. W., Jhoo, ... Woo, J. I. (2002). The prevalence of dementia in older people in an urban population of Korea: The Seoul Study. *Journal of the American Geriatric Society*, *50*, 1233-1239.
- Lezak, M. D., Howieson, D. B., & Loring, D. W. (2004).

  \*Neuropsychological Assessment (4<sup>th</sup> Ed). New York: Oxford University Press.
- Lough, S., Kipps, C. M., Treise, C., Watson, P., Blair, J. R., & Hodges, J.
  R. (2006). Social reasoning, emotion, and empathy in frontotemporal dementia. *Neuropsychologia*, 44, 950–958.
- Mathew, R., Bak, T. H., & Hodges, J. R. (2011). Screening for cognitive dysfunction in Corticobasal Syndrome: Utility of Addenbrooke's Cognitive Examination. *Dementia and Geriatric Cognitive Disorders*, 31, 254-258.
- Mathuranath, P. S., Nestor, P. J., Berrios, G. E., Rakowicz, W., & Hodges, J. R. (2000). A brief cognitive test battery to differentiate Alzheimer's disease and frontotemporal dementia. *Neurology*, 55, 1613-1620.
- Mayeux, R., Reitz, C., Brickman, A. M., Haan, M. N., Manly, J. J., Glymour, M. M., ... Morris, J. C. (2011). Operationalizing diagnostic criteria for Alzheimer's disease and other age-related cognitive impairment—Part 1. *Alzheimer's & Dementia*, 7, 15–34.
- McClintock, S. M., Husain, M. M., Greer, T. L., & Cullum, C. M. (2010). Association between depression severity and neurocognitive function in major depressive disorder: A review and synthesis. *Neuropsychology*, 24(1), 1-34.
- McDowell, I., Kristjansson, B., Hill, G. B., & Hébert, R. (1997).

  Community screening for dementia: the Mini-Mental State

  Examination (MMSE) and Modified Mini-Mental State Exam

  (3MS) compared. *Journal of Clinical Epidemiology*, 50(4), 377-383.
- McKhann, G. M., Knopman, D. S., Chertkow, H., Hyman, B. T., Jack, C.

- R. Jr., Claudia H. ... Phelps, C. H. (2011). The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & Dementia*, 7, 263–269.
- Meyer, G. J., Finn, S. E., Eyde, L., Kay, G. G., Moreland, K. L., Dies, R.
  R., ... Reed, G. M. (2001). Psychological testing and psychological assessment: a review of evidence and issues. *American Psychologist*, 56, 128-165.
- Mioshi, E., Dawson, K., Mitchell, J., Arnold, R., & Hodges, J. R. (2006). The Addenbrooke's Cognitive Examination revised (ACE-R): A brief cognitive test battery for dementia screening. *International Journal of Geriatric Psychiatry*, 21(11), 1078-1085.
- Mohs, R. C., Rosen, W. G., & Davis, K. L. (1983). The Alzheimer's disease assessment scale: an instrument for assessing treatment efficacy. *Psychopharmacology Bulletin*, *19*, 448-450.
- Molloy, D. W., Standish, T. I., & Lewis, D. L. (2005). Screening for mild cognitive impairment: comparing the SMMSE and the ABCS.

  Canadian Journal of Psychiatry, 50, 52-58.
- Morris, J. C., Storandt, M., McKeel, D. W., Rubin, E. H., Price, J. L., Grant, E. A., & Berg, L. (1996). Cerebral amyloid deposition and diffuse plaques in "normal" aging: Evidence for presymptomatic and very mild Alzheimer's disease. *Neurology*, 46(3), 707-719.
- Murphy, K. J., Troyer, A. K., Levine, B., & Moscovitch, M. (2008). Episodic, but not semantic, autobiographical memory is reduced in amnestic mild cognitive impairment. *Neuropsychologia*, 46(13), 3116-3123.
- Nadler, J. D., Relkin, N. R., Cohen, M. S., Hodder, R. A., Reingold, J., & Plum, F. (1995). Mental status testing in the elderly nursing home population. *Journal of Geriatric Psychiatry and Neurology*, 8(3), 177-183.
- Nasreddine, Z. S., Phillips, N. A., Bedirian, V., Charnonneau, S.,

- Whitehead, V., Collin, I., ... Cherthow, H. (2005). The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. *Journal of the American Geriatric Society*, 53, 695-99.
- National Institute for Health and Clinical Excellence. (2006). Dementia.

  Supporting People with Dementia and Their Carers in Health and

  Social Care (NICE Clinical Guideline 42). London: The National

  Institute for Health and Clinical Excellence.
- Nordlund, A., Rolstad, S., Klang, O., Lind, K., Pedersen, M., Blennow, K., ... Wallin, A. (2008). Episodic memory and speed/attention deficits are associated with Alzheimer-typical CSF abnormalities in MCI. *Journal of the International Neuropsychological Society*, 14(4), 582-590.
- Palmer, K., Backman, L., Winblad, B., & Fratiglioni, L. (2008). Mild cognitive impairment in the general population: occurrence and progression to Alzheimer disease. *American Journal of Geriatric Psychiatry*, 16, 603–611.
- Petersen, R. C., Roberts, R. O., Knopman, D. S., Geda, Y. E., Cha, R. H., Pankratz, ... Rocca, W. A. (2010). Prevalence of mild cognitive impairment is higher in men: The Mayo Clinic Study of Aging.

  Neurology, 75(10), 889-897.
- Petersen, R. C. (2004). Mild cognitive impairment as a diagnostic entity. *Journal of Internal Medicine*, 256, 183-194.
- Petersen, R. C., Roberts, R. O., Knopman, D. S., Boeve, B. F., Geda, Y.
  E., Ivnik, R. J., Smith, G. E., & Jack Jr, C. R. (2009). Mild cognitive impairment: Ten years later. *Archives of Neurology*, 66(12), 1447-1455.
- Pfeiffer, E. (1975). A short portable mental status questionnaire for the assessment of organic brain deficit in elderly patients. *Journal of the American Geriatric Society*, 23, 433-441.
- Pfennig, A., Littmann, E., & Bauer, M. (2007). Neurocognitive

- Impairment and Dementia in Mood Disorders. *The Journal of Neuropsychiatry and Clinical Neurosciences*, *19*, 373–382.
- Plassman, B. L., Langa, K. M., Fisher, G. G., Heeringa, S. G., Weir, D. R., Ofstedal, M. B., ... Wallace, R.B. (2007). Prevalence of dementia in the United States: The aging, demographics, and memory study. *Neuroepidemiology*, 29(1-2), 125-132.
- Randolph, C., Tierney, M. C., Mohr, E., & Chase, T. N. (1998). The
  Repeatable Battery for the Assessment of Neuropsychological
  Status (RBANS): preliminary clinical validity. *Journal of Clinical*& Experimental Neuropsychology, 20, 310-319.
- Reitan, R. M. (1958). Validity of the trail-making test as an indicator of organic brain damage. *Perceptual Motor Skills*, 8, 271-6.
- Reyes, M. A., Lloret, S. P., Gerscovich, E. R. (2009). Addenbrooke's Cognitive Examination validation in Parkinson's disease. *European Journal of Neurology*, *16*, 142-147.
- Reilly S., Challis D., Burns A., & Hughes J. (2004). The use of assessment scales in Old Age Psychiatry services in England and Northern Ireland. *Aging & Mental Health*, 8, 249-55.
- Riddha B, & Rossor M. (2005). The Mini Mental State Examination. *Practical Neurology*, *5*, 298-303.
- Ritchie, K., & Fuhrer, R. (1996). The validation of an informant screening test for irreversible cognitive decline in the elderly: performance characteristics within a general population sample. *International Journal of Geriatric Psychiatry*, 11, 149-56.
- Roberts, J. S., Karlawish, J. H., Uhlmann, W. R., Petersen, R. C., Green, R. C. (2010). Mild cognitive impairment in clinical care: A survey of American Academy of Neurology members. *Neurology*, 75(5), 425-431.
- Robine, J., & Michel, J. (2004). Looking forward to a general theory on population aging. *Journal of Gerontology*, 59A(6), 590-597.
- Roth, M., Tym, E., Mountjoy, C., Huppert, F. A., Hendrie, H., Verma, S.,

- & Goddard, R. (1986). CAMDEX. A standardised instrument for the diagnosis of mental disorder in the elderly with special reference to the early detection of dementia. *British Journal of Psychiatry*, 149, 698-709.
- Royall, D. R., Mahurin, R. K., & Gray, K. F. (1992). Bedside assessment of executive cognitive impairment: The Executive Interview. *Journal of American Geriatric Society*, 40, 1221-1226.
- Sangren, P. V. (1929). Comparative validity of primary intelligence tests. *Journal of Applied Psychology, 13*, 394-412.
- Schatzberg, A. F. (2002). Major depression: Causes or effects? *American Journal of Psychiatry*, 159, 1077–1079.
- Sahadevan, S., Saw, S. M., Gao, W., Tan, L., Chin, J. J., ye Hong, C., & Venketasubramanian, N. (2008). Ethnic differences in Singapore's dementia prevalence: The Stroke, Parkinson's Disease, Epilepsy, and Dementia in Singapore Study. *Journal of the American Geriatric Society*, *56*, 2061–2068.
- Sampson, E. L., Blanchard, M. R., Jones, L. Tookman, A., & King, M. (2009). Dementia in the acute hospital: prospective cohort study of prevalence and mortality. *The British Journal of Psychiatry*, 195, 61-66.
- Saunders, N., L., J. & Summers, M. J. (2011). Longitudinal deficits to attention, executive, and working memory in subtypes of mild cognitive impairment. *Neuropsychology*, 25(2), 237–248.
- Sbordone, R. J., Saul, R. E., & Purisch, A. D. (2007). Neuropsychology for psychologists, health care professionals, and attorneys (3<sup>rd</sup> Edition). Taylor & Francis.
- Sechrest, L. (1963). Incremental validity: A recommendation. *Educational* and *Psychological Measurement*, 23, 153-158.
- Seshadri, S., Beiser, A., Au, R., Wolf, P. A., Evans, D. A., Wilson, ...
  Chui, H. C. (2011). Operationalizing diagnostic criteria for
  Alzheimer's disease and other age-related cognitive impairment—
  Part 2. *Alzheimer's & Dementia*, 7, 35–52.

- Setia, M., Islam, A. M., Thompson, J. P., & Matchar, D. B. (2011).

  Stakeholders' perspective on issues and challenges associated with care and treatment of aging-related cognitive impairment disorders in Singapore. *International Psychogeriatrics*, 23, 1421-1432.
- Shepherd, I., & Leathem, J. M. (1999). Factors affecting performance in cross-cultural neuropsychology: From a New Zealand bicultural perspective. *Journal of the International Neuropsychological Society*, *5*, 83–84.
- Shulman, K. I., Herrmann, N., Brodaty, H., Chiu, H., Lawlor, B., Ritchie,K., & Scanlan, J. M. (2006). IPA survey of brief cognitivescreening instruments. *International Psychogeriatrics*, 8, 281-94.
- Schulz, R. & Martire, L. M. (2004) Family Caregiving of Persons with Dementia: Prevalence, health effects, and support strategies.

  American Journal of Geriatric Psychiatry, 12(3), 240-249.
- Silverman, J. M, Breitner, J. C., Mohs, R. C., Davis, K. L. (1986).

  Reliability of the family history method in genetic studies of

  Alzheimer's disease and related dementias. *American Journal of Psychiatry*, 143, 1279-1282.
- Solomon, P. R., Hirschoff, A., Kelly, B., Relin, M., Brush, M., DeVeaux, R. D., & Pendlebury, W. W. (1998). A 7 minute neurocognitive screening battery highly sensitive to Alzheimer's disease. *Archives of Neurology*, 55, 349-55.
- Statistics New Zealand. (1995). *New Zealand Now: 65 plus*. Wellington: Statistics New Zealand.
- Statistics New Zealand. (2000). *Population Aging in New Zealand*. Wellington: Statistics New Zealand
- Statistics New Zealand (2002). *Population Structure and Internal Migration*. Wellington: Statistics New Zealand.
- Steffens, D. C., Fisher, G. G., Langa, K. M., Potter, G. G., & Plassman, B. L. (2009). Prevalence of depression among older Americans: the Aging, Demographics and Memory Study. *International Psychogeriatrics*, 21(5), 879-888.

- Storey, J. E., Rowland, J. T. J., Conforti, D. A., & Dickson, H. G. (2004). The Rowland Universal Dementia Assessment Scale (RUDAS): a multicultural cognitive assessment scale. *International Psychogeriatrics*, 16, 13–31.
- Sunderland, T., Hill, J. L., Mellow, A. M., Lawlor, B. A., Gundersheimer,
  J., Newhouse, P. A., & Grafman, J. H. (1989). Clock drawing in
  Alzheimer's disease. A novel measure of dementia severity.
  Journal of the American Geriatric Society, 37, 725-729.
- Tabachnick, B. G., & Fidell, L. S. (2007). *Using Multivariate Statistics* (5<sup>th</sup> *Edition*). Boston: Allyn and Bacon.
- Teng, E. L., & Chui, H. C. (1987). The Modified Mini-Mental State (3MS) examination. *Journal of Clinical Psychiatry*, 48, 314-18.
- Teng, E. L., Hasegawa, K., Homma, A., Imai, A., Larson, E., Graves, A.
  ... Chui, D. (1994). The Cognitive Abilities Screening Instrument
  (CASI): A practical test for cross-cultural epidemiological studies
  of dementia. *International Psychogeriatrics*, 6, 45-58.
- Tombaugh, T. N., McDowell, I., Kristjansson, B., & Hubley, A. M. (1996). Mini-Mental State Examination (MMSE) and the modified MMSE (3MS): A psychometric comparison and normative data. *Psychological Assessment*, 8(1), 48-59.
- Von Dras, D. D., & Blumenthal, H. T. (1992). Dementia of the aged:
  Disease or atypical-accelerated aging? Biopathological and
  psychological perspectives. *Journal of the American Geriatrics Society*, 40(3), 285-294.
- Wechsler D. (1997). Wechsler Adult Intelligence Scale Third Edition (WAIS–III). San Antonio: Pearson Education.
- Wilson, B. A., Cockburn, J. M., & Baddeley, A. D. (1985). *The Rivermead Behavioural Memory Test*. Bury St Edmunds: Thames Valley Test Co.
- Wimo, A., Winblad, B., & Jönsson, L. (2010). The worldwide societal costs of dementia: Estimates for 2009. *Alzheimer's and Dementia*, 6(2), 98-103.

- Whitmer, R. A., Sidney, S., Selby, J., Johnston, S., & Yaffe, K. (2005).
  Midlife cardiovascular risk factors and risk of dementia in late life.
  Neurology, 64(2), 277-281.
- World Health Organisation. (1992). The ICD-10 classification of mental and behavioural disorders. Clinical descriptions and diagnostic guidelines. Geneva: Author.
- Wright, D. B. (1997). Understanding statistics: an introduction for the social sciences. London: Sage Publications.
- Yoshida, H., Terada, S., Honda, H., Ata, T., Takeda, N. Kishimoto, Y., ... Kuroda, S. (2011). Validation of Addenbrooke's cognitive examination for detecting early dementia in a Japanese population. *Psychiatry Research*, 185, 211-214.

### APPENDIX I: SURVEY INFORMATION SHEET

# The Use of Cognitive Screening Instruments in New Zealand

#### **INFORMATION SHEET**

### Who is doing this research?

My name is Heidi Strauss and I am a student at Massey University, currently undertaking research as partial requirement of completing a Doctorate degree in Clinical Psychology (DClinPsych). The main research supervisor for this project is Professor Janet Leathem of Massey University's Wellington campus.

### What is this research about?

This project involves a survey to determine which cognitive screening instruments are most commonly used by specialist clinicians, how they are used, and which factors determine the choice of a specific screen. The findings of this survey may reveal that clinicians are satisfied with current screens, that currently used screens need to be adapted to the New Zealand context, or that a completely new screen may need to be developed.

## Who can participate?

You are invited to complete the survey, which will take approximately 10 minutes of your time.

Potential participants are being recruited via email, special inserts into the newsletters of various professional bodies, and/or via personal recruitment at psychiatry and neurology conferences. Participants would be psychiatrists, geriatricians, psycho-geriatricians, neurologists, and neuro-psychologists. The aim is to recruit at least 100 respondents, as this would ensure findings that are statistically meaningful and valid.

### What are my rights as a participant?

Completed surveys would be held in a central and secure site, and responses entered into a database for the purposes of statistical analyses. Responses will be logged anonymously and data will only be available to the researcher and research supervisor. All data will be stored for 5 years, after which it will be destroyed.

You are under no obligation to accept this invitation. Completion and submission of the questionnaire implies consent. You have the right to decline to answer any particular question.

Feel free to contact the researcher or supervisor if you have any further questions about the project. You are welcome to request a copy of the research findings once the study is complete.

Thank you

Heidi Strauss

Researcher:	Supervisor:
Heidi Strauss	Professor Janet Leathem School of Psychology Wellington Campus Massey University New Zealand
	Telephone: 04 801 5799, Ext 62035 Email: J.M.Leathem@massey.ac.nz

Completion and submission of the following questionnaire implies your consent to participating in the research.

Please **click HERE** if you would like to continue and participate in this research.

This project has been reviewed and approved by the Massey University Human Ethics Committee: Southern A, Application 08/60.

If you have any concerns about the conduct of this research, please contact Dr John O'Neill, Chair, Massey University Human Ethics Committee: Southern A, telephone 06 350 5799 x 8771, email: <a href="https://humanethicsoutha@massey.ac.nz">humanethicsoutha@massey.ac.nz</a>.

## APPENDIX II: SURVEY QUESTIONNAIRE

# The Use of Cognitive Screening Instruments in New Zealand

All going well, you have been directed here from the preceding <u>information sheet</u> about this survey.

#### **Instructions**

Thank you for participating in this study. The questionnaire contains 14 questions, most of which are tick-box questions with the option of adding extra information if required.

The questionnaire requires roughly 10 minutes of your time.

Your responses are anonymous and data will be held in a secure file with no linkage back to the respondent.

The information you provide will enable increased understanding of the nature and extent of the use of brief cognitive screening instruments in New Zealand and how useful they may or may not be. We appreciate your input.

Please complete all the sections below if possible. You have the right to decline to answer any particular question.

### **PLEASE NOTE:**

If at any stage you would like to check your previous answers to any questions please scroll up and down the document. Do not use the back-button on your tool bar, as this will take you

out of this survey without saving your answers.

Many thanks for your assistance with this survey.

### **Section A - Participant Demographics**

Please respond by choosing the options that best represent your situation.

	your profes sional discipl ine?	Geriatric psychiatry Neuro-psychiatry Geriatric medicine Neurology Psychology Other If other, please specify
A 2	What is your age (in years) ?	Please select one years
A 3	What is your gende r?	Male Female
A 4	How many years of clinica I practi ce?	Please select one
A 5	What is the pr imary settin g of your clinica I practi ce?	Please select one    If other, please specify

# **Section B - Cognitive Screening Instruments**

B1 With which clinical populations do you use cognitive brief screening instruments?	Dementia
--	----------

Age-related cognitive impairment  Depression  Traumatic brain injury  Neurotoxic injury
Electroconvulsive therapy patients  Alcohol & drug related disorders  Other  If other, please specify

# B2. How often do you use the following screening instruments for cognitive function?

(Please use key below)

		Never	Seldom	Sometimes	Of	ten	Routinely			
						0	1	2	3	4
B2a MMSE (Mini-Mental State Examination)						0	0	0	0	0
B2b 3MS (Modified Mini-Mental State Examination)							0	0	0	0
B2c CASI (Cognitive Abilities Screening Instrument)						0	0	0	0	0
B2d	FAS (Verbal Fluency Test)					0	0	0	0	0
B2e	CDT (Clock d	Irawing tes	st)			0	0	0	0	0
B2f	MEAMS (Mid State)	dlesex Ex	amination	of Mental		0	0	0	0	0
B2g	ACE-R (Adde - Revised)	enbrook's	Cognitive	Examinatio	n	0	0	0	0	0
B2h	h 3WR (Three Word Recall)					0	0	0	0	0
B2i	TMT (Trail ma	aking Test	)			0	0	0	0	0
B2j	<b>7MS</b> (7-Minut	te Screen)				0	0	0	0	0

B2k	ABCS (AB Cognitive Screen)	0	0	0	0	0
B2I	CAST (Cognitive Assessment Screening Test)	0	0	0	0	0
B2 m	AMT (Abbreviated Mental Test)	0	0	0	0	0
B2n	<b>DECO</b> (Deterioration Cognitive Observee)	0	0	0	0	0
B20	DQ (Dementia Questionnaire)	0	0	0	0	0
В2р	HVLT (Hopkins Verbal Learning Test)	0	0	0	0	0
B2q	IQCODE (Informant Questionnaire on Cog. Decline in Elderly)	0	0	0	0	0
B2r	IQCODE-SF (IQCODE - Short Form)	0	0	0	0	0
B2s	Mini-Cog	0	0	0	0	0
B2t	MIS (Memory Impairment Screen)	0	0	0	0	0
B2u	NCSE (Neurobehavioral Cognitive Status Examination, also known as Cognistat)	0	0	0	0	0
B2v	SPMSQ (Short Portable Mental Status Questionnaire)	0	0	0	0	0
B2 w	T&C (Time and Change)	0	0	0	0	0
B2x	Other If others, please specify	0	0	0	0	0
		0	0	0	0	0
		0	0	0	0	0
B3. P	lease state the three cognitive screening instr	uments	s <u>you u</u>	se mos	t often	in

# descending order:

1.	
2.	
3.	



# The role of cognitive screening instruments in clinical practice

# B4.) Please rate the role of cut-off scores in your use of cognitive screening instruments:

Rating scale for these questions is as follows:

		0	1	2	3		4		
		Never	Seldom	Sometime	ofte	en Ro	outinely		
					0	1	2	3	4
B4a	Cutoff scores alone determine diagnosis					0	0	0	0
B4b	Cutoff scores determine whether further assessment is indicated			0	0	0	0	0	
B4c			m diagnosis, clinical interview		0	0	0	0	0
B4d		ores confi clinical in	•	osis	0	0	0	0	0

**B5)** How important would you rate the following factors in test administration? Rating scale for these questions is as follows:

		0	1	2	3		4		
		Not important	Somewhat important	Importan	t Ver impor		Crucial		
					0	1	2	3	4
В5а	Standard	lised admi	nistration		0	0	0	0	0
B5b	Formal tr	aining			0	0	0	0	0
B5c	Supervis	ed practica	al training		0	0	0	0	0

B5d	Flexible administration according to patient needs	0	0	0	0	0
omment	s:					
		_				

# **Training and Experience**

# B6) Please rate your level of training and experience in each of the following screening measures:

(Please use key below)

	0	1	2		3	4			
	No formal training or practical experience	Some practical experience	Some formal training and practical experience	prac expe	ensive ctical rience nly	tra	Extensive training and practical experience		
				0	1	2	3	4	
В6а	MMSE (Mini-	-Mental State Exa	0	0	0	0	0		
B6b	3MS (Modifie	ed Mini-Mental Sta	0	0	0	0	0		
B6c	CASI (Cogni Instrument)	0	0	0	0	0			
B6d	FAS (Verbal	0	0	0	0	0			
B6e	CDT (Clock of	drawing test)		0	0	0	0	0	
B6f	MEAMS (Mid State)	ddlesex Examinat	ion of Mental	0	0	0	0	0	
B6g	ACE-R (Add - Revised)	enbrook's Cogniti	ve Examination	0	0	0	0	0	
B6h	3WR (Three Word Recall)				0	0	0	0	
B6i	TMT (Trail m	naking Test)		0	0	0	0	0	
В6ј	<b>7MS</b> (7-Minu	ite Screen)		0	0	0	0	0	

B6k	ABCS (AB Cognitive Screen)	0	0	0	0	0
B6I	CAST (Cognitive Assessment Screening Test)	0	0	0	0	0
B6 m	AMT (Abbreviated Mental Test)	0	0	0	0	0
B6n	<b>DECO</b> (Deterioration Cognitive Observee)	0	0	0	0	0
B6o	DQ (Dementia Questionnaire)	0	0	0	0	0
В6р	HVLT (Hopkins Verbal Learning Test)		0	0	0	0
B6q	IQCODE (Informant Questionnaire on Cog. Decline in Elderly)		0	0	0	0
B6r	IQCODE-SF (IQCODE - Short Form)	0	0	0	0	0
B6s	Mini-Cog	0	0	0	0	0
B6t	MIS (Memory Impairment Screen)	0	0	0	0	0
B6u	NCSE (Neurobehavioral Cognitive Status Examination, also known as Cognistat)	0	0	0	0	0
B6v	SPMSQ (Short Portable Mental Status Questionnaire)	0	0	0	0	0
B6 w	T&C (Time and Change)	0	0	0	0	0
B6x	Other If other, please specify	0	0	0	0	0

# Factors determining choice of specific cognitive screening instruments

B7	With regards to the screening instrument <b>you most commonly use</b> (as answered in Question B3), how confident are you that it is valid and reliable?	0	0 - 20 % 21 - 40 %
		0	41 - 60 %
			61 - 80 %
		0	81 - 100 %

# B8.) How important would you rate the following factors in determining your use of a particular cognitive screening instrument?

Rating scale for these questions is as follows:

		0	1	2	3	3	4			
		Not important	Somewhat important	Important	Ve impo		Crucial			
						0	1	2	3	4
B8 a	Widespread use					0	0	0	0	0
B8 b	Validity & reliability statistics					0	0	0	0	0
B8 c	Availability					0	0	0	0	0
B8 d	Research about usefulness in your setting					0	0	0	0	0
В8 е	Time required	to use an	d score			0	0	0	0	0
B8f	Cost					0	0	0	0	0
B8 g	Comprehensiv	ve coveraç	je			0	0	0	0	0
B8 h	Known and trusted					0	0	0	0	0
B8i	Other factors If other factors	s, please s	pecify			0	0	0	0	0

## Section C - Have your say

Do you have any further comments? Please feel free to add them below.

To submit your results, please click on the **Submit this information** button.

If you wish to wipe your answers, click on the *Clear your answers* button. With submission of your answers, you imply consent to participate in this study.

Submit this information.

Clear your answers.

Thank you for your time in completing this questionnaire!

Your help is appreciated.

# Thank You!

This project has been reviewed and approved by the Massey University Human Ethics Committee: Southern A, Application 08/60.

If you have any concerns about the conduct of this research, please contact Dr John O'Neill, Chair, Massey University Human Ethics Committee:

Southern A, telephone 06 350 5799 x 8771,

email: humanethicsoutha@massey.ac.nz.