SCREENING FOR AND DIAGNOSING DEMENTIA IN AN ELDERLY RESIDENTIAL HOME POPULATION: A VALIDATION STUDY.

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DECLARATION

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ABSTRACT

Background: With the projected increase in the elderly population and expected rise in the prevalence of dementia, particularly in low-and-middle-income countries, early case-identification is necessary for planning and delivering clinical services. The effectiveness of dementia screening depends on the availability of suitable screening tools with good sensitivity and specificity to confidently distinguish normal age-related cognitive decline from dementia. The aims of this research study were to report on the prevalence of cognitive impairment (dementia and Mild Cognitive Impairment-MCI), and to assess the performance of selected screening tools and a neuropsychological battery of tests in a heterogeneous local population.

Methodology

A cross-sectional study was conducted in a heterogeneous elderly South African population and consisted of three stages of data collection. In the first stage, cognitive screening measures were administered to a group of 302 participants, aged +60 years, living in a residential facility for the aged. The second stage consisted of a sub-sample of 140 participants who were assessed for cognitive impairment based on the Diagnostic and Statistical Manual of Mental Disorders 4th Edition-Text Revised criteria (DSM-IV-TR). Criteria A and B for Alzheimer's and Vascular dementia were applied to assign a diagnosis of dementia without reference to aetiology. The participants were also assessed for Mild Cognitive Impairment (MCI), based on the criteria of the International Working Group on Mild Cognitive Impairment. Of the 140 participants in stage two, 117 were administered a neuropsychological battery of tests in the third stage. The influence of demographic variables and the sensitivity, specificity and optimum cut-off scores were determined for the

following seven selected screening measures, individually and in combination: the Mini-Mental State Examination (MMSE), Subjective Memory Complaint (SMC), Subjective Memory Complaint Clinical (SMCC), Subjective Memory Rating Scale (SMRS), Deterioration Cognitive Observee (DECO), Subjective Memory Complaint Clinical (SMCC) and the Clock Drawing Test (CDT). The sensitivity and specificity of the neuropsychological tests in the detection of dementia were also determined.

Results

Eleven (7.9%) dementia and 38 (27.1%) MCI cases were diagnosed. Performance on the screening measures was influenced by race, age and education. Using ROC analyses, the SMCC, MMSE and CDT were found to be moderately accurate in screening for dementia with AUC >.70. Neuropsychological test performance was influenced by the age, gender, race and education level of participants. With the exception of the Digit Span (forward), Digit Span (total), COWAT-A, Narrative Memory Test (delayed recall), Token Test and the Luria Hand Sequence Test, all the neuropsychological test measures displayed significance in distinguishing between the three classification groups (controls, MCI, dementia).

Conclusion

SMCC's are valid screening questions as a first level of 'rule-out' screening. The MMSE can be included at a second stage of screening at general hospital level and the CDT in specialist clinical settings. Several measures from the neuropsychological battery of tests evaluated have discriminant validity and diagnostic accuracy for the differential diagnosis of cognitive disturbances in an elderly heterogeneous South African population.

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TABLE OF CONTENTS

TABLES

FIGURES

PAPERS

Paper 1: Ramlall S, Chipps J, Bhigjee AI, Pillay BJ. Screening a heterogeneous elderly South African population for cognitive impairment: The utility and performance of the Mini-Mental State Examination, Six Item Screener, Subjective Memory Rating Scale and Deterioration Cognitive Observee. *African Journal of Psychiatry* 2013; **In Press.**	Chapter 4
Paper 2: Ramlall S, Chipps J, Pillay BJ, Bhigjee AI. Mild Cognitive Impairment and Dementia in a heterogeneous elderly population: prevalence and risk profile. *African Journal of Psychiatry* 2013; **In Press.**	Chapter 5
Paper 3: Ramlall S, Chipps J, Bhigjee AI, Pillay BJ. The Sensitivity and Specificity of Subjective Memory Complaints and the Subjective Memory Rating Scale, Deterioration Cognitive Observee , Mini-Mental State Examination, Six Item Screener and Clock Drawing Test in Dementia Screening. Dementia and Geriatric Cognitive Disorders; Printed online July 2013.	Chapter 6
Paper 4: Ramlall S, Chipps J, Bhigjee AI, Pillay BJ. Durban dementia study: Rey Auditory Verbal Learning, Rey Complex Figure, Narrative Memory and Digit Span normative data for the elderly. **Submitted to South African Journal of Psychology for publication.** *Paper 5:* Ramlall S, Chipps J, Bhigjee AI, Pillay BJ. Durban dementia study: Norms for Clock Drawing Test, Controlled Word Association Test, Digit Symbol Test, Luria Hand Sequencing and Trail Making Test for the elderly. **Submitted to South African Journal of Psychology for publication.** Paper 6: Ramlall S, Pillay BJ, Chipps J, Bhigjee AI.BJ. The sensitivity and specificity of a neuropsychological battery of tests for discriminating Dementia and Mild Cognitive Impairment in the elderly.	Chapter 7

CHAPTER 1

INTRODUCTION

1.1 Overview of dementia

Dementia is a degenerative and usually progressive disease of the brain that affects mainly elderly persons. It manifests with varying types and degrees of cognitive disturbances, functional disturbances and, ultimately, physical impairments. As the condition progresses, it precludes those affected from being able to function independently and requires a host of medico-legal, ethical, social, medical and safety considerations. Dementias may be caused by primary degenerative disease processes, vascular pathology or manifest secondary to general medical conditions (hypothyroidism) or head trauma. There are many causes which may vary in their onset and presentation. However, it is largely an insidious condition as age-related cognitive changes begin to set in and are assumed by family members to be an 'acceptable' age-related change. Despite the absence of any specific treatment for most of the dementias, tangible benefits to both sufferers and loved ones or caregivers derive from early recognition of the condition. Early recognition is possible through the use of screening measures. While there are a wide range of such measures available and in use in South Africa, they have not been validated for this population, resulting in this three stage cross-sectional epidemiological study to identify suitable and valid screening measures for a local elderly population. The thesis is submitted as a compilation of papers published in peer-reviewed journals, as per the University's rules.

This chapter provides a background on dementia and its implications for ageing populations, outlines the burden of dementia internationally and in South Africa, reviews mild cognitive impairment as a precursor to dementia, and outlines the screening tools for dementia internationally and in the South African public health sector. It presents the problem statement and study research question, as well as the aim and objectives, the significance of the study and the study outline.

1.2 The Implications of the Increasing Worldwide Aged Population

Globally, the ageing population is increasing, with the number of older persons aged 65 years and more expected to increase from an estimated 420 million in 2000 to almost a billion by 2030 (O'Bryant, Gavett et al. 2008), and the population aged over 60 years is expected to rise to two billion by 2050 (United Nations 2009). Furthermore, the aged population in developing countries is set to increase from 59% to 71% of the world's total ageing population (O'Bryant, Gavett et al. 2008). Approximately 37% of the European population is projected to be 60 and over, while 10 per cent of the population of Africa is projected to be over 60 in 2050; this represents a doubling from 5% in 2000. South Africa's ageing population is projected to increase from 3.1 million to 4.6 million over the next 25 years (Ferreira and Kowal 2006).

While increased life expectancy reflects positively on health service provision and overall quality of life in general, it also presents challenges related to the preservation of the optimum physical, mental health and functional capacity of the aged. The ageing population has serious implications for health, healthcare delivery systems and the economics of health and the country as a whole (O'Bryant, Humphreys et al. 2008). Of particular concern are the

problems associated with cognitive decline and impairment in the elderly. It is estimated that this will result in 4.6 million new cases of dementia worldwide each year, with the rates in developed countries being predicted to increase by 100% between 2001 and 2040 (Ferri, Prince et al. 2005), and globally from 87% to 438% between 2010 and 2050 (Prince, Bryce et al. 2013).

Currently, 54% of dementia sufferers reside in low or middle income countries (LMIC), with numbers expected to double every 20 years (Alzheimer's Disease International 2010; Prince, Bryce et al. 2013). In 2010, there were 4.66 million people aged over 60 years in southern sub-Saharan Africa, and using a crude estimated prevalence of 2.1%, the number of people with dementia will increase by 70%, from 0.10 million in 2010 to 0.17 million in 2030, and by 100% to 0.20 million in 2050 (Prince, Bryce et al. 2013). The estimated prevalence of dementia in Africa is 1.6%, lower than other world regions (4%-6.4%)(Ferri, Prince et al. 2005).

These projections translate into a considerable burden, both in fiscal terms as well as in terms of suffering of patients and their caregivers and families (Cherbuin, Windsor et al. 2008; Kumar, Anstey et al. 2008; Shaji, Jotheeswaran et al. 2010; World Health Organisation and Alzheimer's Disease International 2012). The total estimated worldwide costs of dementia were US$ 604 billion in 2010. Although almost 70% of these costs were incurred in Western Europe and North America, there is a predicted shift of costs in low- and middle-income countries (LMIC), where large treatment gaps currently exist, from the informal to formal sectors. It has been estimated that annually, on average, a resident with dementia requires 229 more hours of care than one without dementia, this amounting to a mean

additional cost of $3,865 per patient (O'Brien and Caro 2001). The financial implications are therefore large (Wimo, Jonsson et al. 2013), and necessitate careful planning to manage its associated health and economic challenges. The need to address the global impact of dementia have been formalised in the 'Declaration on a Global Response to Dementia (Anstey, Cherbuin et al. 2008) and 'Dementia: A Public Health Priority' (World Health Organisation and Alzheimer's Disease International 2012).

1.3 Burden of Dementia

There are 7.7 million new cases of dementia each year, which translates into one new case of dementia in the world every four seconds (World Health Organisation and Alzheimer's Disease International 2012). The impact of dementia can be understood from three inter-related levels: the individual, the family and society (directly through government expenditure and indirectly such as through lost productivity), its total cost to society and its people are being not easily quantifiable (Shaji, Jotheeswaran et al. 2010). For patients, it leads to cognitive and functional deterioration, behavioural challenges, increased use of health and social services, complicated clinical management of other co-morbid conditions, and increased risk for medical conditions such as delirium, falls, motor vehicle accidents, incontinence, fractures, infections and increased mortality (Callahan, Hendrie et al. 1995). For family and caregivers, dementia can lead to financial and emotional stress. Family members, usually elderly spouses, care for 66% to 75% of demented people at home. The progressive nature of the dementia syndrome has particularly negative effects on the caregiver. Most studies find high levels of anxiety, depression, chronic fatigue, anger and the use of psychotropic medications in caregivers compared with the general population. Recent data have suggested that caregiver burden can be an important determinant of the

severity and frequency of demented patients' behavioural problems and contribute to the need to place patients in an institutional setting(Boustani, Peterson et al. 2003).

While the global age standardised death rate for Alzheimer's disease (AD) and other dementias of 6.7 per 100,000 for males and 7.7 per 100,000 females, rates in India are 13.5 per 100,000 males and 11.1 per 100,000 females, with AD being the fourth leading cause of death in the Asia Pacific region (Shaji, Jotheeswaran et al. 2010). The associated mortality rates are high, with up to 51.3% in Brazil (Nitrini, Caramelli et al. 2005), and 70% of elderly aged 75 years and more in Nigeria dying within five years of diagnosis (Perkins, Hui et al. 2002), highlighting the challenges faced specifically by LMIC in meeting the challenges of dementia. The treatment gap for dementia, estimated at 50% in high-income countries, is as high as 90% (Dias and Patel 2009) in low-income countries such as India (Dias and Patel 2009; Shaji, Jotheeswaran et al. 2010), highlighting the need for both early recognition and the availability of comprehensive management services to be accessible to all.

While there is as yet no cure for dementia, delaying the progression from Mild Cognitive Impairment (MCI), a pre-dementia state, to AD by even one year could have significant savings implications (Peterson, Smith et al. 1999). Early recognition also allows families and sufferers to enlist the necessary support and ensure appropriate planning around living arrangements, finances and advance directives to be undertaken timeously.

Addressing the change in the worldwide demographic profile and the associated morbidity (especially that related to cognitive decline in the elderly) is "among the most important challenges facing scientists, health-care providers, policy-makers, the business community,

and governments worldwide" (Naylor, Karlawish et al. 2012). In recognition of the challenges posed by the growing burden of dementia, the University of Pennsylvania formulated a set of four recommendations to address the pending health crisis:

1. identifying and developing novel treatments;
2. improving gains from clinical trials,
3. enabling better patient options by early identification of individuals at risk for AD;
4. providing care to patients and families throughout the illness (Naylor, Karlawish et al. 2012).

A more global call to address the challenges of dementia is echoed by the World Health Organization (WHO),with its dedicated comprehensive publication entitled 'Dementia: A public health priority' in 2012.The Director-General of WHO warns of the 'catastrophic' cost of care associated with dementia, which is likely to rise higher than its prevalence, thus identifying dementia as a public health priority(World Health Organization 2012).

1.4 Mild Cognitive Impairment

Described as a transitional stage between normal ageing and early AD, mild cognitive impairment (MCI) describes a clinical state were an individual has a memory complaint (may be corroborated by an informant), objective evidence of memory impairment with normal general cognition, intact activities of daily living and does not meet criteria for dementia (Petersen, Stevens et al. 2001). MCI is a distinct clinical category and individuals with MCI can be distinguished from normal and mildly-demented individuals. Dementia antecedents described prior to Petersen's MCI definition in 2001 were the Clinical Dementia Rating Scale (CDR)(Morris 1997) stage 0.5 and the Global Deterioration Scale (GDS) stage 3. The Clinical

Dementia Rating (CDR) is a numeric scale used to quantify the severity of symptoms of dementia (i.e. its 'stage'). The CDR is based on a structured-interview protocol administered by a medical doctor, with an assessment being made on the patient's cognitive and functional performance in six areas: memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. The scores are combined to obtain a composite score ranging from 0 through 3 (Morris 1997).

Table 1: Clinical Dementia Rating Scale score interpretation

Composite Rating	Symptoms
0	none
0.5	very mild
1	mild
2	moderate
3	severe

The GDS is a clinician-administered semi-structured assessment of patient and carer. It is broken down into seven different stages: stages 1-3 are the pre-dementia stages and stages 4-7 are the dementia stages. Beginning in stage 5, an individual can no longer survive without assistance. Within the GDS, each stage is numbered (1- 7), given a short title (i.e., forgetfulness, early confusion) followed by a brief listing of the characteristics for that stage (Reisberg, Ferris et al. 1982).

In 2004, the International Working Group on MCI published a consensus report that MCI is a useful clinical and research entity with a heterogeneous aetiology, presentation and variable course. The diagnostic criteria were refined to include ‘evidence of decline over time on

objective cognitive tasks' and 'minimal impairment in complex instrumental functions.' Four subtypes of MCI were characterised based on the presence of amnesia and the presence of impairment in a single or multiple cognitive domains such as: amnestic MCI single-domain, non-amnestic MCI single-domain, amnestic MCI multi-domain and non-amnestic MCI multi-domain (Winblad, Palmer et al. 2004). The multi-domain subtypes appear to represent more advanced stages of the condition(Hughes, Snitz et al. 2011). Deficits in verbal memory, psychomotor speed and executive functions were found to be predictive of conversion to AD in individuals with amnestic MCI (Tabert, Manly et al. 2006).

The heterogeneity of the condition was confirmed in the Goteborg study, where impairment in five major cognitive domains were found in those with MCI (Nordlund, Rolstad et al. 2005). Even in those diagnosed with amnestic MCI, deficits were identified in other cognitive domains, highlighting the importance of comprehensive assessments, irrespective of the presenting complaints of patients (Kramer, Nelson et al. 2006). Subtyping is intended to identify more homogenous clinical subgroups and have limited validity and utility currently, with further refinement of their clinical and biological markers being recommended (Hughes, Snitz et al. 2011; Han, Kim et al. 2012). However, a study by Sachdev et al. found that the MCI subtypes have different aetiologies and outcomes with distinctive sex-dependent risk profiles (Sachdev, Lipnicki et al. 2012).

When followed over a four-year period, individuals with MCI declined cognitively at a faster rate than normal individuals, but at a lower rate than those with mild AD (Petersen, Smith et al. 1999). The presence of diabetes and pre-diabetes has also been shown to hasten the progression from MCI to dementia (Xu, Caracciolo et al. 2010). The conversion rate from

MCI to dementia reported in one study was 11.1% over a three year period, the authors suggesting that the diagnostic criteria be modified (Ritchie, Artero et al. 2001).

The Third Canadian Consensus Conference on the Diagnosis and Treatment of Dementia provide a detailed review on the concept, neuropathological basis and diagnosis of MCI and Cognitive Impairment Not Dementia CIND, with recommendations to clinicians on the clinical approach to MCI and suitable screening and diagnostic tools (Chertkow, Nasreddine et al. 2007). Regarding the 'treatment' of MCI, there was support for recommending a general 'healthy lifestyle' (physical exercise, nutrition, smoking, mental stimulation) and reduction of vascular risk factors (Massoud, Belleville et al. 2007).

A systematic review of studies, which included 42 publications, found great variability in the reported incidence and prevalence of MCI across 42 publications (Ward, Arrighi et al. 2012). Contributory factors were a lack of consistency in definitions (age-associated memory impairment - AAMI, cognitive impairment no dementia - CIND, MCI and amnestic MCI - a MCI). The incidence of MCI was 21.5% to 71.3%, and its prevalence ranged from 3% to 42% (Ward, Arrighi et al. 2012).

While several screening measures have been identified for MCI, they have limited value in predicting its course and outcome (Lonie, Tierney et al. 2009). Only five robust studies were identified in a meta-analysis of the Mini-Mental State Examination(MMSE) for MCI detection (Mitchell 2009). Based on these studies, a provisional conclusion is that the MMSE has 'very limited value' in MCI diagnosis, with a 'modest' rule-out value (Mitchell 2009). The Informant Questionnaire on Cognitive Decline in the Elderly, IQCODE, an informant

questionnaire, may have utility in MCI recognition (Isella, Villa et al. 2006). The presence of subjective memory complaints had a meta-analytic pooled sensitivity of 37.4% and specificity of 86.9% for MCI, and may be a reasonable approach to excluding MCI (Mitchell 2008). Individuals with MCI are at increased risk of developing Alzheimer's disease, yet the economic impact of MCI is yet to be determined (Lin and Neumann 2013). Progression rates, factors that drive costs, and models of the cost-effectiveness of interventions for MCI are needed to inform 'payers, providers and policymakers' to make informed decisions(Lin and Neumann 2013).

Despite its usefulness as a clinical entity, the definition and epidemiology of MCI require further refinement in the following areas: identifying appropriate and sensitive psychometric and functional diagnostic measures; establishing reliable methods to monitor the course of MCI; and calculating population estimates of MCI in diverse ethnic and cultural groups (Luis, Loewenstein et al. 2003). More recently, a clinically defined pre-MCI stage has been described. This stage is characterised by distinct cognitive, functional, motor, behavioural and radiological features that fall between the 'no cognitive impairment' (NCI) and MCI elderly, and shows greater progression to MCI compared to those with NCI (Duara, Loewenstein et al. 2011). The validity of pre-MCI as a clinical entity has been confirmed in a longitudinal study over three years, where distinct pre-MCI subtypes were identified with increased progression to MCI or dementia (Loewenstein, Greig et al. 2012). While much research is focussed on dementia, there is a growing interest and an increasing body of research data on pre-dementia states (Albert, DeKosky et al. 2011; Sperling, Aisen et al. 2011). This is likely fuelled by the failure of a cure for dementia to materialise, as well as the

realisation that, in view of the long pre-clinical phase of AD, greater value lies in identifying pre-dementia states where intervention is more likely to impact on the burden of disease.

1.5 Screening for Dementia

While in America, Australia and Europe, policies and programs for dementia are relatively well-established, in low socio-economic countries these are less so (Kalula and Petros 2011). Studies to date have revealed a much lower prevalence of dementia in developing countries compared to developed nations (Kalaria, Maestre et al. 2008). Nonetheless, the overall burden of dementia necessitates the establishment of effective screening and diagnostic programs in developing countries if the predicted surge is to be managed appropriately. While the prevalence and burden of dementia has been studied in developed and some developing countries, such as Nigeria (Ogunniyi, Baiyewu et al. 2000) and India (Chandra V 1998), similar large scale studies have not been conducted in South Africa.

Given the host of competing medical and social priorities and the apparent relatively low incidence of dementia in general, routine screening is not feasible. However, factors distinguishing those at risk need to be identified, and effective screening tools need to be available to inform those who warrant more intensive investigation and assessment. Although there is no real treatment for dementia, current management options are not limited to improving patients' cognition but also target multiple outcomes, such as improving functional autonomy, decreasing institutionalization, decreasing associated behavioural problems, limiting automobile crashes and accidental falls, and lowering caregiver stress. It is therefore important for screening programmes to be implemented so

that patients can be identified and, together with their caregivers, benefit from these supportive interventions.

It is also important for the cost implications of dementia to be borne in mind when contemplating implementing new programmes. Fortunately, the considerable cost savings resulting from early recognition and treatment of dementia has been borne out by studies conducted internationally (Peterson, Smith et al. 1999; Sager, Hermann et al. 2006).A comprehensive economic evaluation of early assessment for dementia due to Alzheimer's disease (AD) in the United Kingdom concluded that there were both cost savings and health benefits associated with early identification, despite significant up-front costs(Getsios, Blume et al. 2012).

1.6 Screening for Dementia in the South African Public Health Sector

In the South African public health sector patients are first seen at primary health care clinics (PHC) that are serviced by non-specialist nursing staff. There is currently no policy informing the practice of routine screening at this level, patients may be referred for further evaluation or the symptoms may be dismissed as due to 'normal ageing.' In general, the nurses are both untrained and reluctant to address problems of a 'mental' or psychiatric nature. These problems usually require more contact time than general physical ailments, adding to the clinical burden in busy, often understaffed, PHCs.

From a PHC, patients may be referred to a District Level Hospital where non-specialist doctors may evaluate the patient's cognition functioning further and investigate for contributory medical causes. Specialist nurses, with mental health expertise, are unlikely to

be present. No policy exists at this level to guide the assessment or management of patients presenting with cognitive problems. The Mini-Mental State Examination (MMSE) is the cognitive assessment measure that is most widely known, but is neither routinely nor generally used at District Hospitals.

Patients in turn may be referred from District Hospitals to Regional or Tertiary Hospitals where specialists are available. At the specialist level, psychiatrists, neurologists and clinical psychologists would be able to administer tests that are more complex and comprehensive, and which have high specificity as well as sensitivity. In addition, a neuropsychological battery may be administered at this point to establish a diagnosis as well as to monitor decline. This referral pattern varies across geographical areas dependent on the proximity and accessibility of Regional Hospitals to the District Hospitals. Two Tertiary Hospitals exist in KwaZulu-Natal Province (KZN), one of which offers a monthly Memory Clinic Service, attended by geriatric medicine specialists, neurologists, psychiatrists, psychologists, nurses, social workers and speech therapists. A similar multidisciplinary memory clinic exists in the Western Cape Province (Kalula, Ferreira et al. 2010).

1.7 Problem Statement

Psychometric instruments to screen and diagnose dementia have largely been developed and standardized on Western, English-speaking societies, that have high levels of education. The South African population differs greatly with respect to race, culture, language, literacy and discrepancies in the quality and quantity of education. These factors can impact on the performance and validity of these instruments in the local context. Dementia screening and diagnostic instruments need to be validated on the local population before they can be

endorsed for general population screening. The development of new tools is beyond the scope of this research project, in view of the significant resource investment required, and it was deemed prudent not to 're-invent the wheel'. It was therefore decided to first evaluate the performance of screening and diagnostic instruments that have been validated outside of South Africa, and base the decision on whether to adapt them or develop new instruments on the emanating data.

1.8 Research Question

Are the screening and diagnostic instruments evaluated in this study, which have been developed and validated outside South Africa, valid for use in the local South African population?

1.9 Aim and Objectives

The main aim of the study was to evaluate the performance and utility of a set of screening measures and a battery of neuropsychological tests for dementia screening in a heterogeneous local population. The secondary aims were to establish the influence of demographic variables (age, gender and race) and educational level on the screening and neuropsychological test scores.

The objectives of the study were:

1. To establish the utility and validity of subjective measures, objective measures and an informant questionnaire in screening for dementia.

   Papers: Paper 1 (Chapter 4), Paper 2 (Chapter 5) and Paper 3 (Chapter 6)

2. To establish whether combining screening measures would increase their sensitivity in screening for dementia.

   Paper: Paper 3 (Chapter 6).

3. To establish the optimal cut-off points for identifying dementia on the various screening measures and neuropsychological tests.

   Papers: Paper 3 and Papers 4 and 5 (Chapter 6 and Chapter 7).

4. To establish the utility and validity of a neuropsychological battery of tests for the diagnosis of dementia in the South African context.

   Paper: Paper 4 (Chapter 7).

1.10 Type of Study and Method

The research was based on an epidemiological framework and the method included three stages of data collection: screening, clinical evaluation and neuropsychological testing. The study was intended to address routine clinical needs and the study stages were modelled to simulate the local health service structure.

1.11 Significance of the Study

The results of this study could have implications for the following areas:

- Clinical policy guidelines on screening: It is intended that the results of this study will either indicate that the currently available tools are valid for use in South Africa or not. If not, consideration will need to be given to either adaptation of existing tools or the development of new tools. This will, in turn, assist in developing policy guidelines for dementia screening and diagnosis in public sector health facilities.

- Referral policy: The screening policy will necessitate improving the current referral and staffing systems at the various levels of care, and ensure better management of these patients. Accessing services will not only enable appropriate diagnosis and treatment, where possible, but will provide a support facility for care givers and families affected by dementia.
- Increasing knowledge and awareness of dementia and cognitive impairment in the elderly: There is currently limited information and awareness of cognitive problems in the aged, locally. The publication of local data will sensitize health care professionals.
- Identifying valid screening tools will inform the training and curriculum for health professionals.
- Advocacy: While there are widespread public awareness and advocacy movements for dementia in Western and European settings, there is much less public awareness and mobilization locally. It is hoped that the data will be able to mobilise political support towards the development of a national policy on dementia.

1.12 Definition of Terms

The terms and their descriptions used in this study are presented in Table 1.2.

Table 2: Terms and descriptions

Term	Description
Age associated cognitive decline (AACD)	The concept of mild impairments in multiple cognitive domains but not of sufficient severity to constitute the diagnosis of dementia.
Age associated memory impairment (AAMI)	The concept of increasing memory impairment with age. References memory function in the elderly cohort to young normal adult subjects.
Cognitive Impairment Not Dementia (CIND)	Individuals who are cognitively impaired but do not meet the diagnostic criteria for dementia
Dementia	A disturbance characterized by impairment in short and long-term

Term	Description
	memory, associated with impairment in abstract thinking, impaired judgment, other disturbances of higher cortical functioning or personality change. The disturbance is severe enough to interfere significantly with work or usual social activities or relationships with others.
Informant screening measure	Assessments based on the observations of caregivers or family-members
Mild cognitive impairment (MCI)	Characterized by memory impairment, without impairment in daily functioning; the transitional stage normal ageing and early dementia.
Multi-domain screening measures	Assessments based on performance in more than one cognitive domain e.g. memory, executive function, language and visuospatial skills
Objective screening measures	Assessments based on participant's performance on administered cognitive tasks
Single-domain screening measures	Assessments based on performance in one cognitive domain e.g. memory or executive function
Subjective memory complaints/impairment (SMC/SMI)	Subjective reports of memory disturbances of patients with no reference to objective findings.
Subjective screening measures	Assessment based on self-reports of participants

1.13 Outline of the Study

Chapter 2 reviews the literature relating to the epidemiology of dementia, and highlights the main professional considerations inherent in the design and use of psychometric instruments. Ethical issues pertaining to dementia research and the use of psychometric instruments are also addressed.

Chapter 3 presents the methodological framework of the overall study, reviews the relevant theoretical literature, and outlines the study sample, inclusion and exclusion criteria, data collection, management and analysis methods, as well as reliability, validity and ethical considerations.

Chapter 4 is paper 1: Screening a heterogeneous elderly South African population for cognitive impairment: The utility and performance of the Mini-Mental State Examination, Six Item Screener, Subjective Memory Rating Scale and Deterioration Cognitive Observee

Chapter 5 is paper 2: Mild Cognitive Impairment and Dementia in a heterogeneous elderly population: prevalence and risk profile

Chapter 6 is paper 3: The Sensitivity and Specificity of Subjective Memory Complaints and the Subjective Memory Rating Scale, Deterioration Cognitive Observee, Mini-Mental State Examination, Six Item Screener and Clock Drawing Test in Dementia Screening

Chapter 7 is paper 4: The sensitivity and specificity of a neuropsychological battery of tests for discriminating Dementia and Mild Cognitive Impairment in the elderly.

Chapter 8 concludes this thesis and presents the key findings and study limitations, highlight priorities for future research and propose a model for addressing cognitive deterioration within the local public care health setting.

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

The increasing prevalence of dementia worldwide, and particularly in poorly-resourced low-income countries, will pose a challenge to healthcare services. The WHO believes that dementia should be made a national health and social priority, and that investing in systems that will improve care to all those affected. Dementia screening addresses the 'pre-diagnosis' stage of the WHOs proposed seven-stage model for planning dementia services (World Health Organisation and Alzheimer's Disease International 2012).

The literature review includes references from the 1970s, as the most researched screening tool, which is still in use today, the MMSE, was developed during that decade. Epidemiological studies on dementia and a large number of assessment instruments have been the subject of researchers in developed countries for several decades, with low-middle income countries lagging in this respect. As the literature on the relevant areas pertaining to this study is considerable, emphasis was placed on those studies that have particular relevance for the South African social and health environment. The review will provide a brief overview of:

- The incidence and prevalence of dementia, to appreciate the need for screening instruments as well as to calculate their sensitivity and specificity.
- Screening for dementia, including screening tools and their use in low- and middle-income families.

- Professional considerations for psychometric testing, with specific reference to norms, cultural adaptations, methodological considerations, language and translation, cultural values and test-setting, education influences and ethical aspects pertaining to dementia screening.

In addition, it should be noted that each published paper that forms part of this dissertation provides more specific and detailed literature reviews relevant to that paper and will not be repeated in this review.

2.2 Incidence and Prevalence of Dementia

Dementia, a syndrome characterised by clinically significant impairment in multiple cognitive domains and associated functional impairment, has become a world health priority due to the increase in the aged population and the associated financial, health and social implications (World Health Organisation and Alzheimer's Disease International 2012). The global prevalence in those aged 60 years and over is estimated to be 3.9%, with a global annual incidence of approximately 7.5 per 1000 population (Ferri, Prince et al. 2005). In a study of two populations from non-industrialized and industrialized countries, using identical methods and the same group of investigators, the age-standardized annual incidence rates in Yoruba (Nigerian) and African Americans (Indianapolis) were 1.35% and 3.24% for dementia, and 1.15% and 2.52% for AD respectively (Hendrie HC 2001). The overall incidence of AD in those 65 years and older in a rural community in India was 4.7 per 1000 person-years, lower than the rate of 17.5 per 1000 person years in a reference US population (Chandra, Ganguli et al. 1998).

Dementia prevalence varies widely across studies, with methodological variables, such as definitions, study design, characteristics of the sample, and methods of assessment and diagnosis, having a significant effect on the rates reported. In a meta-analysis of studies of dementia carried out in some European countries between 1980 and 1990, the overall prevalence for the five-year age groups is presented in Table 2.1 (Hofman A 1991).

Table 3: Dementia prevalence according to age categories

Age group	Prevalence
60-64 years	1.0%,
65-69 years	1.4%
70-74 years	4.1%,
75-79 years	5.7%,
80-84 years	13.0%
85-89 years	21.6%
90-94 years	32.2%

For persons under 75 years, the prevalence was slightly higher in men than women, compared to those over 75 years old (Hofman A 1991). A meta-analysis of epidemiological studies conducted since 1980, using DSM III diagnostic criteria for diagnosing dementia, found an exponential increase in the prevalence of dementia with age, with the prevalence of dementia doubling every six years, and the prevalence of AD doubling every 4.2 years. A decrease in the rate of increase after the age of 80 suggests that dementia may be age-related rather than ageing-related (Ritchie, Kildea et al. 1992; Ritchie and Kildea 1995). This suggests that there is a critical age period when individuals are at greater risk; should they live beyond this age without declining cognitively, they are no longer at risk for dementia. While this has clinical implications, it also offers insight into the pathophysiology of the

dementing process. Three per cent to 11% of those older than 65, and 25%-47% of those older than 85 had dementia (Boustani, Peterson et al. 2003).

A comparison between the six European studies included in the EURODEM meta-analysis (Rocca, Hofman et al. 1991) and seven methodologically robust studies of dementia prevalence in developing countries concluded that dementia and AD were much rarer in developing than in the developed countries (Prince 2000). While differences in methodological issues may be contributory factors to discrepancies in dementia prevalence, the role of genetic and environmental risk factors in the geographical differences also need to be explored (Prince 2000).

The most recent and detailed estimate of the global prevalence of dementia, based on a systematic review and meta-analysis, indicates that: 35.6 million dementia sufferers worldwide in 2010 are expected to increase to 65.7 million in 2030 and 115.4 million in 2050; 58% of worldwide dementia sufferers in 2010 resided in low-middle income countries and is expected to increase to 63% in 2030 and 71% in 2050 (Prince, Bryce et al. 2013). However, encouraging news has emerged from a two-decade comparison of dementia prevalence in the United Kingdom with researchers reporting a 1.8% lower than expected prevalence. The findings support a cohort effect in dementia prevalence (Matthews, Arthur et al. 2013). These findings also suggest the potential protective effects of healthier lifestyles. However, Lancet editor-in-chief Richard Horton, while welcoming the findings, cautions against governmental deprioritisation of dementia care and research (Anderson 2013).

The prevalence figures for dementia in residential facilities vary widely between countries and across different types of facilities sampled. A study conducted among residential homes in a borough of London revealed that two thirds of the residents suffered from dementia (Mann, Graham et al. 1984). A UK study that surveyed private and council residential and nursing homes as well as long-stay hospitals, found the prevalence of dementia to range from 52% to 71% (Mathews and Dening 2002). A Swedish city population was found to have 30% of moderately demented and 6% of severely demented residents (Dehlin and Franzen 1985). A Mexican city study reported a prevalence of dementia of 16% in two nursing homes (Alvarado-Esquivel, Hernandez-Alvarado et al. 2004). Accuracy of prevalence data is further compounded by the under-recognition of dementia within nursing homes. A recent Scottish survey reported existing levels of dementia diagnosis of 58% with a possible 31.8% of additional unidentified cases(Lithgow, Jackson et al. 2012).

Data on the prevalence of dementia within residential settings in South Africa were not available. However, two local studies have been conducted in community settings, with the prevalence of dementia in a Cape Coloured elderly sample being 8.6%. This figure must be viewed with circumspection, as a diagnosis of dementia was based on mental status examination and the administration of a modified MMSE (Ben-Arje O 1983). A more recent study conducted in the Free State reported a dementia prevalence of 7.7% (Van der Poel and Heyns 2012) and was based on the 10/66 protocols (Prince, Graham et al. 2004).

2.3 Screening for Dementia

Screening refers to a public health service programme offered to improve the health of a nation; it is intended to reduce the risk of a disease and does not guarantee diagnosis or cure (Department of Health 2000). It is defined by the Department of Health (2000) as:

> *Screening is the systematic application of a test or enquiry to identify individuals at sufficient risk of a specific disorder to warrant further investigation or direct preventive action, amongst persons who have not sought medical attention on account of symptoms of that disorder.*

An alternate definition has been proposed by Wald (2000):

> *a public health service in which members of a defined population who do not necessarily perceive they are at risk of, or are already affected by, a disease or its complications are asked a question or offered a test to identify those individuals who are more likely to be helped than harmed by further tests or treatment to reduce the risk of disease or its complications.*

However, this definition has been criticised for being 'unwieldy and unclear' (Department of Health 2000).

Screening for dementia in the absence of a cure poses ethical and practical challenges (Ashford 2008). However, the United States' Preventive Services Task Force (USPSTF) describes the benefits of early recognition of cognitive impairment in the elderly for clinicians, patients and their caregivers/families. In the absence of formal recommendations for routine screening, the USPSTF findings was that current evidence did not support the

routine screening of individuals in whom cognitive impairment was not suspected (Boustani, Peterson et al. 2003).

Dementia meets the criteria for an appropriate condition for screening based on its seriousness, high prevalence and the presence of a pre-clinical stage (MCI). A successful screening intervention also requires the availability of valid screening tests which should have wide accessibility, be simple to administer, inexpensive and not be associated with discomfort or morbidity. In addition, screening tests need to be valid, reproducible and be able to detect pre-clinical stages of the disease (Herman, Gill et al. 2002). Of particular relevance to low-income countries, where there is a scarcity of trained staff and specialised psychiatric facilities, is the recommendation that quick and low-cost means, that do not require specialised training, are necessary to assess psychiatric disorders. Further, the ideal instrument is described as one that is 'comprehensive, psychometrically sound and valid across cultures, age, gender, socio-economic and language groups (Chipimo and Fylkesnes 2010).

An effective screening test is one that affords early detection of a condition without producing large numbers of false positive or false negative results. Test accuracy is quantified by its sensitivity and specificity (Ashford 2008), as well as the positive and negative predictive values (Herman, Gill et al. 2002), both of which will be outlined.

a. Sensitivity and Specificity

Sensitivity refers to the probability of a positive test in the presence of dementia, i.e. how likely it is for a test to pick up the presence of a disease in a person who has it.

Specificity refers to the probability of a negative test in the absence of dementia (Herman, Gill et al. 2002), or how likely it is for a test to exclude a person who does not have the disease. A test should have both high sensitivity and high specificity, but there are trade-offs resulting in false positives and false negatives. Acceptable levels of Sensitivity and Specificity are determined by the context of the screening (a community setting may require a lower sensitivity compared to a clinical), and the clinical and cost implications of 'missing' a case (false negative) versus incorrect labelling of a true case (false positive) (Stephan, Kurth et al. 2010). The ideal screening test should emphasise sensitivity even if this comes at the expense of specificity, in contrast to diagnostic tests, which should favour specificity over sensitivity (Lezak, Howieson et al. 2004).

b. Positive and Negative Predictive Values (PPV, NPV)

The ability of a tool to identify (rule-in) a condition with minimal false negatives is referred to as 'case-finding' or the 'precision' of a test, and is measured by the positive predictive value (PPV). This value represents the probability that an individual with a positive screening result actually has dementia. Conversely, the ability of a tool to 'rule out' a diagnosis with minimal false positives is known as 'screening', and is reported as the negative predictive value (NPV), representing the probability that an individual with a negative screening result does not have dementia(Herman, Gill et al. 2002; Mitchell and Malladi 2010). The ideal property of a 'rule-out' test is a high sensitivity, while the ideal 'rule-in' test has a high specificity. High sensitivity corresponds to high NPV and high specificity corresponds to high PPV (Florkowski 2008). For clinicians, the PPV and NPV are the most relevant (Flicker, Logiudice et al. 1997).

c. Area under the Receiver Operating Characteristic Curve (AUC)

Sensitivity and Specificity are a function of the cut-off value selected for the tool being assessed. Receiver Operating Characteristics (ROC) analysis provides the Sensitivity and 1-Specificity for each possible cut-score of a tool. The area under the ROC curve (AUC) summarises the diagnostic accuracy of a tool on all possible cut-off scores, giving equal weighting to Sensitivity and Specificity. Sensitivity and Specificity values can be set at a fixed desired percentage and the corresponding cut-off score can be generated (Greiner, Pfeiffer et al. 2000). ROC analysis also allows for the comparison of the discriminatory validity of different cognitive tests (Ritchie and Fuhrer 1992; Kukull, Larson et al. 1994). The maximum value for the AUC is 1.0, thereby indicating a (theoretically) perfect test (i.e., 100% sensitive and 100% specific). Tests with AUC values of <.8 are considered as having 'questionable utility'(Stephan, Kurth et al. 2010), but the interpretation of AUC scores in Table 2.2 were found to be more appropriate for this study (Swets 1988).

Table 4: Interpretation of AUC values

AUC* VALUE	INTERPRETATION
0.5	non-informative
0.5<AUC< O.7	less accurate
0.7< AUC < 0.9	moderately accurate
0.9<AUC<1	highly accurate
AUC =1	perfect

*AUC=Area under the curve

Sensitivity and specificity vary depending on the prevalence of the disease in different populations (Stephan, Kurth et al. 2010) and there is no consensus on what the acceptable level of sensitivity, specificity, PPV, or NPV are for dementia screening. One

metric measuring of overall diagnostic effectiveness is the Youden index (J), which is a function of sensitivity and specificity. The Youden index occurs at the cut-point that optimizes the biomarker's differentiating ability when equal weight is given to sensitivity and specificity (Schisterman, Perkins et al. 2005). Another metric, suggested by the Ronald and Nancy Reagan Research Institute, is a Sensitivity and Specificity value of >80% for biomarkers (The Ronald and Nancy Reagan Research Institute of the Alzheimer's Association and the National Institute on Aging Working Group 1998). In the absence of a recommendation for psychometric values, 80% can be used as a benchmark figure to guide decisions on optimum sensitivity and specificity cut-off values.

2.3.1 Screening Tools for Dementia

Screening for dementia can be based on the presence of biological markers or on the performance on psychometric tests. Genetic screening has yielded limited data on risk and is associated with significant ethical issues (Boustani, Peterson et al. 2003). Recently, there have been significant advances in the identification of biochemical markers, both for dementia and pre-dementia states. The workgroup tasked with developing criteria for symptomatic pre-dementia stages developed two sets of criteria viz: “(1) core clinical criteria that could be used by healthcare providers without access to advanced imaging techniques or cerebrospinal fluid analysis, and (2) research criteria that could be used in clinical research settings and clinical trials”. These include biomarkers based on imaging and cerebrospinal fluid measures, but considerable work is required before these biological markers are sufficiently validated and standardised for application in community settings (Albert, DeKosky et al. 2011).

The 2011 revised National Institute of Ageing-Alzheimer's Association criteria for the diagnosis of AD makes a semantic and conceptual distinction between AD pathophysiological processes and clinically observable syndromes which was not evident in the 1984 diagnostic criteria(Jack, Albert et al. 2011). Biomarker evidence has been integrated into the diagnostic formulations for probable and possible AD dementia for use in research settings, while the core clinical criteria for AD dementia will continue to be the cornerstone of the diagnosis in clinical practice. It is expected that biomarkers will improve the pathophysiological diagnostic specificity once they have been validated. The two classes of biomarkers are based on the biology which they measure:

- biomarkers of brain amyloid-beta (Ab) protein deposition (low CSF Ab42 and positive PET amyloid imaging) and
- biomarkers of downstream neuronal degeneration or injury (elevated CSF total tau and phosphorylated tau; decreased 18fluorodeoxyglucose (FDG) uptake on PET in temporo–parietal cortex; disproportionate atrophy on structural magnetic resonance imaging in medial, basal, and lateral temporal lobe, and medial parietal cortex) (McKhann, Knopman et al. 2011).

Psychometric screening tests of cognitive deterioration in the elderly can generally be divided into 3 categories:

- Brief clinical examinations of mental status sampling a wide range of mental activities;
- Short batteries of neuropsychological tests targeting highly specific cognitive functions; and

- Questionnaires based on the observations by informants of behavioural changes over a given time (Ritchie K 1992).

All three categories of tests were evaluated in our research. The reasons for the choice of instruments/ measures for this study are discussed in Paper 3, Chapter 6, accompanied by a brief description of each measure.

In a comprehensive review of the history of cognitive screening tests, almost 150 were identified (Ashford 2008). Despite the large number and variety of tests, Ashford concluded that the tests couldn't adequately account for dementia due to the continuum that exists from normal age-related cognitive decline to mild dementia, and the cultural and ethnic influences on test item performance.

According to Ritchie and Fuhrer, screening instruments presently available have imperfect discriminability, due both to an absence of a biological marker for senile dementia and the subsequent reliance on non-specific behavioural indicators. There is no agreement on which behaviours should be measured and there are challenges associated with cross-cultural assessment of cognitive functioning (Ritchie and Fuhrer 1992; Ritchie and Fuhrer 1996). Screening tests also vary in diagnostic accuracy and administration time, and it is therefore not surprising that no single instrument has been identified for screening and diagnosis for all settings (Heun, Papassotiropoulos et al. 1998; Holsinger 2008).

In a review of the accuracy of screening tests by the United States Preventative Services Task Force (Boustani, Peterson et al. 2003), three methodological problems are cited that

make assessment of the accuracy of screening tests for dementia difficult. These are: the limited degree to which many screening instruments had been researched; the use of a variety of reference standards for the diagnosis of dementia, and the variations in study sample sizes. Of all the studies that evaluated screening instruments for dementia, the proportion that met acceptable methodological standards was low. The MMSE was identified as the best studied and a clinically feasible screening tool for the primary care setting. Other instruments may have clinical utility, but there was insufficient evidence as to whether these tests could screen elderly patients effectively (Boustani, Peterson et al. 2003).

It is beyond the scope of this review to summarise the nature and merits of the wide variety of screening tests available. Mitchell and Malladi conducted meta-analyses of screening tests and categorised them as either multi-domain or single-domain screening or case-finding tools for dementia in 2010. Studies in both community and specialist settings were included. Brief (less time than the MMSE administration time) single domain tests were defined as those that focussed mainly on one domain of cognitive function such as orientation, memory or executive function. Fifteen categories of single-domain tests were evaluated. Brief (similar to the MMSE administration time i.e. 9-15 minutes) multi-domain tests which could serve as alternatives to the MMSE were also evaluated. Their key findings are summarised below:

- Single-domain tests in primary care settings: the sensitivity and specificity was 69.5% and 82.5% respectively (less specific but equally sensitive to the MMSE). In specialist settings, the sensitivity and specificity was 76.6% and 81.9% respectively (almost

equivalent accuracy to the MMSE). Single-domain tests were suggested to be an efficient first step in screening for cognitive impairment (Mitchell and Malladi 2010).

- Multi-domain tests in community settings with low prevalence of dementia: tests of less than 10 minutes' duration had an overall sensitivity of 72.0% and an overall specificity of 88.2%. The MMSE or the Abbreviated Mental Test Score (AMTS) were recommended for the primary care setting, while the Six-item Cognitive Impairment Test (6 CIT) or the MINI-COG are appropriate for specialist settings. The MMSE was found to be optimal for screening while the AMTS was superior for case-finding (Mitchell and Malladi 2010).

2.3.2 Screening for Dementia in Low- and Middle-Income Countries

The evaluation of dementia in low- and middle-income countries (LMIC) requires special considerations. Apart from general conceptual issues, a host of methodological factors must be addressed in order to generate valid data including cultural factors. The issue of illiterate and uneducated populations impact on both the prevalence and assessment of cognitive impairment, making it more realistic to aim for 'culture-fair' as opposed to 'culture-free' tests (Chandra, Ganguli et al. 1994).

Based on a comprehensive review of methodological issues relevant to dementia studies in LMIC, the 10/66 Dementia Research Group report that "as yet, there is no screening instrument for dementia, or combination of instruments designed to diagnose dementia, that is well enough validated across a wide range of cultures to allow it to be used uncritically in cross-cultural research" (Prince, 2000, p28). The authors suggest that it would

be useful to develop a one-stage culture- and education-fair diagnostic package which could be administered by a lay interviewer and validated for cross-cultural use (Prince 2000).

To redress the imbalance in LMIC, where 66% of the world's dementia population reside and which enjoys only 10% of the world's dementia research efforts, the 10/66 Dementia Research Group has developed protocols for population-based research that aim to redress this imbalance as well as the methodological challenges highlighted above. The Group has validated a diagnostic methodology for developing countries. However, the methodology is suited to research settings and not practical for routine clinical application (Prince, Graham et al. 2004; Prince, Ferri et al. 2007).

Using these protocols, one-phase surveys have been conducted in ten LMIC (Prince, Ferri et al. 2007), excluding a more recent South African study conducted in the Free State Province, South Africa(Van der Poel and Heyns 2012). The protocols consist of a collection of a comprehensive core minimum data set using cross-culturally validated assessments that includes demographic, clinical, risk, anthropometric, caregiver, service-delivery and biomarker indices (Prince, Ferri et al. 2007). The protocols are well suited to research agendas, but would need modification for application in routine clinical settings.

2.4 Professional Considerations for Psychometric Testing

When choosing, administering and interpreting psychometric tests, professional principles must be applied and cognisance taken of socio-political and cultural factors relevant to the population being tested. In South Africa, the legacy of apartheid has impacted on the image of psychological testing, which is viewed with suspicion and confusion(Burke 2009), and

must be taken into consideration when planning the implementation of widespread screening using psychometric tools. The history of psychological testing is tainted by apartheid practices such as the discriminatory testing of IQs which were prevalent since its inception (Eaton, Schwellnus et al. 2008).

The late, former Prime Minister of South Africa, Hendrik Verwoerd, who was considered the father of apartheid in SA, was also a professor of applied psychology. According to Nicholas, 2008, during the apartheid era, most measures of intelligence were mainly aimed at assessing white, English-and-Afrikaans-speaking individuals. Tests were standardised for whites only, thus advantaging them for school placement programmes and other situations that required an assessment. IQ tests with English norms were inappropriately used on other race groups, who were not proficient in the language of administration, and who therefore scored substantially lower than the population on whom the norms were standardised. This was allegedly done with the intention of proving the superiority of the English speaking population (Nicholas 2008). Nell asserts that Intelligence Quotient (IQ) testing, an ability measurement which is one of the professional foundations of clinical neuropsychology, has a racist taint (Nell 2000). The application of neuropsychological testing for cognitive assessments of the elderly therefore needs to be guided by sound theoretical principles to ensure fairness in both application and interpretation. This can serve to ensure that test results are valid and free of controversy.

The gold standard in psychological testing is that the constructs underlying tests and interview questions must have a common, shared existence in the minds of the test maker and test taker (Nell 2000). The absence of appropriate normative data can give rise to the

misuse of tests and has the potential to perpetrate injustices (Saunders 1998) such as the SA Wechsler Adult Intelligence Scale (WAIS), which inflated the full scale IQ scores by close to a standard deviation, with the resultant effect of depriving significantly impaired individuals of compensation. It was argued that psychometric test scores that were misleadingly low could deny clients jobs for which they qualified and conversely, scores that appeared too high may have deprived clients of the compensation to which they were entitled (Nell 2000).

Disregard for socio-cultural, language and educational influences can have socio-political repercussions. For example, in their endeavours to adapt Luria's Neuropsychological Investigation (LNI) for Zulu-speaking individuals in SA, Tollman and Msengana found that minor changes were required for its use in westernized English and Afrikaans-speaking urban South Africans. Major changes were however necessary for Zulu-speaking individuals when probing for higher intellectual functions. Accurate responses depended, to an 'alarming' degree, on the level of education of the test user. Differences in values assigned to individual versus group needs between Zulu and White subjects were also noted (Tollman and Msengana 1990).Although comprehensive guidelines have since been published to guide the culturally fair use of psychometric tests in South Africa(Foxcroft and Roodt 2006), these findings highlight the challenges associated with the administration and interpretation of tests on different racial groups within our country.

2.4.1 Psychological test norms

Cognitively normal ethnic minorities in America are more likely to be misdiagnosed as impaired compared to Whites, suggesting that not all tasks are functionally equivalent (Manly and Espino 2004). Whenever a cross-cultural comparison is made, better scores are

observed in the cultural group who is responsible for developing the test (Ardila 2005). Discrepancies in the results of the same test between cultural groups highlight the importance of using appropriately corrected norms when interpreting results, and Nell warns that a multitude of interpretive cautions apply even to the best of norms (Nell 2000).

Norms refer to the performance of a particular group, and should be appropriate for different age ranges, education and cultural groups, as there are assumptions underlying the norms of each group. One set of norms cannot automatically be assumed to be appropriate for another cultural group (Uzzel 2004). Although establishing separate test norms for ethnic minorities may help to account for variability of educational and cultural experiences and prevent misdiagnoses, variability of the experiences within ethnic groups may decrease the accuracy of these norms. Manly and Espino (2004) however believe that separate norms do not address the variables related to culture, race and education that underlie ethnic group differences on cognitive test performance. Their view is that separate ethnic group norms may lead to increased misunderstanding of racial and ethnic group differences, and become unwieldy and impractical. They suggest that, instead, direct and more meaningful and predictive variables that underlie test performance across cultural groups should be identified that could serve to increase both the accuracy of cognitive assessments and the validity of all instruments used in diagnosing dementia (Manly and Espino 2004).

Establishing norms is however not a simple exercise, with the contention that a test can have scores, but has no norms until its construct validity has been established. It is only once the underlying constructs are known, that scores become norms. Failure to meet this

condition may lead to injustice in situations where jobs or disability benefits are based on performance. Good norms are reportedly rare and are said to have little reliability or worth if basic methodological requirements are not met (Nell 2000). In seeking to establish normative data, the researcher or clinician therefore has to first ensure the validity of the test being administered, and then gather sufficient scores from representative cultural, education and age groups in order to generate norms.

Nell is critical of the attention given to psychometric test development, asserting that "cross cultural psychology has made little progress on the construct validation of psychological tests in the developing countries." He further charges that "mainstream neuropsychological assessment seems content with its Western focus and indifferent to the needs of psychologists and their clients outside the countries of Western Europe and North America" (Nell, 2000, p.85-86). He suggests that the way forward to break the vicious circle of uncertain construct validity, lack of norms and the resulting ambiguity of psychological assessments is to acknowledge that test scores, being the raw material from which constructs are made, are the 'royal road' to constructs, and that scores have priority over constructs. Construct validity can be established by assembling score collections on convergent tests from large samples that are representative of the target ethno-cultural group (Nell 2000). Tests however may require cultural adaptation to ensure that construct validity is maintained.

2.4.2 Cultural Adaptations of Psychological Tests- Methodological Considerations

Fairness in test development is defined as “equal treatment in context and purpose of testing and comparable opportunity to demonstrate abilities on the construct the test is intended to measure”(American Psychological Association 1999).The International Test Commission’s Test Adaptation Guidelines recommends that test administrators should strive to ensure that clients receive a linguistically, culturally and clinically competent evaluation (Judd, Capetillo et al. 2009). Furthermore, they advise that the development and /or adaptation of valid and reliable test measures to assess non-western ethnic groups must be based on empirical investigations (Sugarman 2004). The challenges of cross-cultural assessments are typified in the results of a study conducted by Gurland et al, in which five dementia screening scales were administered to Black, Hispanic and White elderly participants. Using the publisher’s scoring methods resulted in ‘drastically’ different scores and hence rates of cognitive impairment. The discrepancies were ascribed to the difference in sensitivities of the scales as well as to their socio-cultural bias. Adjusting the cut-off points partially addressed the shortcomings (Gurland, Wilder et al. 1992).

Important reasons for adapting assessment measures include enhancing fairness, reducing costs, saving time and facilitating comparative studies. Adaptation of tests also enables the comparison of newly developed measures to existing norms, interpretations and other available information about established and respected measures. There are three important areas of considerations when adapting measures that relate to administration, item format

and time limits. The validity of tests can also be compromised by the culture, language and dialect of the test takers, as well as by the administrative and measurement skills of the practitioners (Foxcroft and Roodt 2005).

In the absence of existing instruments that have proven to be cross-culturally equivalent and psychometrically sound in one culture with high face validity, Flaherty et al proposed a stepwise validation for cross-cultural equivalence when a new instrument has to be prepared. Five major dimensions of cross-cultural equivalence should be achieved in the following order: content, semantic, technical, criterion and conceptual equivalence. They acknowledge that their method is both rigorous and difficult, but nonetheless essential in the absence of biological markers for psychiatric phenomena (Flaherty, Gaviria et al. 1988).

Geisinger (1994), in a comprehensive review of translation and adaptation issues, emphasizes that, even when two groups speak the same language, instruments may need to be adapted to accommodate cultural differences. The preference for the term 'adaptation' over 'translation' is intended to document that attention to culture, wording and content are necessary when embarking on test revisions. After assessing the need for adaptation, he proposed an intensive series of ten-steps to adapt a measure for a new cultural context(Geisinger 1994). The Association of Test Publishers provides a similar guideline of 13 steps for improving test adaptation practices and increasing the validity of adapted tests. In addition, they dispel myths about adapting tests, and suggest popular linking designs for connecting scores on the source and target language versions of the test. They caution that cross-cultural studies should not be 'one-shot affairs', and that researchers should be vigilant to potential flaws and have a responsibility to engage in on-going monitoring, re-

investigation and re-evaluation of reliability and validity (Hambleton and Patsula 1999). Conversely, there is concern that culturally appropriate tests might be too culture specific and thus lose their validity, because the data they generate ceases to be comparable cross-culturally within the population (Griffin-Pierce, Silverberg et al. 2008).

Given the scientific rigor and considerable investment in resources that would be required to develop new measures or adapt existing measures for an ethnically and linguistically diverse South African population, the researchers in this study opted to first assess the validity of measures that are in use and that have been well researched. The findings of this study could be used to determine whether these measures need adaptation or whether new measures need to be developed. Another consideration for this study was whether the measures being used should be translated into any of the eleven official languages of the country. South Africans speak more than 25 different languages, 11 of which are official. The South African Language Policy aims to promote the equitable use of all 11 languages and redress the marginalisation of indigenous languages (Department of Arts and Culture 2002). While there are strong underlying socio-political undercurrents to language use in South Africa(Wright 2012), the implications of the language of administration of psychometric tests, the language contained within the tests and the issue of the translation of tests into indigenous languages require attention to multiple arising issues. To be considered are the complexities of test validity and cultural fairness on one hand, and practical issues of cost and the availability of human and fiscal resources on the other. A commonly adopted approach is that of translating existing instruments into local languages. However, the question arises as to whether translation addresses language equity and test-fairness.

2.4.3 Language and Translation

The language in which assessments are conducted impacts on the test outcome, with examinees being disadvantaged when assessments are conducted in a language they are not comfortable with. Examinees should be free to choose the language in which they would like the assessment to be conducted (Manly and Espino 2004). Elders tested in the language they were most comfortable in performed best on cognitive measures (Yano, Grove et al. 2000).While the ideal of having an examiner who shares the same cultural and linguistic background as the examinee is rarely feasible, lack of regard for language and communication barriers can impact on the reliability and validity of the tests (Manly and Espino 2004).

While clinicians and researchers have attempted to use Western developed tools on local groups by translating them into the local languages, extreme caution is recommended on the uses of appropriate methods to adapt measures into other languages. Furthermore, the accuracy of translated tools need to be checked using established guidelines (Manly and Espino 2004).Literal translations may be fraught with limitations, as languages vary greatly in their idiosyncrasies, fluency and complexity. Translations need to honour language and cultural equivalence if the psychometric properties of the original test are to be preserved. Again, it is recommended that accepted guidelines should be adhered to when embarking on translations (American Psychological Association 1999).

When translating instruments and administration instructions, it is necessary to ensure functional and cultural equivalence, in addition to linguistic equivalence, to guard against validity threats. Both the instructions and tests used across languages need to be equivalent

to provide equal opportunity to the examinee to demonstrate the skill under study (Bender, Garcia et al. 2010).Linguistic equivalence (LE) usually refers to translating and back translating of instructions and instruments. Its main goal is to make certain that the words and linguistic meanings used in both versions are the same. However, a limitation is that the same stimuli may result in different responses or outcomes due to differences in cultural interpretation, familiarity or frequency of occurrence, thus introducing bias. Instruments and elicitation procedures must be scrutinized to ensure equal opportunity to demonstrate the target ability. Back translation has limited usefulness in ensuring the semantic, socio-cultural and thematic relevance between source and target tests (Bender, Garcia et al. 2010). Functional equivalence (FE) is achieved when the instructions and instruments elicit the same target behaviour (Greenfield 1997). Meaning and content validity may be distorted during translation and FE ensures examination and validation of the same construct. A 'decentering' or 'dual-focus' approach are suggested methods of ensuring FE. Cultural equivalence (CE) considers how respondents will interpret a given direction or test item, and develops items that tap the same cultural meanings for each cultural linguistic group. In the presence of LE and FE, test items may still have different salience for different linguistic and cultural groups due to distinct cultural and historical influences on interpretation of concepts.

Metric equivalence (ME) refers to the difficulty of the specific item expressed in two distinct languages. Some items may be rendered more or less complex when translated and words selected in the translation may have different frequencies of occurrence and may influence ability. When developing psychometric instruments, there are ways of determining item difficulty conventionally. Attention to LE, FE, CE, ME are therefore critical to reduce validity

threats in cross cultural research (Pena 2007). Techniques such as Item Characteristic Analysis should be used to develop tests that function the same way in multiple cultures, and thus obviate variability in difficulties that may arise during the translation process (Gibbons, van Belle et al. 2002).

The following example indicates the importance of preserving both linguistic and cultural relevance when translating instruments from source texts to target texts:

> Original English item: If there are five sparrows perched on the power lines point to the fattest pig unless there are two witches on the roof in which case point to the winking black cow.'
>
> Spanish version back-translated into English:' If there are five[non-word] hung on the energy lines point to the fattest cedar tree less there are two witches on the roof in which case point to the black cow of wink.'(Bender, Garcia et al. 2010)

The majority of tests and questionnaires in use originated in English, and attempts to translate them into second languages have largely resulted in instruments that are of unacceptable quality, with errors in phonology, syntax, and pragmatics of language, resulting in test bias, validity threats and ultimately questionable conclusions. The resultant linguistic deficiencies in translated tests can hinder intelligibility and comprehension, and consequently jeopardize validity and reliability. Errors in translation extend beyond the linguistic basis to the socio-cultural dimensions of test translation, with the possibility of socio-cultural artefacts being introduced at individual test item or at the level of instructions.

Translation has its roots in linguistics, semiotics, computer science, anthropology, and philosophy. Appropriateness in translation can and should be defined by community-specific norms. As all translation acts involve two languages and two cultural traditions, a choice has to be made between the target or source standards of behaviour and norms. Capturing acceptability in the target group may be more important than preserving adequacy and maintaining reliability and validity of the test measures, and the data yielded from them i.e. test translators, should therefore favour the target audience norms. The potentially serious implications of errors in translation underscore the importance of interdisciplinary collaboration in adapting instruments. An appropriate balance between acceptability and adequacy can be achieved by translators who are knowledgeable of both the purpose of the neuropsychological tests as well as the socio-cultural and linguistic norms of the target audience (Bender, Garcia et al. 2010).There is convincing evidence that adaptations should therefore be done in consultation with, among others, local cultural experts, linguists and anthropologists (Uzzel 2004).

It is evident from the above overview that translating instruments is in itself a scientifically rigorous and complex task. It was therefore decided to perform this study on participants who were proficient, confident and comfortable to speak in English, although it may not have been their first-language, with the decision on the need for translation to be based on the data generated.

2.4.4 Cultural Values and Test-Setting

The process and content of psychometric testing are both Western concepts and culturally biased (Ardila 2005), with 'Western' referring to the countries of Western Europe and North America. The core psychological meaning of Westernization, according to Nell, is 'test-wiseness'. Test-taking is intrinsic to Western society, and test-wiseness is most powerfully acquired through the formal education system. The major influences on the degree of Westernization are urbanization and schooling (Nell 2000).

Cognitive abilities, as currently measured by psychometric tests, therefore represent, at least in their contents, cultural learned abilities. Western test procedures focus on over-learned information, not on the potential to learn, thus working to the advantage of those who have actualized their potential, and against those who have potential that has yet to be realized. Scores obtained are therefore generally higher in examinees from Western as opposed to other cultures. Based on neuropsychological test performance, ethnic minorities are often judged to be cognitively impaired more often because few cognitive measures have been validated cross-culturally. Even when socio-economic, demographic and educational variables are accounted for, discrepancies in test scores persist (Manly and Espino 2004). Quoting Taylor,1999, test situations have been described as serving a 'gate keeping' function that favours test-wise Western subject, and serves the examiner and not the examinee (Sugarman 2004).

The process and context of psychometric testing are influenced by the values, attitudes, beliefs and interpersonal behaviour of the test-administrator as well as the individual being tested. The performance of non-Western individuals subjected to such testing is likely to be

affected by these variables, thus confounding the results obtained. There are at least eight different culture-dependent values that underlie cognitive testing, which represents a social situation that is governed by implicit cultural rules, these being: one-to-one relationship, background authority, best performance, isolated environment, special type of communication, speed, internal or subjective issues, and the use of specific testing elements and strategies (Ardila 2005).

There are several reasons why ability assessments are not successful when applied cross-culturally such as: values and meanings, modes of knowing and communication patterns (Greenfield 1997). The responses to standard questions on test items are influenced by cultural values and meanings, and the 'expected' (Western-culture laden) responses may therefore not be forthcoming(Ardila 2005).

Both the content of and responses to test items need to be modified to accommodate cultural variables if bias is to be reduced or avoided (Jett 2006). While speed of performance may be the skill targeted, prudence and caution are more highly valued in many African societies than quickness. Although speed is important, most of the meaningful tasks in life do not require problem solving or decision making in the small number of seconds typically allocated for the solution of timed IQ test problems (Nell 2000).Westernized and non-Westernized people also differ in terms of the relative importance that is given to individual needs as opposed to group needs (Uzzel 2004). Western culture idealizes individualism, independence and autonomy with the latter symbolizing maturity. Many traditional, non-Western societies however, are modelled on communal living, where the individual identity is secondary to and dependent upon a person's affiliation to a group. Psychometric tests

focus on individual knowledge and performance but, in certain cultural contexts, knowing may be a collective endeavour (Mkhize 2004). Ubuntu, “a man is a man through others,” embraces the notion of group solidarity (Arnoldi-Van der Walt 2000), highlighting the African view that an individual exists in the context of a society, and self-report questionnaires could therefore pose challenges (Uzzel 2004). Traditional Asian cultures also place greater emphasis on the family or extended family as the primary organism, although this is changing in contemporary Asia (Wong and Fujii 2004). Similar family dynamics characterise Indian and African families in South Africa, who are also succumbing to Western influence**.**

The use of interpreters during cross-cultural consultations is not without limitations. Interpreters need to be trained in the nature of interviewing and psychological assessment and have a clear understanding of their role; otherwise they could invalidate the information obtained. Translators need to understand the idiosyncrasies and subtle nuances of both languages as well as the social meanings attached to words and phrases. Equivalent indigenous terms or words cannot always be found in the language into which the instructions and verbal items are being translated (Uzzel 2004).

Levels of comfort and confidence during test sessions vary. Stereotype threat, demonstrated across race and gender, can affect test performance. It is the result of a test taker diverting attention from the task at hand due to the fear that his performance will confirm a negative stereotype about the group he belongs to (Manly and Espino 2004). Erroneous or biased conclusions emanating from testing without due sensitivity to

stereotype threat can have socio-political repercussions, particularly in countries like South Africa, where racial stereotyping may evoke unpleasant memories of the apartheid era.

Standardizing the assessment method is important in order to avoid misjudgements, of which the clinician is often unaware (Lewis-Fernandez and Diaz 2002). Formal language used in test instructions represent a form of 'academic knowledge', difficult for those with limited education to understand. Tasks performed in the test context may have no relevance to the examinee in a cultural context, thus impacting on effort and outcome. Examinees' attitude toward the test situation can significantly influence test performance. It is generally assumed that a patient will strive for best performance, but this is based on the Western value of 'achievement motivation', and varies across cultures. Examinees may be intimidated by the rigid and standardized administration of tests, and may be afraid or embarrassed (Ardila 1995).

In South Africa, literacy levels are relatively low, and those with poor literacy may not be used to test situations and score very low on tests due to different learning opportunities (Nell 2000). It was thought that the effects of culture could be controlled if verbal items were eliminated, however, cross-cultural differences have been observed in both verbal and non-verbal tests, and performance on visuo-perceptual and visuo-constructive ability tasks can be significantly influenced by culture (Rosselli and Ardila 2003). Given that performance is influenced by a host of variables ranging from culture, ecological/environmental demands, and primary language, to patterns of abilities, familiarity and educational level, rather than attempting to develop culture free/fair tests, Ardila proposed that it may be more appropriate to suppose a continuum, ranging from 'heavily culturally loaded' to 'highly

culturally reduced' tasks (Ardila 1995). He further recommends that if it is not possible for the examiner and examinee to be of the same cultural background, that examiners should familiarize themselves with the cultural background of the examinee, and that behavioural and qualitative scaleS should be used in cultures where a solid psychometric tradition does not exist. It is prudent to assess the degree of test-wiseness of examinees early on to determine whether it is appropriate to use a test. Consideration could be given to the use of other forms of assessment such as behavioural observation and informant questionnaires (Uzzel 2004). Cultural biases in tests should be identified, and tests that are universal and less culture-dependent, and new interpretation strategies and norms for different cultural groups should be used or developed (Ardila 2005).

Given the number and nature of considerations and challenges associated with the development or adaptation of cognitive measures for a heterogeneous local population, it was neither feasible nor pragmatic from the perspective of time or resource availability to attempt to develop new tools for the purposes of this study. It was therefore decided to first evaluate the performance of existing tools, with minimal if any adaptations, administered in English to a mixed group of English-speaking elderly, and to determine firstly, whether adaptation is indicated and secondly, if so, the nature of the adaptation required.

2.4.5 Education and cognitive performance

In the meta analysis conducted by Anstey and Christensen (2000), education was the most important non-biological correlate of cognitive performance in many studies, and formal education was the most crucial variable in cognitive test scores (Ostrosky-Solis 2004) . Increases in test performance have been detected with as little as 2-3 years of Western-

style schooling (Nisbett and Norenzayan 2002). In South African paint workers and farm labourers, years of education were the single largest moderator of test performance (Nell 2000). The largest contribution to performance variance on psychometric tests (Nell 2000), more so than does ethnicity or the traditional variables of age, sex and socio-economic status (Caetano 2004), is made by a 'cultural variable' that includes education and urbanization.

The effects of formal education however overshadow the effects of urbanization when both are controlled for, despite the existence of an 'acculturation' construct that describes a hierarchy which embraces both variables. This hierarchy extends from rural illiterate, to urban illiterate, to rural literate, to urban literate (Kendall, Verster et al. 1988). Thus, the education and social (urban or rural) backgrounds are significant factors when administering and interpreting psychometric scores in a country such as South Africa, where 50% of the population reside in rural areas, and discrepancies exist in the quality of education received by different socio-ethnic groups of people.

School in itself represents a sub-culture that is based on the assumptions and values of scientific and technologically orientated societies. As cognitive testing evaluates those abilities that educated people are trained in, schooled subjects significantly outperform illiterate individuals in cognitive testing. This does not imply that illiterates are deficient or inferior, but that they have different abilities (Ardila 2005), which would be culturally determined e.g. in a hunting community, an illiterate individual may have skills that make him adept to hunt skilfully, yet those skills may not be measurable in a test based on skills acquired during an academic schooling career.

Based on cognitive reserve theory, low education levels are regarded as a risk factor for cognitive decline, and are most commonly measured in the years of formal education received. However, years of education has been found to be an inadequate measure of the educational experience among multicultural elderly people. While it may be possible to adjust statistically for years of education, differences in quality of education are not so easily adjusted for. However, adjusting for the quality of education may improve the specificity of certain neuropsychological measures across racial groups, and has been shown to be useful in addressing disparities in test performance (Manly, Jacobs et al. 2000).

Reading level or literacy has been shown to be the strongest predictor of test performance for all African-American elders, regardless of Caribbean or US birth (Byrd, Sanchez et al. 2005). Older African Americans performed poorly in comparison with older Whites on episodic memory tests. Using logistic regression analyses, reading level was the only variable that explained this difference (Fyffe, Mukherjee et al. 2011).

Literacy, which is not dependent on years of education, age or ethnicity, may therefore, be a more sensitive proxy for cognitive reserve than years of education. It more accurately reflects quality of education experience, native ability and those driven to betterment beyond the confines of school (Manly and Espino 2004). When measured by reading level, it has been shown to be an important factor when assessing cognition among diverse older adults. Interpretation of performance on verbal and non-verbal cognitive measures, being more dependent on knowledge of literacy or reading skills than years of education, may be more accurate if literacy levels were routinely used(Manly and Espino 2004).

Age-related cognitive decline has been noted to be more rapid in those with low education levels, which are often cited as a risk factor for AD and other dementias (Manly and Espino 2004). However, not all studies support the association between low education and risk for dementia. In the Ibadan and Indo-US studies, low educational levels co-existed with very low dementia incidence and prevalence figures (Ogunniyi, Baiyewu et al. 2000; Chandra, Pandav et al. 2001) despite these sites having used 'the most rigorously developed culture- and education-fair diagnostic procedures' (Prince 2000). Literacy correlated with slowing of age-related decline, but low education was not a risk factor for cognitive decline (Manly, Touradji et al. 2003).One reason for discrepant findings on the association between dementia and education could be the choice of assessment instruments, which are influenced by educational and cultural variables (Chandra, Ganguli et al. 1994).

Caution is however advised in controlling for educational variables in dementia studies, as several intermediary variables related to educational levels impact on the educational status of people, namely: socio-economic factors, race and poverty influence access to and quality of education, and cultural values influence attitudes towards academia, learning and ambition (Ostrosky-Solis 2004). The latter variables in turn can exert their individual influences on the risk for dementia, highlighting the complex genetic and socio-environmental risk factors underlying the risk for dementia.

Differences in educational levels, often assessed by the number of formal schooling years of subjects, are often adjusted for in dementia research designs, based on the assumption that all subjects have received the same standard of education. There are considerable

discrepancies in the quality of education received, especially for minority groups, which may confound results, despite matching groups carefully for 'years of education'. In America, considerable differences in educational levels between ethnic groups and Whites, noted to be larger among >65 year olds and non-Whites, may impact on the differential rates of dementia among people of different ethnic backgrounds (Manly, Jacobs et al. 2002).

In addition, functional capacities, such as the ability to engage in household activities, are prone to cultural biases, and require normative data for different ethnic and cultural groups (Ardila and Rosselli 2004). Expected roles and responsibilities differ across cultural settings, with higher levels of independent living being expected in Westernized societies. Asian and African communities traditionally care for the elderly within extended family units, which are less demanding on the elderly. All older adults in an Indian cohort who lived with their families in cognitively undemanding environments may not have met the 'functional impairment' criteria for dementia due to low family expectations or the traditional respect of Indians for elders (Chandra, Pandav et al. 2001). Hence, interpretation of scores on functional assessment instruments needs to be interpreted within the context of local cultural expectations and norms.

South Africa's apartheid system gave rise to racially-segregated schools, with large quality differentials in resource allocations, which resulted in qualitative differences in academic performance (van der Berg 2007). This legacy manifests in the inability to compare 'years of education' between individuals of different racial groups, and has relevance for the comparison of test performance across racial groups. Within racial groups, socio-economic and rural/urban divides also result in differential educational opportunities, making it

difficult to generalize about the quantity or quality of education received by any group. These factors therefore present challenges when examining the education variable in relation to dementia risk, as well as when choosing instruments that are fair to all.

2.5 Ethical Issues

The evaluation of groups that are racially, ethnically and culturally diverse raises complex ethical issues. Many may question the need or rationale for subjecting the elderly and those with cognitive impairment to scientific research. There are however scientific, public health and ethical rationales for examining dementia in the context of race and ethnicity. Based on the ethical principles of justice and beneficence, all racial and ethnic groups, irrespective of socio-economic and educational status, should have equal access to research and treatment (Weiner 2008).

A variety of factors can influence test performance, namely: pain and fatigue, true biological differences in performance based on ethnicity, and differences in the experience of examiners working cross-culturally. It is important to remember that group differences in performance could also be due to other intermediate variables such as socio-economic status, quality of education, levels of acculturation, literacy, test-wiseness, and racial socialization – i.e. stereotype threat(Brickman, Cabo et al. 2006).

In discussing ethical issues pertinent to neuropsychological testing, the question remains as to whether race and culture should be considered. Although most neuropsychological tests in use are inherently biased towards non-Hispanic, White, normative cohorts, differences in neuropsychological test performance cannot be attributed solely to race or ethnicity. These

should be viewed as markers of other intermediate variables such as socio-economic status, quality of education and acculturation that can impact on test performance (Brickman, Cabo et al. 2006). While good normative data maximizes the diagnostic utility of neuropsychological tests, race specific norms need to be used cautiously, given the social and political sensitivities associated with race, especially in some contexts, e.g. South Africa. Due to the heterogeneity within racial and ethnic groups, the generation of norms, stratified by age and education for every test for every group may be neither possible nor practical. Questions regarding who is competent to design, translate, administer and interpret tests also raises many ethical and practical challenges (Brickman, Cabo et al. 2006).

The core ethical consideration in culturally and linguistically diverse African settings is how to cater for this diversity during test selection, administration, interpretation and reporting. An additional challenge for Africa is to develop practitioners with multicultural awareness and worldview. The provision of services by professionals who are not competent may be as unethical as the denial of services on account of inadequately trained staff. Examiners should therefore immerse themselves in the test-taker's world, by acquiring knowledge of the test-taker in relation to his cultural, family, linguistic, educational and socio-economic background and heritage (Foxcroft 2002). On-going empiric research is needed to provide guidance about neuropsychological evaluation of ethnically and linguistically different people (Brickman, Cabo et al. 2006).

2.6 Conclusion

This literature review provides a brief overview of some of the issues pertinent to screening for cognitive impairment, using instruments that were developed outside of South Africa, in a population characterised by diversity in race, culture, language, socio-economic status and education level. The information provides a contextual background to the study and complements the specific literature reviews in each of the published papers. The review also highlights some of the challenges associated with psychometric assessments of the elderly in a multiracial setting. Gaps in the literature remain, with very few empirical studies of this nature having been conducted locally.

CHAPTER 3

METHODOLOGY

3.1 Introduction

This chapter details the study population, the sample size, inclusion and exclusion criteria, the data collection instrument and pilot study, how the data was collected, managed and analysed, as well as reliability, validity and the ethical considerations.

3.2 Study population

The eThekweni Municipality is home to 3.4 million people (Census 2011), of whom 165 393 (4.9%) are 65 years and older, of whom 103 383 (62.5%) are women and 62 010 (37.5%) are men. Those aged 65 years and greater constitute 4.8% of the municipality's population; this is an increase from 4.2% in 2001. The racial composition of the municipality is Asian (Indian) (17.0%), Black (73.6%), Coloured (2.5%), and White (6.5%). There has been an improvement in the education levels from 1996 with 4.2% of the municipality's population having no schooling, 37.6% with a Grade 12 level of schooling and 12.1% with tertiary education. The majority of the population (572 746) reside in formal dwellings with 149 289 residing in informal dwellings and 40 188 living in traditional homesteads(Lehohla 2012).

This study was conducted in a group of retirement homes administered by a non-governmental organisation (NGO). The residential facilities ranged from frail care to independent living, and cater for all ethnic groups and socio-economic classes, representing a cross-section of the local elderly population.

3.3 Study Sample and Size

The study participants were residents aged 60 years or older (N=1371) living in a group of residential homes run by a non-governmental organisation in eThekwini Municipality. A two-step sampling design was used to estimate an appropriate sample size to firstly administer the screening tools, and secondly, to undertake a clinical assessment, which constituted the gold standard against which the screening tools were validated. The sample size was also calculated in two steps. The first step calculated an overall sample size based on a sensitivity and specificity of 85% for the MMSE(Mitchell 2009). In the absence of data on the prevalence of dementia in local residential homes, a conservative estimate of20% was used, based on the reported ranges of 16% (Alvarado-Esquivel, Hernandez-Alvarado et al. 2004) to 75% (Matthews and Dening 2002). A precision of 9.05% was selected to artificially increase the sample size to about 300 so that an adequate number of screen positives would be detected. Step 2 selected a sub-sample of this group to measure the screening tool against a gold standard. The sub-samples included a random selection of cases (screen positives) and non- cases (screen negatives). These values were then input parameters for a 2-by-2 table analysis supposing 85 % sensitivity and specificity, using a 2 -by-2 unstratified table analysis(Epicalc 2000). In order to get the suitably narrow confidence intervals for 'Specificity', 'Sensitivity,' 'Predictive value of +ve result' and 'Predictive value of -ve result', a number of samples were taken, resulting in favourable confidence intervals (Epicalc 2000), as presented in Table 3.1

Table 5: Assumptions for sample size calculation

Precision (W):	9.05 %
Estimated prevalence in the target population (P):	20 %
Confidence Intervals:	95 %
Expected specificity of MMSE	85 %
Expected sensitivity of MMSE .	85%

STEP 1

Based on the methodology detailed by Buderer (Buderer 1996), an overall sample size was calculated. Once the parameters had been specified, the number of potential cases was calculated and a sample size for sensitivity was calculated using:

$$TP + FN = (Z(\alpha/2) * SN(1-SN))/(W*W)$$

$$N1 = (TP + FN)/P$$

The number of non-cases was calculated, and a sample size for specificity was calculated using:

$$FP + TN = (Z(\alpha/2) * SP(1-SP))/(W*W)$$

$$N2 = (TP + FN)/P$$

The larger of the two sample sizes was selected. The results were as follows:

Width of CI: 0.1

Estimated sensitivity 0.85

Estimated specificity 0.85

Estimated population prevalence 0.2

Sample size for sensitivity 301

Sample size for specificity 76

Final sample size: 302.

Step 1: An initial sample of 302 of residents was to be randomly selected from the sampling frame. The screening tool would be administered to the sample that would then be classified into "MMSE cases" and "MMSE non-cases" using standard cut-off points on the MMSE. Assuming a dementia prevalence of 20% in residential homes, we expected to find approximately 60 cases of dementia after the initial screening.

Step 2: A random sample of "MMSE cases" and a random sample of "MMSE non-cases" would then be selected from the sample selected in Step 1. In the event that there were fewer than 60 'cases', all 'cases' would be included.

3.4 Inclusion and Exclusion Criteria

The following inclusion and exclusion criteria were used to identify study participants:

Inclusion criteria:

- 60 years and older,
- a minimum of eight years of formal schooling,
- ability to speak, read and write in English,
- ability to give written, informed consent.

Exclusion criteria:

- residents with severe physical, mental or sensory handicaps that precluded their engagement in the assessment procedures.

3.5 Data collection

The data was collected in 3 stages:

1. Screening

2. Clinical diagnosis
3. Neuropsychological testing

The study received ethical approval from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal.

3.5.1 Stage 1 Screening

In stage 1, participants were screened for the presence of cognitive impairment and depression. The method, instruments administered and the statistical analyses employed in this stage are described below.

a. Method

Screening assessments were conducted by a trained senior psychiatric registrar at the residences of 302 participants. All 302 participants were assessed for the presence of a subjective memory complaint (SMC) by asking the question: 'Are you experiencing any difficulty with your memory?' The Subjective Memory Rating Scale (SMRS)(Li Wang, van Belle et al. 2004) was administered to those participants who replied 'yes' to the SMC question. A multi-domain cognitive screening tool, the Mini-Mental State Examination (MMSE)(Folstein, Folstein et al. 1975) was administered to all participants. The DECO (Ritchie and Fuhrer 1996) was administered to available informants who had monthly contact with the study participants for at least two years. Depression was identified using the Geriatric Depression Scale (GDS)(Brink, Yesavage et al. 1982) employing a cut-off score of $\geq$11.

b. Instruments

Five measures of cognitive impairment were administered:

I. *Subjective Memory Complaint (SMC):* The SMC is a single domain screening measure assessing memory through a 'yes/no' response to the question: 'Are you experiencing any difficulty with your memory?'

II. *A subjective memory rating scale (SMRS) (Li Wang, van Belle et al. 2004):* This is a 5-item single domain scale that assesses subjective deterioration of memory over a 10-20 year period in five situations. Each item is scored on a 5-point Likert scale. The maximum score that may be obtained on this scale is 25 and a score of $\geq$20 suggest memory impairment. While there is no information on the sensitivity and specificity of the SMRS, subjective memory questionnaires have a pooled sensitivity and specificity of 43% and 85.8%, respectively (Mitchell 2008). There are at least fifteen variations of the use of a single question, and at least ten sets of questions in the literature(Abdulrab and Heun 2008) to assess subjective memory impairment. The SMRS used in this study has not been as extensively researched as the CAMDEX (Roth, Tym et al. 1986) subset of items(Schmand, Jonker et al. 1996; de Jager and Budge 2005) and the MAC-Q(Crook, Feher et al. 1992; Hanninen, Reinikainen et al. 1994; Hanninen, Hallikainen et al. 1995; Mattos, Lino et al. 2003). The MAC-Q has recently been found to be greatly affected by affect and was not recommended for cognitive screening (Reid, Parkinson et al. 2012). The Memory Complaint Scale has only recently been proposed for further research(Vale, Ballieiro-Jr et al. 2012). The SMRS was chosen for its brevity, simplicity and scoring method - characteristics that could lend it to easy administration by non-

professionals, translation into local languages and utility for elderly with low literacy, should it prove to have validity for dementia screening.

III. *Deterioration Cognitive Observee (DECO):(Ritchie and Fuhrer 1996)*This is a multi-domain 19-item screening test which is considered to be not affected by the participant's education as it relies on an informant to complete the questionnaire *(Ritchie and Fuhrer 1996).* At a cut-score of ≤24, the DECO has a sensitivity of 79% and specificity of 90% in detecting dementia(Ritchie and Fuhrer 1996). The DECO has discriminability for mild, moderate and severe dementia(Ritchie and Fuhrer 1992) and has been found to be useful in predicting mild and moderate dementia in South Africa(Lenger, deVilliers et al. 1996). The DECO was therefore chosen above the more widely researched IQCODE(Jorm, Scott et al. 1991).

IV. *Mini-Mental State Examination (MMSE)(Folstein, Folstein et al. 1975):* It is a multi-domain clinician-administered tool that yields a maximum score of 30. The most widely used cut-off score for cognitive impairment is ≤23. In community settings, the MMSE has a pooled sensitivity and specificity of 85.1% and 85.5% respectively (Mitchell 2009); its sensitivity and specificity in the South African population have not been determined. The MMSE's limitations relate to its 'floor' and 'ceiling' effects and age, gender, ethnicity and education level have been shown to influence its performance(Escobar, Burnam et al. 1986). In cross-cultural settings, race has been shown to influence scores despite adjusting for education(Tombaugh and Mc Intyre 1992). MMSE scores have also been shown to be affected by the educational level of individuals; the effect of education has been shown to be greater than that due to gender, race and social class(Escobar, Burnam et al. 1986; Tombaugh and Mc Intyre 1992; Scazufca, Almeida et al. 2009).The MMSE was

selected as it is the most widely used screening instrument in clinical and research settings(Mitchell 2009; Scazufca, Almeida et al. 2009),despite the emergence of many new tools over the last ten years(Escobar, Burnam et al. 1986).To our knowledge, its validity in the local setting has not been determined, yet this is necessary in order to be able to reference other screening tools against it in future. Its recently introduced copyright restrictions and related costs may prevent its widespread use in low-resource settings in the future.

V. *Six-Item Screener (SIS)*(Callahan, Unverzagt et al. 2002)*:* This is a brief multi-domain tool comprising three temporal orientation items and the three recall items of the MMSE, resulting in a maximum total score of six. It has been found to be reliable and has the full psychometric properties of the full MMSE. Using a cut-off score of $\leq$3, the SIS has a sensitivity and specificity of 88.7% and 88% respectively for the diagnosis of dementia (Callahan, Unverzagt et al. 2002).

c. Statistical analysis

The data for all tools were analysed using IBM® *SPSS*®19, and the significance for all tests set at $p<.05$. Cognitive impairment cases were classified using the identified cut-off scores for 'cases' for each test. Sensitivity and specificity (95% Confidence Intervals (CIs)) of the SMRS, SMC, SIS and DECO were calculated against the MMSE cognitive impairment 'cases'. Numerical variables were tested for normality using Kolmogorov-Smirnov Z. Data were then compared for differences between 'cases' and non-cases for cognitive impairment for all tests using parametric-tests and non-parametric tests (Chi-square or Fisher Exact Test (X^2), Mann Whitney (U) and Kruskall Wallis (K) tests),and for related samples the Wilcoxon signed-rank test (W). Direct

logistic regression was performed to assess the impact of race, age and years of education on the classification of cognitive impairments as defined by MMSE 'cases'.

3.5.2 Stage 2 Clinical diagnosis

In this stage, a subsample of participants that were screened in stage 1 was assessed clinically for cognitive impairment and diagnoses were assigned. The method, diagnostic categories and criteria, assessment tool and statistical analyses are described below.

a. Method

The participants for this stage were 51 screen positives (≤23) on the MMSE and a random selection of the 251 screen negatives in stage 1, described above. The resulting sample of 140 participants included 38 screen positives (13 either refused or were unavailable) and 102 screen negatives.

Clinical diagnostic evaluations were conducted in English by three psychiatrists, who were blind to the results of the screening stage. A standardised clinical assessment tool (Annexure 9.7) developed for the study was administered. Following the clinical diagnostic assessments, a consensus panel consisting of a senior neurologist, senior clinical psychologist and psychiatrist assigned the diagnoses of dementia, major depression-current and delirium according to DSM IV-TR criteria(American Psychiatric Association 2000). Participants who did not fulfil the criteria for dementia or MCI were categorised as 'non-cases'. A DSM-IV-TR(American Psychiatric Association 2000) diagnosis of dementia is based on, firstly, the development of multiple cognitive deficits manifested by both memory impairment as well as one of four areas (aphasia,

apraxia, agnosia, executive functioning) of cognitive disturbances; and secondly, these cognitive deficits should also cause significant impairment in social or occupational functioning(American Psychiatric Association 2000).Sub-typing of the dementias was not done.

A diagnosis of Mild Cognitive Impairment (MCI) was based on the recommendations of the International Working Group on Mild Cognitive Impairment and requires the presence of subjective cognitive impairment (self or informant reported), objective evidence of cognitive impairment in the presence of high scores for ADL and normal or minimally-impaired IADL functions(Winblad, Palmer et al. 2004).MCI diagnostic subtypes of amnestic MCI, single domain (aMCIsd), multi-domain (aMCImd) non-amnestic MCI single domain (naMCIsd) were based on the presence or absence of amnesia and the presence of single or multiple cognitive domains of impairment(Petersen 2004). Those participants who did not meet criteria for Dementia or MCI were classified as non-cases.

For ethical reasons, all participants who were assigned a clinical diagnosis of dementia were offered blood tests (full blood count [FBC], blood glucose, thyroid functioning test [TFT], syphilis serology [RPR] and Vitamin B12 and folate levels) as well as a CT scan of the brain, without contrast.

Clinical classification *("Gold Standard")*

For the purposes of this study, the following apply:

- *Dementia* was diagnosed using the Diagnostic and Statistical Manual of Mental Disorders 4th Edition-Text Revised (DSM IV-TR). Criteria A and B for Alzheimer's and Vascular Dementia were applied to assign a general diagnosis of dementia without

reference to aetiology. A clinical diagnosis was used as the "gold standard" for dementia (Knopman, DeKosky et al. 2001; Alagiakrishnan 2010).

- *Mild Cognitive Impairment (MCI)* was diagnosed using the criteria contained in the *Report of the International Working Group on Mild Cognitive Impairment*. These were: the presence of subjective cognitive impairment (self or informant reported), objective evidence of cognitive impairment in the presence of high scores for activities of daily living (ADL) and normal or minimally-impaired instrumental activities of daily living (IADL) functions.(Winblad, Palmer et al. 2004)Subjective memory impairment was through solicited self-report and objective evidence of cognitive impairment was based on the performance of participants on the various cognitive domains assessed in the clinical evaluation (Stage 2).
- *Non-dementia controls* were those participants who did not meet the criteria for dementia. The *Controls were those* participants who did not meet the criteria for MCI or for dementia.

b. Instruments

A standardised clinical data sheet was designed for completion by assessing psychiatrists.

- Standardised clinical assessment tool (Annexure 9.7): The assessment tool used in the study included the following sections: a historical review of the participant's cognitive status, a review of the medical, surgical, family, medication and substance use history, a review of social and functional activities, a physical (including neurological) examination and a comprehensive mental state examination. The assessment of functional abilities was based on participant self-report as the residential setting precluded access to informants. Participants were classified as

being functionally unable to perform specified activities of daily living (ADL) and instrumental activities of daily living (IADL) tasks only after medical causes for the inability were excluded. Content validity was based on the Diagnostic and Statistical Manual, Fourth edition, Text Revised (DSM IV-TR) criteria for Dementia, Major Depression and Delirium. Face validity of the tool was established through review of the tool by a group of psychiatrists, neurologists and psychologists. Although the assessing psychiatrists underwent intensive training in order to standardise the assessments, inter-rater reliability was not formally established.

- *Subjective Memory Complaint-Clinical (SMCC):* The SMCC is a single domain screening measure that is used to assess memory through affirmative responses to seven questions on memory recall problems experienced at least once a week over the last year. The participant is presented with seven commonly occurring situations requiring memory recall, six short-term items and one long-term item (Table 3). The evaluation of SMCC is distinguished from SMC by the specification of duration, frequency and nature of the memory complaint. As memory behaviours occur in specific behavioural contexts and most memory questionnaires focus on context-free memory domains, we decided to evaluate specific memory behaviours. This is based on the behavioural specificity hypothesis that 'individuals are capable of accurately reporting memory-related problems in everyday life, provided that questions are specific to the behaviours in question'(Hertzog, Park et al. 2000). The descriptive subjective memory items used in our study were based on commonly encountered clinical experiences of patients in a psychiatric hospital setting which were further specified for duration and frequency. Two psychologists and three psychiatrists were asked to examine the items to ensure face validity.

The SMCC was coded as positive if the participant reported difficulties with at least one of the seven situations presented. A positive association has been shown between the type and number of SMCs and objective cognitive performance, with 'finding one's way around familiar streets' identified as being one type of memory complaint that was more likely than others to be associated with cognitive impairment (Amariglio, Townsend et al. 2011).

c. Statistical analysis

The data was analysed according to diagnostic categories of dementia and MCI. Differences in age and education between the diagnostic groups were tested using Independent Samples Kruskall Wallis Tests. Associations between diagnostic categories and demographic variables, the presence of risk factors and retained functionality in IADL were tested using Pearsons' Chi square Test or Fisher Exact Tests (where sample sizes were small). Significance was set at $p<.05$.

3.5.3 Stage 3 Neuropsychological testing

The third stage involved the administration of a neuropsychological battery of tests to participants who were diagnostically assessed in stage 2.

a. Method

One hundred and seventeen participants (including nine with dementia and 30 with MCI) from stage 2 were included in this stage. The 108 participants who did not meet the criteria for MCI or for dementia represented the control group. Clinical psychologists administered ten tests, in English, in a single session, at the participants'

residences. The psychologists were blind to the screening test results and diagnostic status of the participants.

b. Instruments

The eleven neuropsychological tests were categorized according to the five cognitive domains assessed, and consisted of verbal memory and learning, executive function, language, visuo-spatial/perceptual, attention and working memory.

i. *Verbal Memory and Learning: The Rey Auditory Verbal Learning Test (RAVLT)*(Lezak, Howieson et al. 2004; Strauss, Sherman et al. 2006): This is a simple test of memory consisting of five free-recall Trials of a 15 item list of nouns. After an interference period, Trial 6, recall is tested immediately and again after 20 minutes. Administration time is 10-15 minutes.

ii. *Executive function: Trail Making Test (TRAILS)*(Reitan 1955; Lezak, Howieson et al. 2004; Strauss, Sherman et al. 2006): The TRAILS is an assessment of attention, speed, visual-motor tracking and mental flexibility. In Part A, subjects are asked to connect consecutively numbered circles on a sheet and in Part B, they connect consecutively numbered and lettered circles alternately without lifting pencil from paper. Administration time is 5-10 minutes, and the score is expressed as the time in seconds taken to complete the tasks.

iii. *Clock Drawing Test*(Freedman, Leach et al. 1994): This is a screening test for dementia that assesses visual-spatial, constructional and executive functions. Numerous versions of drawing the clock have been published with varying administration instructions and scoring systems. In this study, the free-

drawing version with the ’10 past 11’ time setting was used using Rouleau’s 10-point scoring system (Rouleau, Salmon et al. 1992; Rouleau, Salmon et al. 1996).

iv. *Luria hand sequence*(Lezak, Howieson et al. 2004; Weiner, Hynan et al. 2011): An assessment of programmed motor tasks in which subjects are required to imitate a cycle of three hand motions performed by the examiner. After three guided attempts, the subjects are required to repeat them without guidance. The test score is based on the number of correctly completed cycles.

v. *Mazes*(Lezak, Howieson et al. 2004): Mazes test planning and foresight and subjects are required to complete mazes of varying complexity. Scores are expressed in the time taken for completion.

vi. *Language: Controlled Oral Word Association Test (COWAT/FAS)*: (Lezak, Howieson et al. 2004) The test consists of three one-minute word-naming trials using the letters “F-A-S”, with subjects asked to name as many words as they can in one minute that begin with each of the given letters. The score is the sum of all acceptable words produced in the three one-minute trials. The COWAT/Animal test requires subjects to name as many animals as they can in one minute.

vii. *Short story comprehension and recall* (Lezak, Howieson et al. 2004): A short story is presented to a subject who is then required to narrate the story to the examiner. The test simulates the memory demands of everyday life situations. It measures the retention capacity when the immediate memory span is exceeded, as well as the contribution of meaning to retention and

recall. A South African adaptation of the Cowboy Story, A Farmer from Transkei, was used in this study.

viii. *Token test*(Short version)(De Renzi and Vignolo 1962; Lezak, Howieson et al. 2004)*:* The token test utilizes 20 paper tokens of various shapes, sizes and colours. Subjects are instructed to complete 36 commands related to the tokens which requires the ability to identify the tokens correctly and obey the instructions.

ix. *Visuo-spatial/perceptual: Rey Osterreith/Rey Complex Figure(RCF)*(Lezak, Howieson et al. 2004): This is a test of visuo-constructive skill, visual memory, attention and planning. A subject is first asked to copy a complex figure presented to him, and is expected to reproduce the figure from memory immediately or after a 20 minute delay. Various scoring systems are in use and are based on specific details on the figure that are reproduced.

x. *Attention and Working memory: Digit Span*(Wechsler 1997): A measure of short term memory. Subjects are required to repeat a sequence of numbers presented verbally by the interviewer. The subject then listens to a sequence of numbers and repeats them in reverse order. In both parts, the length of each sequence of numbers presented increases as the subject correctly responds.

xi. *Digit symbol***:**(Wechsler 1997) A test of psychomotor performance that requires subjects to correctly pair randomly presented numbers with nonsense figures as paired on a table. Subjects are given 90 or 120 seconds respectively, and the score is based on the number of correctly paired items.

c. Statistical analysis

Data were analysed using IBM SPSS® v21.0 (IBM Corp 2012). MedCalc® v12.5.0 (MedCalc Software 2012) was used for the Random Operating Curve (ROC) analysis. For the generation of norms, data was tested for normality and differences in demographic variables of the participants were tested using parametric and non-parametric tests as appropriate. Descriptive statistics for each test was calculated, including quartiles, by race, age group, gender, and education group and differences in means of tests were compared in the different genders race groups and educational categories using Kruskall-Wallis tests for Independent Samples or Mann-Whitney U Tests for Independent samples as appropriate. The descriptive statistics for each test were calculated for each of the diagnostic groups (MCI and dementia) as well as for the non-cognitively impaired controls.

For the determination of the sensitivity and specificity of the tests for MCI and dementia, descriptive statistics were calculated for demographic variables, and mean neuropsychological scores were calculated for each of the groups. Between-group comparisons were undertaken using non-parametric Kruskal-Wallis Tests and Chi-square Tests (including Fisher Exact Tests where appropriate).

For all cognitive tests, differences were tested using non-parametric Kruskall-Wallis tests and 95% confidence intervals were calculated. After establishing the discriminant validity of these tests for MCI and Dementia, ROC analyses were used to summarise the diagnostic accuracy of the tests on all possible cut-off scores, giving equal weighting to sensitivity and specificity. This allowed comparison of the discriminatory

validity and diagnostic accuracy of the different cognitive tests (Ritchie and Fuhrer 1992; Kukull, Larson et al. 1994), and the ranking of the sensitivities and specificities of the various tests. ROC curves and the sensitivities and specificities were produced for each of the tests for Dementia (n=9) compared with the performance of non-dementia participants (Controls + MCI; n=108).

Similar comparisons were done between MCI (n=30) and Controls (n=78). For each test measure, the area under the curve (AUC) was calculated with 95% confidence intervals. Optimal cut-off scores (Youden Index) and associated sensitivity and specificity values were generated for each test for dementia and MCI respectively. Swets' interpretation of AUC scores were used in this study: 0.5=non-informative; 0.5<AUC$\leq$ O.7 = less accurate; 0.7< AUC $\leq$ 0.9 = moderately accurate; 0.9<AUC<1 = highly accurate and the perfect test has an AUC = 1 (Swets 1988). For those tests where the area beneath the curve was significant, we selected the cut-off score on each one that gave the optimum sensitivity to cases, balanced against the optimum specificity for the comparator group.

3.6 Choice of Screening and Neuropsychological Tests

As described in the literature review, several practical and professional considerations affect the choice of psychometric tests, particularly in the context of culturally, linguistically and educationally diverse populations. The first consideration was whether to use existing tests or develop a new test. As outlined in the literature review, the development of a new test is a multi-disciplinary process requiring extensive resources and iterant review and refining stages. Given that there are a large number of tests in use globally, it seemed prudent to

first establish if one or more of them could suffice, with additional adaptation for local relevance and validity.

The second consideration was whether to first adapt the chosen tests before determining their performance characteristics on the local population. Given the racial (within each of which there exist further cultural, ethnic and acculturation differences), linguistic and educational differences within the sample, test adaptation would entail the creation of several versions of any single test to ensure cultural fairness and equivalence, in addition to construct validity. This would clearly exhaust the parameters of this small study. Furthermore, it did not appear prudent to modify tests without first establishing what, if any, limitations or biases they posed in the local population, given that little or no baseline data from South Africa was available for most of the chosen tests.

The researchers therefore opted to first establish the performance of the tests in English-speaking participants of all race groups who had a minimum of eight years of formal schooling. English is not the first language of all participants, but self-reported proficiency in reading, writing and understanding the language was required to ensure any related barriers did not compromise the comprehension of test instructions and test content, and hence adversely affect test performance. Admittedly, the quality of the years of education would not be equal among participants. However, it was hoped that the emerging data would create a starting point to begin further exploration of the degree to which these tests were significantly affected by at least race and education. Our findings would thus serve to inform future decisions about the need to adapt existing tests or embark on the development of new tests.

3.7 Data management

All the completed data collection material was stored in sealed envelopes in a locked room at the King George V Hospital until they were given to the researcher on a weekly basis. They were then stored in her locked office at the University of KwaZulu-Natal, where she entered the data into SPSS. Access to the digital data on the computer was password protected and the raw data was only available to the researcher and her supervisor. The data collections sheets will be retained in a locked room in the Department for five years after which they will be destroyed.

3.8 Research Framework

This study used two frameworks, an epidemiological screening framework and the cognitive reserve theory of dementia, both of which are detailed further.

3.8.1 Epidemiological Framework

Epidemiology refers to the scientific study of the distribution and determinants of disease frequency in humans (Duff, Humphreys-Clark et al. 2008). While classic epidemiological research designs are applied to psychiatric research, psychiatric case definition remains a challenge, despite major advances in psychiatric classification systems, (Tsuang, Tohen et al. 1995; O'Bryant,Waring et al. 2008) due to the lack of pathognomonic biological markers. Cognitive impairment in the elderly exists on a continuum from 'normal' age-related changes to pre-clinical/asymptomatic degenerative changes before the clinical features of dementia manifest. Despite advances made in the identification of biological markers for dementia (Albert, DeKosky et al. 2011;Jack, Albert et al. 2011; McKhann, Knopman et al.

2011) diagnosis remains a clinical exercise augmented by the use of psychometric instruments or measures. Despite its limitations, epidemiological designs offer useful strategies to address critical clinical issues that rely on knowledge of the nature, cause and prognosis of psychiatric disorders(Tsuang, Tohen et al. 1995).

A cross-sectional design was chosen to assess a defined group of elderly, where the entire spectrum of cognitive capacity (i.e. normal to age-related decline to dementia) could be described and quantified. Several advantages of a cross-sectional design are cited: access to clinical and non-clinical participants, the ability to interview participants (useful in psychiatric disorders), and prevalence estimates(psychiatric disorders may have low incidence but their chronicity allow for the calculation of incidence based on prevalence figures(Tsuang, Tohen et al. 1995). A cross-sectional design is particularly relevant to multi-cultural settings, as it has been shown that African Americans, American Indians and Xhosa-speaking groups cognitive decline in the elderly is often viewed as a normal accompaniment of ageing and not a pathological condition warranting medical attention. This has implications for estimates of disease prevalence as well as intervention opportunities.

While the significant advances in psychiatric epidemiology are acknowledged, the remaining challenges, which are relevant to this study, are the development and implementation of accurate assessment tools for studying disorders affecting the elderly, especially those living in developing countries, as well as undertaking research to determine needs and to plan programmes(O'Bryant, Waring et al. 2008).It is hoped that this study will contribute toward redressing the gap in the literature on the use of cognitive assessment instruments in the elderly in low-income settings, and that the contribution of data emanating from the study

could be useful in estimating the need for cognitive screening in the elderly in residential settings as well as suggest an evidence-based screening programme.

3.8.2 Cognitive Reserve Theory of Dementia

The concept of cognitive reserve (CR) was suggested as far back as 1988, when a study revealed pathological features of Alzheimer's Disease (AD) with many neocortical plaques in the brains of clinically normal elderly nursing home residents(Katzman, Terry et al. 1988). The associated findings that these residents had higher brain weights and greater numbers of neurons led the authors to advance the concept of 'reserve.' Briefly, cognitive reserve refers to the non-linear relationship between the degree of neuro-pathological abnormalities and the clinical severity of manifested brain injury whether due to disease (dementia) or damage (traumatic brain injury)(Stern 2003).

Reserve may be conceptualized as either an active or a passive process. In the passive model, brain reserve (also referred to as neuronal reserve) refers to the amount of damage that the brain can tolerate before the damage manifests clinically. The threshold model, first described by Satz in his seminal paper of 1993 and cited by Stern (2003), is based on 'brain reserve capacity' (BRC), a hypothetical construct, which states that there is a critical threshold (threshold model) of BRC which, when exceeded, allows for the emergence of clinical signs and symptoms. Hence, greater BRC would confer protection to the manifestation of illness while low BRC would render subjects more vulnerable (Stern 2003).

The active models of reserve suggest that the brain actively compensates for brain damage. This could be due to two mechanisms viz. cognitive reserve when the brain 'activates' brain

networks or cognitive paradigms that are less susceptible to disruption, or compensation, where brain structures or networks not normally used by individuals with intact brains begin to be used(Stern 2002).

In the threshold model, the reserve would arise from additional synapses or an increased number of redundant neuronal networks, while cognitive reserve refers to the 'software', implying resilience of the cognitive paradigm or the adoption of an alternate paradigm to approach a cognitive task(Stern 2002).The threshold model can be applied to explain the findings of pathognomonic plaques in brain specimens of individuals who displayed no clinical features of AD during life. It can also be used to support the research findings that individuals with larger heads or greater educational level are less likely to have AD or severer forms of AD. Genetic factors, variation in nutritional and cognitive stimuli *in utero,* childhood development, as well as educational or vocational environment, are all possible contributory factors to CR, and can therefore influence the incidence and prevalence of AD (Lee 2003). While most of the screening and assessment psychometric tests are biased in favour of those educated within a Western educational system, CR adds another dimension to the interpretation of the effects of education on test performances.

Viewed as a feature of brain structure and/or function that acts as a modifying factor between pathology and performance on neuropsychological tasks or clinical outcomes, CR poses practical challenges: being a hypothetical construct, as direct measures of reserve are not available. In additions, developing and testing models of CR are challenging, as the risk factors (brain pathology) and the moderating variable (reserve) are directly measurable. In light of these challenges, the utility of the concept of reserve is being questioned with the

recommendation that it be subjected to on-going refinement and construct validation(Jones, Manly et al. 2011).

On a practical level, there is evidence to suggest that cognitive reserve is potentially modifiable at an individual level. Socio-economic status, education, leisure and cognitive activities both at age 40 and in late life have been shown to be predictors of CR (Reed, Dowling et al. 2011). Social engagement and participation in physical and cognitively stimulating activities can lower dementia risk by increasing cognitive reserve (Karp, Paillard-Borg et al. 2006). The concept of CR therefore has potential value in supporting interventions that could reduce the risk or increase the resilience of individuals for cognitive decline.

Cognitive reserve theory has implications for screening for and diagnosing dementia. Although the neurobiological basis of CR is not well understood, good measures of performance are needed in order to measure performance and pathology(Bennett and Barnes 2011). If screening measures are intended to detect disease in the early stages, the implication is that our screening and diagnostic efforts are currently only targeting the disease after it manifests clinically. Although several biological markers (Jack, Albert et al. 2011; McKhann 2011) have been identified for AD in particular, their use is currently recommended only for research settings (McKhann, Knopman et al. 2011). Furthermore, their prohibitive costs are unlikely to allow for their routine use in the local setting. Hence, psychometric screening instruments remain the most cost-effective screening measures available currently.

The choice of specific tests for screening and neuropsychological testing are described further in Papers 3 (chapter 6) and 5 (chapter 7) respectively.

3.9 Limitations

Several limitations are identified in the methods used in this study.

a. Study population

The ideal sample for a study of this nature would have been community-dwelling elderly. This would have represented a more naturalistic setting. Our use of participants living in a residential setting has potential biases. Many reasons underlie the decision of elderly individuals and their families to opt for residential living. These include financial, social and health reasons. The challenges and burden associated with living with an individual with cognitive impairment has been shown to increase the likelihood of institutionalisation(Boustani, Peterson et al. 2003); conversely, the loneliness and isolation of living apart from family is also known to impact negatively on mental health and can therefore be a risk factor for cognitive decline(Fillit, Butler et al. 2002; Williams, Plassman et al. 2010).

b. Sampling

Ideally, a stratified sample, equally representative of all race groups, would have enabled comparisons to be made between race groups. Unfortunately, all race groups were not equally represented in the population, with very low numbers of Black residents being compounded by a low level of education, resulting in their failure to meet inclusion criteria.

Accessibility to the residents also proved a challenge. Sampling initially commenced with a random selection of residents, generated electronically from the residential database. This proved to be extremely time-consuming, and resulted in a very low yield of residents who agreed to participate and met the inclusion criteria. It was then decided to revert to convenience sampling which entailed approaching every resident in each building systematically according to residential door numbers until the desired number of participants was attained. It is noteworthy that several buildings had to be revisited due to the numbers of residents who were not present during the first round of visits.

c. Language and cultural factors

In a multiracial, multi-linguistic setting, the choice of language is a challenge. To obviate some of the confounding effects of language differences between investigators and participants, it was decided to conduct the study in English only and to restrict participation to those who were proficient in speaking, reading and writing English. This was necessitated also by the use of screening instruments that were available in English and were not validated in the local languages. This however does not eliminate the many potential biases due to language and cultural factors that can influence performance on psychometric instruments, as discussed in the literature review.

d. Choice of instruments

As discussed in the literature review, choosing suitable, valid and culture-fair instruments remains a challenge in a setting where dementia has not been much

researched and where cost factors preclude large-scale epidemiological and validation studies.

e. Time lag between assessments

The total duration of the data collection spanned eight months. Each of the three stages had to be completed prior to the commencement of the next stage as subsamples from the preceding stage formed the sample for the next stage. Hence, sensitivities and specificities of the screening instruments were based on diagnoses made one to two months later. While there could theoretically have been deterioration in the cognitive status of participants in this interval, we do not believe that this would have substantially impacted on the data. A similar lag existed between clinical assessments and neuropsychological testing.

3.10 Ethical considerations

The study received ethical approval from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal, BF 200/09.

3.11 Conclusion

This is the first study done locally to attempt to simulate a naturalistic clinical approach to the assessment of cognitive impairment in the elderly. By commencing with the evaluation of a variety of existing screening measures at 'community' level (stage 1), it is hoped that measures that have both practical utility and scientific validity will be identified that can be considered for widespread clinical application. The second stage explores the clinical

diagnostic assessment of participants who screen positive on the various measures evaluated in the screening stage. One newly developed screening measure, the Subjective Memory Complaint- Clinical (SMCC) was also incorporated at this stage and its utility and validity as a screening measure was examined. Assessments of the functional status of participants with respect to basic and instrumental activities of daily living were also evaluated for their potential utility and validity as screening measures; their use in screening is supported by a small but growing and important literature.

CHAPTER 4

UTILITY AND VALIDITY OF SCREENING TOOLS FOR COGNITIVE IMPAIRMENT

4.1 Introduction

This chapter reports on the data from the first stage of data collection, namely the administration of the screening instruments. The instruments were compared to the Mini Mental State Examination, as it is the most widely used and researched screening instrument. The researcher was responsible for designing and defining the research, data analysis, interpreting the data, and writing up the paper.

4.2 Background

The District health system in South Africa requires patients using public health services to make initial contact with primary health care personnel who serve as a 'gateway' to District, Regional and Tertiary hospitals, with specialists being available at the latter two. Due to the shortage of mental health care professionals in South Africa, there is a need to identify screening measures that are suitable for use at primary health care clinics and/or District hospitals. A variety of screening measures (subjective, objective and informant) were evaluated to ascertain which would be most suitable for local use.

4.3 Aim

The aim of the first stage was to investigate the performance of cognitive screening measures in a sample of elderly participants of different race groups.

4.4 Methodology

Three hundred and two residents were conveniently sampled and administered four cognitive and one depression screening measure in their homes: Subjective Memory Complaint, Mini Mental State Examination, Subjective Memory Rating Scale and Deteriorative Cognitive Observee and the Geriatric Depression Scale.

4.5 Study Outcome

The data is reported in Paper 1, **"Screening a heterogeneous elderly South African population for cognitive impairment: The utility and performance of the Mini Mental State Examination, Six Item Screener, Subjective Memory Rating Scale and Deteriorative Cognitive Observee"** accepted for publication in the African Journal of Psychiatry.

4.6 Paper 1

Screening a heterogeneous elderly South African population for cognitive impairment: The utility and performance of the Mini-Mental State Examination, Six Item Screener, Subjective Memory Rating Scale and Deterioration Cognitive Observee

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Abstract

Objective: With the expected increase in the elderly population and prevalence of dementia, particularly in low-and-middle-income countries, reliable and culturally appropriate cognitive screening tools are necessary. Screening tools have not been widely researched for cross-cultural validity in South Africa (SA). The aim of this study was to report on the prevalence of cognitive impairment, and to assess the performance and utility of subjective, objective and informant screening tools in a heterogeneous community sample. **Method:** A sample of 302 elderly participants (>60 years) living in residential homes in a large city in South Africa were screened for the presence of cognitive impairment using objective (Mini-Mental State Examination [MMSE] and Six Item Screener-[SIS]), subjective (Subjective Memory Complaint [SMC]and Subjective Memory Rating Scale [SMRS]) and informant (Deterioration Cognitive Observee [DECO]) screening tools**.** All tools were compared to the MMSE and the influence of demographic variables on the performance on these tools was considered**. Results:** Significantly lower MMSE scores were found in participants aged 80-89 years (p=.023) and those who had 8-11 years of education (p=.002). For every one additional year of education, participants were 0.71 times less likely to screen positive on the MMSE. Differential item functioning on various components of the MMSE was demonstrated due to the effects of education, race and gender. There was significant differential performance between the recommended and alternate attention/concentration items (p<.001) with the alternate item favouring better performance. Based on the MMSE cut-off score of $\leq$ 23, the prevalence of cognitive impairment was 16.9%; the prevalence yielded by the remaining tools ranged from 10.5% using the DECO to 46% as determined by the presence of a SMC. Using the MMSE as the reference standard for the presence of cognitive impairment, the SIS, SMC, SMRS and DECO had sensitivities of 82.3%, 54.6%, 17.0% and 37.5%, and specificities of 71.3%, 57.6%, 87.4% and 96.7% respectively. Age and race influenced performance on the MMSE, SIS and SMRS. **Conclusion**: Different types of cognitive screening tools yielded varying sensitivities and specificities for identifying cognitive impairment when compared to the MMSE. The influence of race, age and education on test performance highlights the need for suitable, culture-fair screening tools. Locally, the alternate item for attention/concentration should be preferred.

Keywords: Screening; Dementia; MMSE; Subjective Memory Complaints; South Africa

Introduction

South Africa has the second largest elderly population in Sub-Saharan Africa[1] with the population aged 60 years and older projected to increase from 7.1% in 1996 to 8.4% in 2014.[2] However, the serious consequences of population ageing do not appear to be planned for as evidenced by the lack of a national dementia care policy. There is a lack of recent data on morbidity as well as a paucity of research particularly in the areas of cognitive, mental and physical functioning of the elderly.[3] Dementia, a condition largely affecting the aged, requires specialised services, few of which exist either in the public or private health sector in South Africa. The projected increase in the prevalence of dementia, especially in lower and middle income countries (LAMIC), and the resultant increase in demand for services 'needs to be met by adequately prepared and resourced services…'.[4] The Kyoto Declaration identified the recognition and treatment of dementia at primary health care level as a first priority.[5] Recognition of dementia requires the use of screening tools to identify individuals who warrant intensive clinical diagnostic evaluation. The validation of screening tools in the local context is an important first step in this process.

Dementia poses a significant health and economic burden to society.[6] It is the 11th leading cause of years lived with disability (YLDs) at a global level, and accounts for 2% of total YLDs.[7] The annual cost of caring for people with dementia in the UK and USA are $10 billion and $100 billion respectively.[8] Economic models suggest that early dementia diagnoses are more cost effective[4] and that a delay of progression from Mild Cognitive Impairment (MCI) to Alzheimer's Disease (AD), even by one year, could have significant cost implications for health and social services.[9] Early diagnosis and intervention is therefore recommended[10] and actively promoted in high-income countries (HIC),[4] despite widespread routine screening not being recommended by the United States Preventive Services Task Force.[11] MCI, an intermediate stage between normal age-associated cognitive decline and dementia, shows substantial variation in reported prevalence, but may be present in up to 42% of elderly populations.[12] It is associated with disability and neuropsychiatric symptoms.[13] Together with dementia, it therefore also requires early detection if any significant impact is to be made on the burden posed by cognitive impairment in the elderly.

Screening initiatives are compounded by refusal rates as high as 50%,[14] with a survey conducted in the USA and Europe revealing low levels of acceptance by the elderly and the perception that screening was harmful.[15] Dementia screening enjoys a low priority in low and middle income country (LAMIC) healthcare systems that face considerable burdens relating to communicable diseases.[16,17] Fifty-eight percent of people with dementia currently live in LAMIC and this figure will increase to 70% in 2025 and to 71% by 2050.[12] The treatment gap for dementia is as high as 90%[18] in these countries compared to 20%-50% in HIC.[19] Empirical data on dementia in LAMICs is limited,[6] with a dearth of large

community-based epidemiological studies[20] and only seven methodologically robust studies being identified by the 10/66 Dementia Research Group in 2000.[21]

Due to existing resource constraints and competing health priorities, a cost-effective strategy for dementia is needed. Screening tools, largely the product of Western psychological paradigms,[22] are ability assessments that are not culture-fair,[23] and they therefore pose challenges to being used among diverse cultural, ethnic, language and literacy populations in LAMIC, as well as within and between HIC.[24,25] Screening tools need to be brief, easy to administer, clinically acceptable, effective, minimally affected by education, gender and ethnicity,[26] and have sound psychometric properties. At the same time, it is recommended that similar screening tools should be used in LAMIC and HIC to facilitate comparisons between studies, and that such tools should be reliable and administrable by both paraprofessionals and trained non-professionals.[20]

To date, few studies have been conducted in SA to evaluate the performance of screening tools that are commonly in use. The MMSE has been used in a homogenous population as a diagnostic tool without comment on its psychometric properties.[27] In another study involving ten patients, it was concluded that the MMSE was an 'out-dated and inadequate' screening tool.[28] The utility of the DECO[29] as an informant screening tool has been assessed in a pilot study and found to be a sensitive measure for mild and moderate dementia and its use recommended, with minor modifications, in community studies.[30]

The aims of this study were to calculate the prevalence of cognitive impairment, evaluate the performance of the Mini-Mental State Examination (MMSE),[31] the Six Item Screener (SIS)[32], the presence of a subjective memory complaint (SMC), Subjective Memory Rating Scale (SMRS)[33] and the Deterioration Cognitive Observee scale (DECO) in identifying cognitive impairment in a heterogeneous elderly South African population. We also sought to establish the degree to which race, age, education level and depression may influence the performance of these screening tools.

Method

This study was conducted in a group of retirement homes administered by a non-governmental organisation (NGO) in Durban, KwaZulu-Natal, South Africa between August and October 2010. The residential facilities ranged from frail care to independent living, and cater for all ethnic groups and socio-economic classes, representing a cross-section of the local elderly population. A sample of 302 was assessed to have adequate power to provide caseness in screening. Inclusion criteria were: residents who were 60 years and older, with a minimum of 8 years of formal schooling, the ability to speak, read and write in English and the ability to give written, informed consent. Exclusion criteria were residents with severe physical, mental or sensory handicaps that precluded their engagement in the assessment

procedures. A random sample was initially selected electronically from a database of the 1371 residents. There was a high refusal rate and many residents were not at home which resulted in a low yield of participants. To address this, the approach was revised to a door-to-door convenience sampling method that included all residents who were available on the day of screening and who agreed to participate. A total of 733 residents were screened of which 302 met the inclusion criteria. Of the remaining 431 (58.8%), 155 failed to meet the inclusion criteria, 227 declined and 49 were unavailable.

The study received ethical approval from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal. Screening assessments were conducted at the participants' residences by a trained senior psychiatric registrar using the MMSE, SMRS and the DECO. The Six Item Screener (SIS), comprising a subset of the MMSE items was also analysed separately as it has the potential to substitute the MMSE, especially in resource-constrained clinical environments where lengthy administration time may be a significant deterrent to regular screening. The SMRS was administered to those participants who replied 'yes' to the question: 'Are you experiencing any difficulty with your memory?' The SMRS defines five specific contexts of memory impairment with respect to duration (last 10-20 years) whereas the SMC documents the presence of subjective awareness of memory problems in general. In the MMSE, the terms for orientation to place were modified to accommodate the local geographical context and two of the three registration/recall items were substituted. The DECO was administered to available informants who had monthly contact with the study participants for at least two years. Depression was identified using the Geriatric Depression Scale (GDS)[34] employing a cut-off score of $\geq$11. The psychometric properties of the tests are reported in Table 1.

Table 1. Psychometric properties of dementia screening tests

Domains measured	Method of administration	Sensitivity & Specificity	Reliability	Validity
MMSE[31]				
11 items: Orientation, registration, attention/concentration, calculation, recall, naming, repetition, comprehension, writing, construction.	▪ Interviewer administered ▪ 7-10 Minutes ▪ Cut-off score: 23/24	85.1% & 85.5% [35]	▪ Cronbach α= .54-96 [36] ▪Interrater=.9 Test Retest =.80-.95 ▪ Kendall Coefficients= .7 [31]	Content: Good: Concurrent: Correlates with WAIS,[31] Reisberg Global Deterioration Scale & Blessed Dementia Scale[37]
SIS[32]				
6 items 3 item temporal orientation and 3 item recall	▪ Interviewer administered ▪ 3 minutes ▪ Cut-off score: 4/5	88.7% & 88.0%	Test-retest moderate (Kappa=.52) (Shah)	Not available
DECO[29]				
Changes in behaviour noticed over 1 year in-activity level, semantic and visual memory, memory for places, events and procedures, visuo-spatial performance and new skill learning	▪ Informant administered ▪ 11-15 minutes ▪ Cut-off score: 24/25	79% & 90 %	▪ Inter-rater =.87 ▪ Test Retest = .92	Not available
SMRS[33]				
Changes in remembering names, faces, friends, appointments and judging the time	▪Self-administered ▪5 minutes ▪Cut-off score: 19/20	43.0% (pooled) & 85.8%[38]	▪Cronbach α= .6.[33]	▪Face validity at 70,75, and 80, ▪Hazard ratios: 6.0 (95% CI 52.1–18), 3.2 (95% CI 51.6–6.2) and 1.6 (95% CI 50.86–3.1)[33]

Statistical analysis

The data for all tools were analysed using IBM® SPSS®19, and the significance for all tests set at $p<.05$. Cognitive impairment cases were classified using the identified cut-off scores for 'cases' for each test as indicated in Table 1. Sensitivity and specificity (95% Confidence Intervals (CIs)) of the SMRS, SMC, SIS and DECO were calculated against the MMSE cognitive impairment 'cases'. Numerical variables were tested for normality using Kolmogorov-Smirnov Z. Data were then compared for differences between 'cases' and non-cases for cognitive impairment for all tests using parametric-tests and non-parametric tests (Chi-square or Fisher Exact Test (X^2), Mann Whitney (U) and Kruskall Wallis (K) tests),and for related samples the Wilcoxon signed-rank test (W). Direct logistic regression was performed

to assess the impact of race, age and years of education on the classification of cognitive impairments as defined by MMSE 'cases'.

Results

Following an analysis of the participants' race, age and education levels, the results for each of the tools are presented separately.

Demographics

The age of the participants ranged from 60 to 94 years (mean 73.5 ± 7.7) and the female to male ratio was 2.6. More than half of the participants were White (168, 55.6%), followed by Coloureds (67, 22.2%), Asian (58, 19.2%) and 9 (3.0%) were Black[1]. The mean number of years of formal education was 10.4 ± 2.2 years and ranged from a minimum of eight years to a maximum of 19 years. Seventy per cent of participants had a high-school education and 8.9% had a tertiary education.

There was a significant association between race and age (White 75.1 and Asian 70.9 years of age, *K*=15.8, p=.001) and race and years of education (White 10.8 and Coloured 9.6, K=22.6, p<.001). Years of education was also associated with gender (Male 10.7 and Females 10.3 years, *U*=1.0, *p*=.047).

Mini Mental State Examination (MMSE) and Six Item Screener (SIS)

The MMSE was administered to all 302 participants and scored using both the recommended and the alternate items for the assessment of attention/concentration.[2] Over half of the participants (184, 60.9%) scored higher on the alternate item, 92 (30.5%) scored the same and 26 (8.6%) lower. This resulted in a significantly higher MMSE total using the alternate (mean 26.0 ±3.0 95%CIs [25.7, 26.4]) compared to the recommended item (mean 24.8 ± 3.4 95%CIs [24.4, 25.2]) Wilcoxon Signed-Ranks Test, T=9.9, p<.001. The final MMSE score was based on the better score between the recommended and alternate items.[37] Using a cut-off score of ≤23, 51 (16.9%) participants screened positive for cognitive impairment and 251 (83.1%) screened negative.

The mean MMSE score was 26.2 ±2.9, with scores ranging from 15 to 30. Lower MMSE scores were significantly associated with increased age groups[3] (*K*=9.6, *p*=.023), lower education groups[4] (*K*=12.5, p=.002) and race (Whites scoring higher) (*K*=25.3, *p*<.001).

[1] Traditionally, the elderly among people of colour are cared for by their families within the community.
[2] Copyright restrictions preclude further description of these items.
[3] Age groups were 60-69, 70-79, 80-89, >90 years.
[4] Education groups were 8-11, 12, >12 years

Comparing the performance of different participant age groups on the recommended vs the alternate attention/concentration items of the MMSE, no significant differences were noted (K=2.8, p=.422 and K=3.6, p=.311 respectively). However, participants with 8-11 years' education scored significantly lower on the recommended (*K*=22.3, p<.001) compared to the alternate item (K=7.3, p=.03). Similarly, there were significant differences for the race groups in the recommended item score (Blacks scoring lower) (*K*=23.0, p<.001) but not for the alternate item score (*K*=3.6, p=.315). The mean score for Blacks on the recommended item was 1.7±1.5 compared to a mean score of 4.8±0.7 on the alternate item (W=2.6, p=.011).

Direct logistic regression was used to report the effect of race, age and education together, and the relative contribution of each of the variables to the MMSE categories. The full model containing all the predictors were statistically significant (X^2 (n=302, 5) =19.8 *p*<.001), indicating that the model was able to distinguish between cases with and without cognitive impairment. It explained between 6.4% (Cox and Snell R square) and 10.7% (NagelKerke R Squared) of the variance in classification of cognitive impairment, correctly classifying 82.8% of cases. As shown in Table 2, only education made a statistically significant contribution to the model. The odds ratio of 0.71 for years of education was less than one, indicating that for every additional year of education, respondents were 0.71 times less likely to be classified as suffering from cognitive impairment as identified by the MMSE.

Table 2: Logistic regression predicting likelihood of classification as dementia using the MMSE score

Step 1*	B	se	Wald	df	*p-value*	Exp(B)	95% C I for EXP(B)	
							Lower	Upper
Age	.03	.02	1.50	1	.22	1.03	.98	1.07
Years of education	-.35	.10	11.57	1	.001*	.71	.58	.86
Race (White)			3.35	3	.34			
Race (Asian)	.48	.42	1.320	1	.25	1.61	.71	3.65
Race (Coloured)	.03	.42	.01	1	.94	1.03	.46	2.33
Race (Black)	1.16	.77	2.26	1	.13	3.19	.71	14.43
Constant	-.25	1.89	.02	1	.90	.78		

* Significance set p<.05. Variable(s) entered on step 1: age, race, and years of education. B=un standardized coefficients; se=standard error; Wald=Wald test; df-degrees of freedom; Cp-value= significance; Exp (B) = odd ratios and CI=confidence intervals

In considering the effect of these variables on individual items, education levels significantly influenced the performance on the following: geographical orientation (K=8.1, p=.017), recommended (K=22.3, p=.001), and alternate attention/concentration (K=7.3, p=.026), repetition (K=7.3, p=.026) and construction items (K=13.5, p=.001).

There were significant differences between the race groups (with Black participants scoring consistently lower than other race groups) on 3 orientation items (*K*=9.3, *p*=.025; *K*=9.3, *p*=.025; *K*=16.3, *p*=.001), as well as on the attention/concentration (*K*=23.0, *p*=.000), naming (*K*=10.7, *p*=.014), repetition ' (*K*=21.4, *p*=.001), comprehension of verbal (*K*=17,0, *p*=.001), and written command (*K*=12.7, *p*=.005) items.

Gender accounted for significant differences in 2 orientation items (*K*=2.7, *p*=.006) and (*K*=2.1, *p*=.036), the recommended (*K*=2.7, *p*=.007), and the alternate attention/concentration items (*K*=2.5, *p*=.015). Females performed better on all these items except for the recommended attention/concentration item.

In comparing the screen positives on the MMSE (n=51) with the screen negatives (n=251), there were significant differences in the positive and negative screen group for years of education, MMSE, SIS and GDS scores, but there was no significant association between MMSE screen positives and GDS positive categories (Table 3).

Table 3: Comparison of Participants with positive vs negative screen on MMSE

Item	**Screen positive MMSE <24 N=51 (16.9 %)**	**Screen negative MMSE ≥24 N=251 (83.1%)**	**Statistic**	***P***
Age	74.2 ± 7.6	73.4 ± 7.8	*T*=0.66	.51
Race Asian	13 (25.5%)	45 (17.9%)	X^2=4.3	.182
Black	3 (5.9%)	6 (2.4%)		
Coloured	12 (23.5%)	55 (21.9%)		
White	23 (45.1%)	145 (57.8%)		
Gender Female	32 (62.7%)	187 (74.5%)	X^2=2.9	.086
Male	19 (37.3%)	64 (25.5%)		
Years of education	9.4 ±1.7	10.6 ±2.2	*T*=3.6	<.001*
Depression (GDS positive ≥11)	20 (40%)	80 (31.9%)	X^2=1.2	.265
MMSE /30	21.0 ±2.2	27.2 ±1.7	*U* =11.4	<.001*
SIS score /6	3.2 ±1.5	4.9±0.9	*U* =8.0	<.001*
SIS positive <=4	42 (82.4%)	72 (28.75)	X^2=52.0	<.001*

Age and Years of Education were compared using Independent Samples T-Tests. MMSE, SIS scores were compared using Independent Samples Mann-Whitney U Tests. Gender, Race, GDS and SIS categories were compared using Pearson Chi-square Tests. *Significance level set as p<.05.

In addition to the full MMSE, the SIS was analysed to determine its sensitivity and specificity to screen for cognitive impairment. The SIS score was significantly affected by race (K=8.2, p=.041) and age groups (K=7.8, p=.049) but not by gender (U=-0.3, p=.806,) or education groups (K=1.1, p=.578). Using the SIS with a cut of ≤ 4, 114 (37.7%) participants screened positive for cognitive impairment. Testing whether the SIS categories could be used to

predict cognitive impairment as measured by the MMSE resulted in a sensitivity of 82.3 %, 95% CIs[68.7%, 91.1%] and a specificity of 71.3%, 95% CIs[65.2%, 76.7%].

Subjective Memory Complaint (SMC) and Subjective Memory Rating Scale (SMRS)
Subjective memory complaints were reported by one hundred and forty participants (46%) but its presence was not significantly associated with race (X^2=4.7, p=.193), gender (X^2=0.8, p=.438), age (U=1.8, p=.07) or education (U=0.8, p=.426). There was no significant association between the presence of SMCs and MMSE scores (U=1.2 p=.235). SMCs were significantly associated with depression (X^2=18.4, p<.001).

Using the MMSE scores to assign caseness, the presence of SMCs had a sensitivity of 54.6%, 95% CIs [44.2%, 64.7%] and a specificity of 57.6%, 95% CIs [50.5%, 64.4%] in identifying possible cognitive impairment cases.

The SMRS was administered to 140 participants who reported a SMC, with the mean SMRS score being 17.7, ±1.9, and a range of 15-24. The distribution of scores was not influenced by gender (U=0.9, p=.389) or educational level (K=5.5, p=.07) but was significantly associated with race (K=8.9, p=.03) and age group (K=14.7, p=.02). There was no significant association between SMRS categories and MMSE scores (U=0.6 p=.548).

Using the recommended cut-off of ≥20 to determine screen positives, 20 (14.3%) screened positive on the SMRS and 120 (85.7%) screened negative. There was a significant association between age, race and depression (Table 4) and screen categories.

Table 4: Comparison of Participants with positive vs negative screen on SMRS

Item	**Screen positive SMRS ≥20 N=20 (14.3%)**	**Screen negative ≤19 SMRS N=120 (85.7%)**	**Test**	***P***
Age	69.3 ±6.5	75.2±7.7	T=3.3	.001*****
Race			X^2=14.1	.002*****
Asian	9 (45%)	15 (12.5%)		
Black	1 (5%)	5 (4.2%)		
Coloured	6 (30%)	31 (25.8%)		
White	4 (20%)	69(57.5%)		
Gender			X^2=0.2	.681
Female	15 (75%)	90 (75%)		
Male	5 (25%)	30 (25%)		
Years of education	10.6 ±2,6	10.2 ±1.9	U=0.3	.753
Depression (GDS)	14(70%)	50(41.7%)	X^2=5.5	.019*
SMRS score	21.2±1.3	17.1±1.2	U=7.3	<.001*****

Age was compared using Independent Samples T-Tests. Years of Education, SMRS and MMSE were compared using Independent Samples Mann-Whitney U Tests. Gender and race were compared using Pearson Chi-square Tests.*Significance level set as p< .05.

Using the MMSE scores to assign caseness, the SMRS had a sensitivity of 17.0%, 95% CIs [8.5%, 30.3%] and specificity of 87.4%, 95% CI [78.1%, 93.2%].

Deterioration Cognitive Observee (DECO)

Of the 207 participants (64.7%) who provided details of eligible informants, 76 (36.7%) were contactable and were able to complete a DECO. Of these, 20 (9.7%) completed all 19 items on the DECO. This was due to two DECO items consistently having high missing values. These were writing letters (37, 48.7% completion rate) and reminding a person of a conversation (39, 51.3% completion rate). Adjusting for the denominator to take into consideration missing items, made no difference to caseness, and the decision was made to assign all missing data a score of zero.

The average DECO score was 30.9 ± 5.8, ranging from 4 to 38. Using the recommended cut off score of ≤24 (maximum score=38), eight (10.5%) screened positive for cognitive impairment. There were significant differences between the screen positives and screen negatives for gender and the DECO score (Table 5).

Table 5: Comparison of Participants with positive vs negative screen on DECO

Item		**Screen positive =<24/38 N=8(10.5%)**	**Screen negative >24/38 N=68 (89.5%)**	**Statistic**	***P***
Age		75.3 ±8.5	70.5±6.4	*T*=1.9	.06
Race	Asian Coloured White	1 (13%) 4 (50%) 3(37%)	A 18 (26.5%) C 16 (23.5%) W 34(50%)	X^2=2.4	.338
Gender	Female Male	2 (25%) 6 (75%)	43 (63.2%) 25 (36.7%)	X^2=4.3	.06*
Years of education		10.6 ±3.3	9.8 ±1.6	*U*=0.3	.807
DECO score		16.6 ±5.9	32.5 ±2.6	*U*=4.6	<.001*

Age was compared using Independent Samples T-Tests. Years of Education, and DECO were compared using Independent Samples Mann-Whitney U Tests. Gender and race were compared using Pearson Chi-square Tests. *Significance level set as p< .05.

Using the MMSE scores to assign caseness, the DECO was found to have a sensitivity of 37.5%, 95% CI [6.3%, 64.2%] and specificity of 96.7%, 95% CI [87.5%, 99.4%].

Discussion

The benefits of early identification of dementia, even in the absence of disease-modifying pharmacological agents, are well-recognised.[4] MCI, while regarded as a pre-dementia stage, has been shown to have a variable course and lends itself to implementation of risk management if diagnosed early.[39] There is therefore a need for the early recognition of cognitive impairment (dementia and MCI) at community and primary care level for which validated and simple tools are necessary. This study provided measures of prevalence of

cognitive impairment using different tools, assessed the performance of a number of cognitive screening instruments and quantified the degree to which race, age and education level influenced their performance. It also highlighted the challenges associated with screening.

Prevalence estimates of cognitive impairment

Using the different tools, the 'prevalence' of cognitive impairment in this population was 16.9% using the MMSE and ranged from 10.5% (DECO) to 46.3% (SMC). The tools also had widely varying sensitivities (17%-82%) and specificities (57.6%-96.7%) when compared with the MMSE.. These discrepant figures suggest that the various instruments, while measuring cognitive impairment, may have different underlying constructs and hence may not be readily comparable with each other. The detail of the performance of each test is discussed below.

Performance of Tools

The first set of screening tools was objective measures of cognitive impairment. The MMSE is the most widely used cognitive screening test[35] and may remain the best screening tool for primary care clinicians to rule in or rule out a diagnosis of dementia.[40] In our study, the MMSE identified 51 while the SIS identified twice the number (114) of participants with possible cognitive impairment. Compared with the MMSE, the SIS showed good sensitivity and specificity suggesting that it may be a useful screening tool as an alternative to the MMSE locally. This confirms findings from an international study where a good correlation was demonstrated between the MMSE and SIS in a community-based sample.[32] Subsequent studies have been divided on its efficacy with one study yielding lower sensitivities[41] and another finding it a reliable and effective tool for dementia but not MCI detection.[42] In view of the large difference in case identification between the MMSE and the SIS, the relative merits of using the MMSE or the SIS locally is best determined once the validity of the MMSE is established against the gold standard of a clinical diagnosis of cognitive impairment.

The second set of screening tools assessed subjective cognitive impairments. Subjective knowledge and awareness of memory deficits (meta-memory)[38] are frequently reported by the elderly. In our study a prevalence of 46% of SMC was found. A UK study, using a primary health-care sample, reported a 46.5% prevalence of any cognitive complaint in the elderly, with an increase in prevalence occurring with increasing age and among females.[43] Conversely, a recent study reports the prevalence of a lack of awareness of memory deficits ranging from 63% to 81% across three LAMICs and that absence of awareness is associated with depression, dementia severity, socio-economic status and education in different sites.[44] In community settings, 20% of individuals with SMC are likely to have dementia and 30% MCI.[38] Establishing the presence of SMCs may prove useful as they have been associated with characteristic neuro-imaging changes in the temporal and hippocampal

regions,[45] and may represent a degree of cognitive impairment that is not currently measurable by objective tests.[46] SMCs may therefore represent a simple and cost-effective way of identifying underlying impairment which would obviate the need for validated tools and trained administration staff. However, despite SMCs being a diagnostic criterion for MCI,[10] there is a lack of consistency in how SMCs are defined.[47] The construct underlying subjective impairment may be influenced by cultural variables and may account for the large variation in MCI prevalence across LAMIC.[13] The implication of the lack of a consistent definition of subjective memory impairment is illustrated in our findings where two subjective measures yielded markedly different results.

In our study, 46.3%of participants reported the presence of a subjective memory complaint (SMC) and of these the SMRS identified 14.3% as being possibly cognitively impaired. While the discrepancy could be attributed to the SMRS being a more specific and detailed measure of subjective cognitive impairment, this is not supported by the differences in sensitivities of the two measures as compared against the MMSE.

The third set of tools included the informant questionnaire, the DECO. Informant assessments have several advantages over patient administered screening tools. Direct information about a decline in daily functioning can be elicited from those who know the patient well.[30] While brief cognitive screening tests, short neuro-psychological batteries and informant questionnaires have comparable discriminability, informant observations are less influenced by the educational levels of subjects being screened and retained discriminability in mild dementia.[48] Informant questionnaire may therefore prove valuable for local community screening where informants may be more readily available than in residential facilities; they may also have utility in settings where low educational levels of the elderly may limit the use of the MMSE.

Of the 76 respondents on the DECO, 73.7% were unable to respond to all 19 items. Informants were unable to respond to letter writing and remembering a conversation items which may be similar to other studies which identified the items pertaining to household appliances, handling of money and writing as necessitating replacement with culturally suitable alternatives[29] to improve the potential of the DECO to be a 'useful instrument to diagnose dementia cross-culturally in SA'.[30] Using the MMSE as a gold standard, our study revealed a much lower sensitivity than that obtained in a pilot study in a small cross-cultural South African sample. The DECO in the latter study had a sensitivity of 79% and a specificity of 90%, a good correlation with the MMSE ($r=0.625$; $p<0.01$) and validity for the diagnosis of mild and moderate dementia.[30]

The unavailability of informants for 75% of the participants in the study, including none for Black participants, is much higher than that reported in the literature (viz. 19%[49] and 5%[50]) and limits proper evaluation of the validity of the DECO and the generalizability of our

findings. However, the substantial lack of informants raises the question of the utility of this tool in a residential setting. Social support in the elderly has clinical implications, identifying this group as being at risk for cognitive disorders. Studies confirm the role of social integration and the quality and quantity of social relationships in maintaining cognitive vitality,[51] reducing the risk for AD[52,53] decreasing psychiatric morbidity,[54,55] influencing physical health[55] mortality risk,[55,56] predicting quality of life,[57] and reducing the rate of memory decline[58] in the elderly. On the basis of the implied low levels of regular family contact, subsequent low response rate and low sensitivity, the utility of the DECO as a screening instrument suitable for use in this population appears to be limited.

Influence of demographic variables and depression
Race, age and years of education were shown to affect the performance of the measures used in our study.

Race: There was a significant association between race and the SIS, SMRS and specific items of the MMSE. The recommended and alternate attention/concentration items ' are not equivalent[37] and this was evidenced in the poorer performance of participants of different races on the recommended item and suggesting that the alternate item should be preferred in this heterogeneous sample . However, there were two issues to consider here namely, there were only 9 black participants in the study and there were significant differences between race groups in terms of age and years of education. Replication of these results in a larger sample will confirm the validity of these associations.

The differences between race groups for individual items on the MMSE largely disappeared with the use of the better score between the 2 attention/concentration items. This suggests that, in the local population, the use of the recommended attention/concentration item of the MMSE does not demonstrate cross-cultural equivalence,[59] and may need to be adapted according to the cultural, demographic and educational profile of the population being screened. Age, educational level, ethnicity and language of administration have been shown to influence frequency of errors and scores on the MMSE.[60] Attempts have been made in many countries to translate and adapt the MMSE for local use.[20,61] The relative difficulty of certain items has been shown to vary between ethnic groups within the United States[24] and a study comparing UK and USA dementia populations suggested that the MMSE items may not be dynamically equivalent even within Western race groups.[25] Establishing separate test norms for different racial groups may help to improve the accuracy of tools. Alternatively, direct and more meaningful and predictive variables that underlie test performance across cultural groups may serve to increase the validity of the instruments used to diagnose dementia.[62]

Age: Although age is a risk factor for dementia, dementia is not an inevitable consequence of ageing, and its effects cannot be dismissed as representing psychometric bias. In keeping

with previous studies that showed a decrease in MMSE scores as age increases,[37] scores in our sample were significantly lower in older participants (p=.023) although the mean age of those screening positive was not significantly greater than those screening negative (p=.74). There exists a complex relationship between MMSE scores, age and educational level which may have implications for the cut-off score.[37] Age effects were also evident with the SIS (p=.049) and SMRS scores where screen positives were significantly younger (p=.001); however, no age effect was evident with the SMC measurement. This could possibly be explained on the basis of younger participants retaining awareness of the details of their subjective cognitive status (measures on the SMRS) while the simpler measure of SMC was not confounded by age-effects.

Education: Education has been found to be the most important non-biological correlate of cognitive performance[63-65] and the 'cultural variable,' which includes education and urbanization, making it the largest contributor to performance variance on psychometric tests[66,67] more so than ethnicity or the traditional variables of age, sex and socio-economic status.[68] MMSE scores were confounded by the level of education (p=.02) of participants in this study. A previous local study found no correlation between education and MMSE scores,[30] which could be attributed to the adaptations (especially on the educationally biased items) made to the MMSE administered in that study. Education levels significantly influenced the performance on individual MMSE items which confirms earlier research on the differential item performance attributable to education, race, ethnicity and language, and its use in educationally disadvantaged populations has been questioned.[69] Given the significantly poorer performance of participants with lower education levels on the recommended attention/concentration item the alternate item would preferred for local MMSE administration. Performance on the SIS was not significantly associated with education (p=.578) suggesting that this subset of MMSE items are less influenced by education effects and that it could be a useful alternative to the MMSE locally.

General population studies have consistently demonstrated that a lower educational level is associated with an increased probability of scoring below the recommended MMSE cut point,[70] and literacy is suggested to be a more sensitive proxy for cognitive reserve than years of education.[71] Although the MMSE (with modifications) has been used in illiterate populations,[72] there are reports of numerous challenges[20,72] due to the complex relationship that exists between literacy and dementia risk and prevalence.[62] As there is a higher prevalence of illiteracy among the elderly in LAMIC[73] these challenges may be compounded.

Discrepancies in both the quantity and quality of education[62] between racial groups, especially among the elderly in South Africa who would have been exposed to education during the apartheid era, will impact on test performance. Among South Africans aged 60 years and older, two-thirds of Blacks and Asians and half of Coloureds had less than five years of education and rural Blacks had a literacy rate of 29%.[74] In our study, each year of

formal education was found to reduce the likelihood of screening positive on the MMSE by a factor of 0.71 thus warranting caution in its widespread local use without further evaluation and possible adaptation. The finding also highlights the important role of education and cognitive stimulation in increasing brain reserve capacity and protecting against disease manifestation. The SMCs (p=.426) and SMRS scores (p=.07) were not significantly influenced by the level of education of participants and assessments of subjective memory may offer a possible solution to the challenges posed by educational influences on test performance.

Cognitive impairment has been documented in geriatric depression[75,76] and the frequent co-existence of dementia and depression suggests that the two conditions share a complex association with each other.[77] Depression may be an early manifestation of dementia[78] or a risk factor for its development.[79,80] However, in our study, a screen positive on the MMSE was not significantly associated with depression (p=.109). SMCs have also been shown to be associated with depression[81,82] and this was evident in our study where the presences of SMCs(p<.001) as well as screen positives on the SMRS (p=.019) were found to be significantly associated with depression. The utility of subjective measures of cognitive impairment should therefore always be assessed in conjunction with mood disorders in the elderly.

Challenges of screening

The study faced two challenges in conducting screening in this population, one being the refusal of residents to participate, and the other being the low number of contactable informants on which to conduct the DECO. Nearly a third of the local residents refused to participate in the study; this is contrary to the view that the elderly in developing countries are more likely to co-operate in studies due to the attraction of 'free' health care and other incentives for participation.[20] In a recent comparison between the elderly in the US and the UK, 39.4% and 32.1% of respondents respectively found screening to be unacceptable.[15] Refusal rates in high income countries vary from 19%[83] to 50%,[84] and among those agreeing to be screened, 47.7% of those screening positive refused further assessments, perceiving themselves to have no cognitive deficits; older Blacks were more likely than Whites to refuse screening.[84] Due to the low numbers of Blacks in our sample, racial differences in acceptance of screening is yet to be determined locally. A lack of awareness of dementia and possible anxiety about being diagnosed may have contributed to the low level of acceptance in our sample. However, it is important, if screening initiatives are to be successful, that reasons for refusal are formally identified so that they can be addressed. A second challenge was the low numbers of contactable informants (N=76; 25.2%), which posed a significant constraint on both screening and diagnostic activities, as the information provided by collateral sources are invaluable for the diagnosis and management of cognitive disorders. In a local study among Xhosa-speaking Black, a 69.4% agreement was reported between clinicians' and relatives' perceptions of normal and abnormal cognition,[85]

highlighting the importance of caregivers' observations about cognitive decline when making an assessment of cognitive decline.

Limitations of study

This study had a number of limitations which affects the generalizability of the findings. Firstly, the sample represented an urban setting within a non-governmental organization in KwaZulu-Natal. Secondly, the restricted inclusion criteria may have precluded participation of the elderly with severe dementia. Thirdly, there was a high participant refusal rate. Fourthly, the majority of the sample was White. Fourthly, the validity of the various instruments is better measured against the gold standard of a clinical diagnosis of cognitive impairment. Lastly, the low number of respondents on the DECO, including the lack of Black respondents, limits the generalizability of its performance.

Recommendations

The study highlights the need for further investigation in the use of screening measures in other populations, using larger sample sizes and conducting household surveys among the elderly who are cared for by family-members. This will be especially important since collateral information may be more easily obtained from their care givers. In view of the widely discrepant performance between the attention/concentration items it is recommended that the alternate item be used when administering the MMSE locally.

Conclusion

Despite the identified limitations, the study is the first local study to estimate the prevalence of cognitive impairment in this setting and to evaluate the performance of different types of screening instruments for cognitive impairment among the diverse race groups in the country. The performance of the screening tools in this study confirms the concerns raised about the validity of instruments developed for culturally homogeneous Western populations[30] that are used in populations that are demographically and educationally heterogeneous. In addition, the estimated burden of cognitive impairment is significant and highlights the need for increased awareness in a 'super-aging society'[86] of the importance of screening and the need for an appropriate, valid screening tool for health workers in clinical settings and for cross-cultural research[21].

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CHAPTER5

CLINICAL DIAGNOSIS OF DEMENTIA

5.1 Introduction

This chapter reports on the data from the second stage of data collection viz. the clinical assessment of participants. Prevalence data for MCI (with sub-types) and dementia (without sub-types) as well as the risk profile are included. The diagnosis of dementia was based on the gold standard of a clinical diagnosis, with the prevalence rates being necessary to calculate the sensitivity and specificity of the screening instruments. The researcher was responsible for designing and defining the research, conducting the data analysis and interpretation, and writing up the paper.

5.2 Background

In the absence of diagnostic biomarkers for dementia, diagnosis is based on clinical criteria. There is very little prevalence data on dementia for the South African population, the ideal being to have prevalence data based on community studies. The study therefore provides a useful benchmark for prevalence in the setting of old-age residential facilities. Prevalence figures were necessary to determine the sensitivity and specificity of the various screening measures.

5.3 Aim

To determine the prevalence of dementia (and MCI) in the study sample, and to describe the demographic and clinical risk profile of the studied sample for cognitive impairment.

5.4 Methodology

A sub-sample of the participants who were screened for dementia were examined clinically and assigned diagnoses of dementia and MCI. A standardised clinical assessment tool was developed for the study by the researcher. The researcher was responsible for conducting the majority of the clinical assessments (assisted by two other clinicians).

5.5 Study Outcome

The data is reported in Paper 2, **"Mild Cognitive Impairment and Dementia in a heterogeneous elderly population: prevalence and risk profile"** accepted for publication in the African Journal of Psychiatry.

5.6 Additional Data

CT scans of the brain, without contrast, were performed on four participants, while the results of previously done MRI scans were available for two others who refused CT scans. All scans revealed evidence of vascular pathology in the brain. However, the sample of those who were imaged is too small for any meaningful conclusions to be arrived at.

Table 5.1 Brain Imaging Results of Participants Diagnosed with Dementia

Study Number	Age/ Gender	Ix/Date	Abnormalities
227	68F	MRI 14/2 2011	Multiple areas of hyper-intensities in white matter bilaterally; lacunar infarcts in BG bilaterally
71	70F	MRI 17/01/2005	Periventricular white matter hyper-intensity, focal foci of white matter hyper-intensity-ischaemic leuco-encephalopathy
33	92F	CT 26/05/2011	Atrophic changes, mural calcification of internal carotid arteries
186	69F	CT 26/05/2011	Old infarct in MCA distribution with cystic encephalomalacia; prominence of cerebral sulci and cerebellar folia
208	87F	CT 26/05/2011	Old infarct in mid-R parietal lobe, linear hypodensity in R external capsule; diffuse hypodensity of white matter periventricular and centrum semi-ovale?2.3cm meningioma in L posterior fossa
229	87F	CT 26/05/2011	Old infarct in R MCA distribution;localised atrophy of R temporal lobe; white matter hypodensities periventricular and centrum semi-ovale-chronic ischaemic changes from small vessel disease. Mural calcification of vertebral and internal carotid arteries; ectatic basilar artery.

5.7 Paper 2

Mild Cognitive Impairment and Dementia in a heterogeneous elderly population: prevalence and risk profile

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Abstract

Background and Objective Despite a predicted surge in the prevalence of dementia, especially in developing countries, there is a dearth of South African data on prevalence and associated risk factors. This paper presents information on the demographic, clinical and risk profile of Mild Cognitive Impairment and dementia in a sample of elderly South Africans within a residential setting. **Methods** One hundred and forty participants residing in a group of residential homes for the elderly were assessed by psychiatrists and assigned diagnoses of dementia or Mild Cognitive Impairment (MCI). Participants diagnosed with dementia were also offered haematological investigations and a CT scan of the brain. **Results** The sample consisted of 140 participants comprising 46.4% White, 29.3% Coloured, 20% Asian and 4.3% Black participants. There were 97 (69.3%) females and 106 (75.7%) participants had less than 12 years of education. Eleven (7.9%) dementia and 38 (27.1%) MCI cases were diagnosed. Increasing age was associated with cognitive impairment (MCI and dementia) (p=.020) but there was no association between gender and cognitive impairment (p=.165). MCI was significantly associated with a lower education level (p=.036) and no association was found between depression (current-p=.646; past-.719) and dementia or MCI. In the total sample, the presence of vascular risk factors ranged from 66.4% (hypertension) to 14.3% (stroke). Subjective memory complaints were significantly associated with cognitive impairment (p=.001). Except for the use of the telephone (p=.225) and the television (p=.08), impairment in all domains of instrumental activities of daily living that were assessed were significantly associated with a dementia diagnosis. **Conclusions** The study showed that cognitive impairment was associated with increasing age and low education levels. The presence of vascular risk factors places this population at risk for future cognitive decline.

Key words: dementia, mild cognitive impairment, prevalence, risk factors, instrumental activities of daily living

Background

With the elderly population in lower and middle income countries (LAMIC) predicted to increase from 60% in 2001 to 71% by 2040, dementia rates are expected to increase between 100% to 300% in these regions.[1] Dementia costs for Africa have been conservatively estimated to be in the region of US$2.9 billion.[2] To address this financial and clinical burden in lower and middle income countries, data on the local prevalence of dementia and its associated risk factors are important. In the absence of disease-modifying pharmacotherapeutic options, decreasing the prevalence of dementia may be achieved by modifying risk factors or lifestyle.[3] Therefore the early identification and management of risk factors and early diagnosis of dementia, can contribute to a reduction in the burden of disease and result in significant cost savings.[4]

While dementia is a huge public health challenge in high income countries (HIC), with high prevalence rates reported,[5,6] it appears that the prevalence may be lower in LAMIC.[7] Large prevalence studies conducted in Nigeria[8] and India[9] reported figures of 2.29% and 0.84% respectively. In two large cross-country studies, one comparing African and American Blacks[8] and the other comparing rural populations from India and America,[9] it was found that the prevalence rates of dementia and Alzheimer's Dementia (AD) were significantly lower for participants in the lower income countries. Similar findings have emerged from prevalence studies in Latin America and China.[7] The lower prevalence rates in LAMIC has also been confirmed in the Delphi consensus study suggesting that factors such as methodology, differential survival rates and/ or differences in the risk profile (low levels of

cardiovascular risk and hypolipidaemia) in LAMIC populations may be contributing to the lower rates.[1]

While the incidence and prevalence of dementia have been extensively studied in Western and European countries[5] there remains a dearth of similar studies from Africa. The few studies conducted in Africa prior to 2000 used small samples and was reported to have used 'non-standardised clinical assessments'.[10] Recent studies from Africa reported prevalence figures ranging from 2.6% to 8.1%. [11, 12, 13] Dementia studies from South Africa include a Western Cape sample of Coloured[1] people,[14] with a prevalence of 8.6%, and a Free State sample of indigenous Sotho-speaking elderly Black,[15] which reported a prevalence of 7.7%.

This paper describes the clinical and risk profile of a sample of elderly participants who were assessed for the presence of dementia and MCI. In addition, the value of functional assessments and subjective memory complaints in case-finding are also explored.

Method

The study consisted of three stages: 1) Administration of dementia screening tools; 2) Clinical diagnostic evaluation for dementia; and 3) Administration of a neuropsychological battery of tests.

The study population were residents (N=1450) of a group of homes for the elderly in Durban, KwaZulu-Natal, South Africa. The homes are administered by a non-governmental

[1] In South Africa, four racial groups are recognized viz Asian (Indian), Black, Coloured and White.

organisation (NGO) and cater for frail care, assisted and independent living people 60 years and older.

An initial conveniently selected sample (n=302) was selected to undergo screening for cognitive impairment using the Mini-Mental State Examination (MMSE). Inclusion criteria were: residents who were 60 years and older, a minimum of 8 years of formal schooling, the ability to speak, read and write in English and the ability to give written, informed consent. Exclusion criteria were: residents with severe physical, mental or sensory handicaps that precluded their engagement in the assessment procedures.

This paper describes the results of the second stage of the study, the clinical diagnostic evaluation for dementia. The target population for this stage was 51 participants who screened positive ($\leq$23) on the MMSE and a random selection of the 251 participants who screened negative. The resulting sample of 140 participants included 38 screen positives (13 either refused or were unavailable) and 102 screen negatives.

Clinical diagnostic evaluations were conducted in English by three psychiatrists, who were blinded to the results of the screening stage. A standardised clinical assessment tool was developed for the study. The assessment tool included the following sections: a historical review of the participant's cognitive status, a review of the medical, surgical, family, medication and substance use history, a review of social and functional activities, a physical (including neurological) examination and a comprehensive mental state examination. The assessment of functional abilities was based on participant self-report as the residential setting precluded access to informants. Participants were classified as being functionally

unable to perform specified activities of daily living (ADL) and instrumental activities of daily living (IADL) tasks only after medical causes for the inability were excluded. Content validity was based on the the Diagnostic and Statistical Manual, Fourth edition, Text Revised (DSM IV-TR) criteria for Dementia, Major Depression and Delirium. Face validity of the tool was established through review of the tool by a group of psychiatrists, neurologists and psychologists. Although the assessing psychiatrists underwent intensive training in order to standardise the assessments, inter-rater reliability was not formally established.

Following the clinical diagnostic assessments, a consensus panel consisting of a senior neurologist, senior clinical psychologist and psychiatrist assigned diagnoses of dementia, major depression-current and delirium according to DSM IV-TR criteria.[16] Participants who did not fulfil the criteria for dementia or MCI were categorised as 'non-cases'. A DSM-IV-TR[16] diagnosis of dementia is based on, firstly, the development of multiple cognitive deficits manifested by both memory impairment as well as one of four areas (aphasia, apraxia, agnosia, executive functioning) of cognitive disturbances; and secondly, these cognitive deficits should also cause significant impairment in social or occupational functioning.[16] Sub-typing of the dementias was not done. A diagnosis of Mild Cognitive Impairment (MCI) was based on the recommendations of the International Working Group on Mild Cognitive Impairment and requires the presence of subjective cognitive impairment (self or informant reported), objective evidence of cognitive impairment in the presence of high scores for ADL and normal or minimally-impaired IADL functions.[17] MCI diagnostic subtypes of amnestic MCI, single domain (aMCIsd), multi-domain (aMCImd) non-amnestic MCI single domain (naMCIsd) were based on the presence or absence of amnesia and the presence of single or

multiple cognitive domains of impairment.[18] Those participants who did not meet criteria for Dementia or MCI were classified as non-cases.

For ethical reasons, all participants who were assigned a clinical diagnosis of dementia were offered blood tests (full blood count [FBC], blood glucose, thyroid functioning test [TFT], syphilis serology [RPR] and Vitamin B12 and folate levels) as well as a CT scan of the brain, without contrast. The study received ethical approval from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal.

Statistical Analysis

The data was analysed according to diagnostic categories of dementia and MCI. Differences in age and education between the diagnostic groups were tested using Independent Samples Kruskall Wallis Tests. Associations between diagnostic categories and demographic variables, the presence of risk factors and retained functionality in IADL were tested using Pearsons' Chi square Test or Fisher Exact Tests (where sample sizes were small). Significance was set as $p<.05$.

Results

Demographic details

Of the 140 participants assessed, 97 (69.3%) were female and 43 (30.7%) were male. The average age of the participants was 75.2 years (± 8.9). There were 65 (46.4%) White, 41 (29.3%) Coloured, 28 (20%) Asian and 6 (4.3%) Black participants. Proficiency in English was

an inclusion criterion for the study. It was the first language for 123 (87.9%) of the participants, followed by Xhosa (7%), then Afrikaans (4.3%) and isiZulu (4.3%), and other languages (2.9%). Eleven (7.9%) participants had more than 12 years of education and 106 (75.7%) had less than 12 years of education.

Most participants (132, 94.3%) were in independent living residences with seven (5%) in assisted living. One hundred and four (72.9%) reported that they lived alone and 32 (22.9%) were either living together or married. A government pension was the sole source of income for ninety-seven (69.3%) participants. The demographic data according to the diagnostic categories are presented in Table 1. Significant associations were found between the diagnostic categories and the mean age and mean years of education of the participants.

Table 1: Demographics according to Diagnostic Categories

Item	**Dementia (n=11)** n (%)	**MCI (n=38)** n (%)	**Non-cases (n=91)** n (%)	**Statistic**	***P***
Race					
Asian	0 (0%)	6 (15.8%)	22 (24.2%)	X^2=15.0	.078
Black	1 (9.1%)	2 (5.3%)	3 (3.3%)		
Coloured	1(9.1%)	15(39.5%)	25 (27.5%)		
White	9 (81.8%)	15 (39.5%)	41 (45.1%)		
Gender					
Female	9 (81.8%)	30 (78.9%)	58(63.7%)	X^2=3.7	.165
Male	2 (18.2%)	8 (21.1%)	33 (36.3%)		
Age	77.2 ± 7.9	75.8 ±8.1	72.1 ±6.8	*K*=7.9	.020*
Years of education	10.3 ±2.6	9.3 ±1.6	10.3 ±2.1	*K*=6.6	.036*

Age and Years of Education were compared using Independent Samples Kruskal-Wallis or Fisher Exact Tests. Gender and Race was compared using Pearson Chi-square Tests. *Significance level set as p< .05.

Clinical diagnostic categories

Eleven (7.9%) cases of dementia and 38 (27.1%) cases of mild cognitive impairment (MCI) were diagnosed, with 91 (61%) participants not meeting criteria for dementia or MCI (non-cases).

Six of the 11 participants who were diagnosed with dementia agreed to have blood tests performed, and no abnormalities were detected apart from elevated blood glucose in two participants who were known sufferers of diabetes mellitus. Of the 11 participants, four new CT scans, one previously done CT and one previously done MRI scan were reviewed with all scans revealing evidence of vascular pathology in the brain, with evidence of old infarcts in three of the CT scans.

Of the 38 cases of MCI, 18(47.4%) represented amnestic MCI, single domain (aMCIsd), 12 (31.6 %) were amnestic MCI, multi-domain (aMCImd) and 8 (21.0 %) were non-amnestic MCI single domain (naMCIsd). No cases of non-amnestic MCI multiple domain (naMCImd) were identified. No cases of delirium were identified and thirteen participants (9.3%) were diagnosed with major depression.

The 91 non-cases comprised a mixture of participants with varying degrees of cognitive and functional impairment. Impairment in executive functioning was present in 28 (30.8 %) and memory impairment in 36 (39.6%) of these participants. Twenty of the 91(22.0%) would have met the criteria for MCI but were significantly functionally impaired in at least one instrumental activity of daily living domain and were therefore excluded; 17 of the 91(18.7%) who were functionally impaired failed to meet the cognitive impairment criteria for dementia.

Risk factor profile

To establish a risk profile, the prevalence of clinical factors was determined for each diagnostic category and compared to 'non-cases' (Table 2).

Table 2: Presence of Risk Factors within Diagnostic Categories

	Dementia (n=11)	MCI (n=38)	Non-cases (N=91)	Total (n=140)	X^2	P Value
Vascular Risk Factors						
Stroke	4 (36.4 %)	6 (15.8 %)	10 (11 %)	20 (14.3 %)	$X^2=4.8$	.065
Blackouts	3 (27.3 %)	10 (26.3 %)	8 (8.8 %)	21 (15 %)	$X^2=8.0$	.012*
High Cholesterol	3 (27.3 %)	11 (28.9 %)	30 (33 %)	44 (31.4 %)	$X^2=0.3$	.879
High blood pressure	4 (36.4 %)	22 (57.9 %)	67 (73.6 %)	93 (66.4 %)	$X^2=7.8$	.024*
Heart attack	0 (0 %)	5 (13.2 %)	21 (23.1 %)	26 (18.6 %)	$X^2=4.1$	.117
IHD/Angina	3 (27.3 %)	12 (31.6 %)	22 (24.2 %)	37 (26.4 %)	$X^2=0.9$	.649
Modified Hachinski score category >=5	3 (27.3 %)	3 (7.9 %)	7 (7.7 %)	13 (9.3 %)	$X^2=4.5$	.120
Lifestyle Risk Factors						
Cigarettes Current or Past	8 (72.7 %)	24 (63.2 %)	75 (82.4 %)	107 (76.4 %)	$X^2=1.7$	.795
Alcohol Current or Past	7 (63.6 %)	18 (47.4 %)	35 (38.5 %)	60 (42.9 %)	$X^2=0.5$	.833
Engages in any exercise	6(54.5%)	6 (15.8%)	22 (24.2%)	34(24.3%)	$X^2=7.0$	.031*
Psychological Risk Factors						
MDD Current	1 (9.1 %)	2 (5.3 %)	10 (11 %)	13 (9.3 %)	$X^2=1.0$	.646
MDD Past	2 (18.2 %)	12 (31.6 %)	24 (26.4 %)	38 (27.1 %)	$X^2=.8$	.719
[#]Presence of at least one Subjective Memory Complaint (SMCC)	10 (90.9 %)	38 (100 %)	32 (35.2 %)	80 (57.1 %)	$X^2=51.6$	.001*
Other Risk Factors						
Family Dementia	0 (0 %)	4 (10.5 %)	7 (7.7 %)	11 (7.9 %)	$X^2=1.3$	.687
Head injury	1 (9.1 %)	9 (23.7 %)	16 (17.6 %)	26 (18.6 %)	$X^2=1.2$	.535
Diabetes Mellitus	4 (36.4 %)	8 (21.1 %)	25 (27.5 %)	37 (26.4 %)	$X^2=1.2$	.530

All risk factors were compared using Independent Samples Pearson Chi-square Tests and Fisher Exact Tests.
*Significance level set as $p < .05$. [#]SMCC was defined for a specified minimum duration (previous one year), frequency (at least once a week) and sub-type (memory for names, places, events).

A number of significant associations between risk factors and diagnostic categories were found. Firstly, there were significant associations between the diagnostic groups and self-reported "blackouts" (transient periods of loss of consciousness for which a medical diagnosis had not been established at the time of assessment). Only 8.8% of non-cases reported a history of blackouts compared to 27.3% of participants with dementia and 26.3% of participants with MCI (p=.012).

Secondly, a significant negative association was found between reported high blood pressure and cognitive impairment (dementia and MCI). Seventy three point six percent of non-cases reported a history of high blood pressure compared to 36.4% of participants with dementia and 57.9% of participants with MCI (p=.024).

Thirdly, a significant association with exercise was found with participants with dementia reporting more engagement in physical exercise (54.5%) compared to participants with MCI (15.8%) and non-cases (24.2%; p=.012).

Lastly, there was a significant association between the presence of a subjective memory complaint assessed clinically (SMCC) and the presence of dementia. Ninety point nine percent of participants with dementia compared to 35.2% of non-cases (p<.001) reported the presence of an SMCC. (SMCC is a diagnostic criterion for MCI). The presence of a SMCC was not significantly associated with the presence of major depression(X^2=0.86, p=.355).

Physical and functional impairment profile

In addition to clinical risk factors, the presence of physical impairment (Table 3) and the capacity to perform instrumental activities of daily living (Table 4) and diagnostic categories were also compared.

Two significant associations were found between physical impairments and diagnostic groupings (Table 3).

Table 3: Presence of Physical Impairments within Diagnostic Categories

	Dementia (n=11)	**MCI (n=38)**	**Non-cases (N=91)**	**Total (n=140)**	X^2	**P Value**
Uses walking aid	4 (36.4 %)	11 (28.9 %)	23 (25.3 %)	38 (27.1 %)	$X^2=0.7$	.686
Visual problems	6 (54.5 %)	35 (92.1 %)	72 (79.1 %)	113 (80.7 %)	$X^2=7.8$	.019*
Use of visual aids	6 (54.5 %)	33 (86.8 %)	77 (84.6 %)	116 (82.9 %)	$X^2=5.7$	.051
Hearing problems	5 (45.5 %)	18 (47.4 %)	23 (25.3 %)	46 (32.9 %)	$X^2=6.8$	.036*
Use of hearing aids	2 (18.2 %)	1 (2.6 %)	5 (5.5 %)	8 (5.7 %)	$X^2=3.4$	.178

All risk factors were compared using Independent Samples Pearson Chi-square Tests and Fisher Exact Tests. *Significance level set as $p < .05$. #SMCC was defined for a specified minimum duration (previous one year), frequency (at least once a week) and sub-type (memory for names, places, events).

In terms of visual impairments, more participants with MCI reported visual impairments (92.1%) as compared to participants with dementia (54.5 p=.019). More participants with dementia (45.5%) and MCI (47.4%) also reported hearing impairments as compared to non-cases. (25.3%; p=.036).

The ability to perform ADLs and IADLs has diagnostic significance for dementia. In evaluating the functional profile of participants, significant differences were found between dementia, MCI and non-cases for the following activities: Use of public transport, meal preparation, taking medication, shopping, and using the microwave and washing machine (Table 4). All participants reported being able to use a radio.

Table 4: Retained Functionality in IADL

	Dementia (n=11)	MCI (n=38)	Non-cases (N=91)	Total (n=140)	X^2	P Value
Telephone use	10(90.9%)	38 (100%)	88 (96.7%)	136 (97.1%)	X^2=2.7	.225
Public transport (*NA=15)	4(40%)	33 (100%)	78 (95.1%)	115 (89.3%)	X^2=22.3	<.001*
Meal preparation (NA=7)	8 (80%)	34 (97.1%)	87 (98.9%)	129 (92.1%)	X^2=7.0	.024*
Operating TV (NA=3)	10(90.9%)	35 (100%)	91 (100%)	136 (97.1%)	X^2=5.7	.080
Operating microwave (NA=5)	7(70%)	36 (94.7%)	85 (97.7%)	128 (91.4%)	X^2=9.0	.010*
Operating washing machine) (NA=8)	7(70%)	34 (94.4%)	83 (96.5%)	124 (88.6%)	X^2=7.6	.016*
Taking medication (NA=7)	5 (55.6%)	38 (100%)	80 (93%)	123 (87.9%)	X^2=13.6	<.001*
Shopping (NA=3)	7 (63.6%)	37 (100%)	84 (94.4%)	128 (91.4%)	X^2=12.1	.002*

IADL were compared using Independent samples Pearson Chi-square Tests and Fisher Exact Tests.
*Significance level set as p < .05.
*NA=Data either not available or not-applicable

Discussion

Prevalence of Dementia and MCI

Dementia prevalence: The study identified a dementia prevalence of 7.9%, similar to prevalence rates reported in homogeneous South African populations (8.6%,[14] and 7.7%[15]) but greater than the mean age-adjusted prevalence estimate for dementia in LAMIC of 5.3%.[3]. The range of prevalence figures in Africa could be attributed to differences in population age structures, genetics and lifestyle,[3] but could also be due to methodological factors in the assessment and assignment of a diagnosis. Methodological factors may

include variations in the use of accurate, standardised diagnostic measures and variations in clinical opinion of what constitutes 'significant' impairment in social and occupational functioning. 'Impairment' also varies according to cultural expectations of the elderly with regard to their functional activities and hence influences the definition of 'functional impairment' in different socio-cultural settings.[3]

While our prevalence figure lies within the range reported for LAMIC countries, our sample is drawn from a residential, not a community or a nursing home setting. International prevalence figures for dementia in elderly residential homes vary from 36.7%-58%.[19,20,21,22] Prevalence figures vary according to the admission criteria and the heterogeneity in the types of residential facilities and data from LAMIC are scarce. In the United Kingdom, where almost 5% of people aged 65 years or older live in institutions, two thirds of the elderly in residential homes [23] and 62% of the elderly residing in private and council residential and nursing homes were found to have dementia. [24] The prevalence of dementia in Mexican nursing homes is 16.1%.[25]

An important factor emerging from our study was that none of these residents had been previously diagnosed with dementia or MCI. The under-recognition of dementia is not unique to our setting as rates of under-recognition range from 31.8%[21] for dementia in Scotland to 70% for mild dementia in Hong Kong.[20] Our findings therefore identify a need for increasing the awareness of dementia among the personnel working in residential settings for the elderly.

A limitation in our findings has been the exclusion of those unable or too impaired to engage consensually in the assessment procedures and this may have contributed to the relatively low prevalence of dementia of 7.9% in our study. Further large scale community studies are needed to confirm the prevalence of dementia in South Africa.

MCI prevalence: MCI was diagnosed in 27% of our sample, which is similar to the prevalence rates of 3% to 42%[26] reported in the literature. The wide range has been attributed to the lack of standardization of the definition and diagnostic criteria of MCI.[26] Diagnostic consistency across studies will assist in establishing the true burden posed by MCI in the elderly. This is important as the reported annual conversion rate of MCI to Alzheimer's dementia is 10-15%[27] in high risk clinical populations and 4.2% in the general population.[28]

Despite existing diagnostic criteria for MCI,[27,29] the lack of appropriate and sensitive neuropsychological and functional measures[30] poses challenges to its consistent application and interpretation. Challenges in assigning this diagnosis include the fact that subjective memory deficits lack clear definition,[31] and the interpretation of what constitutes 'minimal' impairment in IADL in the context of MCI. This is important as it has been shown that impairment in IADL impacts significantly on the prognostic value of MCI with respect to progression to dementia.[32,33,34,35] Delaying the progression of MCI to dementia by one year will result in significant cost savings,[36] therefore objective measurement criteria for MCI and IADL are essential.

The most prevalent subtypes of MCI in our study was aMCIsd (47.4%) followed by aMCImd (31.6%). The risk of converting to dementia is increased when cognitive domains in addition

to memory (multi-domain) are impaired.[37] Those with single domain MCI are reported to revert to normal cognitive functioning with greater frequency than those with multi-domain impairment.[28] This places almost a third of those diagnosed with MCI in our sample at high risk for progressing to dementia and targets them for close monitoring. However, although MCI subtypes have diagnostic validity and clinical utility,[38,28] MCI is a heterogeneous condition[39] both aetiologically and prognostically and the clinical significance of these subtypes are best evaluated in a prospective study.

Challenges in the evaluation of cognition: The evaluation of cognition in the elderly, especially in in LAMICs, is compounded by numerous practical and technical issues.[40,41] A major challenge is the validity and sensitivity of the diagnostic criteria applied. Diagnostic criteria should help to clearly distinguish normal from pathological cognitive impairment. While ninety one participants in our study did not meet the criteria for dementia or MCI, they were found to have varying levels of cognitive and functional deficits. Cognitive impairment in the elderly exists on a continuum ranging from normal, subjective cognitive impairment (pre-MCI),[42] MCI to dementia. In addition, impairment in multiple cognitive domains are present many years before a diagnosis of dementia (AD) is made.[43] Even though the DSM criteria are widely used, the ICD-10 sets a higher threshold for dementia compared to DSM-III-R[44] and a ten-fold difference in the rate of dementia diagnosis using six separate classification systems has been demonstrated.[45] The literature has been criticised for failing to provide clear guidance on standards against which functional and cognitive impairments should be measured.[32] Current diagnostic criteria define a 'narrow category of unambiguous dementia characterised by marked impairment'.[46] The limitations of the

current DSM IV-TR diagnostic system has the potential to under-estimate the prevalence of dementia with significant socio-clinical implications.[47]

Similar diagnostic challenges are encountered with MCI diagnosis. Different definitions of MCI have been shown to significantly influence the annual conversion rates from MCI to dementia.[17] MCI diagnosis requires the demonstration of the 'preservation of independence in functional abilities.' While abilities may appear to be overtly preserved, subtle impairments related to time and precision may be present that are not readily measurable[29] and could still impact on the autonomy of individuals. In addition, consensus is required on the level of impairment in IADL that distinguishes MCI from dementia and normal ageing.[33] These issues have significant clinical and ethical implications for clinicians, patients and their families.

Risk factors and dementia

The prevalence of several clinical risk factors for cognitive impairment in our sample, compounded by the low level of protective factors, identifies this population as a vulnerable group in need of preventative interventions.

Demographic risk factors: In keeping with the literature, there was a progressive and statistically significant (p =.020) increase in the mean age of participants from the MCI to Dementia categories in our study. The results also suggest an increasing progression of cognitive impairment with age. Increasing age has been identified as the 'most consistent risk factor for dementia worldwide'[3,48] and for dementia in LAMIC countries.[9,49,50,51]

In terms of gender, in our study, there were more than twice as many female participants (97 females, 43 males), and females were more prevalent in all diagnostic categories but the differences were non- significant. Our findings are similar to the Indo-US study,[52] where the prevalence of dementia was not associated with gender. Females have been shown to be at increased risk for dementia in developed regions as well as Asian countries, but this association was not clear for African and Latin American countries.[3] Hormonal factors have been implicated in the differential risk of women,[53] however other protective factors may exist that are unique to women in developing countries; identification of such factors could be useful in reducing the risk to women in developed countries.

We were not able to show an association between race and the prevalence of cognitive impairment due to the low representation of Asians, Blacks and Coloureds in our sample (Table 1). While trends are changing, it is not common local practice for the elderly to be placed in old-age homes, especially among Asian and Black families, which may account for the low representation in our sample. Nigerian Africans have been found to have a lower prevalence of AD compared to their American-African counterparts.[8] While different environmental risk factors may be implicated,[54] the clinical and molecular aetiologies of dementia have been found to differ among races[55] contributing to racial differences in risk for the various types of dementia. It is therefore necessary for local studies to be conducted to establish the risk profile of the different race groups in South Africa.

Lastly, education is said to be protective against dementia through its contribution to cognitive reserve[56] and our results indicated a significant difference in years of education between the MCI group compared to the dementia group. However, years of education may

not be a sensitive measure of education in our sample where there are discrepancies in the quality of education received by different race groups. Two strategies are suggested to deal with education in this context, namely the use of literacy as a marker and the use of informants for screening of dementia. Literacy has been proposed as a more accurate measure of education.[57] African Americans performed significantly lower than White Non-Hispanics on several cognitive tests despite controlling for demographics and years of education. These differences in performance disappeared after controlling for literacy levels,[58] highlighting the importance of accommodating for education effects when interpreting test results. It may be useful for local researchers to measure literacy as part of the assessment of dementia in future. The second strategy of using informant surveys may offer an opportunity to overcome the challenges posed in assessments due to differences in educational level. The use of informants in cognitive evaluations has been shown in different cultures to be as effective as cognitive assessments and has the advantage of not being biased by educational level. [59,60] Unfortunately in our studywe did not have access to informants.

Clinical risk factors: Described as a 'tidal wave on the horizon,[61] dementia in LAMICs has been shown to be the most important independent contributor to disability in the elderly.[62] In the absence of specific treatment, attention has to be focussed on identifying and modifying risk factors. Optimum and aggressive control of hypertension, diabetes, weight, smoking, and vascular risk factors and the need for exercise have been identified as potential preventative strategies.[63,64]

Vascular dementia accounts for about 30% of the total dementia prevalence.[3] Vascular risk factors were most prevalent in our study. The history of a stroke among the dementia cases (36.4%) was high even though this did not reach statistical significance. There was also radiological evidence of vascular pathology in all six of the dementia participants for whom scans were available, three of whom had evidence of infarcts. Temporality was not established in our study, but it is known that 10% of patients develop dementia after a first stroke and a third after recurrent stroke.[65] The acute stroke patient of today, may be the dementia referral of tomorrow. There is therefore a need for stroke neurologists and cognitive physicians to work more closely,[63] to ensure optimum management of this high risk population and early detection of cognitive impairment.

Hypertension was present in 66.4% of the participants: 36.4% in dementia, 57.9% in MCI and 73.6% in the non-case group, p=.024. This represents a high burden and raises concern as hypertension has been associated with an increased risk of cognitive decline and dementia[66,67,3] as well as a higher rate of progression from MCI to dementia.[58] While there is no compelling evidence that dementia can be prevented by modifying vascular risk factors,[68] a more complete understanding of the pathophysiology, and aetiology of dementia, especially in different population groups,[3,68,69] will serve to better inform clinicians. Optimum management of vascular disease is nonetheless necessary for healthy ageing.[68] Diabetes, also shown to increase the risk of dementia in the elderly,[70-60] was not significantly more prevalent in the dementia group compared to the MCI and 'non-case' groups. 36.5%, 212.1%, 27.5%; p=.530). However, low dementia case numbers (<4) also prevent us identifying diabetes as being associated with dementia in our sample. A fifth (21.1%) of those diagnosed with MCI in our study had diabetes mellitus, identifying them at

higher risk, as diabetes has been shown to substantially increase the progression from MCI to dementia.[71]

Physical and mental exercise, social engagement, and nutrition and stress management are important factors in maintaining cognitive vitality and protecting against the development of dementia.[72] A comprehensive review of the evidence has also confirmed the negative impact of social isolation and the protective effect of exercise on cognitive health.[73] Of concern in our study was the fact that the participants were found to be physically inactive with less than a quarter of participants engaging in any physical exercise. Given the significant medical implications of a sedentary life, this is an important and simple intervention that can reduce risk for both physical and cognitive decline.

Subjective memory complaints: More than 50% of our sample reported the presence of a subjective memory complaint. . A significant association was found between the presence of a SMC and the presence of dementia (x^2=51.6, p=.001). In our study, a SMC was present in 90.9% of those diagnosed with dementia. The prevalence of SMC in the community varies from 25-50%[74] and is present in 42.8% of dementia sufferers and 38.2% with MCI.[75] As with any subjective measure, assessing for the presence of SMCs poses challenges. The lack of standardisation of the definition of SMCs across studies complicates the interpretation of results as[31] different criteria may refer to different underlying cognitive constructs. However, the presence of SMC has been associated with cerebral white matter lesions in the absence of objective cognitive impairment,[76] implying that they may have diagnostic validity. The diagnosis of SMC should therefore be standardised based on criteria that include age and nature of onset, course, duration and frequency.[31] This may result in better

correlation between subjective and objective measures of disease and improve the validity and predictive value of SMCs for dementia.

The mean number of memory complaints per participant in our study increased significantly with increasing cognitive impairment from MCI to Dementia (p=.001). The presence of subjective memory complaints (SMC), also referred to as subjective memory impairment (SMI), and subjective cognitive impairment (SCI), is regarded as a pre-MCI stage which has a mean duration of 15 years.[42] Elderly individuals with SMC may be at a fourfold increase of dementia or a two fold increase of depression. [77] However, an association between SMC and depression, past or current, was not found in our study.

The utility index of SMC has recently been assessed as 'good' for ruling out a diagnosis of dementia but 'poor' for ruling in a diagnosis of dementia as there is only a 20%-30% chance of dementia or MCI being present in those with SMC.[75] However, there is evidence for its use in brief screening programmes.[75] In the local context of a severe shortage of mental health professionals[78], further evaluation of the clinical correlates and utility of SMCs may clarify its potential as a simple, cost-effective screening measure towards meeting the challenges associated with the predicted upsurge in the prevalence of dementia.

Functional assessments: A diagnosis of dementia requires the confirmation of cognitive decline of sufficient severity to cause functional impairment. The concise definition of the functional status of patients is necessary for optimum care planning[79] as greater impairment has been associated with earlier institutionalization, decreased quality of life, death, increased caregiver burden, and increased health and care costs.[80]

In our study, the preservation of activities of daily living (IADL) functions in the dementia category ranged from 40% for the independent use of public transport to 90.9% for the use of a telephone. With the exception of the ability to use a telephone and the television, preservation of functionality in the remaining IADL domains assessed significantly distinguished those with dementia from those without (Table 3). In our sample, the use of the telephone was an ability that was best preserved amongst all diagnostic categories, suggesting that this might be an ability that is relatively resistant to deterioration. Inter-task difference analyses have revealed that finances, meal preparation, housekeeping and shopping are the earliest functions to deteriorate, while telephone use appeared to be more resistant.[80] Loss of skills related to independent medication management, shopping, housekeeping and use of public transport have also been shown to significantly impact on time to incident dementia.[35]

In LAMIC, where low education levels are more prevalent than in HIC, screening tools with minimal education bias are necessary. Cognitive decline contributes to functional impairment and is expressed among instrumental activities before basic activities of daily living.[80] IADL require a high degree of executive skills and executive dysfunction has been correlated with IADL disability.[79] Functional scales therefore have the potential to be used as screening tools, and have less education bias than cognitive tests.[81] Several IADL scales are in use and even though their psychometric properties need to be further established,[82] they have been shown to discriminate between the demented and non-demented as well as detect mild dementia with minimum effects of age, gender and education.[81]

IADL scales have been shown to be 'reliable, sensitive and responsive' and useful in dementia screening in a heterogeneous Indian population,[83] with acceptable efficiency for dementia screening.[84] They have been shown to compare favourably against the MMSE when administered by General Practitioners and have the advantage of being simple and non-threatening to administer.[85]

It has been shown that subjects who performed poorly on IADL were more likely to develop dementia ten years later.[33] IADL assessments are useful as diagnostic aids in memory clinics, and are able to predict the onset of dementia at one and two year follow-up.[86] IADL assessments also have the potential to distinguish between clinical stages along the continuum from subjective to objective cognitive impairment. Specific areas of IADL impairment show discriminative and predictive power for Subjective Cognitive Impairment (SCI) and MCI.[87] The inclusion of IADL impairment in the diagnosis of MCI has been shown to significantly improve dementia prediction in those who have MCI.[35] These findings support the need for the further evaluation of IADL scales as screening tools for dementia in the local setting especially as they require low skill in administration. The limitations of IADL scales can be addressed by enhancing self-report through collateral corroboration,[86] standardizing performance-based assessments that include measures of accuracy and speed,[35] and improving the psychometric properties by establishing validity.

LIMITATIONS OF STUDY

While this study provides useful information on the demographic and risk profile of a heterogeneous South African elderly population, the nature of the sample and its small size,

the low numbers of Black participants, and the low number of dementia cases limit the generalizability of our findings. Inter-rater reliability should have been formally quantified. The study is however useful in defining the risk profile of this elderly population and provides a platform for the introduction of risk management interventions.

CONCLUSION

The quantification of the prevalence of cognitive impairment in a non-clinical sample highlights its under-recognition locally. The prevalent risk factors call for increasing the awareness of dementia in the general population combined with active medical outreach to non-clinical populations. The reported lower prevalence of dementia in LAMIC highlights the need for risk factors as well as 'protective' social and contextual determinants of health and dementia, the 'new epidemiology',[88] to be studied. Dementia in LAMICs deserve further epidemiological research to address the growing burden,[89] better define risks and devise novel approaches to prevention, early detection and adequate treatment.[3]

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CHAPTER6

SENSITIVITY AND SPECIFICITY OF SCREENING MEASURES

6.1 Introduction

This chapter reports on the findings with respect to the sensitivity and specificity of the seven screening measures used in all three stages of data collection: the first stage screening 302 residents using five measures, the second stage using the SMCC the third stage, the CDT. The researcher was responsible for designing and defining the research, collecting some of the data, the data analysis and interpretation, and writing up the paper.

6.2 Background

For screening to be valid and cost-effective, appropriate instruments with good discriminant ability for normal versus abnormal cognitive functioning are essential. While the performance of many screening measures has been extensively researched in Europe and America, and to a lesser extent in developing countries, such data on South African populations are lacking. Establishing the sensitivity and specificity of measures for local use is necessary to guide appropriate referral of at-risk individuals to higher levels of medical care. False positives will result in undue alarm in those affected and place undue strain on our limited resources, especially specialist level care. False negatives will deprive sufferers and their families of timely interventions and support to optimally address the challenges of living with dementia.

6.3 Aim

To determine the degree of accuracy of the measures under study to identify elderly individuals with cognitive impairment, to measure the sensitivity and specificity of the measures at the recommended cut-off scores, and to determine the cut-off score that will generate the optimum balance between the sensitivity and specificity for each measure.

6.4 Methodology

Receiver operating characteristics (ROC) analysis was done to generate the Area under the curve (AUC) for each of the seven screening measures evaluated (MMSE, SIS, SMC, SMCC, SMRS, DECO, CDT). Sensitivity and specificity at the recommended cut-off scores are listed, cut-off scores that would generate sensitivity and specificity levels of 80% respectively are indicated, and cut-off scores that will generate optimum sensitivity/specificity ratios are suggested.

6.5 Study Outcome

The data is reported in Paper 3, "**The Sensitivity and Specificity of Selected Screening Instruments for Dementia"** published online in the Journal of Dementia and Geriatric Cognitive Disorders in July 2013.

6.6 Additional Data-Mild Cognitive Impairment

Data is also included in Table 6.1 below for the properties of the measures screened for clinically significant cognitive impairment (dementia and MCI) and for MCI, as well as the sensitivity and specificity for MCI versus controls in Table 6.2.

Table 6: Sensitivity and Specificity for controls vs cognitively impaired (dementia and MCI)

Measure	Sensitivity % (95% CI)	Specificity% (95% CI)	PPV% (95% CI)	NPV% (95% CI)	ROC Area under curve (95% CI)
MMSE ≤23	38.7 (25.5-53.7)	79.1 (69.0-86.6)	50.0 (33.6-66.3)	70.5 (60.6-78.9)	.656 (.561-.750)
SMC	67.3 (52.3-79.6)	63.7 (52.9-73.4)	50.0 (37.6-62.4)	78.4 (66.9-86.7)	n/a
SMRS ≥20	27.2 (13.9-45.7)	90.9 (74.5-97.6)	75.0 (42.8-93.3)	55.5 (41.5-68.8)	.774 (.662-.887)
DECO	25.0 (4.4-64.4)	50.0 (35.4-64.5)	7.6 (13.4-26.5)	80.0 (60.8-91.5)	.630 (.388-.872)
SIS ≤4	55.1 (40.3 – 69.1)	49.5 (38.8-60.5)	36.9 (26.2-49.1)	67.1 (54.4-77.8)	.504 (.404-.603)
CDT ≤6	23.1 (11.7-39.7)	91.0 (81.8-96.0)	56.2 (30.5-79.2)	70.2 (60.3-78.8)	.559 (.445-.673)

PPV= Positive predictive value, NPV= Negative predictive value, MMSE= Mini-Mental State Examination, SIS= Six Item Screener, SMC= Subjective Memory Complaints, SMCC= Subjective Memory Complaints Clinical, SMRS=Subjective Memory Rating Scale, DECO= Deterioration Cognitive Observee, CDT= Clock Drawing Test, ROC=Receiver operating characteristics

Table 7: Sensitivity and Specificity for MCI vs controls

Measures	Sensitivity % (95% CI)	Specificity% (95% CI)	PPV% (95% CI)	NPV% (95% CI)	ROC Area under curve (95% CI)
MMSE ≤23	31.6 (17.5-48.7)	79.1 (69.3-86.9)	29.5 (21.8-38.1)	38.7 (21.9-57.8)	.618 (.528-.702)
SMC	68.4 (51.4-82.5)	63.7 (53.0-73.6)	44.1 (31.2-57.6)	82.9 (72.0-90.8)	n/a
SMRS ≥20	30.8 (14.4-51.8)	90.9 (75.6-98.0)	72.7 (39.1-93.7)	62.5 (47.4-76.0)	.729 (.643-.803)
DECO	16.7 (2.8-63.9)	92.3 (74.8-98.8)	33.3 (5.5-88.5)	82.8 (64.2-94.1)	.833 (.429-.991)
SIS ≥4	57.9 (40.8-73.7)	49.5 (38.8-60.1)	32.4 (21.5-44.8)	73.8 (60.9-84.2)	.511 (.421-.600)
CDT ≤6	16.7 (5.7-34.7)	91.0 (82.4-96.3)	41.67 (5.3-72.3)	74.0 (64.0-82.4)	.494 (.369-.619)

PPV= Positive predictive value, NPV= Negative predictive value, MMSE= Mini-Mental State Examination, SIS= Six Item Screener, SMC= Subjective Memory Complaints, SMRS=Subjective Memory Rating Scale, DECO= Deterioration Cognitive Observee, CDT= Clock Drawing Test, ROC=Receiver operating characteristics

SMCC was not evaluated as it was used as a diagnostic criterion for MCI

6.7 Results and Discussion

Cognitively impaired vs Controls: Using a AUC value of >0.7 as a measure of a 'moderately accurate' measure, the SMRS (0.774) is potentially useful to distinguish controls from individuals with cognitive impairment (dementia and MCI diagnoses). The SMRS has a high specificity and positive predictive value but a very low sensitivity. The MMSE, although showing high specificity, was found to have low sensitivity (38.7%). However, this must be interpreted with caution as these figures are based on a cut-off score of ≤23;

MCI vs Controls: The SMRS (.729) and DECO (0.833) are moderately accurate in distinguishing controls from MCI participants, with both measures having sensitivities in excess of 90% but low sensitivities. The SMRS with its high specificity and high positive predictive suggests it has utility as 'rule-in' test for MCI and should be evaluated further. The MMSE is very specific but has low sensitivity at the cut-off score of <=23.

Relatively little literature exists on screening for MCI compared to dementia, with a systematic review on screening for MCI identified several measures with high sensitivities. However, the specificities of the measures against psychiatric and neurological disorders and their predictive validity were lacking (Lonie, Tierney et al. 2009). Research efforts have included the potential value of the MMSE for MCI screening, given its widespread use in dementia. Although the validity of the MMSE was confirmed in a study where the scores of MCI subjects were significantly lower than controls ($p<.001$), the MMSE was noted to be less accurate in the presence of depression (Benson, Slavin et al. 2005). Arising from a Nigerian study, which reported a 5.2% prevalence of MCI, a cut-off score of $\geq$17 on the MMSE has been suggested for MCI with 'healthy' adults scoring from 12-30(Onwuekwe 2012).

The effects of education on MMSE performance are well-documented (Tombaugh and Mc Intyre 1992). In a study of a largely Caucasian, highly educated sample (mean education level of 17.1 years), the cognitively impaired group (dementia and MCI) was compared to controls. A MMSE cut-off score of 27 (sensitivity of 69% and specificity of 91%) or 28 (sensitivity and specificity of 78%) was proposed (O'Bryant, Humphreys et al. 2008). These studies highlight the need for further evaluation of the MMSE for MCI screening, with

special regard to appropriate cut-off scores, which are appropriate to the education levels of the studied populations.

The clock-drawing test (CDT) has also been studied for its potential as a screening measure for MCI. It has been found to better differentiate healthy controls from MCI while the MMSE was better at differentiating MCI from dementia (Umidi, Trimarchi et al. 2009). Using different scoring methods, the CDT significantly differentiated MCI and non-MCI subjects. One study explored the value of combining screening measures, with the clock drawing test (CDT) being the focus of two such studies. Combining the MMSE and the CDT (mini-clock) was found to be reasonably accurate in distinguishing MCI from controls. The mini-clock had a ROC value of 0.855 compared to values of 0.821 forthe MMSE and 0.779 for the CDT respectively (Cacho, Benito-Leon et al. 2010).

Informant questionnaires may also have utility in MCI screening. Using a two-dimensional graded response model, the IQCODE has been shown to be useful for screening for MCI in a memory clinic setting(Sikkes, van den Berg et al. 2010).Based on their finding of a poor correlation between SMC and objective memory performance, the continued inclusion of SMC as a diagnostic criterion for MCI has been questioned as it may reduce the diagnostic accuracy of MCI(Lenehan, Klekociuk et al. 2012).While the diagnostic criteria for MCI may well evolve over time, the value of SMCs in the early evolution of cognitive impairment in the elderly is being increasingly recognised (Alzheimer's Association 2013).

6.8 Conclusion

As attention is increasingly focused on identifying earlier and pre-clinical stages of dementia, identifying valid screening measures will enable clinicians to recognise MCI. This will facilitate the institution of measures that could prevent the progression of MCI to dementia.

6.9 Paper 3

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and Geriatric
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Original Research Article

The Sensitivity and Specificity of Subjective Memory Complaints and the Subjective Memory Rating Scale, Deterioration Cognitive Observee, Mini-Mental State Examination, Six-Item Screener and Clock Drawing Test in Dementia Screening

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Key Words
Screening · Mini-Mental State Examination · Subjective memory complaints · Sensitivity · Specificity

Abstract
Background: The effectiveness of dementia screening depends on the availability of suitable screening tools with good sensitivity and specificity to confidently distinguish normal age-related cognitive decline from dementia. The aim of this study was to evaluate the discriminant validity of 7 screening measures for dementia. ***Methods:*** A sample of 140 participants aged ≥60 years living in a residential facility for the aged were assessed clinically and assigned caseness for dementia using the *Diagnostic and Statistical Manual of Mental Disorders,* 4th edition, text revised diagnostic criteria. Sensitivity and specificity of a selection of the following screening measures were tested using receiver operating characteristic (ROC) analysis for individual and combined tests: the Mini-Mental State Examination (MMSE), Six-Item Screener (SIS), Subjective Memory Complaint, Subjective Memory Complaint Clinical (SMCC), Subjective Memory Rating Scale (SMRS), Deterioration Cognitive Observee (DECO) and the Clock Drawing Test (CDT). ***Results:*** Using ROC analyses, the SMCC, MMSE and CDT were found to be 'moderately accurate' in screening for dementia with an area under the curve (AUC) >0.70. The AUCs for the SIS (0.526), SMRS (0.661) and DECO (0.687) classified these measures as being 'less accurate'. At recommended cutoff scores, the SMCC had a sensitivity of 90.9% and specificity of 45.7%; the MMSE had a sensitivity of 63.6% and a specificity of 76.0%, and the CDT had a sensitivity of 44.4% and a specificity of 88.9%. Combining the SMCC and MMSE did

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not improve their predictive power except for a modest increase when using the sequential rule. ***Conclusion:*** The SMCC is composed of valid screening questions that have high sensitivity, are simple to administer and ideal for administration at the community or primary health care level as a first level of 'rule-out' screening. The MMSE can be included at a second stage of screening at the general hospital level and the CDT in specialist clinical settings. Sequential use of the SMCC and MMSE will improve the specificity of the former and the sensitivity of the latter.

Introduction

Almost 60% of the world's dementia population resides in lower- and middle-income countries, with this figure predicted to increase to over 70% by 2050 [1]. Mild cognitive impairment (MCI) is an intermediate stage between the cognitive changes associated with normal aging and early dementia [2], and its prevalence ranges from 3 to 45% [3], with an annual conversion rate from MCI to dementia ranging from 6 to 25% [2].

The challenges associated with identifying people with dementia are a significant barrier to its optimum management [4], and may contribute to treatment gaps as high as 90% [5]. In addition, despite limitations in currently available treatment, early detection of dementia through screening is beneficial for risk assessment and management [6], and is associated with high cost savings [7].

Screening refers to the use of measures to identify individuals at sufficient risk of a specific disorder to warrant further investigation or direct preventive action [8]. The ability of a measure to 'rule out' or 'rule in' the likely presence of a condition with minimal false positives and minimal false negatives is captured by quantification of its sensitivity, specificity and positive or negative predictive values [9, 10]. In view of the considerable burden posed by dementia [11] and MCI [12], and the absence of pathognomonic biological markers for dementia [13], there is a need to identify suitable, effective screening measures that have been validated locally. The challenges associated with cross-cultural cognitive assessments are well documented [13–15]. Effective screening requires measures that are widely accessible, simple to administer, inexpensive, culturally appropriate, valid and reliable, that cause minimum discomfort and are sensitive to preclinical detection of disease states [9]. This is particularly important in low-income countries, where the language and culture may be very different from those where the measures have been developed. In addition, measures only suitable for applying in a research context must be distinguished from those that have practical utility in daily clinical settings in low-resource countries. Given the severe shortage of mental health professionals in low-income countries, including South Africa, measures need to be suitable for administration by lay or nonspecialist health care workers at busy primary care clinics, with minimum cost implications [16].

Cognitive decline in the elderly is believed to exist on a continuum ranging from normal age-related changes, to subjective impairment, MCI and dementia [17–19] with accompanying biomarker models being proposed [18]. Subjective ratings of health have been shown to be associated with impairment in functional and cognitive status [20] and brief self-reports, which can be easily obtained, have shown potential for predicting cognitive decline [21]. While the literature has traditionally focused on measures of objective cognitive impairment, there is increasing focus on the significance and measurement of subjective cognitive impairment, especially subjective memory impairment or subjective memory complaints.

The reported prevalence of subjective memory complaints varies widely from 26 [22] to 57% [23] depending on whether they are spontaneously reported or solicited, the types of

Dement Geriatr Cogn Disord 2013;36:119–135
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questions used to establish their presence, the nature of the sample (community vs. clinical) and age [24]. Objective cognitive impairment may be present in almost 50% of individuals with subjective memory complaints [25, 26], warranting clinicians to further investigate self-reports. Identifying valid measures of subjective cognitive impairment may therefore prove useful and have the potential to overcome some of the limitations related to the cross-cultural validity of objective cognitive assessment tools [27–29].

Subjective memory complaints have been associated with the presence of depression in the elderly [30] as well as increased risk for dementia [31]. Longitudinal studies confirm the association between subjective memory complaints and subsequent cognitive decline [17, 19, 32, 33]. The validity of subjective impairment as a correlate of organic pathology is supported by its association with neuroradiological changes in the absence of objective impairment [34, 35]. There is also a significant association between subjective memory complaints and cerebral white matter lesions which is independent of cognition and depression [36]. While the presence of subjective memory complaints correlates with a 20- to 30-percent likelihood of a diagnosis of dementia or MCI, their absence may be a 'reasonable' method of ruling out these conditions [24].

The aim of this study was therefore to evaluate the discriminant validity of 7 screening measures [Subjective Memory Complaint (SMC), Subjective Memory Rating Scale (SMRS), Deterioration Cognitive Observee (DECO), Mini-Mental State Examination (MMSE), Six-Item Screener (SIS) and Clock Drawing Test (CDT)] individually and in combination, the intention being to recommend a set of screening measures which could be applied in the multiracial, multilinguistic South African population in the primary health care context.

Methods

This study was a component of a study on dementia conducted in a group of homes for the elderly in Durban, KwaZulu-Natal, South Africa, which housed a total of 1,371 residents at the time of the study in 2010–2011. The homes are administered by a nongovernmental organization and cater for those needing frail care, and assisted and independent living for people aged 60 years and older. Inclusion criteria for the entire study were: residents who were 60 years and older, had a minimum of 8 years of formal schooling, were able to speak, read and write in English and give written, informed consent. Exclusion criteria were: residents with severe physical, mental or sensory handicaps that precluded their engagement in the assessment procedures.

The methodology and choice of instruments were designed to simulate local clinical practice at different levels of care. The 3 stages consisted of: (1) administration of dementia screening measures to a sample of the residents; (2) clinical diagnostic evaluation for dementia in a subsample of those screened, and (3) administration of neuropsychological measures to those assessed clinically.

Stage 1 consisted of 302 participants who were conveniently sampled to be screened for the presence of cognitive impairment. All 302 were administered the SMC and the MMSE [37]. For those participants who reported the presence of a subjective memory complaint, the SMRS [38] was also administered. If an informant was available, the informant DECO scale [39] was also administered (n = 76), with the results of this stage being reported separately elsewhere [40].

For stage 2, 140 (46.4%) of the 302 screened participants (38 screen positives and 102 randomly selected screen negatives on the MMSE) had a clinical diagnostic evaluation conducted in English by psychiatrists [41]. The psychiatrists were blinded to the results of the screening in stage 1 and used a standardized clinical diagnostic assessment tool developed for this stage of the study. While several formal and well-researched tools exist for dementia diagnosis [42–44], many are applicable only in research contexts, this having implications for cost and skills in administration, while others require the presence of an informant [45–48], which is not always possible. The structured questionnaire used in our study consisted of two components and was designed to simulate naturalistic clinical practice in respect of cognitive assessment of the elderly. Firstly, it contained items for the evaluation of clinical and historical risk factors for dementia and included a subjective cognitive impairment measure [Subjective Memory Complaint Clinical (SMCC)].

Dement Geriatr Cogn Disord 2013;36:119–135
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Secondly, it included the mental state examination (comprising bedside cognitive assessments of memory, language, praxis and executive functioning), self-reported assessments of functional abilities (basic and instrumental activities of daily living) and a physical examination. Following the clinical diagnostic assessments, a consensus panel consisting of 3 specialists (neurologist, clinical psychologist and psychiatrist) assigned diagnoses of dementia, current major depression and delirium according to the *Diagnostic and Statistical Manual of Mental Disorders,* 4th edition, text revised (DSM-IV-TR) criteria [49] and MCI [50] to all 140 participants. The panel was blinded to the participants' performance scores on the various screening measures. In the third stage, 117 participants completed a battery of neuropsychological measures which included the CDT [51]. The overall study received ethical approval from the Biomedical Research Ethics Committee of the University of KwaZulu Natal and the elderly gave written, informed consent to participate.

Clinical Classification ('Gold Standard')

For the purposes of this study, the following applies: dementia was diagnosed using the DSM-IV-TR. Criteria A and B for Alzheimer's and vascular dementia were applied to assign a general diagnosis of dementia without reference to etiology. A clinical diagnosis was used as the 'gold standard' for dementia [52, 53].

MCI was diagnosed using the criteria contained in the report of the International Working Group on Mild Cognitive Impairment. These were: the presence of subjective cognitive impairment (self- or informant-reported), objective evidence of cognitive impairment in the presence of high scores for activities of daily living and normal or minimally impaired instrumental activities of daily living functions [50]. Subjective memory impairment was assessed through solicited self-report and objective evidence of cognitive impairment was based on the performance of participants in the various cognitive domains assessed in the clinical evaluation (stage 2).

Nondementia controls were those participants who did not meet the criteria for dementia. The controls were those participants who did not meet the criteria for MCI or for dementia.

Screening Measures

Although there are almost 150 cognitive screening measures cited in the literature [54], there is no consensus on what domains should be measured [13].

Seven screening measures were chosen with regard to relevance and utility in low-resourced contexts and with the view to developing an assessment algorithm for widespread local implementation. Apart from the neuropsychological battery of tests, all the measures used in this study were deemed to be suitable for use by nonspecialist clinical personnel and, except for the DECO, were not dependent on the availability of an informant.

One of the challenges associated with interpreting the significance of subjective memory complaints has been identified as the inconsistency in its definition across studies [55]. By utilizing 3 different assessment measures for subjective memory complaint (1–3 below), we hoped to identify one that would be most sensitive and useful for screening.

(1) Subjective Memory Complaint. The SMC is a single-domain screening measure assessing memory through a 'yes/no' response to the question: 'Are you experiencing any difficulty with your memory?'

(2) Subjective Memory Complaint Clinical. The SMCC is a single-domain screening measure assessing memory through affirmative responses to 7 questions on memory recall problems experienced at least once a week over the last year. The participant is confronted with 7 commonly occurring situations requiring memory recall, 6 short-term and 1 long-term items (table 3). The evaluation of the SMCC is distinguished from the SMC by the specification of duration, frequency and nature of the memory complaint. As memory behaviors occur in specific behavioral contexts and most memory questionnaires focus on context-free memory domains, we decided to evaluate specific memory behaviors. This is based on the behavioral specificity hypothesis that 'individuals are capable of accurately reporting memory-related problems in everyday life, provided that questions are specific to the behaviours in question' [56]. The descriptive subjective memory items used in our study were based on commonly encountered clinical experiences of patients in a psychiatric hospital setting which were further specified for duration and frequency. Their face validity was confirmed by 2 psychologists and 3 psychiatrists. The SMCC was coded as positive if the participant reported difficulties with at least 1 of the 7 situations presented. A positive association has been shown between the type and number of subjective memory complaints and objective cognitive performance, with 'finding one's way around familiar streets' identified as being one type of memory complaint that was more likely than others to be associated with cognitive impairment [57].

Dement Geriatr Cogn Disord 2013;36:119–135
DOI: 10.1159/000350768

(3) Subjective Memory Rating Scale. This is a 5-item single-domain scale that assesses subjective deterioration of memory over a 10- to 20-year period in 5 situations [38]. Each item is scored on a 5-point Likert scale. The maximum score that may be obtained on this scale is 25 and a score of ≥20 suggests memory impairment. While there is no information on the sensitivity and specificity of the SMRS, subjective memory questionnaires have a pooled sensitivity and specificity of 43 and 85.8%, respectively [24]. There are at least 15 variations of the use of a single question, and at least 10 sets of questions in the literature [55] to assess subjective memory impairment. The SMRS used in this study has not been as extensively researched as the CAMDEX [58] subset of items [59, 60] and the MAC-Q [61–64]. The MAC-Q has recently been found to be greatly affected by affect and was not recommended for cognitive screening [65]. The Memory Complaint Scale has only recently been proposed for further research [66]. The SMRS was chosen for its brevity, simplicity and scoring method – characteristics that could lend it to easy administration by nonprofessionals, translation into local languages and utility for elderly with low literacy, should it prove to have validity for dementia screening.

(4) Deterioration Cognitive Observee. This is a multidomain 19-item screening test which is considered not to be affected by the participant's education as it relies on an informant to complete the questionnaire [39]. At a cutoff score of ≤24, the DECO has a sensitivity of 79% and specificity of 90% in detecting dementia [39]. The DECO has discriminability for mild, moderate and severe dementia [13] and has been found to be useful in predicting mild and moderate dementia in South Africa [67]. The DECO was therefore chosen above the more widely researched IQCODE [68].

(5) Mini-Mental State Examination. It is a multidomain clinician-administered tool that yields a maximum score of 30. The most widely used cutoff score for cognitive impairment is ≤23. In community settings, the MMSE has a pooled sensitivity and specificity of 85.1 and 85.5%, respectively [69]; its sensitivity and specificity in the South African population have not been determined. The MMSE was selected as it is the most widely used screening instrument in clinical and research settings [69, 70], despite the emergence of many new tools over the last 10 years [71]. To our knowledge, its validity in the local setting has not been determined, yet this is necessary in order to be able to reference other screening tools against it in future. Its recently introduced copyright restrictions and related costs may prevent its widespread use in low-resource settings in the future.

(6) Six-Item Screener. The SIS [72] is a brief multidomain tool comprising 3 temporal orientation items and the 3 recall items of the MMSE, resulting in a maximum total score of 6. It has been found to be reliable and has the full psychometric properties of the full MMSE. Using a cutoff score of ≤3, the SIS has a sensitivity and specificity of 88.7 and 88%, respectively, for the diagnosis of dementia [72].

(7) Clock Drawing Test. This is a screening test for dementia [73] that assesses visuospatial, constructional and executive functions and is classified as a single-domain test [74]. In this study, the free-drawing version with the '10 past 11' time setting instruction was used. The 10-point scoring method of Rouleau et al. [75, 76] was used and a cutoff of ≤6 was applied. The CDT has been shown to have good correlation with the MMSE. It is nonthreatening to patients and has been identified as a good screening test for moderate and severe, but not mild, dementia. Lower scores are obtained with increasing age, low education and depression. It has the advantage over other screening tests in that the clock drawings can serve as a visual record of the cognitive status of an individual which can be compared over time [77].

The quoted sensitivities and specificities of the above measures emanate from studies conducted in countries other than South Africa and are in reference to a diagnosis of dementia only.

Measures of Predictive Validity for Dementia versus Nondementia

Though community settings may require screening measures with a lower sensitivity compared to clinical settings [10], sensitivity and specificity of >80% were set as acceptable levels for the measures [78]. The ability of a measure to case-find or 'rule in' dementia with minimal false negatives is its positive predictive value (PPV), and the ability of a measure to screen or 'rule out' a diagnosis with minimal false positives is its negative predictive value (NPV) [9, 79]. The PPV and NPV are considered most relevant for clinicians [80]. More often receiver operating characteristic (ROC) curves are used where the area under the ROC curve (AUC) summarizes the diagnostic accuracy of a tool on all possible cutoff scores, giving equal weighting to sensitivity and specificity and allowing for the comparison of the discriminatory validity of different cognitive tests [13, 81]. Though AUC values of <0.8 are considered of 'questionable utility' [10], in this study, AUC values of 0.5 were classified as noninformative; 0.5 < AUC ≤ 0.7 less accurate; 0.7 < AUC ≤ 0.9 moderately accurate; 0.9 < AUC < 1 highly accurate with the perfect test having an AUC = 1 [82]. In this study, the Youden index (J) was used as a specific metric measurement of overall diagnostic effectiveness as a function of optimal sensitivity and specificity [83].

Dement Geriatr Cogn Disord 2013;36:119–135
DOI: 10.1159/000350768

Statistical Analysis

The data were analyzed in 3 components: demographic details, performance of the 7 measures, and performance of the combined screening measures. Data were analyzed using IBM SPSS19 and ROC curves were calculated using MedCalc software. The demographic variables included age, gender, race and education level; average test scores and the proportion of participants with cognitive impairment were calculated for each of the classification categories and compared using χ^2 tests. The clinically assigned diagnoses (dementia and MCI) were used as the gold standard to calculate the sensitivity, specificity, PPV and NPV for the subjective and objective screening tools using their standard cutoff values. In addition, for each tool, the AUC with 95% confidence intervals (CIs), optimal cutoff scores (Youden index), and cutoff values for set sensitivities and specificities of 80% were calculated using ROC analysis.

The single-domain (SMCC) and multidomain (MMSE) screening measures that each displayed the best accuracy for screening (AUC >0.70) were then combined to determine whether the 2 tests together provided any additional information for dementia prediction over that given by either test alone. Three different methods were used: logistic regression, the compensatory ('or') rule and the conjunctive ('and') rule [84]. Differences in the sensitivity and specificity of individual and combinations of tests were evaluated using 95% CIs.

The SMCC and MMSE were entered simultaneously to determine which variables independently predicted dementia when adjusting for scores on the remaining tests. Two stepwise approaches were used (forward and backward) with the SMCC forced into the model and the MMSE as candidate for stepwise entry. The probability was 0.05 for stepwise entry and 0.10 for removal, and because similar models were elicited using forward and backward stepwise methods, only results from the forward stepwise regressions are reported. The odds ratios and CIs were reported for each measure, and the percentage of those correctly classified as demented is reported. ROC curves and the AUC were generated to graphically and quantitatively reflect the ability of the combined models derived from logistic regression to discriminate between dementia and nondementia controls.

Results

The demographic results will be followed by a review of the performance of the 7 measures and the results of the analysis of the combination of the tests that performed the best.

The 140 participants comprised 97 (69.3%) females and 43 (30.7%) males with an average age of 75.2 ± 8.9 years. There was a significant association between increasing age and increasing cognitive impairment ($F = 5.0$, $p = 0.008$; table 1). There were 65 (46.4%) white, 41 (29.3%) colored, 28 (20%) Asian and 6 (4.3%) black participants. One hundred and six participants (75.7%) had less than 12 years of education and 11 (7.9%) participants had more than 12 years of education; significant differences were found in education levels between controls and MCI participants ($p = 0.041$) (table 1).

While all 140 of the sample had MMSE, SIS and SMCC scores, SMRS scores were only available for those who reported the presence of subjective impairment (n = 69), and DECO scores were only available for those participants who had contactable informants (n = 34) [40]. The prevalence data for dementia and MCI are reported fully in a separate paper [41].

Table 1 also reports on the performance of the various assessment measures. The prevalence of screen positives on the various measures was compared across the three classification groups (dementia, MCI, controls) using standard cutoff scores. All the measures, except for the SIS and DECO, were significantly different between the classification groups. The MMSE, SMCC, SMRS and CDT were able to significantly discriminate between controls and those with MCI and dementia (table 1).

Table 1. Demographic and psychometric data according to diagnostic categories

	Dementia (n = 11; 7.9%)	MCI (n = 38; 27.1%)	Controls (n = 91; 65%)	Statistic	p
Age	77.2±7.9	75.8±8.1	72.1±6.8	F = 5.0	0.008*
Race				χ^2 = 15.0	0.078
Asian	0	6 (15.8)	22 (24.2)		
Black	1 (9.1)	2 (5.3)	3 (3.3)		
Colored	1 (9.1)	15 (39.5)	25 (27.5)		
White	9 (81.8)	15 (39.5)	41 (45.1)		
Gender				χ^2 = 3.7	0.165
Female	9 (81.8)	30 (78.9)	58 (63.7)		
Male	2 (18.2)	8 (21.1)	33 (36.3)		
Years of education	10.3±2.6	9.3±1.6	10.3±2.1	F = 3.3	0.041*
Performance of assessment measures					
SMC present	7 (63.6)	26 (68.4)	33 (36.3)	χ^2 = 12.5	0.002*
SMCC ≥1	10 (90.9)	38 (100) [a]	32 (35.2)	χ^2 = 61.4	<0.001*
SMRS ≥20	1 (14.3)	8 (30.8)	3 (9.1)	χ^2 = 4.5	0.080
DECO ≤24	1 (50)	1 (16.7)	3 (11.5)	χ^2 = 2.6	0.301
MMSE ≤23	7 (63.6)	12 (31.6)	19 (20.9)	χ^2 = 8.5	0.010*
SIS ≤4	5 (45.5)	22 (57.9)	46 (50.5)	χ^2 = 0.8	0.712
CDT ≤6	4 (44.4)	5 (16.7)	7 (9)	χ^2 = 7.5	0.009*

Figures in parentheses are percentages. Spearman's χ^2 test and Fisher's exact test were used. Significance set at 95%, * $p < 0.05$.

[a] The presence of at least 1 SMCC was a diagnostic requirement for MCI.

Performance of the Seven Measures

Table 2 summarizes the ROC analysis data for each of the measures (excluding SMC[1]) with sensitivity, specificity, PPV, NPV and AUC values for detecting dementia based on their recommended cutoff scores. In addition, the optimum cutoff scores that should be applied to optimize the trade-off between sensitivity and specificity are reported, together with the recommended cutoff scores if a fixed sensitivity or specificity of 80%, respectively, was required.

Using the acceptable level of 80% for sensitivity, only the SMCC had a sensitivity >80% (90.9%), followed by the MMSE with a sensitivity of 63.6%. In terms of specificity, the SMRS (81.4%), DECO (87.5%) and CDT (88.9%) achieved a specificity >80%; however, the MMSE had a specificity of 76% (table 3). With the exception of the SMCC and SIS, adjusting the cutoff scores in order to optimize the balance between sensitivity and specificity values resulted in increasing one at the expense of the other being lowered. Increasing the cutoff score of the MMSE from ≤23 to ≤24 increased its sensitivity from 63.6 to 81.8% (table 2). The SIS, comprising a subset of MMSE items, was evaluated for its potential to replace the MMSE, which is considered by some to be too lengthy for administration. However, in this study, the SIS displayed sensitivity and specificity values <50%, with an AUC of 0.526 (p = 0.777).

The NPVs ranged from 88.9% for the SMRS to 98.3% for the SMCC identifying the measures as having a good 'rule-out' value (not dementia cases), thus good for screening. All the measures recorded very low PPVs ranging from 6.8% for the SIS to 25.0% for the CDT, suggesting a poor 'rule-in' value (finding possible dementia cases).

[1]This categorical measure was not suitable for ROC analysis.

Table 2. Predictive validity of screening measures for dementia

	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	AUC (95% CI) p value	Optimum cutoff caseness (sensitivity, specificity in %) Youden index	Cutoff score, sensitivity 80%, specificity in %[a]	Cutoff score, sensitivity in %, specificity 80%[b]
SMCC	90.9 (57.1–99.5)	45.7 (37.0–54.7)	12.5 (6.5–22.2)	98.3 (89.9–99.9)	0.717 (0.635–0.790) p = 0.004*	>0 (90.9, 45.7) J = 0.37	>0.4, 80, 51.0	>2.1, 52.1, 80
SMRS	14.3 (0.8–58.0)	81.4 (68.7–89.9)	8.3 (0.4–40.2)	88.9 (76.7–95.4)	0.661 (0.537–0.771) p = 0.05	>16 (100, 32.3) J = 0.32	>16, 80, 46.9	>18, 22.3, 80
DECO	50.0 (2.7–97.3)	87.5 (70.1–96.0)	20.0 (1.0–70.1)	96.6 (80.4–99.8)	0.687 (0.506–0.835) p = 0.462	≤17 (50, 93.8) J = 0.44	≤32, 80, 41.3	≤27, 50.0, 80
MMSE	63.6 (31.6–87.6)	76.0 (67.5–82.9)	18.4 (8.3–34.9)	96.1 (89.7–98.7)	0.770 (0.691–0.838) p < 0.001*	≤24 (81.8, 66.7) J = 0.49	≤24, 80, 67.6	≤23, 63.6, 80
SIS	45.5 (18.1–75.4)	47.3 (38.5–56.2)	6.8 (2.5–15.9)	91.0 (80.9–96.3)	0.526 (0.349–0.703) p = 0.777	>4 (54.6, 52.7) J = 0.07	>3, 80, 23.8	>5, 19.9, 80
CDT	44.4 (15.3–77.3)	88.9 (81.0–93.9)	25.0 (8.3–52.6)	95.0 (88.3–98.2)	0.732 (0.642–0.810) p = 0.012*	≤5 (44.4, 91.7) J = 0.36	≤9, 80, 50.5	≤6.8, 44.4, 80

Using De Long et al. [85], binomial exact CI for AUC, and optimal Youden index (J = sensitivity and 1 – specificity) were calculated. Significance set as p < 0.05 (asterisk). [a] Sensitivity set at 80%. [b] Specificity set at 80%.

However, only the SMCC (AUC = 0.717, p = 0.004), MMSE (AUC = 0.770, p < 0.001) and CDT (AUC = 0.732, p = 0.012) had AUC scores of >0.70, thereby meeting the criteria for 'moderate reliability' as screening tools and warranting further investigation [82].

The SMCC had moderate discriminatory power to correctly classify those with and without dementia (AUC = 0.717, p = 0.004) and potential utility as a single-domain screening test. At the standard cutoff scores of >1, the SMCC had a sensitivity of 91% and a specificity of 46%. This means that the presence of at least 1 subjective memory complaint correctly identified 91% of the 11 participants with dementia, but only correctly distinguished 46% of the 129 nondementia participants as such. In terms of whether the measure would predict the probability of having dementia, the proportion of people with a positive SMCC score who had dementia was low (PPV = 13%), but the proportion of people with a negative SMCC score who did not have dementia was high (NPV = 98%), thus confirming that the SMCC would be useful for 'ruling out' dementia.

With these findings, it appeared that the SMCC could be used as an appropriate first-step screening measure where false positives would be included for further screening. The SMCC measure had a high reliability (internal consistency) with a Cronbach's alpha of 0.745, with 2 of the 7 individual items significantly associated with dementia. These were: 'difficulty remembering what happened in the last few days' ($\chi^2 = 8.5$, p = 0.008) and 'difficulty remembering the names of people you have known a long time' ($\chi^2 = 5.6$, p = 0.025) (table 3).

Dement Geriatr Cogn Disord 2013;36:119–135
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Table 3. Performance of SMCC items

Item		Dementia (n = 11)	Nondementia (n = 129)	Test
1	Difficulty remembering things that had happened in the last few days?	7 (63.6%)	30 (23.3%)	$\chi^2 = 8.5$, p = 0.008*
2	Difficulty remembering the names of common objects?	2 (18.2%)	12 (9.3%)	$\chi^2 = 0.9$, p = 0.302
3	Difficulty remembering where you left your belongings?	5 (45.5%)	35 (27.1%)	$\chi^2 = 1.7$, p = 0.294
4	Difficulty remembering the names of people you have known for a long time?	8 (72.7%)	47 (36.4%)	$\chi^2 = 5.6$, p = 0.025*
5	Difficulty remembering the names of people who you had met within the last week?	6 (54.5%)	44 (34.1%)	$\chi^2 = 1.8$, p = 0.200
6	Difficulty finding your way around your home?	1 (9.1%)	4 (3.1%)	$\chi^2 = 1.1$, p = 0.340
7	Difficulty finding your way around other places (e.g. shopping center/home of a friend/relative/church)?	1 (9.1%)	7 (5.4%)	$\chi^2 = 0.3$, p = 0.489

Differences were tested using Fisher's exact test. Significance was set at 95%, * $p < 0.05$.

The SMCC also displayed higher sensitivity (90.9 vs. 63.6%), PPV (12.5 vs. 10.6%) and NPV (98.3 vs. 94.6%) than the SMC. The SMCC defines the duration, frequency and nature of the memory complaints as opposed to the SMC, which merely confirms the presence of any subjective memory complaint. These results suggest that defining subjective cognitive impairment with greater specificity may result in higher predictive validity.

The MMSE was also found to have moderate discriminative ability as a screening measure for dementia (AUC = 0.770, $p < 0.001$), confirming its utility as a multidomain screening test. At the standard cutoff score of ≤23, the MMSE had a sensitivity of 63.6% and a specificity of 76%, meaning that the MMSE at that cutoff score correctly identified 63.6% of the 11 participants who had dementia, and misclassified 24% of the 129 participants without dementia as having dementia. Increasing the cutoff score to ≤24 improved the sensitivity of the MMSE to 81.8% while reducing its specificity to 66.7%.

The MMSE NPV was high with 96.1% of participants with a negative test not having dementia, but it had a low PPV with 18.4% of participants with a positive test actually having dementia.

The CDT also showed potential as a screening measure [86] and displayed a similar moderate discriminability to the MMSE in identifying participants with and without dementia (AUC = 0.731, p = 0.012). At standard cutoff scores of ≤6, the CDT had a sensitivity of 44.4% and a specificity of 88.9%. Reducing the cutoff score to ≤5 did not improve the sensitivity but increased the specificity to 91.7%.

The CDT NPV was also high with 95% of participants with a negative test not having dementia, but the CDT PPV was low with 25% of participants with a positive test actually having dementia. The findings from this study confirmed that the CDT would also be useful for screening and 'ruling out' dementia.

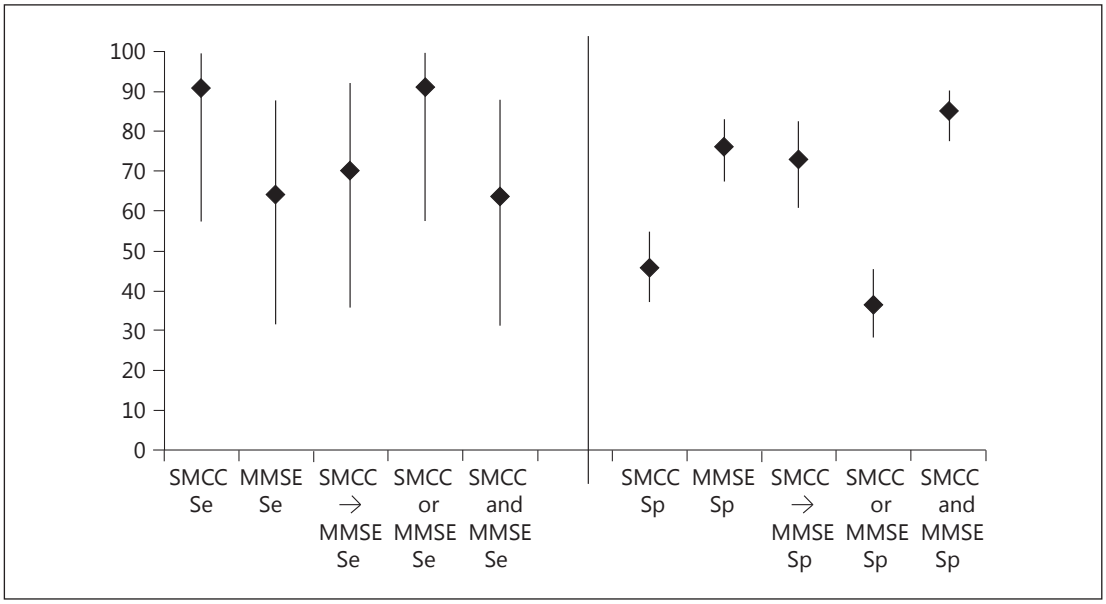

Fig. 1. Sensitivity and specificity of combination of measures (95% CI). Se = Sensitivity; Sp = specificity.

Combining Screening Measures

Combining measures in parallel or sequentially can address the challenges of the 'trade-off' between sensitivity and specificity [9, 80, 84]. The SMCC (a single-domain measure) and the MMSE (a multidomain measure) were combined in 4 different ways and tested for improvements in accuracy of screening for dementia compared to the use of the MMSE or SMCC alone (table 4).

Sequential Combination. Starting with the single-domain measure, followed by the multi-domain measure, all participants who screened positive on the SMCC (n = 80) were selected for further screening. The MMSE results on the 80 participants identified 26 as scoring ≤23. Sequentially combining the MMSE with SMCC increased the discriminatory power of the MMSE with the AUC increasing from 0.770 (95% CI 0.62–0.919, p = 0.004) to 0.774 (95% CI 0.602–0.945, p = 0.005) (table 4), and resulted in an increased sensitivity of 70% (95% CI 35.4–91.9, n.s.) and a decreased specificity of 72.9% (95% CI 60.7–82.5, n.s.) (fig. 1).

Compensatory Combination. Using the compensatory rule, the two measures were combined by classifying participants as screen positive if either measure had a positive result. Consistent with this interpretation, combining two tests in this manner should increase sensitivity above that of either test used alone. However, because only participants with negative results on both tests are classified as controls, the specificity of the combination cannot be greater than that of either test [84].

Combining the presence of a positive SMCC *or* a positive MMSE score resulted in 92 participants meeting caseness for dementia on either of these measures (n = 92), compared to 80 on the SMCC and 38 on the MMSE. Combining these tests reduced the discriminatory power of the measures (AUC = 0.637, 95% CI 0.49–0.783, p = 0.133) (table 4) and resulted in a sensitivity of 90.9% (95% CI 57.1–99.5), which was similar to the SMCC but higher than the MMSE (n.s.). The sensitivity for these 36.4% (95% CI 28.3–45.4) screen positives was lower than that in the SMCC (n.s.) and significantly lower than that in the MMSE individually (fig. 1).

Conjunctive Combination. Using the conjunctive rule, two tests are combined by classifying patients as having dementia if the patient scored positive on both tests. Such a combi-

Dement Geriatr Cogn Disord 2013;36:119–135
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Table 4. Predictive validity measures of various combinations of SMCC and MMSE

Cases	Sensitivity	NPV	Specificity	PPV	AUC	p
SMCC alone (n = 80, 57.1%)	90.9 (57.1–99.5)	98.3 (89.9–99.9)	45.7 (37.0–54.7)	12.5 (6.5–22.2)	0.717 (0.635–0.790)	0.004*
MMSE alone (n = 38, 27.1%)	63.6 (31.6–87.6)	96.1 (89.7–98.7)	76.0 (67.5–82.9)	18.4 (8.3–34.9).	0.770 (0.691–0.838)	<0.001*
Sequential rule (SMCC → MMSE) (n = 80 → 26, 32.5%)	70 (35.4–91.9)	94.4 (83.7–98.6)	72.9 (60.7–82.5)	26.9 (12.4–48.1)	0.774 (0.602–0.945)	0.005*
Compensatory rule (either test is positive) (n = 92, 65.7%)	90.9 (57.1–99.5)	97.9 (87.5–99.9)	36.4 (28.3–45.4)	10.9 (5.6–19.5)	0.637 (0.49–0.783)	0.133
Conjunctive rule (positive on both tests) (n = 26, 18.6%)	63.6 (31.6–87.6)	96.5 (90.7–98.9)	85.3 (77.7–90.6)	26.9 (12.4–48.1)	0.745 (0.572–0.917)	0.007*

Asterisk indicates significance.

nation of tests should improve specificity over that of either test used alone, but the sensitivity of the combination can be no higher than that of either test [84].

When the tests were used individually, 80 and 38 participants screened positive on the SMCC and MMSE, respectively. When a participant screened positive on both measures, only 26 participants met caseness for dementia. Screening positive on both measures resulted in a sensitivity of 63.6% (95% CI 31.6–87.6), similar to that in the MMSE but lower than that in the SMCC (n.s.) (fig. 4). The specificity was 85.3% (95% CI 77.7–90.6), which was significantly higher than that in the SMCC and MMSE (n.s.) on their own (fig. 1). This combination of measures resulted in moderate discriminatory power with an AUC of 0.745 (95% CI 0.572–0.917, p = 0.007) (table 4).

Probability Combination. Logistic regression was used to combine the SMCC and MMSE scores using a mathematical calculation of probability to determine which combination of tests best discriminated individuals with dementia from those without dementia. The SMCC on its own was a significant predictor of group membership (step 1; Wald χ^2 = 5.6, odds ratio = 1.5, 95% CI 1.1–2.0, p = 0.018). With each 1-point increase in SMCC score, participants were 1.5 times more likely to be diagnosed with dementia and the measure correctly classified 92.1% of participants with dementia as having dementia. The addition of the MMSE (step 2; Wald χ^2 = 6.8, p = 0.009) improved the identification of dementia and the discriminatory power of SMCC score and MMSE score combined increased AUC to 0.771 (95% CI 0.610–0.933, p = 0.003). Using the SMCC as a categorical measure (cutoff score of ≥1 SMCC) and combining the 'screen positives' with the MMSE increased the AUC even further to 0.822 (95% CI 0.691–0.953, p < 0.001).

Discussion

The growing burden of dementia, which carries great stigma, and grave social, legal and risk implications for sufferers [80], calls for clinical action to identify the disease in its earliest stages. Early detection of cognitive impairment in low-income countries that have competing health priorities requires the availability of valid measures requiring minimal investment in resources for their administration. In choosing the most suitable screening measures, the decision should be made whether the intention is to detect the presence of cognitive

Dement Geriatr Cogn Disord 2013;36:119–135
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impairment in a community setting (requiring a measure with high sensitivity), or to make a diagnosis in a high-risk, clinical sample which will require a measure that has high specificity [87]. Our study evaluated a range of screening measures with a view to identifying suitable measures with potential for utilization in local clinical settings.

Based on its clinical utility index, the single-domain subjective memory measures appear to be accurate assessments of subjective memory complaints [82] and have a 'good' value for ruling out a diagnosis but are rated as having a 'poor' value for ruling in a diagnosis of dementia [24]. Our study confirmed the utility of the SMCC as a good 'rule-out' measure in our population. The performance of both the SMC and SMCC in our study was superior to the 43% sensitivity and 85.8% specificity reported in a meta-analysis of SMC [74]. The differing performance between SMC and SMCC highlights the need for a standard definition of subjective memory impairment for research or clinical settings [55]. The advantage of the SMCC lies in its brevity of administration and simplicity in scoring. It may easily be used at a community level for screening by community health workers or primary health care nurses where there is a shortage of mental health professionals. In addition, SMCC has minimal training and resource costs, quick administration, easy interpretation and meets the criteria of a test for effective screening [9].

Once participants with subjective memory complaints have been identified, screening with a multidomain tool such as the MMSE would be advised. A meta-analysis of short screening tests in low-prevalence community settings also reported an overall sensitivity of 72% (95% CI 60.4–82.3), and a specificity of 88.2% (95% CI 83.0–92.5) [79] for the MMSE. The performance of the MMSE in the current study sample was less robust. However, changing the recommended cutoff score of ≤23 to ≤24 would increase the sensitivity to 80% but decrease the specificity to 67.6%. Despite its limitations, the MMSE may remain the best tool for primary care clinicians who want to rule in or rule out a diagnosis of dementia, provided the length of administration is acceptable [79]. The length of the MMSE and the training and skill required for its administration, scoring and interpretation may make it more suitable for use at a general hospital level as opposed to busy primary health care settings. While the simplicity and brevity [88] made the MMSE particularly suitable for use in low-resource settings, the recent copyrighting of this tool may make its use prohibitive for clinical and research applications in low-income countries.

The CDT, with an AUC of 0.732, also displayed good discriminant validity. The specificity displayed in our study (88.9%) compares favorably with the published literature which reports a mean of 85%. However, our sensitivity (44.4%) was considerably lower than the published mean of 85% [89]. This difference may be due to this study employing the Rouleau scoring system. One study showed that the Watson method yielded sensitivity and specificity values of 59 and 70%, respectively, while the Sutherland method yielded sensitivity and specificity values of 18 and 100%, respectively, on the CDT in the same cohort of patients [90]. The high NPV of 95.0% in our study identifies the CDT as having a good 'rule-out' value.

The CDT, despite being classified as a single-domain test, can be used to compensate for some of the limitations of the MMSE. It can be applied in the screening of symptomatic individuals in whom the ceiling effect of the MMSE precludes conclusive screening. As the MMSE does not have an item that assesses executive functions, the CDT can be administered to make this assessment. The CDT has been shown to be moderately sensitive and a specific adjunct for detecting executive cognitive impairment in those with a normal MMSE [90]. The CDT is a simple test that has shown good internal consistency and interrater reliability as a measure of executive ability [86]. However, while it is easily administered, scoring systems, which can be both qualitative and quantitative, require some skill in application. In our study, the high specificity of the CDT (88.9%) identifies it as being potentially useful for specialist clinical settings where there are mental health professionals.

Dement Geriatr Cogn Disord 2013;36:119–135
DOI: 10.1159/000350768

As no measures have 100% sensitivity and 100% specificity [87], the ideal screening measure should attempt to achieve maximum sensitivity with maximum specificity, and adjusting the threshold scores should improve sensitivity at the expense of reduced specificity and vice versa [87, 91]. By combining tests that evaluate complementary functions, their discriminant validity can be improved. The combination of the SMCC and MMSE using the logistic regression model provides the best discrimination (AUC >0.80). However, its application in clinical settings is impractical as the calculated scores are arbitrary values that do not share the attributes of the scales of the tests being combined [84]. Of the remaining 3 combination methods, conjunctive and compensatory combinations add minimal value to the predictive validity of the MMSE of SMCC alone, but sequential screening, as described earlier, improves the sensitivity of the MMSE and the specificity of the SMCC and may be the most practical and predictive approach in the local setting.

Neuropathological brain changes are present prior to the clinical manifestation of Alzheimer's dementia [18, 92]. MCI is an important stage in the Alzheimer's dementia continuum and although its course is variable, it is the first clinical harbinger of Alzheimer's dementia. Identifying screening measures that could identify individuals with MCI will create the opportunity to implement risk management strategies pending the availability of pharmacological agents for the prevention of progression to Alzheimer's dementia. The IQCODE has been shown to be useful in diagnosing Alzheimer's dementia, but was less effective in differentiating MCI from subjective memory complaint [93]. In our study, the MMSE, SMRS, SMCC and CDT display the potential to discriminate MCI from those with dementia and the controls (table 1). The sensitivity, specificity, PPV and NPV of these measures will be explored further for MCI screening.

Recommendations and Limitations

Multistage screening is 1 of 5 recognized models of dementia risk prediction [10, 38]. Establishing the presence of SMCC is a simple and effective first step in identifying symptomatic at-risk elderly. It can also be applied to medical patients in whom the presence of dementia should be excluded because cognitive impairment will impact on the care and outcome of comorbid medical conditions. Those screening positive can then be referred for a second level of more intensive screening at the general hospital level using the multidomain MMSE or CDT. Referral for specialist clinical assessments or expensive diagnostic investigations could then be determined by the results of the MMSE or CDT.

The study has some limitations in that the results may not be generalizable to community or clinical populations as our sample was drawn from a residential setting. Secondly, the sample was not demographically representative of the South African population as there was a majority of white patients and females. The inclusion criteria precluded participation by those who may have had severe dementia and were unable to engage in the various assessments.

Conclusion

A recent evaluation of the literature suggested that current risk models for dementia are poor at discriminating between 'at-risk' and 'not at-risk' individuals [10]. Recognition of dementia is ideally made during the early stage of the disease. This is also the time when the distinction between normal age-related cognitive decline and early dementia may be the most difficult to differentiate. Screening tools which have good discriminant validity are necessary to ensure that screening initiatives are both effective and efficient. External vali-

dation of our findings in larger residential samples and in community settings will be useful in confirming the reliability and validity of the assessed measures for widespread local application.

Disclosure Statement

There are no conflicts of interest.

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CHAPTER7

NORMS, SENSITIVITY AND SPECIFICITY OF NEUROPSYCHOLOGICAL TESTS

7.1 Introduction

This chapter reports on the data from the third stage of data collection, in which participants were administered a battery often neuropsychological tests currently used in the South African public sector. The researcher was responsible for designing and defining the research, the data analysis and interpretation, and writing up the paper. The researcher was responsible for designing and defining the research, data analysis and writing the papers.

7.2 Background

The administration of a variety of neuropsychological tests to assess the various cognitive domains potentially affected in dementia form an important component of a comprehensive clinical evaluation of individuals presenting with signs and symptoms of cognitive decline. As with screening measures, these tests must be validated on the population on which they are to be administered to ensure that test performance is appropriately interpreted. Discrepancies in the results of the same test between cultural groups have been reported and highlight the importance of using appropriately corrected norms when interpreting results (Nell 2000), especially in the local multi-cultural context.

Norms refer to the performance of a particular group, and should be appropriate for different age ranges, education and cultural groups, as there are assumptions underlying the norms of each group (Uzzel 2004).

Neuropsychological testing is an important component of a clinically integrative approach to assessing cognitive impairment in the elderly. Neuropsychological testing could be purposively applied to distinguish age-related cognitive deficits from those due to MCI or dementia (Jacova, Kertesz et al. 2007; Salmon and Bondi 2009); neuropsychological testing also allows for the qualitative and quantitative assessment of specific cognitive domains, and is superior to brief cognitive tools whose floor and ceiling effects threaten their validity (Jacova, Kertesz et al. 2007; Salmon and Bondi 2009). There is limited local data on norms for cognition in the healthy elderly as well as those diagnosed with MCI or dementia.

7.3 Aim

To establish the norms and discriminant validity of a battery of neuropsychological tests for cognitive disorders in the elderly.

7.4 Methodology

A neuropsychological battery of ten tests was administered to participants who had been initially screened for dementia and clinically diagnosed as having dementia or MCI. The tests were administered by clinical psychologists.

7.5 Study Outcome

Data on the norms for cognitively unimpaired elderly as well as those with dementia and MCI are presented with separate data for gender, race, age and education groups included. These are reported in Papers 4 and 5:

Paper 4: Durban dementia study: Rey Auditory Verbal Learning, Rey Complex Figure, Narrative Memory and Digit Span normative data for the elderly. **Submitted to the South African Journal of Psychology for publication.**

Paper 5: Durban dementia study: Norms for Clock Drawing Test, Controlled Word Association Test, Digit Symbol Test, Luria Hand Sequencing and Trail Making Test for the elderly.

Submitted to the South African Journal of Psychology for publication.

The sensitivity and specificity of the neuropsychological tests were determined for dementia and MCI and are reported in Paper 6, "**The sensitivity and specificity of a neuropsychological battery of tests in diagnosing Dementia and Mild Cognitive Impairment in an elderly South African population."**

7.6 Paper 4

Durban dementia study: Rey Auditory Verbal Learning, Rey Complex Figure, Narrative Memory and Digit Span normative data for the elderly

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Abstract

The prevalence of dementia is expected to significantly increase, especially in lower and middle-income countries. Due to the limitations of existing brief cognitive screening tools, the distinction between normal ageing and early dementia is often a challenge that requires comprehensive assessment of cognition through the use of specific neuropsychological tests. However, interpretation of these tests depends on the availability of population-specific norms and an appreciation of the impact of demographic variables on test performance. One hundred and seventeen older adults from a group of residential homes for the elderly participated in the study. The memory battery included the Rey Auditory Verbal Learning Test, Rey Complex Figure, Narrative Memory Test and Digit Span. The paper presents norms for the battery of memory tests and highlights the effects of age, education, gender and race on test performance. Black participants scored lower compared to the other race groups on all memory tests. Age, gender and race effects were demonstrated on some tests. The importance of local normative data in a multicultural context is discussed in the context of the results.

Keywords: Elderly, Dementia, Rey Auditory Verbal Learning Test, Rey Complex Figure, Narrative Memory Test and Digit Span.

Introduction

As longevity increases and the world faces the challenges associated with an ageing society, the health impact of cognitive ageing requires both clinicians and researchers to objectively distinguish between normal ageing, cognitive decline and dementia. Cognitive evaluation of elderly is often based on brief screening instruments that are limited by their lack of comprehensiveness (Welsh et al., 1994) and are confounded by age, cultural biases, language, gender, education and floor and ceiling effects (Collie, Shafiq-Antonacci, Maruff, Tyler, & Currie, 1999; Ganguli et al., 1991; Mitrushina, Boone, & D'Elia, 1999). Three major applications of neuropsychological testing in the clinical assessment of the elderly have been identified: diagnostic assessment, evaluation of functional status and planning of interventions (Attix & Welsh-Bohmer, 2006). Due to the considerable overlap between cognitive changes associated with ageing and the early stages of dementia, the commonest indication for neuropsychological testing is diagnostic.

While there are a large number of neuropsychological tests available, their use in South Africa is restricted due to the absence of appropriate norms for the representative samples of elderly (Foxcroft, 2011; Ganguli et al., 2010). As most tests have been developed and standardized for Euro-American populations, failure to consider demographic and cultural influences when interpreting results may lead to misinterpretation and misdiagnosis (Steinberg, Bieliauskas, Smith, Langellotti, & Ivnik, 2005) and compromise their proficiency when applied in the developing world (Kalaria, 2003). Lower mean test scores are routinely obtained in African samples relative to Euro-American test norms (Philippe Rushton & Skuy, 2000). Skuy, Schutte, Fridjohn, and O'Carroll (1999) found scores of one standard deviations (SD) below American norms among African secondary school students on a variety of tests including the

Wechsler Intelligence Scale for Children-Revised (WISC-R), the Rey Auditory Verbal Learning Test, the Stroop Colour Word Test, the Wisconsin Card Sorting Test, the Bender Gestalt Visual Motor Integration Test, the Rey Osterreith Complex Figure Test, the Trail Making Test, the Spatial Memory Task and various Drawing Tasks. Available norms (Lezak, Howieson, & Loring, 2004; Strauss, Sherman, & Spreen, 2006) that are commonly used by practitioners in South Africa are more appropriate for use with the White population of South Africa (Kanjee, 1999). Further, appropriate norms are also essential for neuropsychological assessment used in appropriate neurocognitive classification (S. J. Anderson, 2001). The problem is that when inadequate norms are used, healthy individuals may mistakenly be deemed cognitively impaired. Such misdiagnosis may lead to needless treatment or therapeutic neglect (Anderson, 2001; Mitrushina, et al., 2005; Skuy, Schutte, Fridjhon, & O'Carroll, 2001; Strauss, et al., 2006).

The use and results of neuropsychological tests are confounded by the effects of race or ethnicity, age, gender and education (Collie et al., 1999; Snitz et al., 2009; T. N. Tombaugh, 2004; T.N. Tombaugh & Mc Intyre, 1992). As such the use of these tests in South Africa, with its diverse socio-cultural and linguistic population profile, poses many challenges (Jinabhai et al., 2004; Ngcobo & Pillay, 2008; Pillay, 2012). In a study on the WISC-IV for White and Coloured, Afrikaans, White English and Black Xhosa speaking Grade 7 children, aged 12 to 13 years, stratified for advantaged versus disadvantaged education, the results demonstrated that while language and ethnic variables reveal subtle effects on IQ test performance, quality of education has the most significant effect (Van Der Merwe, 2008).

In this paper we report on the memory tests data from a study conducted in an elderly residential setting in a large city (Ramlall, Chipps, Bhigjee, & Pillay, 2013) and provide

normative data for this cohort. The memory tests namely, the Rey Auditory Verbal Learning Test (Lezak et al., 2004; Strauss et al., 2006), Rey Complex Figure (Lezak et al., 2004), Narrative Prose Memory Test ((Lezak et al., 2004) and Digit Span (Wechsler, 1997b), are commonly used tests in the South African clinical and psycho-legal milieu. Yet adequate norms for the South African older adult do not exist. Practitioners predominantly rely on norms by Lezak et al. (2004), Strauss et al. (2006), Mitrushina et al. (1999) and Anderson, (2000).

Method

Procedure

The study consisted of three stages of cognitive assessments conducted sequentially at approximately 2-3 month intervals at the participants' residences. Participation was voluntary and permission to conduct the study was obtained from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal. In stage one a random sample (n= 302) of residents aged 60 years and older, with a minimum of 8 years of formal schooling, the ability to speak, read and write English and the ability to give written, informed consent was selected and screened for dementia using the Mini-Mental State Examination (MMSE), a subjective memory rating scale (SMRS) and an informant questionnaire, the Deterioration Cognitive Observee (DECO). The second stage involved a comprehensive clinical assessment of 140 participants from stage one. In the third stage participants from stage two had a battery of neuropsychological tests administered to them by two clinical psychologists who underwent intensive training by a senior clinical psychologist and were blind to the participants' performances in the screening and clinical stages of the larger study. The tests were administered, in one session, at the participants' residences.

Participants

Of the 140 participants offered testing, 118 participants agreed to be tested, two had died since stage two of the study and 20 refused or were unavailable. Of the 118 who had agreed, 117 completed the entire battery. One person was unable to complete any of the tests and was excluded. The average time for test completion of the neuropsychology battery was 1.35 (*SD* 0.5) hours [CI 95% 1.3-1.4] with a median of 1.26 hours.

The sample comprised 23 (19.7%) Asian (*M*=71.0; *SD* 7.0), 4 (3.4%) Black (*M*=73.8; *SD* 7.6), 35 (29.9%) Coloured (*M*=73.7; *SD* 7.4), and 55 (47.0%) White (*M*=76.0; *SD* 7.3). There were more Whites in the sample than the other groups with a significant difference between the White and Asian groups (*F* =2.7; *p*=0.05). Regarding age there were 37 (31.6%) in the 60-69 group, 52 (44.4%) in the 70-79 group, 23 (19.7%) in the 80-89 group and 5 (4.3%) in the 90+ group. The mean age was 74.2 (*SD* 7.5). There were significant differences in the mean ages of the different race groups with the White group being the oldest and the Asian group the youngest. English was the first language for 103 (88.0%) of the participants, followed by Afrikaans 6(5.1%), isiZulu 4(3.4%), and other languages 4(3.4%).

The education of the participants was as follows: 87 (74.4%) had 8-11 years, 20 (17.1%) had 12 years, 10 (8.5%) had >12 years of formal education. The mean years of education were 10.1(SD 2.2). There was no significant difference with education between the groups (*M*=75.5; *SD* 9.9; *F*=1.3; *p*=0.265). Eighty-two (70.1%) were male and 35 (29.9%) female. There was no significant gender difference between groups (*M*=74.4; *SD* 7.9; *t* = 0.4; *p*=0.737).

Instruments

The memory tests (which is the focus of this paper) included the: Rey Auditory Verbal Learning Test (Lezak et al., 2004; Strauss et al., 2006), Rey Complex Figure (Lezak et al., 2004), Narrative Prose Memory Test and Digit Span (Wechsler, 1997b).

Data was tested for normality and descriptive statistics for each test was calculated, including 95% confidence intervals, for the total group as well as by diagnostic categories of dementia, MCI and normal. Differences in means of tests were compared in the different genders, race groups and educational categories using Kruskall-Wallis tests for Independent Samples. Test means were also compared to international norms using 95% confidence intervals.

Results

One-way between-groups analysis of variance was conducted to explore the impact of diagnostic category on individual tests. Participants were divided into three groups: Dementia Group (n=9); MCI Group (n=30) and Control Group (healthy older adults) (n=78). The variance contributed by age, education, gender and race on each of the memory tests and subtests, both shared and unique, are presented in Table 1.

RVLT

Norms for the RVLT according to race, age, gender and education are found in Tables 2, 3 and 4. Significant mean score differences were found on Trial I, Trial III and Immediate Recall in the Control and MCI groups for Age, and on Trial III, Trial IV and Sum of I-V for Gender in the Control Group (see Table 2, 3, and 4). Considering Race, the lowest mean was

reported for Black participants (*M*=4.5 *SD* 0.6), followed by Whites (*M*=6.0, *SD* 2.1), Coloured (*M*=6.7, *SD* 2.5) and Asian (*M*=7.1, *SD* 2.7). Generally the data indicates that Black participants' scores are lower than the other groups (See figure 1). However, the low number of Black participants (n=4) limits the significance of this result. Age also affected performance. The mean performance score decreased with age, with the lowest means recorded in the 80-89 year old groups (Table 3). Significant gender differences in the mean scores were observed for the participants' performance on the Trial III, Trial V, and sum of Trial I to V. Males generally scored lower on all subtests of the RAVLT (See Table 3). While age, education, gender and race contributed to 15.5% of the variance in the score of RAVLT (sum I-IV) Age made the largest contribution (β=-.313, p=.001), but Gender (β=.219, p=.014) and Education (β=-.184, p=.041) also made a significant contribution.

< Insert Table1, 2, 3 and 4 here >

Narrative Memory

The norms for the Narrative Memory test for race, age, gender and education are found in Tables 2, 3 and 4. A significant result was obtained for age in the MCI group for delayed recall (see Table 3). The data shows a trend of Black participants scoring lower and White participants the highest especially in the Control group (Table 2). Performance declines with age (Table 3), males perform slightly better (Table 4) and performance increased with education (Table 5). There is a progressive decrease in performance from the Control to MCI and Dementia groups as well as between immediate recall and delayed recall for Race (see Fig 2).

Rey Complex Figure

The normative data for the Rey Complex Figure Test is found in Tables 2, 3 and 4.

Significant differences were found for gender in the Control Group for immediate recall ($p<0.032$) with males scoring higher than females – see Table 3. Approaching significance, a similar trend is observed on delayed recall as well. Although not significant, performance on the RCF is influence by Race (see Table 4 and Figure 5).

Digit Span

Tables 2, 3 and 4 present the norms for the Digit Span Test. Significant differences were found in the mean scores for Race in the Control Group (Table 2). Black participants scored significantly lower in Digit Span forward (*M*=6.5, *SD* 0.7) and Digit Span total (*M*=9.5, *SD* 0.7). While a pattern of general decline was demonstrated with age, the >90 group performed better than the other groups (Figure 10). Higher education also influenced performance (Figure 12)

DISCUSSION

Data from a South African older adult study on dementia was used to establish norms for the Rey Auditory Verbal Learning Test, Rey Complex Figure, Narrative Prose Memory Test and Digit Span. Means and Standard Deviations for Race, Age, Gender and Education are presented for healthy older adults as well as those with MCI and Dementia.

On all of the memory tests Black participants scored lower compared to the other race groups (See Figures 1, 2, 5 and 9). This pattern is consistent in both the verbal and non-verbal tests. Although the number of black participants in the study were low, the authors

believe that this trend is consistent with observations made in clinical practice and is consistent with another study conducted by one of the authors (Pillay, 2008). Comparing these norms to those currently in use, on the RAVLT the mean (sum of Trial 1-5) for the Black (Control Group) in this study is 8.71 points higher than available norms from a similar study in KwaZulu-Natal (S. J. Anderson, 2000) and the mean is 10-12 points lower than western norms (Strauss et al., 2006). On RCF and Digit span these norms are similar to Western norms (Strauss et al., 2006; Wechsler, 1997a) with a variation of ± 1 mean point. The observation of race impacting on the performance of these tests support the existing view elsewhere that 'neurologically normal African Americans consistently earn lower scores than Caucasians on most neuropsychological tests' (Fillenbaum, Huber, & Taussig, 1997; Gladsjo et al., 1999; Lucas et al., 2005; Manly et al., 1998; Manly, Jacobs, Touradji, Small, & Stern, 2002; Moering, Schinka, Mortimer, & Graves, 2004; Pillay, 2008). However this has particular importance within the South African context. In addition to the issues raised earlier, such as, inadequate norms can lead to misinterpretation and misdiagnosis (Steinberg et al., 2005), leading to healthy individuals being mistakenly deemed cognitively impaired, resulting in needless treatment or therapeutic neglect (S. J. Anderson, 2001; Mitrushina et al., 1999; Skuy et al., 1999; Strauss et al., 2006), other critical issues must be considered. Given the oppression, domination and violation of human rights by the White minority in the country under the apartheid system, provision of an equitable health care and the rights of all people in the country is of critical concern (Constitution of the Republic of South Africa). In South Africa the majority population (79%) are Black, 9% Coloured, 9% White, and 2% Asian or Indian (Alexopoulos et al., 2009). The languages spoken vary with 22.7% home language being isiZulu, 16% isiXhosa 36.7% various other African languages. Afrikaans is the home language of 13.6% and

English 9%. Hence the availability of appropriate norms for such a diverse population group is critical.

The date shows that the RAVLT (Trial I, III and delayed recall) for the Control Group and MCI, Narrative Memory (MCI Group delayed) and Digit Span (MCI Group backward) were significantly affected by age. The significant change occurred in the 80 to 89 age range for RAVLT and Narrative Memory. The data support the trend that there is a decline in performance with age in the Control, MCI and Dementia Groups. These results are consistent with other studies indicating that neuropsychology tests are effective in detecting decline in aging (Holtzer et al., 2008). The exception was in the ≥90 range. The small number in this group (n=5) may have contributed to this variation from the trend.

The RAVLT Trial I, Trail III and Trial IV (Control Group) and RCF Control Group Recall were significantly affected by gender. On the Narrative memory females performed better whereas on the RCF Males performed better. Unlike the existing view that there are no gender effects in normal subjects (Mitrushina et al., 1999) this study shows that gender affects performance and this varies with tests.

There were no significant differences attributed to education. This could be due to the level of education in the sample. All participants had eight years and more of formal education.

CONCLUSION

The importance of applying appropriate norms, when using and interpreting neuropsychological assessments, cannot not be overemphasised. Yet many clinicians in South

African continue to use normative data that are not explicitly derived for the groups that they work with. This is especially important given the multicultural context and the history of age, education, gender and race inequalities that exist. This study is one of the first to provide norms for an older South African adult population. These norms will be useful in guiding the correct interpretation of neuropsychological test results in the local multi-ethnic setting contributing to better diagnosis and intervention.

Limitations

One limitation of the study is the relatively small sample size with particularly low numbers of Blacks and dementia cases. The study is also limited in terms of generalizability as it was conducted in only one metropolitan area in South Africa and is not representative of the other cities and provinces in the country.

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Declaration of conflicting interests

The authors declare that they do not have any conflict of interest.

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Table 1: Variance contributed by gender, race, education and age

Tests	R^2	Gender		Race		Education		Age		F	Sig
		β	%	β	%	β	%	β	%		
RAVLT											
Trial I	.058	.127	1.6	.094	.8	.179	3	-.221	4.7	2.790	.030*
Trial II	.053	.133	1.7	.069	.4	.159	2.4	-.228	5	2.622	.039
Trial III	.119	.202	4	.029	.07	.155	2.3	-.327	10.2	4.197	.001**
Trial IV	.057	.156	2.4	.035	.1	.119	1.3	-.250	6	2.744	.032*
Trial V	.142	.253	6.3	.036	.1	.168	2.7	-.327	10.2	8.811	.000**
Sum I-V	.125	.219	4.7	.041	.1	.184	3.2	-.313	9.4	5.131	.001**
Recall	.060	.097	.9	.006	.003	.192	3.5	-.250	6	2.866	.026*
Delayed Recall	.088	.182	3.2	.082	.6	.190	3.4	-.254	6.1	3.781	.006**
TMT-A	.043	-.124	1.5	.146	2	-.034	.1	.234	5.2	2.283	.065
TMT-B	.062	-.027	.07	.110	1.1	-.139	1.8	.280	7.5	2.288	.026*
Narrative Memory											
RECALL	.005	-.033	.1	-.149	2.1	.159	1.1	-.054	.3	1.159	.333
DELAY	.023	-.062	.4	-.185	3.2	.084	.7	-.121	1.4	1.690	.157
RCF											
COPY	-.020	.008	.004	-.088	.7	-.035	.1	.073	.5	.440	.780
RECALL	.087	-.259	.6	-.010	.01	.116	1.3	-.170	2.8	3.748	.007
DELAYED	.107	-.222	4.8	.053	.3	.130	1.6	-.241	5.5	4.491	.002**
DIGIT SPAN											
FORWARD	.091	.059	.3	-.308	8.8	.091	.8	.034	.1	3.910	.005**
BACKWARD	.052	-.014	.01	-.218	4.5	.156	2.3	-.005	.001	2.593	.040*
TOTAL	.104	.037	.1	-.316	9.4	.127	1.5	.017	.03	4.357	.003**

Note: β = standardised coefficients. %= squared part correlations multiplied by 100 to derive a unique percentage for each variable. Total % variance for all variables may be calculated by multiplying R^2 by 100.
* p<0.5 ** p<0.1

Table 2 Performance on Memory Tests by Race

		Race Mean (SD)					K [a]	p value
		Asian (n=23)	Black (n=4)	Coloured (n=35)	White (n=55)	All (N=117)		
RAVLT								
Control Group	Trial I	4.9(2.0)	4.0(1.4)	5.0(2.0)	4.6(1.6)	4.8(1.8)	0.7	0.865
	Trial II	7.3(2.8)	6.0(0)[b]	7.1(2.9)	6.5(1.9)	6.8(2.4)	5.1	0.165
	Trial III	8.3(2.8)	6.0(0)	8.1(3.1)	7.7(2.3)	7.9(2.6)	2.1	0.546
	Trial IV	8.8(2.7)	7.8(0.7)[b]	8.9(3.2)	8.4(2.7)	8.6(2.8)	0.5	0.915
	Trial V	9.6(3.0)	9.5(0.7)	9.0(3.0)	8.9(2.9)	9.1(2.9)	0.8	0.839
	Sum I-V	39.0(11.9)	32.0(1.4)	37.8(12.0)	36.4(10.7)	37.3(11.1)	1.3	0.739
	Recall	7.2(3.8)	3.0(4.2)	6.8(3.7)	6.5(3.4)	6.6(3.6)	2.0	0.565
	Delayed recall	7.3(3.7)	4.5(6.4)	6.2(43)	5.3(3.9)	6.0(4.0)	3.0	0.390
MCI Group	Trial I	4.4(2.3)	4.0(0)	4.5(2.1)	3.8(2.1)	4.2(2.0)	0.8	0.840
	Trial II	6.6(2.4)	5.0(0)	6.1(1.7)	5.3(2.1)	5.8(1.9)	2.4	0.494
	Trial III	7.2(3.7)	5.0(0)	7.4(2.5)	6.3(2.1)	6.9(2.5)	3.1	0.382
	Trial IV	7.2(3.7)	6.0(0)	7.1(1.8)	6.9(3.0)	7.0(2.5)	0.6	0.892
	Trial V	8.6(4.0)	7.9(0)	7.8(2.4)	7.4(2.9)	7.7(2.8)	1.8	0.607
	Sum I-V	34.0(15.0)	25.0(0)	32.8(9.6)	29.6(10.9)	31.6(10.7)	2.0	0.580
	Recall	5.6(4.0)	2.0(0)	6.2(2.7)	5.1(3.1)	5.5(3.0)	3.0	0.392
	Delayed Recall	6.6(3.9)[b]	4.0(0)	5.4(2.1)	5.2(3.5)	5.0(3.0)	1.6	0.655
Dementia Group	Trial I	-	4.0(0)	-	3.3(2.0)	3.3(1.9)	0.04	0.844
	Trial II	-	5.0(0)	-	4.5(1.6)	4.6(1.5)	0.2	0.692
	Trial III	-	4.0(0)	-	5.4(1.7)	5.2(1.6)	1.0	0.321
	Trial IV	-	5.0(0)	-	5.6(2.4)	5.6(2.2)	0.3	0.556
	Trial V	-	7.0(0)	-	5.3(2.4)	5.4(2.4)	1.0	0.321
	Sum I-V	-	25.0(0)	-	24.0(7.4)	24.1(7.0)	0.2	0.697
	Recall	-	2.0(0)	-	3.3(3.1)	3.1(2.9)	0.2	0.692
	Delayed Recall	-	4.0(0)	-	2.4(2.9)	2.6(2.7)	0.2	0.684
NARRATIVE MEMORY								
Control Group	Recall	6.3(4.3)	6.5(2.1)	7.1(4.4)	9.7(4.8)	8.1(4.7)	7.4	0.061
	Delay	5.7(4.2)	5.0(0)	6.0(4.2)	8.0(5.1)	6.8(4.7)	3.8	0.282
MCI Group	Recall	5.4(2.3)	4.8(0)[b]	7.2(2.8)	7.5(4.2)	7.1(3.3)	3.1	0.375
	Delay	4.2(4.2)	3.6 (0)[b]	5.8(3.5)	7.1(4.0)	5.8(3.9)	3.1	0.371
Dementia Group	Recall	-	3.0(0)	-	4.6(4.2)	4.6(4.2)	0.0	1.00
	Delay	-	2.0(0)	-	3.8(4.5)	3.6(4.2)	0.0	1.00
RCF								
Control Group	Copy	30.2(6.8)	32.0(1.4)	29.5(6.9)	31.6(6.4)	30.7(6.5)	2.1	0.558
	Recall	14.1(8.8)	18.8(6.7)	13.4(8.9)	13.1(6.6)	13.5(7.8)	1.4	0.717
	Delayed recall	15.7(7.7)	18.3(3.2)	15.0(8.1)	12.6(6.4)	14.1(7.2)	2.5	0.472
MCI Group	Copy	30.5(6.7)	16.0(0)	32.4(3.9)	56.5(94.5)	40.4(57.1)	2.7	0.420
	Recall	12.9(4.0)	5.5(0)	10.0(4.2)	11.0(7.0)	10.7(5.3)	2.6	0.461
	Delayed	12.8(5.5)	8.5(0)	9.8(5.1)	11.9(6.9)	11.0(5.7)	2.7	0.371
Dementia Group	Copy	-	6.0(0)	-	23.1(10.3)	21.2(11.1)	2.4	0.121
	Recall	-	2.5(0)	-	8.4(7.2)	7.7(7.0)	0.6	0.439
	Delayed	-	2.5(0)	-	6.8(7.6)	6.3(7.3)	0.2	0.697
DIGIT SPAN								
Control Group	Forward	8.7(1.9)	6.5(0.7)	8.1(1.6)	9.8(2.5)	9.0(2.3)	10.9	0.012*
	Backward	5.2(2.0)	3.0(0)	4.4(1.6)	5.4(2.0)	5.0(1.9)	7.3	0.062
	Total	13.9(3.5)	9.5(0.7)	12.5(2.7)	15.2(4.0)	14.0(3.7)	12.1	0.007*
MCI Group	Forward	7.6(0.5)	4.0(0)	8.1(2.0)	7.8(2.5)	7.8(2.1)	3.0	0.399
	Backward	4.4(0.9)	2.0(0)	4.1(1.4)	4.5(2.2)	4.2(1.7)	3.4	0.340
	Total	12.0(0.7)	6.0(0)	12.2(2.6)	12.9(4.5)	12.2(3.4)	3.0	0.384
Dementia Group	Forward	-	4.0(0)	-	9.0(1.1)	8.4(1.9)	2.6	0.109
	Backward	-	2.0(0)	-	4.0(1.1)	3.8(1.2)	2.0	0.159
	Total	-	6.0(0)	-	13.0(1.9)	12.2(2.9)	2.6	0.104

[a] Kruskall Wallis Independent Samples Test [b] adjusted mean

Table 3: Performance on Memory Tests by Age

		Mean (SD)					U	p value
		60-69 (n=37)	70-79 (n=52)	80-89 (n=23)	≥90 (n=5)	All		
RAVLT								
Control Group	Trial I	5.0(1.8)	4.8(1.7)	4.2(1.9)	5.0(0)	4.8(1.8)	0.7	0.577
	Trial II	7.0(2.6)	6.9(2.4)	5.7(1.9)	6.0(0)	6.8(2.4)	1.98	0.577
	Trial III	8.4(2.7)	8.0(2.3)	6.2(3.3)	8.0(0)	7.9(2.6)	3.8	0.279
	Trial IV	9.0(2.8)	8.7(2.7)	6.8(3.2)	9.0(0)	8.6(2.8)	4.08	0.253
	Trial V	9.5(3.2)	9.3(2.6)	7.7(3.0)	8.0(0)	9.1(2.9)	2.9	0.411
	Sum I-V	38.8(11.4)	37.7(10.4)	30.6(12.6)	36.0(0)	37.3(11.1)	3.2	0.369
	Recall	7.2(3.8)	6.5(3.3)	5.9(3.7)	0.0(0)	6.6(3.6)	3.98	0.263
	Delayed recall	6.6(4.0)	6.1(4.0)	4.1(3.7)	0.0(0)	6.0(4.0)	4.96	0.174
MCI Group	Trial I	5.6(1.8)	4.2(1.4)	3.1(2.0)	5.7(3.1)	4.2(2.0)	8.8	0.032*
	Trial II	7.2(1.6)	5.8(1.9)	4.9(1.6)	6.7(2.9)	5.8(1.9)	5.3	0.152
	Trial III	9.2(2.3)	7.1(1.8)	5.2(2.4)	7.7(3.1)	6.9(2.5)	8.2	0.043*
	Trial IV	8.2(1.9)	6.8(2.0)	6.2(2.5)	8.3(4.9)	7.0(2.5)	2.6	0.454
	Trial V	10.6(2.6)	7.2(1.6)	6.9(3.0)	7.7(4.5)	7.7(2.8)	5.9	0.116
	Sum I-V	40.8(8.7)	31.1(7.6)	26.3(10.5)	36.0(17.6)	31.6(10.7)	4.9	0.116
	Recall	7.8(3.3)	4.9(2.5)	4.3(2.8)	8.3(3.1)	5.5(3.0)	6.4	0.095
	Delayed recall	7.2(2.4)	3.9(1.9)	4.1(3.2)	8.3(3.2)	5.0(3.0)	9.7	0.021*
Dementia Group	Trial I		4.0(0)		3.3(2.0)	3.3(1.9)	0.04	0.844
	Trial II		5.0(0)		4.5(1.6)	4.6(1.5)	0.2	0.692
	Trial III		4.0(0)		5.4(1.7)	5.2(1.6)	1.0	0.321
	Trial IV		5.0(0)		5.6(2.4)	5.6(2.2)	0.3	0.556
	Trial V		7.0(0)		5.3(2.4)	5.4(2.4)	1.0	0.321
	Sum I-V		25.0(0)		24.0(7.4)	24.1(7.0)	0.2	0.697
	Recall		2.0(0)		3.3(3.1)	3.1(2.9)	0.2	0.692
	Delayed Recall		4.0(0)		2.4(2.9)	2.6(2.7)	0.2	.684
NARRATIVE MEMORY -								
Control Group	Recall	7.7(4.9)	8.8(4.5)	7.1(5.0)	5.0(0)	8.1(4.7)	1.8	0.611
	Delay	6.7(4.3)	7.6(4.7)	5.7(5.1)[b]	0.0(0)	6.8(4.7)	5.2	0.159
MCI Group	Recall	6.2(3.2)	6.9(3.4)	6.3(2.6)	12.0(1.0)	7.1(3.3)	7.5	0.059
	Delay	5.2(4.2)[b]	5.2(3.2)	4.5(3.4)	12.0(2.0)	5.8(3.9)	8.5	0.037*
Dementia Group	Recall		3.0(0)		4.2(4.2)	4.6(4.2)	0.0	1.00
	Delay		2.0(0)		2.8(4.5)	3.6(4.2)	0.0	1.00
RCF								
Control Group	Copy	30.4(6.4)	31.9(5.0)	27.3(11.0)	26.5(0)	30.7(6.5)	2.2	0.529
	Recall	14.3(7.5)	13.7(7.8)	11.2(8.8)	6.0(0)	13.5(7.8)	2.2	0.528
	Delayed	15.3(6.4)	14.3(7.6)	9.9(8.0)	9.0(0)	14.1(7.2)	3.7	0.290
MCI Group	Copy	32.8(4.0)	28.5(10.2)	61.4(98.1)	30.5(4.9)	40.4(57.1)	0.4	0.947
	Recall	11.3(4.3)	11.2(5.6)	8.9(5.8)	13.8(3.3)	10.7(5.3)	2.96	0.398
	Delayed	11.4(4.3)	11.2(5.6)	8.9(5.8)	13.8(3.3)	10.7(5.3)	3.5	0.318
Dementia Group	Copy		6.0(0)		23.1(10.3)	21.2(11.1)	2.4	0.121
	Recall		2.5(0)		8.4(7.2)	7.7(7.0)	0.6	0.439
	Delayed		2.5(0)		6.8(7.6)	6.3(7.3)	0.2	0.697
DIGIT SPAN								
Control Group	Forward	8.5(2.1)	9.1(2.3)	9.9(2.4)	13.0(0)	9.0(2.3)	5.1	0.161
	Backward	4.5(1.8)	5.4(2.1)	4.9(1.3)	6.0(0)	5.0(1.9)	4.6	0.203
	Total	13.1(3.5)	14.5(3.9)	14.8(3.0)	19.0(0)	14.0(3.7)	5.3	0.149
MCI Group	Forward	8.4(2.3)	7.1(2.0)	7.6(1.7)	10.0(2.6)	7.8(2.1)	4.0	0.259
	Backward	5.0(1.2)	3.6(1.2)	3.8(0.6)	7.0(3.5)	4.2(1.7)	9.9	0.019*
	Total	13.4(2.1)	11.2(3.0)	11.4(2.2)	17.0(6.1)	12.2(3.4)	6.5	0.092
Dementia Group	Forward		4.0(0)		9.0(1.1)	8.4(1.9)	2.6	0.109
	Backward		2.0(0)		4.0(1.1)	3.8(1.2)	2.0	0.159
	Total		6.0(0)		13.0(1.9)	12.2(2.9)	2.6	0.104

[a] Mann-Whitney U Test [b] adjusted mean *Significance p<.05

Table 4: Performance of Memory Test by Gender

		Mean (SD)				
		Male (n=82)	Female (n=35)	**All**	U[a]	P value
RAVLT						
Control	Trial I	4.6(2.1)	4.9(1.6)	4.8(1.8)	1.2	0.214
	Trial II	6.3(2.8)	7.1(2.2)	6.8(2.4)	1.9	0.060
	Trial III	7.1(3.0)	8.4(2.3)	7.9(2.6)	2.1	0.040*
	Trial IV	7.8(3.2)	9.1(2.5)	8.6(2.8)	1.9	0.057
	Trial V	7.9(3.3)	9.8(2.5)	9.1(2.9)	2.4	0.018*
	Σ I-V	33.3(12.5)	39.4(9.8)	37.3(11.1)	2.2	0.027*
	Recall	6.0(3.7)	7.0(3.5)	6.6(3.6)	1.4	0.173
	Delayed recall	4.9(3.8)	6.6(4.1)	6.0(4.0)	1.7	0.088
MCI	Trial I	3.7(2.1)	4.3(2.0)	4.2(2.0)	1.0	0.327
	Trial I	5.3(1.4)	6.0(2.1)	5.8(1.9)	0.9	0.369
	Trial III	5.9(2.4)	7.2(2.6)	6.9(2.5)	1.3	0.206
	Trial IV	6.4(2.0)	7.2(2.7)	7.0(2.5)	0.9	0.395
	Trial V	6.6(2.3)	8.0(2.9)	7.7(2.8)	1.4	0.140
	Σ I-V	27.9(9.6)	32.7(11.0)	31.6(10.7)	1.5	0.140
	Recall	5.1(1.8)	5.7(3.4)	5.5(3.0)	0.049	0.961
	Delayed recall	4.4(1.7)	5.1(3.3)	5.0(3.0)	0.5	0.585
Dementia	Trial I	1.0(0)	3.6(1.8)	3.3(1.9)	1.4	0.168
	Trial II	5.0(0)	4.5(1.6)	4.6(1.5)	0.4	0.692
	Trial III	4.0(0)	5.4(1.7)	5.2(1.6)	1.0	0.321
	Trial IV	5.0(0)	5.6(2.4)	5.6(2.2)	0.6	0.556
	Trial V	3.0(0)	5.8(2.3)	5.4(2.4)	1.2	0.233
	Σ I-V	18.0(0)	24.9(7.0)	24.1(7.0)	1.2	0.243
	Recall	3.0(0)	3.1(3.1)	3.1(2.9)	0.4	0.692
	Delayed recall		2.9(2.7)	2.6(2.7)	1.0	0.310
NARRATIVE						
Control	Recall	8.4(4.8)	7.9(4.7)	8.1(4.7)	0.4	0.712
	Delay	7.3(4.5)	6.6(4.8)	6.8(4.7)	0.7	0.503
MCI	Recall	6.7(2.9)	7.2(3.5)	7.1(3.3)	0.1	0.921
	Delay	5.0(2.8)	6.1(4.2)	5.8(3.9)	0.5	0.587
Dementia	Recall	2.0(0)	4.8(4.1)	4.4(4.0)	0.8	0.429
	Delay	1.7(0)[b]	3.0(4.2)	3.6(4.2)	0.8	0.418
RCF						
Control	Copy	31.4(6.9)	30.3(6.3)	30.7(6.5)	1.0	0.314
	Recall	16.2(8.7)	12.1(6.9)	13.5(7.8)	2.1	0.032*
	Delayed	16.2(7.8)	13.0(6.7)	14.1(7.2)	1.9	0.064
MCI	Copy	31.9(4.1)	42.9(65.3)	40.4(57.1)	0.1	0.882
	Recall	12.9(5.4)	10.0(5.2)	10.7(5.3)	1.0	0.302
	Delayed	13.1(7.2)	10.4(5.2)	11.0(5.7)	0.7	0.507
Dementia	Copy	34.0(0)	19.6(10.8)	21.2(11.1)	1.5	0.121
	Recall	16.0(0)	6.7(6.8)	7.7(7.0)	1.1	0.245
	Delayed	13.0(0)	5.5(7.3)	6.3(7.3)	1.2	0.243
DIGIT SPAN						
Control	Forward	8.7(2.2)	9.2(2.3)	9.0(2.3)	1.0	0.320
	Backward	5.0(2.0)	5.0(1.9)	5.0(1.9)	0.1	0.889
	Total	13.7(3.8)	14.2(3.6)	14.0(3.7)	0.8	0.438
MCI	Forward	7.4(1.7)	7.9(2.2)	7.8(2.1)	0.9	0.384
	Backward	4.1(0.7)	4.3(1.9)	4.2(1.7)	0.2	0.817
	Total	11.6(1.8)	12.4(3.7)	12.2(3.4)	1.0	0.310
Dementia	Forward	9.0(0)	8.4(2.1)	8.4(1.9)	0.0	1.00
	Backward	3.0(0)	3.9(1.2)	3.8(1.2)	0.8	0.421
	Total	12.0(0)	3.9(1.2)	3.8(1.2)	0.6	0.542

a Mann-Whitney U Test [b] adjusted mean *Significance p<.05

Table 5: Performance on Memory Test by Education

		Mean (SD)				K	p value
		8-11 (n=87)	12 (n-20)	>12 (n=10)	**Total**		
RAVLT							
Control Group	Trial I	4.8(1.8)	4.2(1.7)	5.6(1.4)	4.8(1.8)	3.4	0.181
	Trial II	6.8(2.4)	6.3(2.2)	8.0(3.1)	6.8(2.4)	1.3	0.527
	Trial III	7.8(2.4)	7.7(3.1)	9.0(3.4)	7.9(2.6)	0.7	0.704
	Trial IV	8.7(2.5)	8.1(3.3)	9.0(4.0)	8.6(2.8)	0.4	0.816
	Trial V	9.0(2.8)	9.0(3.5)	10.3(2.7)	9.1(2.9)	1.1	0.564
	Sum I-V	37.0(10.1)	36.1(13.5)	41.9(13.9)	37.3(11.1)	0.8	0.666
	Recall	6.3(3.6)	7.3(3.4)	8.0(4.2)	6.6(3.6)	1.5	0.481
	Delayed recall	5.8(3.9)	5.6(4.0)	8.0(4.9)	6.0(4.0)	1.5	0.479
MCI	Trial I	4.0(1.7)	5.0(3.0)		4.2(2.0)	0.7	0.410
	Trial II	5.7(1.9)	6.3(2.4)		5.8(1.9)	0.1	0.712
	Trial III	7.0(2.4)	6.5(3.4)		6.9(2.5)	0.4	0.547
	Trial IV	6.9(2.2)	7.3(3.9)		7.0(2.5)	0.4	0.542
	Trial V	7.9(2.6)	7.0(3.7)		7.7(2.8)	0.6	0.432
	Sum I-V	31.5(9.5)	32.2(15.8)		31.6(10.7)	0.2	0.640
	Recall	5.6(3.1)	5.3(3.0)		5.5(3.0)	0.1	0.754
	Delayed recall	4.8(2.9)	5.7(3.5)		5.0(3.0)	0.1	0.753
Dementia	Trial I	2.9(1.9)		5.0(0)	3.3(1.9)	2.2	0.137
	Trial II	4.4(1.3)		5.0(2.8)	4.6(1.5)	0.09	0.765
	Trial III	4.9(1.7)		6.5(0.7)	5.2(1.6)	1.8	0.176
	Trial IV	4.9(2.0)		8.0(1.4)	5.6(2.2)	3.7	0.054
	Trial V	4.9(1.9)		7.5(3.5)	5.4(2.4)	1.1	0.293
	Sum I-V	21.9(6.0)		32.0(2.8)	24.1(7.0)	3.1	0.078
	Recall	2.4(2.1)		5.5(4.9)	3.1(2.9)	0.8	0.370
	Delayed recall	2.3(2.4)		3.5(4.9)	2.6(2.7)	0.2	0.645
NARRATIVE							
Control	Recall	7.8(4.6)	8.8(4.6)	8.9(5.9)	8.1(4.7)	0.6	0.735
	Delay	6.6(4.5)	7.1(4.8)	8.1(5.6)	6.8(4.7)	0.8	0.680
MCI	Recall	6.9(3.1)	8.0(4.3)		7.1(3.3)	0.5	0.481
	Delay	5.6(3.7)	6.8(4.7)		5.8(3.9)	0.2	0.639
Dementia	Recall	3.4(1.9)		8.0(8.5)	4.4(4.0)	0.4	0.550
	Delay	3.1(3.8)		5.0(7.1)	3.6(4.2)	0.2	0.646
RCF							
Control	Copy	30.3(6.0)	31.4(8.1)	31.9(8.0)	30.7(6.5)	3.4	0.184
	Recall	13.1(7.6)	14.8(8.8)	14.4(7.6)	13.5(7.8)	0.9	0.633
	Delayed	14.0(6.0)	13.6(9.3)	15.7(8.2)	14.1(7.2)	0.1	0.956
MCI	Copy	42.4(63.9)	32.2(5.3)		40.4(57.1)	0.8	0.374
	Recall	10.0(5.4)	13.5(4.3)		10.7(5.3)	1.9	0.058
	Delayed	10.1(5.6)	14.8(5.0)		11.0(5.7)	3.6	0.058
Dementia	Copy	18.3(11.0)		31.3(1.8)	21.2(11.1)	1.4	0.242
	Recall	6.5(5.0)		12.0(14.1)	7.7(7.0)	0.1	0.770
	Delayed	4.9(4.7)		11.3(15.2)	6.3(7.3)	0.3	0.557
DIGIT SPAN							
Control	Forward	8.8(2.2)	9.6(2.3)	9.0(2.3)	9.0(2.3)	1.96	0.374
	Backward	4.8(1.9)	5.5(1.6)	5.5(2.8)	5.0(1.9)	2.4	0.306
	Total	13.7(3.7)	15.1(3.1)	14.5(4.7)	14.0(3.7)	2.9	0.237
MCI	Forward	7.5(2.0)	8.7(2.4)		7.8(2.1)	0.9	0.331
	Backward	4.0(1.2)	5.2(2.9)		4.2(1.7)	0.4	0.550
	Total	11.8(2.7)	13.8(5.3)		12.2(3.4)	0.3	0.564
Dementia	Forward	8.1(2.1)		9.5(0.7)	8.4(1.9)	0.8	0.363
	Backward	3.4(1.1)		5.0(0)	3.8(1.2)	3.3	0.068
	Total	11.6(3.0)		14.5(0.7)	12.2(2.9)	2.9	0.091

[a] Kruskall Wallis Independent Samples Test *Significance p<.05

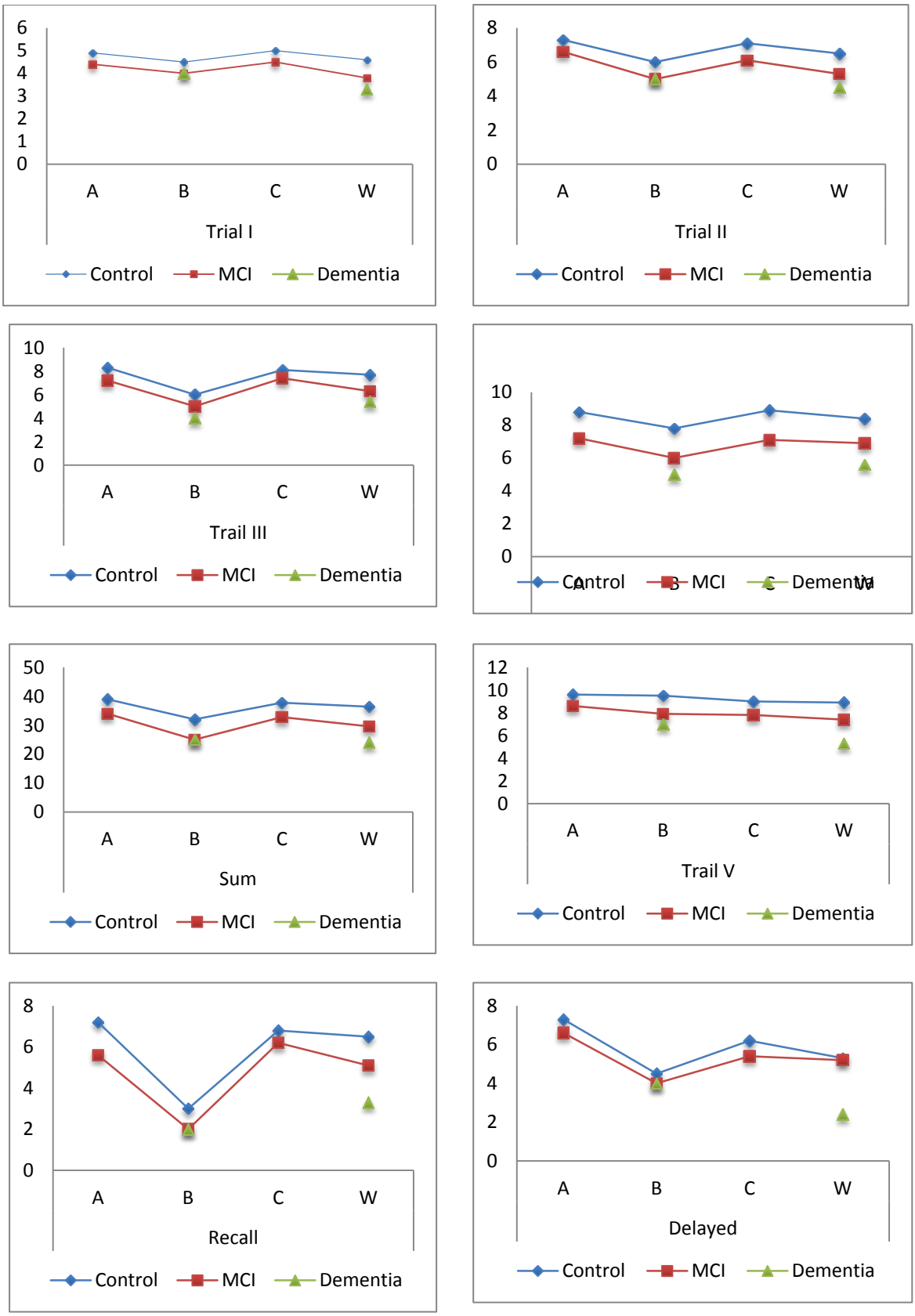

Figure 1. Performance of the Control, MCI and Dementia groups on the RAVLT by Race

Narrative Memory

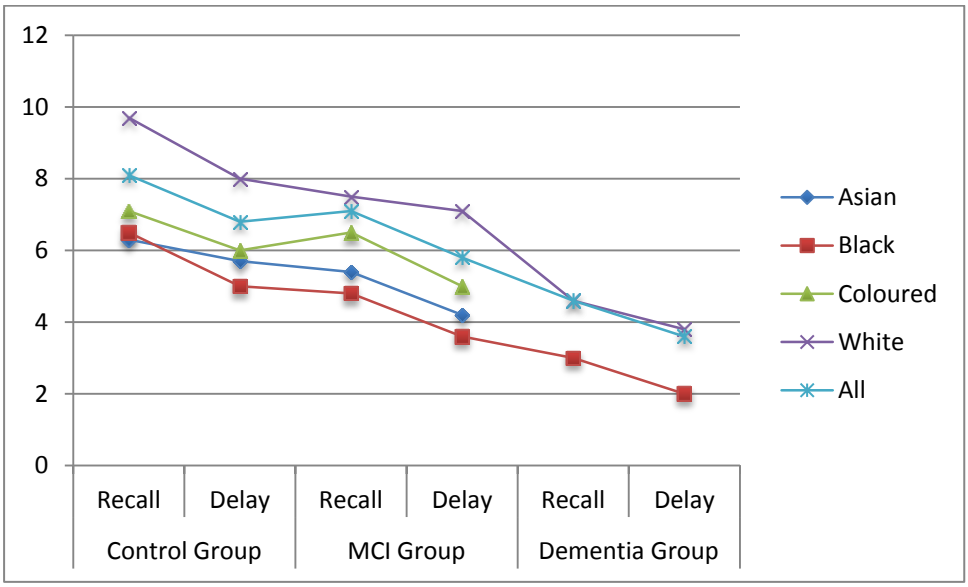

Figure 2 Race

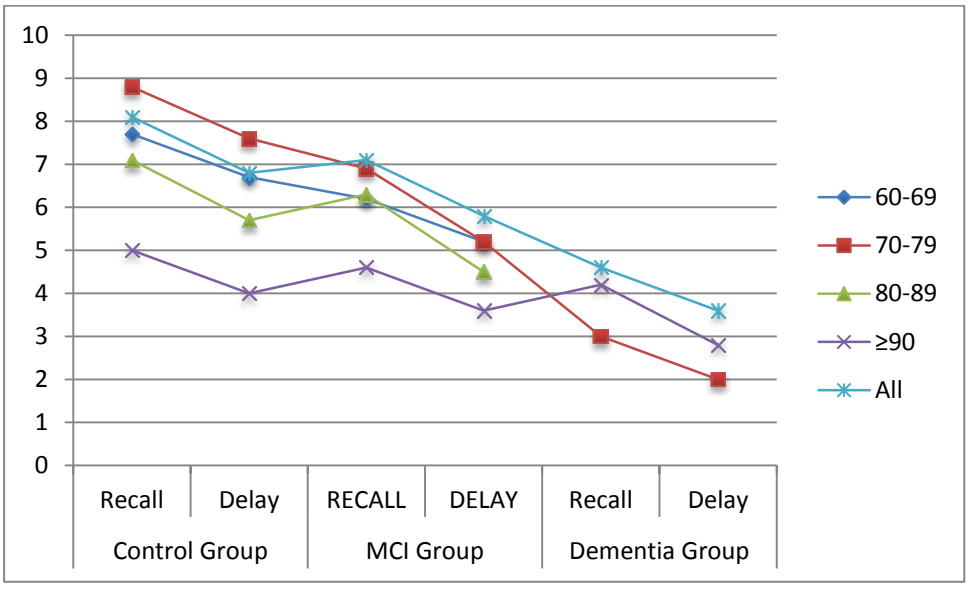

Figure 2 Age

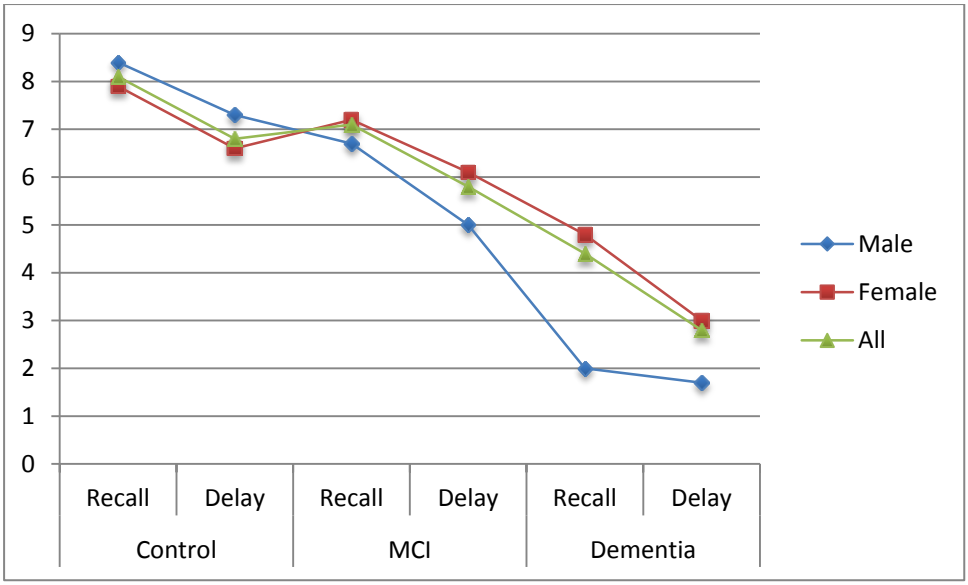

Figure 3: Gender

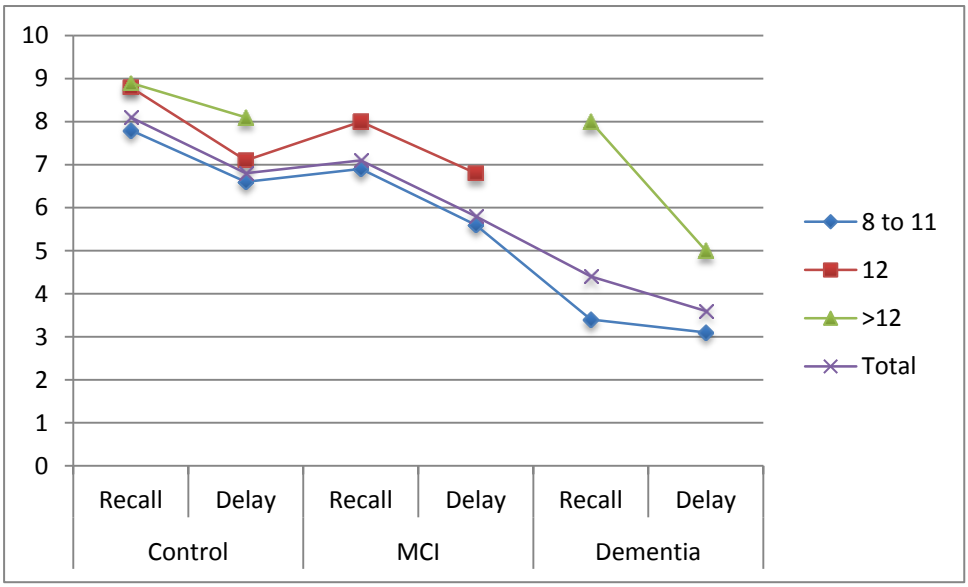

Figure 4: Education

RCF

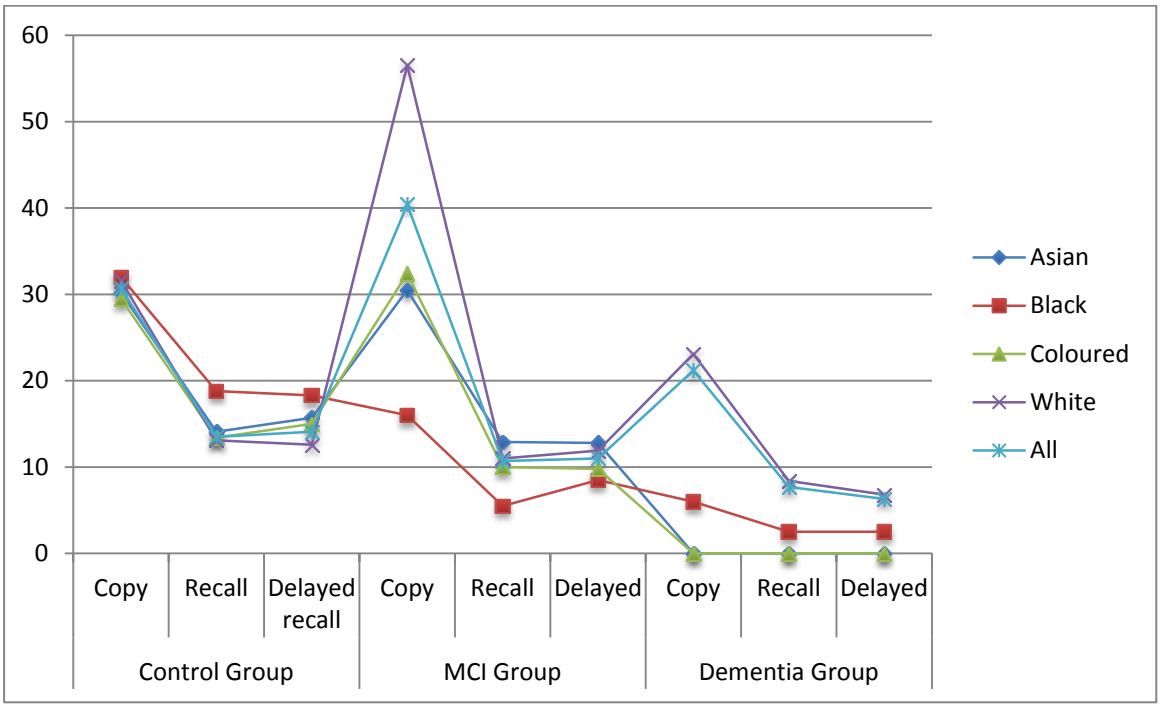

Figure 5: Race

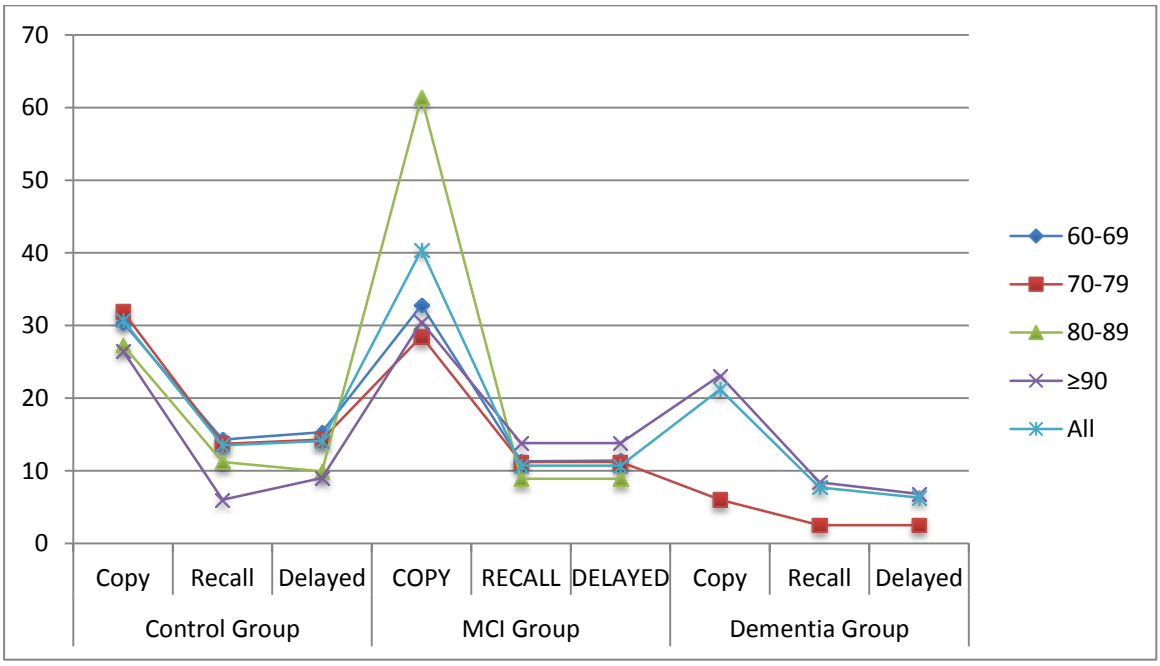

Figure 6 Age

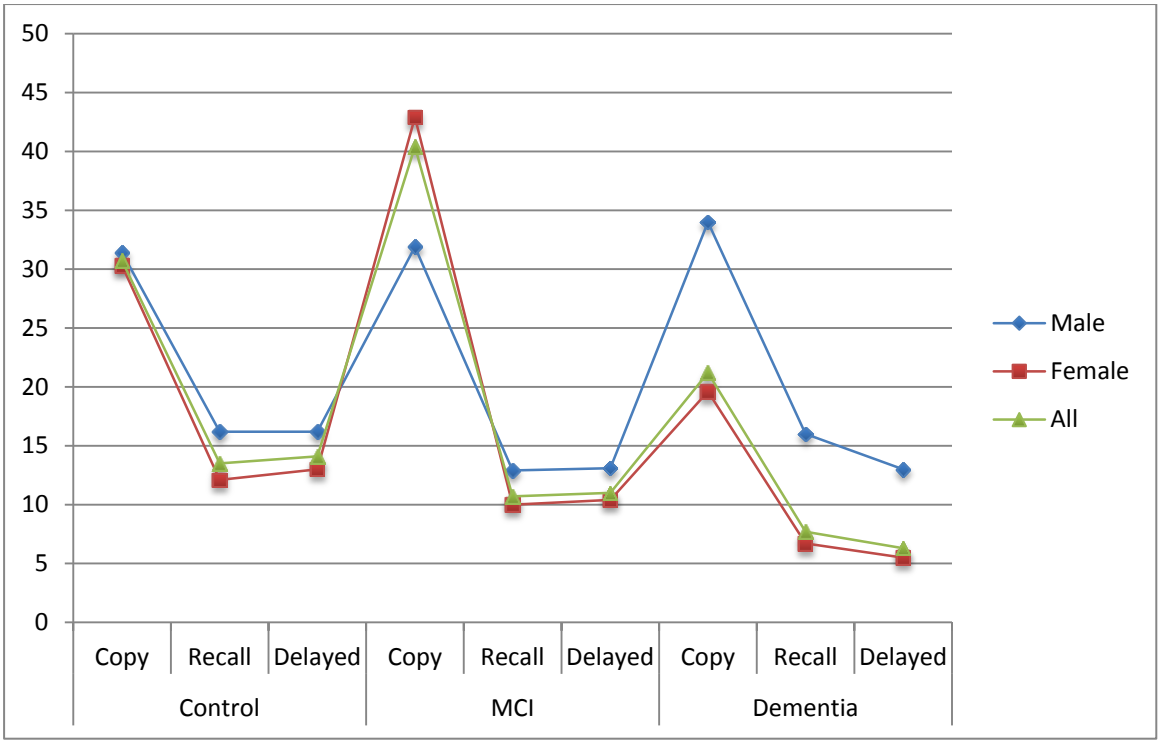

Figure 7 Gender

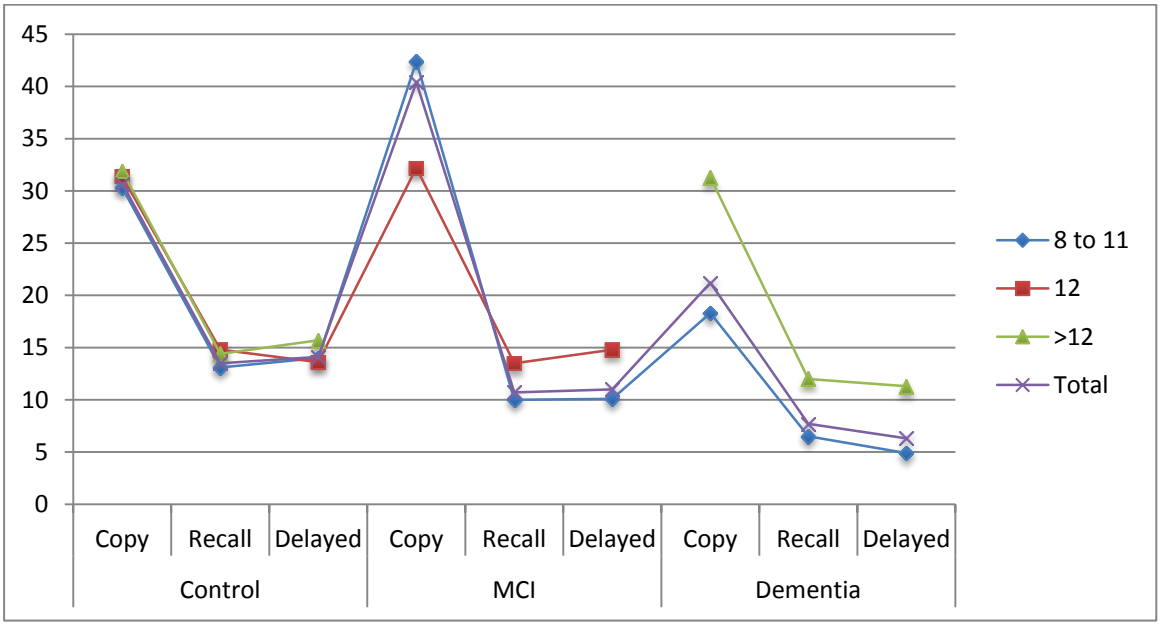

Figure 8 Education

Digit Span

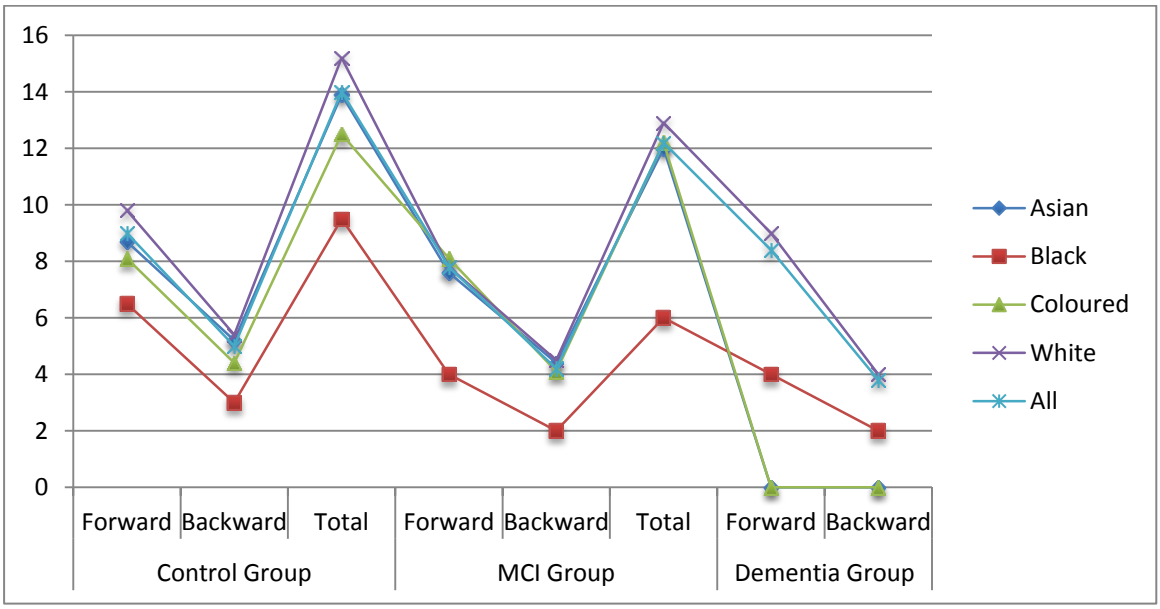

Figure 9 Race

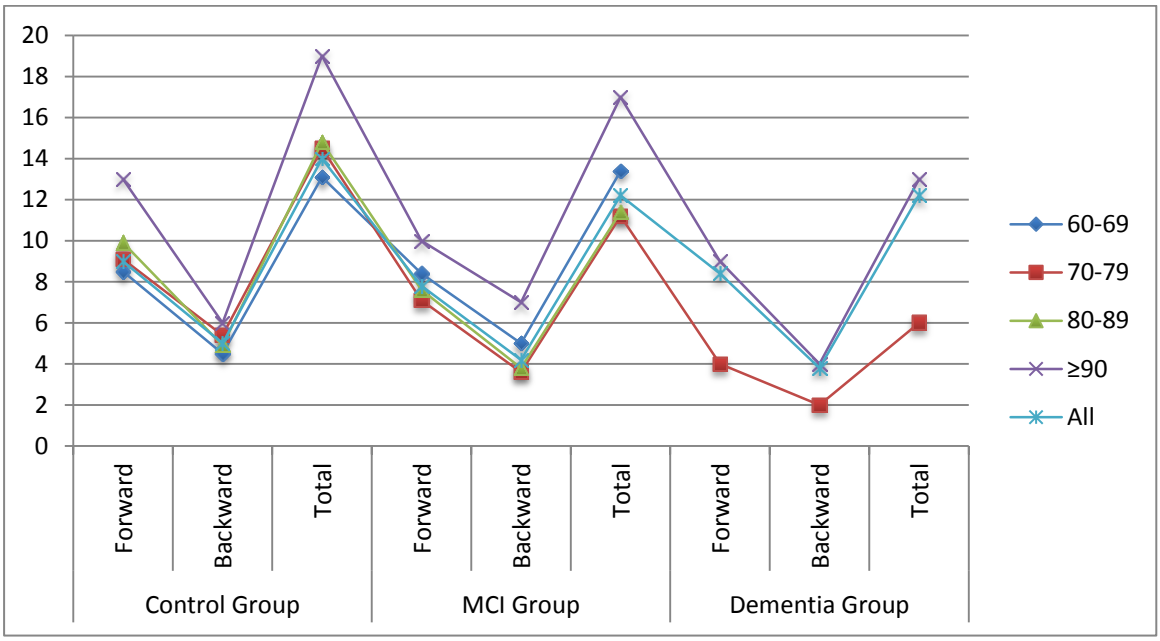

Figure 10 Age

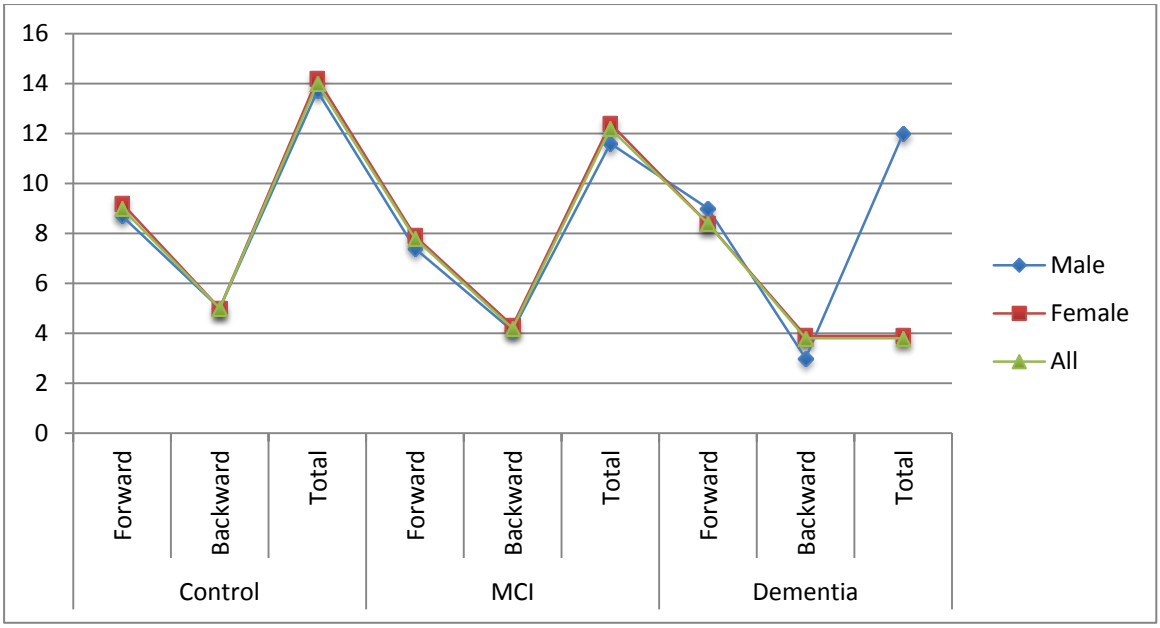

Figure 11 Gender

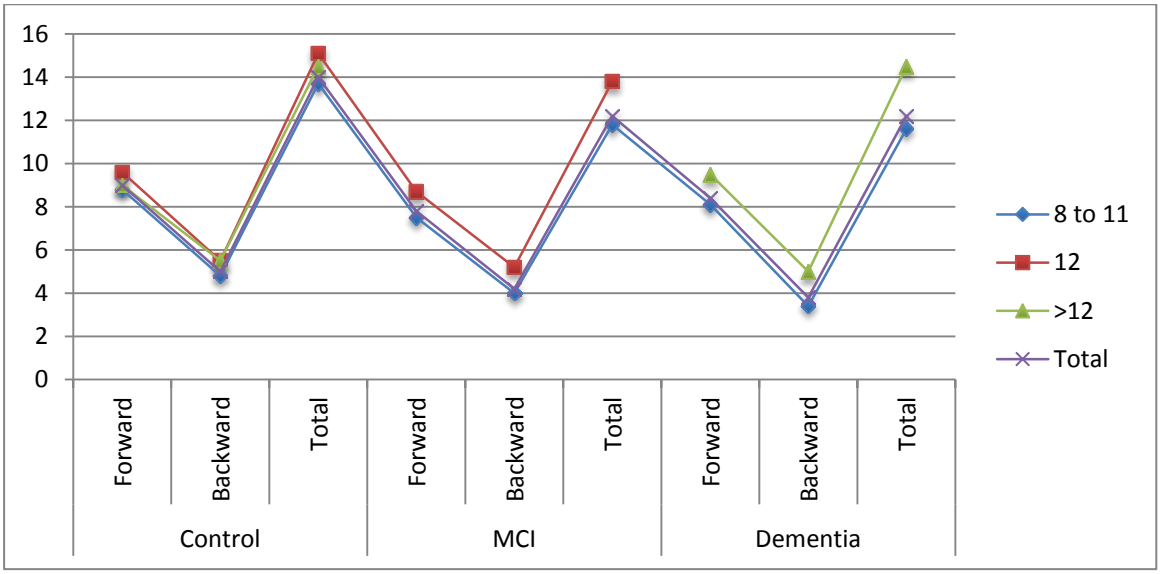

Figure 12 Education

7.7 Paper 5

Durban dementia study: Norms for Clock Drawing Test, Controlled Word Association Test, Digit Symbol Test, Luria Hand Sequencing and Trail Making Test for the elderly

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Abstract

An upsurge in the prevalence of dementia, especially in lower and middle income countries, is expected. Due to the limitations of existing brief cognitive screening tools, the distinction between normal ageing and early dementia is often a challenge and requires a more comprehensive assessment of cognition through the use of specific neuropsychological tests. However, accurate interpretation of these tests depends on the availability of population-specific norms and an appreciation of the impact of demographic variables on test performance. This paper attempts to address this dearth of availability of norms. A sample of 117 elderly participants from a group of residential homes for the elderly was administered a battery of neuropsychological tests by clinical psychologists. Normative data for the Clock Drawing Test, COWAT, Digit Symbol and Luria Hand Sequencing test and Trail Making Test are provided. The effects of age, education, gender and race on test performance is discussed.

Keywords: Clock Drawing Test, Controlled Oral Word Association Test, Digit Symbol, Luria Hand Sequencing Test, Trail Making Test, dementia

Introduction

This paper is the second of two that provides normative data on cognitive screening and neuropsychological assessments, of older adults, in a multicultural setting. The emerging clinical issues as longevity increases and the challenges associated with screening and evaluating an ageing society were discussed in the first paper on normative data for a battery of commonly used memory tests. Cognitive evaluation of elderly is often based on brief screening instruments that are limited by their lack of comprehensiveness (Welsh et al., 1994) and are confounded by factors such as age, cultural biases, language, gender, education and floor and ceiling effects. (Collie, Shafiq-Antonacci, Maruff, Tyler, & Currie, 1999; Ganguli et al., 1991; Mitrushina, Boone, & D'Elia, 1999). In addition, while a large number of neuropsychological tests are available and widely used in South Africa the utility of these instruments are limited by the absence of population-specific norms for representative samples of elderly (Ganguli et al., 2010).

Clock Drawing Test

The Clock Drawing Test (CDT) has been described as the ideal cognitive screening test due to its ease of administration and scoring. It is widely used by many clinicians. The CDT has the ability to assess a range of cognitive abilities and has good psychometric properties (Royall, Cordes, & Polk, 1998; Schramm et al., 2002; Shulman, 2000). The CDT has a .5 correlation with the Mini-Mental State Examination (Shulman, 2000) and has also shown moderate sensitivity and specificity in detecting executive dysfunction in patients with a normal MMSE (Juby, Tench, & Baker, 2002). Supporting its utility in dementia assessment, several studies (Mendez, Ala, & Underwood, 1992; Rouleau, Salmon, Butters, Kennedy, & McGuire, 1992; Royall et al., 1998) confirm earlier findings

of the test in differentiating normal from pathological cognitive decline (Cahn et al., 1996; Tuokko, Hadjistavropoulos, Miller, & Beattie, 1992). In the current study the CDT had an AUC of 0.732, sensitivity of 44.4% and specificity of 88.9% (Ramlall, Chipps, Bhigjee, & Pillay, 2013). Given this background the CDT is therefore considered a very useful screen test in under resourced and overburdened environments such as South Africa and establishing norms for the older adults can be extremely useful.

Cognitive Tests

In addition to the memory test presented in the previous paper, other common cognitive tests that are routinely used in South Africa are the Controlled Word Association Test (Lezak, Howieson, & Loring, 2004), Digit Symbol Test (Wechsler, 1997), Luria Hand Sequencing (Luria, 1980; Weiner, Hynan, Rossetti, & Falkowski, 2011) and the Trail Making Test A and B (Lezak et al., 2004; Reitan, 1955; Strauss, Sherman, & Spreen, 2006). The Controlled Oral Word Association Test (COWAT) is a simple three-word naming trials of letters (F-A-S) and animals measure and is a useful component of any neuropsychological battery as it is able to detect changes in word association fluency often found in various cognitive disorders (Sumerall, Timmons, James, Ewing, & Oehlert, 1997). Performance on the test is affected by age, gender, ethnicity, language and education (B.A. Steinberg, Bieliauskas, Smith, & Ivnik). Regarding the effects of age on phonemic word list generation, performances typically show that, older examinees produce fewer responses (Cauthen, 1978) and commit more errors (Ruff, Light, Parker, & Levin, 1997; Sumerall et al., 1997) than younger examinees. Gender effects suggest the view that females perform moderately better (Cauthen, 1978). Ethnicity and language were

associated with different numbers of responses on the semantic (animals) word list generation task (Kempler, Teng, Dick, Taussig, & Davis). Education was found to correlate positively with task performances (B. A. Steinberg, Bieliauskas, Smith, Langellotti, & Ivnik, 2005)

The Digit Symbol Test is often considered a quick screening instrument for neuropsychological dysfunction where an impairment of any contributing ability will yield a low score (Joy, Kaplan, & Fein, 2004). The two key functions of the test are processing speed and memory. The test is considered more interpretable when administered to older persons or those who are motorically slowed (Kaplan, Fein, Morris, & Delis, 1991). Both age and education effects contribute to the performance on this test with age effect most prominent (Joy, Fein, Kaplan, & Freedman, 2000; Joy et al., 2004; Lezak et al., 2004). Older adults show more variability and women outperform men on this test (Lezak et al., 2004). The test re-test reliability is high with stability coefficients in the .83 to .86 range (Lezak et al., 2004).

The Luria Hand Sequencing is one of the simplest nonverbal tests of executive function that can be readily performed by clinicians. Impaired performance in the Luria test is rare in persons with normal cognition and occurs in < 10% of persons with MCI. Thus, it can be helpful in distinguishing normal and MCI subjects from Alzheimer's disease and fronto-temporal dementia (Weiner et al., 2011). The test may be useful cross-culturally because it is non-verbal and its performance is unaffected by education and only minimally by age. The test may also help to distinguish psychiatric illness from dementing illnesses (Weiner et al., 2011).

The Trail Making Test (TMT) is an assessment of attention, speed, visuomotor tracking and mental flexibility. This is a popular test due to the wide range of cognitive processes that are measured. Normative data on this test vary considerable depending on the characteristics of the sample (Mitrushina et al., 1999) and performance times increase with each decade (Stuss, Stethem, & Poirier, 1987). Age and education play a significant role in this test, which show more prominently on Part B (Lezak et al., 2004). Women may perform slower than men (Ernst, 1987) and ethnicity effects have been demonstrated (Lucas et al., 2005). Performance has been shown to decrease with increasing age and lower levels of education (Tombaugh, 2004).

These tests, briefly discussed above, were developed and standardized for Euro-American populations and its application in the South African context without considering demographic and cultural influences leads to misinterpretation and misdiagnosis (Pillay, 2004, 2008; B. A. Steinberg et al., 2005). Such misdiagnosis may lead to needless treatment and/or therapeutic neglect (Anderson, 2001; Mitrushina, et al., 2005; Skuy, Schutte, Fridjhon, & O'Carroll, 2001; Strauss, et al., 2006). The use of non-standardized norms in South Africa, with its diverse education, socio-cultural and linguistic backgrounds and beliefs, not only poses many challenges but is considered unethical practice (Watts, 2008).

In this paper normative data is provided for the Clock Drawing Test, COWAT, Digit Symbol and Luria Hand Sequencing test and Trail Making Test, from a dementia study for older adults in a residential setting.

Method

Procedure

The study comprised of 3 stages of cognitive assessments, which occurred sequentially in two to three month intervals, at the participants' residences. Participation was voluntary and permission to conduct the study was obtained from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal, Durban, South Africa. In stage one a random sample (N=302) of residents aged 60 years and older, with a minimum of eight years of formal schooling, the ability to speak, read and write English and the ability to give written, informed consent was selected. The Mini-Mental State Examination (MMSE), a subjective memory rating scale (SMRS) and the Deterioration Cognitive Observee (DECO) was used to screen for dementia. The second stage involved a comprehensive clinical assessment of 140 participants from stage one. In the third stage participants from stage two were administered a battery of neuropsychological tests. The tests were administered, in one session, at the participants' residences.

Participants

Of the 140 participants offered testing, 118 participants agreed to be tested, two had died since stage two of the study and 20 refused or were unavailable. Of the 118 who had agreed, 117 completed the entire battery. One person was unable to complete any of the tests and was excluded. The average time for test completion of the neuropsychology battery was 1.35 (*SD* 0.5) hours [CI 95% 1.3-1.4] with a median of 1.26 hours.

<insert Table 1 here>

Table 1 provides a breakdown of the sample in terms of race, age, education and gender. There were more Whites in the sample compared to the other main racial groups. White

participants were also the oldest of the group while the Asian participants were the youngest. The mean years of education were 10.1(*SD* 2.2). There was no significant difference with education between the groups (*M*=75.5; *SD* 9.9; *F*=1.3; *p*=0.265). There was no significant gender difference between groups (*M*=74.4; *SD* 7.9; *t* = 0.4; *p*=0.737). English was the first language for 103 (88.0%) of the participants, followed by Afrikaans 6(5.1%), isiZulu 4(3.4%), and other languages 4(3.4%).

Instruments

A battery of neuropsychological and cognitive screening tests was used. This paper reports on the Clock Drawing Test, COWAT, Digit Symbol and Luria Hand Sequencing test and Trail Making Test.

Results

One-way between-groups analysis of variance was conducted to explore the impact of the diagnostic category on individual tests. Participants were divided into three groups: Dementia Group (n=9); MCI Group (n=30) and Control Group (healthy older adults) (n=78). Means and standard deviations are presented for tests according to race, age, gender and education. The percentage variance contributed by age, education, gender and race on each of the tests and subtests, combined and uniquely, is presented in Table 2.

<insert Table 2 here>

CDT

There was no significant difference in the way the various race groups performed on the CDT. However the means for each race group showed relative variation and the dementia group

performed more poorly than the control and MCI groups. There was no significant age or education effects found. Males perform marginally better than the females on the test.

COWAT

Significant differences ($p<0.034$) were found for race in the COWAT-S (see Table 3). The mean for White participants were significantly higher compared to other participants resulting in a significantly higher COWAT-Total score. Black participants' means were consistently lower when compared to the other race group means. The means for COWAT-A were the lowest and the COWAT-animal means were the highest. Significant gender differences in the mean scores were observed on the COWAT-F ($p<0.002$) and COWAT-A (0.009) for the MCI group. Males scored lower than females on all COWAT categories with the control group doing better than the MCI and Dementia groups. Significant differences in the mean scores were also observed in the MCI group on the COWAT-Animal category ($p<0.015$) with participants who had >12 years of education scoring higher (M=12.2 SD 4.6) than those with less than 12 years of education (M=7.1 SD 4.6).

<insert Table 3 here>

Digit Symbol

Significant differences were found on the Digit Symbol-90 seconds ($p<0.006$) and Digit Symbol-120 seconds ($p<0.024$) for the control group (see Table 3). The Black group performed lower than the other race groups. While there was no significant age effect found, the Dementia group performed lower than the MCI group and the MCI group performed lower than the control group in all age categories. There was also a trend that showed that performance deteriorated with age (Table 4). A significantly lower mean score was observed

in the 8-11 years of education group compared to the >12 year education group for the Digit Symbol-120 seconds in the control group ($p<0.040$).

<insert Table 4 here>

Luria Hand Sequence Test

There were no significant differences found on the Luria Hand Sequence Test for race, age, gender or education (see Table 3, 4, 5, 6). The means for the dementia group in the White race group was lower than the Control group. Age had a deteriorating effect on performance with the Dementia group performing poorer than the Control and MCI groups (Table 4). No gender effects were evidenced (Table 5).

<insert Table 5 & 6 here>

TMT

Table 3 indicates the significant differences found for race on TMT-A for the control group ($p<0.037$) and TMT-B ($p<0.005$). Black (TMT-A) and Coloured (TMT-B) participants took much longer to complete the test compared to White (TMT-A) and Asian TMT-B). Age had a deteriorating effect on performance. Females performed better than males on the test (Table 5).

Discussion

Several investigators have encouraged the development of ethnicity-specific norms for neuropsychological tests as a means of promoting accurate diagnosis in such patients (Anderson, 2001; Lucas et al., 2005; Manly et al., 1998; Pillay, 2008; Watts, 2008). Be this as it may norms for such groups remain limited. In addition, a person's age, intelligence level, education and gender is known to affect performance on neuropsychological tests (Lezak et al., 2004; Mitrushina et al., 1999; Strauss et al., 2006). This study provides normative data and examines the influence of age, education, gender and race on the tests' performance on a group of ethnically diverse elderly participants from a residential setting.

While a significant age difference was only found in the MCI group on the COWAT-S, generally the mean performance scores on most tests support the view that age has a deteriorating effect on performance (see Table 4). This deterioration is most obvious in the dementia groups. Age effects, have been shown to be most prominent in the Symbol Digit Test – with older adults showing more variability (Joy et al., 2000; Joy et al., 2004; Lezak et al., 2004), minimally on the Luria sequencing Test (Weiner et al., 2011), and a significant role on the Trail Making Test – particularly more prominently on Part B (Lezak et al., 2004). Increasing age has been associated with worse performance on the TMT (Ganguli et al., 2010; Tombaugh, 2004) and the COWAT (Ganguli et al., 2010).

It is well known that performances on most neuropsychological tests are highly related to education level of the participants (Mitrushina et al., 1999). In this study, significant education effects were demonstrated on the COWAT-Animal in the MCI Group ($p<0.015$) and on the Digit Symbol among the Control group ($p<0.040$). This indicates that more animals names were articulated by those with higher education on the COWAT-Animal and with increasing education participants coded more items on the Digit Symbol Test.

Education has been found to correlate positively with task performances on the COWAT (B. A. Steinberg et al., 2005) and similar education effects contribute to the performance on the Digit Symbol (Joy et al., 2000; Joy et al., 2004; Lezak et al., 2004). Decreasing level of education has been associated with worse performance on TMT and COWAT (Ganguli et al., 2010). Tombaugh (2004) suggests that performance on the TMT decreases with lower levels of education.

Significant gender effects were observed on the COWAT-F ($p<0,002$) and the COWAT-A ($p<0.000$) in the MCI Group. Female participants generated more words than their male counterparts. A similar trend, although not significant, was also seen in the Dementia Group. This may suggest that males with cognitive impairment perform poorer than the females. Cauthen (1978) showed the gender effects on the COWAT, suggesting that females perform moderately better. On the trail Making Test women have been found to perform slower than men (Ernst, 1987). In this study there is support for this finding in the Control group but the reverse occurs in the MCI and Dementia groups. This may indicate that men are more compromised when cognitively impaired.

Finally significant effects of race were observed on the TMT-A ($p<0.037$), TMT-B ($p<0.0005$), the COWAT-S ($p<0.034$), Digit Symbol 90 seconds ($p<0.006$) and Digit Symbol 120 seconds ($p<0.024$) all in the Control Group. This result suggests that Black and Coloured older adults took longer or perform slower on the TMT compared to Asians and Whites and a similar slower performance was evidenced on the Digit Symbol. This result may support the view that, on timed tests, Black older adult participants may perform slower and timed tests may penalise the person's performance. However these interpretations must be considered cautiously due to the low sample size.

Conclusion

The need for local norms in the evaluation of cognitive functioning cannot be overemphasized. Ethnicity-specific and population-specific norms are useful in guiding the correct interpretation of neuropsychological test results in the South African multi-cultural setting where considerable socio-economic, educational, cultural and language diversity exist. The normative data on older adults presented in this paper will be a welcome resource for many clinicians in South African who have to rely on normative data that are not explicitly derived for the groups that they regularly work with. Further studies of this nature are needed to provide normative data across the developmental life span.

Limitations

A limitation of the study is the relatively small sample size with particularly low numbers of Blacks participants and dementia cases. The study is also limited in terms of generalizability as the study was undertaken in one metropolitan area in the KwaZulu-Natal Province and may not be representative of the population in other areas of the country.

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Declaration of conflicting interests

The authors declare that they do not have any conflict of interest.

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Table 1 Demographic characteristic of participants N=117

	Groups	n (%)	Mean (SD)	statistic	p-value
Race	Asian	23 (19.7%)	71.0 (7.0)*	*F* =2.7	0.05*
	Black	4 (3.4%)	73.8 (7.6)		
	Coloured	35 (29.9%)	73.7 (7.4)		
	White	55 (47.0%)	76.0 (7.3)*		
Age	60-69	37 (31.6%)	74.2 (7.5)		
	70-79	52 (44.4%)			
	80-89	23 (19.7%)			
	90+	5 (4.3%)			
Years of Education *M*=10.1	8-11	87 (74.4%)	73.6 (7.2)	*F*=1.3	0.265
	12	20 (17.1%)	76.4 (7.3)		
	>12	10 (8.5%)	75.5 (9.9)		
Sex	Male	35 (29.9%)	73.9 (6.3)	*t*=0.4	0.737
	Female	82 (70.1%)	74.4 (7.9)		

Age differences compared with *t*-tests and one-way ANOVA post hoc.
*Significance p<.05

Table 2: Variance contributed by gender, race, education and age

	R^2	Gender		Race		Education		Age		F	Sig
		β	%	β	%	β	%	β	%		
CDT	-.004	-.161	2.5	-.079	.6	-.024	.05	-.019	.03	.880	.479
LURIA SCORE	.015	-.018	.03	-.090	.8	.101	1	-.190	3.5	1.431	.228
TMT-A	.043	-.124	1.5	.146	2	-.034	.1	.234	5.2	2.283	.065
TMT-B	.062	-.027	.07	.110	1.1	-.139	1.8	.280	7.5	2.288	.026*
COWAT-F	.051	.197	3.8	-.170	2.6	.072	.5	.052	.3	2.522	.045*
COWAT-A	.090	.162	2.6	-.277	7.2	.085	.7	.022	.04	3.831	.006**
COWAT-S	.065	.023	.05	-.222	4.6	.077	.6	.146	2	3.009	.021*
COWAT ANIMAL	.082	-.039	.1	-.065	.4	.314	9.4	-.065	.4	3.572	.009**
DIGIT SYMBOL 90 SECS	.087	-.035	.1	-.180	3	.180	3.1	-.252	6.1	3.727	.007**
DIGIT SYMBOL 120 SECS	.100	-.073	.5	-.149	2.1	.207	4.1	-.262	6.6	4.196	.003**

Note: β = standardised coefficients. %= squared part correlations multiplied by 100 to derive a unique percentage for each variable. Total % variance for all variables may be calculated by multiplying R^2 by 100.
* p<0.5 ** p<0.1

Table 3: Tests by Race

Test	GROUP	Race Mean (SD)					K [a]	p value
		Asian (n=23)	Black (n=4)	Coloured (n=35)	White (n=55)	All (N=117)		
CDT	Control	8.9(1.2)	8.2(0)[b]	8.4(1.8)	8.8(1.6)	8.7(1.6)	4.2	0.241
	MCI	7.6(2.9)	7.0(0)	8.6(2.3)	8.9(1.4)	8.5(2.0)	2.0	0.570
	Dementia		3.0(0)		7.1(2.7)	6.7(2.9)	1.9	0.166
LURIA SCORE	Control	2.4(1.4)	2.0(0)	2.3(1.7)	2.6(1.3)	2.5(1.4)	0.8	0.839
	MCI	3.0(1.9)	2.0(0)	2.1(1.3)	2.4(1.7)	2.3(1.5)	1.6	0.659
	Dementia				1.9(2.0)	1.9(2.0)		
TMT A	Control	68.1(21.8)	87.0(14.1)	78.5(36.9)	66.4(45.4)	70.8(38.0)	8.5	0.037*
	MCI	80.8(37.1)	112.0(0)	81.8(30.9)	81.2(32.0)	82.4(31.1)	2.2	0.537
	Dementia				86.3(30.7)	86.3(30.7)		
TMT B	Control	123.8(48.3)	151.0(9.9)	199.0(79.8)	142.4(67.0)	154.6(71.8)	12.8	0.005*
	MCI	189.4(73.8)	321.0(0)	187.2(72.3)	195.6(75.1)	195.1(73.8)	2.2	0.528
	Dementia				290.1(221.3)	290.1(221.3)		
COWAT F	Control	7.5(3.2)	2.5(2.1)	6.0(3.1)	7.2(4.4)	6.8(3.8)	5.5	0.140
	MCI	3.8(1.6)	3.0(0)	3.9(2.5)	5.8(4.0)	4.6(3.1)	1.9	0.585
	Dementia				5.1(2.8)	5.1(2.8)		
COWAT A	Control	4.6(3.1)	2.5(2.1)	2.9(2.0)	4.9(3.4)	4.2(3.0)	7.6	0.055
	MCI	1.6(0.9)	1.0(0)	2.4(1.7)	4.5(3.5)	3.0(2.7)	5.5	0.140
	Dementia				3.8(2.4)	3.8(2.4)		
COWAT S	Control	6.8(4.0)	3.5(0.7)	6.3(3.0)	8.9(4.1)	7.6(3.9)	8.7	0.034*
	MCI	3.4(1.1)	2.0(0)	5.5(2.9)	6.5(5.0)	5.4(3.7)	4.4	0.223
	Dementia				5.5(2.8)	5.5(2.8)		
COWAT ANIMAL	Control	13.1(3.9)	8.0(4.2)	10.8(3.5)	12.1(4.4)	11.9(4.1)	4.9	0.180
	MCI	5.8(4.3)	4.0(0)	8.5(3.5)	9.2(3.8)	8.1(3.8)	4.3	0.226
	Dementia				6.5(4.4)	6.5(4.4)		
DIGIT SYMBOL 90 SECS	Control	27.0(11.9)	16.0(4.2)	21.0(10.7)	28.8(9.0)	25.8(10.6)	12.5	0.006*
	MCI	21.4(6.1)	15.0(0)	21.1(8.4)	18.5(7.5)	20.0(7.5)	1.3	0.725
	Dementia				12.9(6.7)	12.9(6.7)		
DIGIT SYMBOL 120 SECS	Control	35.7(15.3)	9.5(13.4)	26.6(14.4)	34.5(15.9)	31.9(15.9)	9.4	0.024*
	MCI	26.6(8.6)	18.0(0)	26.2(10.7)	24.7(9.7)	25.5(9.6)	0.9	0.822
	Dementia				13.9(12.4)	13.9(12.6)		

[a] Kruskall Wallis Independent Samples Test
[b] adjusted mean
*Significance p<.05

Table 4: Tests by Age

Test	Groups	Mean (SD)					U[a]	p value
		60-69 (n=37)	70-79 (n=52)	80-89 (n=23)	≥90 (n=5)	All (N=117)		
CDT	Controls	8.5(1.7)	9.2(1.0)	7.6(2.5)	10(0)	8.7(1.6)	6.2	0.103
	MCI	7.4(3.1)	8.9(1.7)	8.5(2.2)	8.7(0.6)	8.5(2.0)	1.9	0.574
	Dementia	9.0(0)	4.0(1.0)	7.8(3.2)	8.0(0)	6.7(2.9)	3.2	0.359
LURIA	Controls	2.7(1.2)	2.5(1.5)	1.8(1.6)		5.4(1.4)	4.9	0.179
SCORE	MCI	2.2(1.9)	2.3(1.2)	1.8(1.3)	4.3(1.5)	2.3(1.5)	5.4	0.142
	Dementia	5.0(0)	1.5(2.1)	1.8(1.7)		1.9(2.0)	3.3	0.344
TMT-A	Controls	64.4(17.9)	68.6(22.5)	101.8(94.8)	64.0(0)	70.8(38.0)	0.4	0.951
	MCI	86.4(38.1)	84.3(32.4)	83.3(32.7)	65.3(7.1)	82.4(31.1)	1.5	0.679
	Dementia	33.0(0)	95.5(21.9)	89.8(29.5)	107.0(0)	86.3(30.7)	2.8	0.432
TMT-B	Controls	144.8(58.9)	163.8(78.0)	146.5(92.9)	172.0(0)	154.6(71.8)	1.9	0.584
	MCI	178.2(73.9)	194.5(71.9)	204.2(83.6)	195.3(83.7)	195.1(73.8)	0.5	0.922
	Dementia	131.0(0)	159.0(73.5)	401.8(275.2)	265.0(0)	290.1(221.3)	2.8	0.432
	Controls	5.7(3.5)	7.2(3.4)	8.2(5.6)	10.0(0)	6.8(3.8)	5.7	0.130
COWAT-F	MCI	4.0(2.1)	3.9(2.3)	4.3(3.0)	9.0(5.0)	4.6(3.1)	3.5	0.319
	Dementia	7.0(0)	4.5(2.1)	6.0(2.9)	1.0(0)	1.0(0)	3.2	0.369
	Controls	4.0(3.0)	4.0(2.8)	5.2(4.4)	5.0(0)	4.2(3.0)	0.9	0.835
COWAT-A	MCI	1.8(1.1)	2.8(1.8)	2.4(2.3)	8.0(4.0)	3.0(2.7)	7.4	0.060
	Dementia	5.0(0)	2.5(0.7)	5.0(2.2)		3.8(2.4)	3.9	0.277
	Controls	6.4(3.6)	8.1(3.9)	8.7(4.5)	13.0(0)	7.6(3.9)	5.8	0.124
COWAT-S	MCI	3.6(0.5)	4.4(2.6)	5.2(2.6)	13.3(4.5)	5.4(3.7)	8.5	0.036*
	Dementia	9.0(0)	2.5(0.7)	6.5(2.4)	4.0(0)	5.5(2.8)	5.5	0.141
COWAT	Controls	11.3(4.3)	12.1(3.7)	13.6(5.9)	6.0(0)	11.9(4.1)	3.5	0.327
ANIMAL	MCI	11.3(3.9)	12.1(3.7)	13.6(5.9)	6.0(0)	11.9(4.1)	6.4	0.095
	Dementia	13.0(0)	3.0(1.4)	6.3(4.7)	8.0(0)	6.5(4.4)	3.3	0.348
DIGIT	Controls	25.0(9.2)	27.1(11.2)	23.6(13.9)	26.0(0)	25.8(10.6)	0.5	0.918
SYMBOL	MCI	22.6(6.5)	21.4(7.8)	17.7(8.4)	17.7(3.5)	20.0(7.5)	2.4	0.488
90secs	Dementia	28.0(0)	9.0(4.2)	10.5(1.7)	15.0(0)	12.9(6.7)	4.3	0.235
DIGIT	Controls	31.8(13.2)	33.1(16.9)	30.7(18.5)		31.9(15.9)	2.7	0.44
SYMBOL	MCI	28.8(9.2)	26.7(10.0)	22.8(10.7)	24.0(6.6)	25.5(9.6)	1.8	0.624
120secs	Dementia	38.0(0)	3.5(4.9)	11.5(8.1)	20.0(0)	13.9(12.4)	4.9	0.178

[a] Mann-Whitney U Test

*Significance p<.05

Table 5: Test by Gender

Tests	Groups	Mean (SD)			U[a]	p value
		Male (n=82)	Female (n=35)	All (N=117)		
CDT	Controls	9.0(1.5)	8.6(1.6)	8.7(1.6)	1.2	0.212
	MCI	8.7(2.4)	8.4(2.0)	8.5(2.0)	1.0	0.299
	Dementia	10.0(0)	6.3(2.8)	6.7(2.9)	1.6	0.114
LURIA SCORE	Controls	2.6(1.3)	2.4(1.5)	2.5(1.4)	0.3	0.784
	MCI	2.5(1.3)	2.4(1.6)	2.4(1.5)	0.3	0.802
	Dementia	1.0(0)	2.0(2.1)	1.9(2.0)	0.2	0.823
TMT-A	Controls	74.6(51.7)	68.7(28.3)	70.8(38.0)	0.2	0.843
	MCI	98.0(46.0)	77.7(24.5)	82.4(31.1)	1.1	0.270
	Dementia	129.0(0)	80.1(27.4)	86.3(30.7)	1.5	0.127
TMT-B	Controls	144.4(79.5)	159.9(67.7)	154.6(71.8)	1.4	0.173
	MCI	208.3(85.8)	191.1(71.4	195.1(73.8)	0.4	0.677
	Dementia	712(0)	229.9(152.4)	290.1(221.3)	1.5	0.127
COWAT-F	Controls	5.9(3.1)	7.2(4.1)	6.8(3.8)	1.3	0.189
	MCI	1.9(1.3)	5.4(3.0)	4.6(3.1)	3.0	0.002
	Dementia	3.0(0)	5.4(2.9)	5.1(2.8)	0.9	0.380
COWAT-A	Controls	3.7(2.7)	4.4(3.2)	4.2(3.0)	0.9	0.384
	MCI	1.1(0.9)	3.6(2.8)	3.0(2.7)	2.6	0.009
	Dementia	2.0(0)	4.0(2.4)	3.8(2.4)	0.9	0.377
COWAT-S	Controls	7.5(3.8)	7.6(4.0)	7.6(3.9)	0.1	0.899
	MCI	4.0(2.7)	5.9(3.9)	5.4(3.7)	1.4	0.157
	Dementia	4.0(0)	5.7(2.9)	5.5(2.8)	0.4	0.659
COWAT ANIMAL	Controls	11.8(4.1)	11.9(4.2)	11.9(4.1)	0.04	0.966
	MCI	9.3(4.2)	7.8(3.8)	8.1(3.8)	0.8	0.431
	Dementia	3.0(0)	7.0(4.5)	6.5(4.4)	0.883	0.377
DIGIT SYMBOL 90secs	Controls	26.8(11.3)	25.4(10.3)	25.8(10.6)	0.6	0.553
	MCI	17.7(10.1)	20.7(6.6)	20.0(7.5)	0.8	0.447
	Dementia	10.0(0)	13.3(7.1)	12.9(6.7)	0.4	0.826
DIGIT SYMBOL 120secs	Controls	34.6(15.7)	30.5(15.9)	31.9(15.9)	1.0	0.326
	MCI	22.0(12.1)	26.5(8.8)	25.5(9.6)	1.1	0.291
	Dementia	14.0(0)	13.3(7.1)	12.9(6.7)	0.2	0.826

[a] Mann-Whitney U Test

*Significance p<.05

Table 6: Test by Education

Tests	Group	Mean (SD) 8-11 (n=87)	12 (n=20)	>12 (n=10)	Total (N=117)	K[a]	p value
CDT	Controls	8.8(1.8)	8.6(2.1)	8.5(1.4)	8.7(1.6)	0.5	0.765
	MCI	8.5(2.0)	8.5(2.3)		8.5(2.0)	0.8	0.687
	Dementia	6.1(3.1)		8.5(0.7)	6.7(2.9)	0.4	0.550
LURIA SCORE	Controls	2.4(1.4)	2.9(1.3)	2.5(1.8)	2.5(1.4)	1.3	0.517
	MCI	2.1(1.4)	3.2(1.8)		2.3(1.5)	1.5	0.224
	Dementia	1.8(1.9)		2.0(2.8)	1.9(2.0)	0.0	1.00
TMT-A	Controls	69.2(28.0)	80.9(67.0)	63.9(31.5)	70.8(38.0)	0.8	0.681
	MCI	84.9(33.4)	72.7(18.5)		82.4(31.1)	0.5	0.468
	Dementia	86.8(33.4)		84.5(31.8)	86.3(30.7)	0.1	0.739
TMT-B	Controls	159.4(71.6)	157.6(82.9)	116.9(45.7)	154.6(71.8)	3.1	0.217
	MCI	202.0(75.7)	167.7(63.9)		195.1(73.8)	1.1	0.300
	Dementia	304.5(259.7)		247.0(25.5)	290.1(221.3)	0.4	0.505
COWAT-F	Controls	6.7(3.9)	6.3(3.0)	8.0(4.8)	6.8(3.8)	0.5	0.792
	MCI	4.5(2.2)	5.0(5.6)		4.6(3.1)	0.2	0.656
	Dementia	5.2(2.1)		5.0(5.7)	5.1(2.8)	0.0	1.00
COWAT-A	Controls	3.9(3.0)	5.1(2.9)	4.6(3.3)	4.2(3.0)	2.8	0.249
	MCI	2.7(1.8)	4.2(4.8)		3.0(2.7)	0.01	0.916
	Dementia	4.2(2.1)		2.5(3.5)	3.8(2.4)	0.7	0.399
COWAT-S	Controls	7.3(4.2)	8.6(2.8)	7.4(3.4)	7.6(3.9)	1.8	0.406
	MCI	4.8(2.2)	7.8(6.9)		5.4(3.7)	0.1	0.733
	Dementia	5.2(2.8)		6.5(3.5)	5.5(2.8)	0.5	0.500
COWAT ANIMAL	Controls	11.2(3.6)	13.4(4.9)	14.0(4.7)	11.9(4.1)	5.1	0.077
	MCI	7.1(2.9)	12.2(4.6)		8.1(3.8)	5.9	0.015
	Dementia	5.2(4.1)		10.5(3.5)	6.5(4.4)	2.3	0.129
DIGIT SYMBOL 90secs	Controls	24.4(9.7)	28.7(11.0)	31.3(14.4)	25.8(10.6)	5.3	0.072
	MCI	19.7(7.5)	21.2(8.1)		20.0(7.5)	0.1	0.736
	Dementia	12.5(7.8)		14.0(1.4)	12.9(6.7)	1.8	0.180
DIGIT SYMBOL 120secs	Controls	29.3(15.5)	37.9(14.3)	39.3(17.8)	31.9(15.9)	6.4	0.040*
	MCI	25.0(9.4)	27.3(11.3)		25.5(9.6)	0.2	0.640
	Dementia	12.0(14.1)		19.5(0.7)	13.9(12.4)	1.8	0.180

[a] Kruskall Wallis Independent Samples Test

*Significance p<.05

Durban dementia study: Norms for Clock Drawing Test, Controlled Word Association Test, Digit Symbol Test, Luria Hand Sequencing and Trail Making Test for the elderly

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Abstract

An upsurge in the prevalence of dementia, especially in lower and middle income countries, is expected. Due to the limitations of existing brief cognitive screening tools, the distinction between normal ageing and early dementia is often a challenge and requires a more comprehensive assessment of cognition through the use of specific neuropsychological tests. However, accurate interpretation of these tests depends on the availability of population-specific norms and an appreciation of the impact of demographic variables on test performance. This paper attempts to address this dearth of availability of norms. A sample of 117 elderly participants from a group of residential homes for the elderly was administered a battery of neuropsychological tests by clinical psychologists. Normative data for the Clock Drawing Test, COWAT, Digit Symbol and Luria Hand Sequencing test and Trail Making Test are provided. The effects of age, education, gender and race on test performance is discussed.

Keywords: Clock Drawing Test, Controlled Oral Word Association Test, Digit Symbol, Luria Hand Sequencing Test, Trail Making Test, dementia

Introduction

This paper is the second of two that provides normative data on cognitive screening and neuropsychological assessments, of older adults, in a multicultural setting. The emerging clinical issues as longevity increases and the challenges associated with screening and evaluating an ageing society were discussed in the first paper on normative data for a battery of commonly used memory tests. Cognitive evaluation of elderly is often based on brief screening instruments that are limited by their lack of comprehensiveness (Welsh et al., 1994) and are confounded by factors such as age, cultural biases, language, gender, education and floor and ceiling effects. (Collie, Shafiq-Antonacci, Maruff, Tyler, & Currie, 1999; Ganguli et al., 1991; Mitrushina, Boone, & D'Elia, 1999). In addition, while a large number of neuropsychological tests are available and widely used in South Africa the utility of these instruments are limited by the absence of population-specific norms for representative samples of elderly (Ganguli et al., 2010).

Clock Drawing Test

The Clock Drawing Test (CDT) has been described as the ideal cognitive screening test due to its ease of administration and scoring. It is widely used by many clinicians. The CDT has the ability to assess a range of cognitive abilities and has good psychometric properties (Royall, Cordes, & Polk, 1998; Schramm et al., 2002; Shulman, 2000). The CDT has a .5 correlation with the Mini-Mental State Examination (Shulman, 2000) and has also shown moderate sensitivity and specificity in detecting executive dysfunction in patients with a normal MMSE (Juby, Tench, & Baker, 2002). Supporting its utility in dementia assessment, several studies (Mendez, Ala, & Underwood, 1992; Rouleau, Salmon, Butters, Kennedy, & McGuire, 1992; Royall et al., 1998) confirm earlier findings

of the test in differentiating normal from pathological cognitive decline (Cahn et al., 1996; Tuokko, Hadjistavropoulos, Miller, & Beattie, 1992). In the current study the CDT had an AUC of 0.732, sensitivity of 44.4% and specificity of 88.9% (Ramlall, Chipps, Bhigjee, & Pillay, 2013). Given this background the CDT is therefore considered a very useful screen test in under resourced and overburdened environments such as South Africa and establishing norms for the older adults can be extremely useful.

Cognitive Tests

In addition to the memory test presented in the previous paper, other common cognitive tests that are routinely used in South Africa are the Controlled Word Association Test (Lezak, Howieson, & Loring, 2004), Digit Symbol Test (Wechsler, 1997), Luria Hand Sequencing (Luria, 1980; Weiner, Hynan, Rossetti, & Falkowski, 2011) and the Trail Making Test A and B (Lezak et al., 2004; Reitan, 1955; Strauss, Sherman, & Spreen, 2006). The Controlled Oral Word Association Test (COWAT) is a simple three-word naming trials of letters (F-A-S) and animals measure and is a useful component of any neuropsychological battery as it is able to detect changes in word association fluency often found in various cognitive disorders (Sumerall, Timmons, James, Ewing, & Oehlert, 1997). Performance on the test is affected by age, gender, ethnicity, language and education (B.A. Steinberg, Bieliauskas, Smith, & Ivnik). Regarding the effects of age on phonemic word list generation, performances typically show that, older examinees produce fewer responses (Cauthen, 1978) and commit more errors (Ruff, Light, Parker, & Levin, 1997; Sumerall et al., 1997) than younger examinees. Gender effects suggest the view that females perform moderately better (Cauthen, 1978). Ethnicity and language were

associated with different numbers of responses on the semantic (animals) word list generation task (Kempler, Teng, Dick, Taussig, & Davis). Education was found to correlate positively with task performances (B. A. Steinberg, Bieliauskas, Smith, Langellotti, & Ivnik, 2005)

The Digit Symbol Test is often considered a quick screening instrument for neuropsychological dysfunction where an impairment of any contributing ability will yield a low score (Joy, Kaplan, & Fein, 2004). The two key functions of the test are processing speed and memory. The test is considered more interpretable when administered to older persons or those who are motorically slowed (Kaplan, Fein, Morris, & Delis, 1991). Both age and education effects contribute to the performance on this test with age effect most prominent (Joy, Fein, Kaplan, & Freedman, 2000; Joy et al., 2004; Lezak et al., 2004). Older adults show more variability and women outperform men on this test (Lezak et al., 2004). The test re-test reliability is high with stability coefficients in the .83 to .86 range (Lezak et al., 2004).

The Luria Hand Sequencing is one of the simplest nonverbal tests of executive function that can be readily performed by clinicians. Impaired performance in the Luria test is rare in persons with normal cognition and occurs in < 10% of persons with MCI. Thus, it can be helpful in distinguishing normal and MCI subjects from Alzheimer's disease and fronto-temporal dementia (Weiner et al., 2011). The test may be useful cross-culturally because it is non-verbal and its performance is unaffected by education and only minimally by age. The test may also help to distinguish psychiatric illness from dementing illnesses (Weiner et al., 2011).

The Trail Making Test (TMT) is an assessment of attention, speed, visuomotor tracking and mental flexibility. This is a popular test due to the wide range of cognitive processes that are measured. Normative data on this test vary considerable depending on the characteristics of the sample (Mitrushina et al., 1999) and performance times increase with each decade (Stuss, Stethem, & Poirier, 1987). Age and education play a significant role in this test, which show more prominently on Part B (Lezak et al., 2004). Women may perform slower than men (Ernst, 1987) and ethnicity effects have been demonstrated (Lucas et al., 2005). Performance has been shown to decrease with increasing age and lower levels of education (Tombaugh, 2004).

These tests, briefly discussed above, were developed and standardized for Euro-American populations and its application in the South African context without considering demographic and cultural influences leads to misinterpretation and misdiagnosis (Pillay, 2004, 2008; B. A. Steinberg et al., 2005). Such misdiagnosis may lead to needless treatment and/or therapeutic neglect (Anderson, 2001; Mitrushina, et al., 2005; Skuy, Schutte, Fridjhon, & O'Carroll, 2001; Strauss, et al., 2006). The use of non-standardized norms in South Africa, with its diverse education, socio-cultural and linguistic backgrounds and beliefs, not only poses many challenges but is considered unethical practice (Watts, 2008).

In this paper normative data is provided for the Clock Drawing Test, COWAT, Digit Symbol and Luria Hand Sequencing test and Trail Making Test, from a dementia study for older adults in a residential setting.

Method

Procedure

The study comprised of 3 stages of cognitive assessments, which occurred sequentially in two to three month intervals, at the participants' residences. Participation was voluntary and permission to conduct the study was obtained from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal, Durban, South Africa. In stage one a random sample (N=302) of residents aged 60 years and older, with a minimum of eight years of formal schooling, the ability to speak, read and write English and the ability to give written, informed consent was selected. The Mini-Mental State Examination (MMSE), a subjective memory rating scale (SMRS) and the Deterioration Cognitive Observee (DECO) was used to screen for dementia. The second stage involved a comprehensive clinical assessment of 140 participants from stage one. In the third stage participants from stage two were administered a battery of neuropsychological tests. The tests were administered, in one session, at the participants' residences.

Participants

Of the 140 participants offered testing, 118 participants agreed to be tested, two had died since stage two of the study and 20 refused or were unavailable. Of the 118 who had agreed, 117 completed the entire battery. One person was unable to complete any of the tests and was excluded. The average time for test completion of the neuropsychology battery was 1.35 (*SD* 0.5) hours [CI 95% 1.3-1.4] with a median of 1.26 hours.

<insert Table 1 here>

Table 1 provides a breakdown of the sample in terms of race, age, education and gender. There were more Whites in the sample compared to the other main racial groups. White

participants were also the oldest of the group while the Asian participants were the youngest. The mean years of education were 10.1(*SD* 2.2). There was no significant difference with education between the groups (*M*=75.5; *SD* 9.9; *F*=1.3; *p*=0.265). There was no significant gender difference between groups (*M*=74.4; *SD* 7.9; *t* = 0.4; *p*=0.737). English was the first language for 103 (88.0%) of the participants, followed by Afrikaans 6(5.1%), isiZulu 4(3.4%), and other languages 4(3.4%).

Instruments

A battery of neuropsychological and cognitive screening tests was used. This paper reports on the Clock Drawing Test, COWAT, Digit Symbol and Luria Hand Sequencing test and Trail Making Test.

Results

One-way between-groups analysis of variance was conducted to explore the impact of the diagnostic category on individual tests. Participants were divided into three groups: Dementia Group (n=9); MCI Group (n=30) and Control Group (healthy older adults) (n=78). Means and standard deviations are presented for tests according to race, age, gender and education. The percentage variance contributed by age, education, gender and race on each of the tests and subtests, combined and uniquely, is presented in Table 2.

<insert Table 2 here>

CDT

There was no significant difference in the way the various race groups performed on the CDT. However the means for each race group showed relative variation and the dementia group

performed more poorly than the control and MCI groups. There was no significant age or education effects found. Males perform marginally better than the females on the test.

COWAT

Significant differences ($p<0.034$) were found for race in the COWAT-S (see Table 3). The mean for White participants were significantly higher compared to other participants resulting in a significantly higher COWAT-Total score. Black participants' means were consistently lower when compared to the other race group means. The means for COWAT-A were the lowest and the COWAT-animal means were the highest. Significant gender differences in the mean scores were observed on the COWAT-F ($p<0.002$) and COWAT-A (0.009) for the MCI group. Males scored lower than females on all COWAT categories with the control group doing better than the MCI and Dementia groups. Significant differences in the mean scores were also observed in the MCI group on the COWAT-Animal category ($p<0.015$) with participants who had >12 years of education scoring higher (M=12.2 SD 4.6) than those with less than 12 years of education (M=7.1 SD 4.6).

<insert Table 3 here>

Digit Symbol

Significant differences were found on the Digit Symbol-90 seconds ($p<0.006$) and Digit Symbol-120 seconds ($p<0.024$) for the control group (see Table 3). The Black group performed lower than the other race groups. While there was no significant age effect found, the Dementia group performed lower than the MCI group and the MCI group performed lower than the control group in all age categories. There was also a trend that showed that performance deteriorated with age (Table 4). A significantly lower mean score was observed

in the 8-11 years of education group compared to the >12 year education group for the Digit Symbol-120 seconds in the control group ($p<0.040$).

<insert Table 4 here>

Luria Hand Sequence Test

There were no significant differences found on the Luria Hand Sequence Test for race, age, gender or education (see Table 3, 4, 5, 6). The means for the dementia group in the White race group was lower than the Control group. Age had a deteriorating effect on performance with the Dementia group performing poorer than the Control and MCI groups (Table 4). No gender effects were evidenced (Table 5).

<insert Table 5 & 6 here>

TMT

Table 3 indicates the significant differences found for race on TMT-A for the control group ($p<0.037$) and TMT-B ($p<0.005$). Black (TMT-A) and Coloured (TMT-B) participants took much longer to complete the test compared to White (TMT-A) and Asian TMT-B). Age had a deteriorating effect on performance. Females performed better than males on the test (Table 5).

Discussion

Several investigators have encouraged the development of ethnicity-specific norms for neuropsychological tests as a means of promoting accurate diagnosis in such patients (Anderson, 2001; Lucas et al., 2005; Manly et al., 1998; Pillay, 2008; Watts, 2008). Be this as it may norms for such groups remain limited. In addition, a person's age, intelligence level, education and gender is known to affect performance on neuropsychological tests (Lezak et al., 2004; Mitrushina et al., 1999; Strauss et al., 2006). This study provides normative data and examines the influence of age, education, gender and race on the tests' performance on a group of ethnically diverse elderly participants from a residential setting.

While a significant age difference was only found in the MCI group on the COWAT-S, generally the mean performance scores on most tests support the view that age has a deteriorating effect on performance (see Table 4). This deterioration is most obvious in the dementia groups. Age effects, have been shown to be most prominent in the Symbol Digit Test – with older adults showing more variability (Joy et al., 2000; Joy et al., 2004; Lezak et al., 2004), minimally on the Luria sequencing Test (Weiner et al., 2011), and a significant role on the Trail Making Test – particularly more prominently on Part B (Lezak et al., 2004). Increasing age has been associated with worse performance on the TMT (Ganguli et al., 2010; Tombaugh, 2004) and the COWAT (Ganguli et al., 2010).

It is well known that performances on most neuropsychological tests are highly related to education level of the participants (Mitrushina et al., 1999). In this study, significant education effects were demonstrated on the COWAT-Animal in the MCI Group ($p<0.015$) and on the Digit Symbol among the Control group ($p<0.040$). This indicates that more animals names were articulated by those with higher education on the COWAT-Animal and with increasing education participants coded more items on the Digit Symbol Test.

Education has been found to correlate positively with task performances on the COWAT (B. A. Steinberg et al., 2005) and similar education effects contribute to the performance on the Digit Symbol (Joy et al., 2000; Joy et al., 2004; Lezak et al., 2004). Decreasing level of education has been associated with worse performance on TMT and COWAT (Ganguli et al., 2010). Tombaugh (2004) suggests that performance on the TMT decreases with lower levels of education.

Significant gender effects were observed on the COWAT-F ($p<0,002$) and the COWAT-A ($p<0.000$) in the MCI Group. Female participants generated more words than their male counterparts. A similar trend, although not significant, was also seen in the Dementia Group. This may suggest that males with cognitive impairment perform poorer than the females. Cauthen (1978) showed the gender effects on the COWAT, suggesting that females perform moderately better. On the trail Making Test women have been found to perform slower than men (Ernst, 1987). In this study there is support for this finding in the Control group but the reverse occurs in the MCI and Dementia groups. This may indicate that men are more compromised when cognitively impaired.

Finally significant effects of race were observed on the TMT-A ($p<0.037$), TMT-B ($p<0.0005$), the COWAT-S ($p<0.034$), Digit Symbol 90 seconds ($p<0.006$) and Digit Symbol 120 seconds ($p<0.024$) all in the Control Group. This result suggests that Black and Coloured older adults took longer or perform slower on the TMT compared to Asians and Whites and a similar slower performance was evidenced on the Digit Symbol. This result may support the view that, on timed tests, Black older adult participants may perform slower and timed tests may penalise the person's performance. However these interpretations must be considered cautiously due to the low sample size.

Conclusion

The need for local norms in the evaluation of cognitive functioning cannot be overemphasized. Ethnicity-specific and population-specific norms are useful in guiding the correct interpretation of neuropsychological test results in the South African multi-cultural setting where considerable socio-economic, educational, cultural and language diversity exist. The normative data on older adults presented in this paper will be a welcome resource for many clinicians in South African who have to rely on normative data that are not explicitly derived for the groups that they regularly work with. Further studies of this nature are needed to provide normative data across the developmental life span.

Limitations

A limitation of the study is the relatively small sample size with particularly low numbers of Blacks participants and dementia cases. The study is also limited in terms of generalizability as the study was undertaken in one metropolitan area in the KwaZulu-Natal Province and may not be representative of the population in other areas of the country.

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Declaration of conflicting interests

The authors declare that they do not have any conflict of interest.

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Table 1 Demographic characteristic of participants N=117

	Groups	n (%)	Mean (SD)	statistic	p-value
Race	Asian	23 (19.7%)	71.0 (7.0)*	*F* =2.7	0.05*
	Black	4 (3.4%)	73.8 (7.6)		
	Coloured	35 (29.9%)	73.7 (7.4)		
	White	55 (47.0%)	76.0 (7.3)*		
Age	60-69	37 (31.6%)	74.2 (7.5)		
	70-79	52 (44.4%)			
	80-89	23 (19.7%)			
	90+	5 (4.3%)			
Years of Education *M*=10.1	8-11	87 (74.4%)	73.6 (7.2)	*F*=1.3	0.265
	12	20 (17.1%)	76.4 (7.3)		
	>12	10 (8.5%)	75.5 (9.9)		
Sex	Male	35 (29.9%)	73.9 (6.3)	*t*=0.4	0.737
	Female	82 (70.1%)	74.4 (7.9)		

Age differences compared with *t*-tests and one-way ANOVA post hoc.
*Significance p<.05

Table 2: Variance contributed by gender, race, education and age

	R^2	Gender		Race		Education		Age		F	Sig
		β	%	β	%	β	%	β	%		
CDT	-.004	-.161	2.5	-.079	.6	-.024	.05	-.019	.03	.880	.479
LURIA SCORE	.015	-.018	.03	-.090	.8	.101	1	-.190	3.5	1.431	.228
TMT-A	.043	-.124	1.5	.146	2	-.034	.1	.234	5.2	2.283	.065
TMT-B	.062	-.027	.07	.110	1.1	-.139	1.8	.280	7.5	2.288	.026*
COWAT-F	.051	.197	3.8	-.170	2.6	.072	.5	.052	.3	2.522	.045*
COWAT-A	.090	.162	2.6	-.277	7.2	.085	.7	.022	.04	3.831	.006**
COWAT-S	.065	.023	.05	-.222	4.6	.077	.6	.146	2	3.009	.021*
COWAT ANIMAL	.082	-.039	.1	-.065	.4	.314	9.4	-.065	.4	3.572	.009**
DIGIT SYMBOL 90 SECS	.087	-.035	.1	-.180	3	.180	3.1	-.252	6.1	3.727	.007**
DIGIT SYMBOL 120 SECS	.100	-.073	.5	-.149	2.1	.207	4.1	-.262	6.6	4.196	.003**

Note: β = standardised coefficients. %= squared part correlations multiplied by 100 to derive a unique percentage for each variable. Total % variance for all variables may be calculated by multiplying R^2 by 100.
* p<0.5 ** p<0.1

Table 3: Tests by Race

Test	GROUP	Race Mean (SD)					K [a]	p value
		Asian (n=23)	Black (n=4)	Coloured (n=35)	White (n=55)	All (N=117)		
CDT	Control	8.9(1.2)	8.2(0)[b]	8.4(1.8)	8.8(1.6)	8.7(1.6)	4.2	0.241
	MCI	7.6(2.9)	7.0(0)	8.6(2.3)	8.9(1.4)	8.5(2.0)	2.0	0.570
	Dementia		3.0(0)		7.1(2.7)	6.7(2.9)	1.9	0.166
LURIA SCORE	Control	2.4(1.4)	2.0(0)	2.3(1.7)	2.6(1.3)	2.5(1.4)	0.8	0.839
	MCI	3.0(1.9)	2.0(0)	2.1(1.3)	2.4(1.7)	2.3(1.5)	1.6	0.659
	Dementia				1.9(2.0)	1.9(2.0)		
TMT A	Control	68.1(21.8)	87.0(14.1)	78.5(36.9)	66.4(45.4)	70.8(38.0)	8.5	0.037*
	MCI	80.8(37.1)	112.0(0)	81.8(30.9)	81.2(32.0)	82.4(31.1)	2.2	0.537
	Dementia				86.3(30.7)	86.3(30.7)		
TMT B	Control	123.8(48.3)	151.0(9.9)	199.0(79.8)	142.4(67.0)	154.6(71.8)	12.8	0.005*
	MCI	189.4(73.8)	321.0(0)	187.2(72.3)	195.6(75.1)	195.1(73.8)	2.2	0.528
	Dementia				290.1(221.3)	290.1(221.3)		
COWAT F	Control	7.5(3.2)	2.5(2.1)	6.0(3.1)	7.2(4.4)	6.8(3.8)	5.5	0.140
	MCI	3.8(1.6)	3.0(0)	3.9(2.5)	5.8(4.0)	4.6(3.1)	1.9	0.585
	Dementia				5.1(2.8)	5.1(2.8)		
COWAT A	Control	4.6(3.1)	2.5(2.1)	2.9(2.0)	4.9(3.4)	4.2(3.0)	7.6	0.055
	MCI	1.6(0.9)	1.0(0)	2.4(1.7)	4.5(3.5)	3.0(2.7)	5.5	0.140
	Dementia				3.8(2.4)	3.8(2.4)		
COWAT S	Control	6.8(4.0)	3.5(0.7)	6.3(3.0)	8.9(4.1)	7.6(3.9)	8.7	0.034*
	MCI	3.4(1.1)	2.0(0)	5.5(2.9)	6.5(5.0)	5.4(3.7)	4.4	0.223
	Dementia				5.5(2.8)	5.5(2.8)		
COWAT ANIMAL	Control	13.1(3.9)	8.0(4.2)	10.8(3.5)	12.1(4.4)	11.9(4.1)	4.9	0.180
	MCI	5.8(4.3)	4.0(0)	8.5(3.5)	9.2(3.8)	8.1(3.8)	4.3	0.226
	Dementia				6.5(4.4)	6.5(4.4)		
DIGIT SYMBOL 90 SECS	Control	27.0(11.9)	16.0(4.2)	21.0(10.7)	28.8(9.0)	25.8(10.6)	12.5	0.006*
	MCI	21.4(6.1)	15.0(0)	21.1(8.4)	18.5(7.5)	20.0(7.5)	1.3	0.725
	Dementia				12.9(6.7)	12.9(6.7)		
DIGIT SYMBOL 120 SECS	Control	35.7(15.3)	9.5(13.4)	26.6(14.4)	34.5(15.9)	31.9(15.9)	9.4	0.024*
	MCI	26.6(8.6)	18.0(0)	26.2(10.7)	24.7(9.7)	25.5(9.6)	0.9	0.822
	Dementia				13.9(12.4)	13.9(12.6)		

[a] Kruskall Wallis Independent Samples Test
[b] adjusted mean
*Significance p<.05

Table 4: Tests by Age

Test	Groups	Mean (SD)					U[a]	p value
		60-69 (n=37)	70-79 (n=52)	80-89 (n=23)	≥90 (n=5)	All (N=117)		
CDT	Controls	8.5(1.7)	9.2(1.0)	7.6(2.5)	10(0)	8.7(1.6)	6.2	0.103
	MCI	7.4(3.1)	8.9(1.7)	8.5(2.2)	8.7(0.6)	8.5(2.0)	1.9	0.574
	Dementia	9.0(0)	4.0(1.0)	7.8(3.2)	8.0(0)	6.7(2.9)	3.2	0.359
LURIA	Controls	2.7(1.2)	2.5(1.5)	1.8(1.6)		5.4(1.4)	4.9	0.179
SCORE	MCI	2.2(1.9)	2.3(1.2)	1.8(1.3)	4.3(1.5)	2.3(1.5)	5.4	0.142
	Dementia	5.0(0)	1.5(2.1)	1.8(1.7)		1.9(2.0)	3.3	0.344
TMT-A	Controls	64.4(17.9)	68.6(22.5)	101.8(94.8)	64.0(0)	70.8(38.0)	0.4	0.951
	MCI	86.4(38.1)	84.3(32.4)	83.3(32.7)	65.3(7.1)	82.4(31.1)	1.5	0.679
	Dementia	33.0(0)	95.5(21.9)	89.8(29.5)	107.0(0)	86.3(30.7)	2.8	0.432
TMT-B	Controls	144.8(58.9)	163.8(78.0)	146.5(92.9)	172.0(0)	154.6(71.8)	1.9	0.584
	MCI	178.2(73.9)	194.5(71.9)	204.2(83.6)	195.3(83.7)	195.1(73.8)	0.5	0.922
	Dementia	131.0(0)	159.0(73.5)	401.8(275.2)	265.0(0)	290.1(221.3)	2.8	0.432
	Controls	5.7(3.5)	7.2(3.4)	8.2(5.6)	10.0(0)	6.8(3.8)	5.7	0.130
COWAT-F	MCI	4.0(2.1)	3.9(2.3)	4.3(3.0)	9.0(5.0)	4.6(3.1)	3.5	0.319
	Dementia	7.0(0)	4.5(2.1)	6.0(2.9)	1.0(0)	1.0(0)	3.2	0.369
	Controls	4.0(3.0)	4.0(2.8)	5.2(4.4)	5.0(0)	4.2(3.0)	0.9	0.835
COWAT-A	MCI	1.8(1.1)	2.8(1.8)	2.4(2.3)	8.0(4.0)	3.0(2.7)	7.4	0.060
	Dementia	5.0(0)	2.5(0.7)	5.0(2.2)		3.8(2.4)	3.9	0.277
	Controls	6.4(3.6)	8.1(3.9)	8.7(4.5)	13.0(0)	7.6(3.9)	5.8	0.124
COWAT-S	MCI	3.6(0.5)	4.4(2.6)	5.2(2.6)	13.3(4.5)	5.4(3.7)	8.5	0.036*
	Dementia	9.0(0)	2.5(0.7)	6.5(2.4)	4.0(0)	5.5(2.8)	5.5	0.141
COWAT	Controls	11.3(4.3)	12.1(3.7)	13.6(5.9)	6.0(0)	11.9(4.1)	3.5	0.327
ANIMAL	MCI	11.3(3.9)	12.1(3.7)	13.6(5.9)	6.0(0)	11.9(4.1)	6.4	0.095
	Dementia	13.0(0)	3.0(1.4)	6.3(4.7)	8.0(0)	6.5(4.4)	3.3	0.348
DIGIT	Controls	25.0(9.2)	27.1(11.2)	23.6(13.9)	26.0(0)	25.8(10.6)	0.5	0.918
SYMBOL	MCI	22.6(6.5)	21.4(7.8)	17.7(8.4)	17.7(3.5)	20.0(7.5)	2.4	0.488
90secs	Dementia	28.0(0)	9.0(4.2)	10.5(1.7)	15.0(0)	12.9(6.7)	4.3	0.235
DIGIT	Controls	31.8(13.2)	33.1(16.9)	30.7(18.5)		31.9(15.9)	2.7	0.44
SYMBOL	MCI	28.8(9.2)	26.7(10.0)	22.8(10.7)	24.0(6.6)	25.5(9.6)	1.8	0.624
120secs	Dementia	38.0(0)	3.5(4.9)	11.5(8.1)	20.0(0)	13.9(12.4)	4.9	0.178

[a] Mann-Whitney U Test

*Significance p<.05

Table 5: Test by Gender

Tests	Groups	Mean (SD)			U[a]	p value
		Male (n=82)	Female (n=35)	All (N=117)		
CDT	Controls	9.0(1.5)	8.6(1.6)	8.7(1.6)	1.2	0.212
	MCI	8.7(2.4)	8.4(2.0)	8.5(2.0)	1.0	0.299
	Dementia	10.0(0)	6.3(2.8)	6.7(2.9)	1.6	0.114
LURIA SCORE	Controls	2.6(1.3)	2.4(1.5)	2.5(1.4)	0.3	0.784
	MCI	2.5(1.3)	2.4(1.6)	2.4(1.5)	0.3	0.802
	Dementia	1.0(0)	2.0(2.1)	1.9(2.0)	0.2	0.823
TMT-A	Controls	74.6(51.7)	68.7(28.3)	70.8(38.0)	0.2	0.843
	MCI	98.0(46.0)	77.7(24.5)	82.4(31.1)	1.1	0.270
	Dementia	129.0(0)	80.1(27.4)	86.3(30.7)	1.5	0.127
TMT-B	Controls	144.4(79.5)	159.9(67.7)	154.6(71.8)	1.4	0.173
	MCI	208.3(85.8)	191.1(71.4	195.1(73.8)	0.4	0.677
	Dementia	712(0)	229.9(152.4)	290.1(221.3)	1.5	0.127
COWAT-F	Controls	5.9(3.1)	7.2(4.1)	6.8(3.8)	1.3	0.189
	MCI	1.9(1.3)	5.4(3.0)	4.6(3.1)	3.0	0.002
	Dementia	3.0(0)	5.4(2.9)	5.1(2.8)	0.9	0.380
COWAT-A	Controls	3.7(2.7)	4.4(3.2)	4.2(3.0)	0.9	0.384
	MCI	1.1(0.9)	3.6(2.8)	3.0(2.7)	2.6	0.009
	Dementia	2.0(0)	4.0(2.4)	3.8(2.4)	0.9	0.377
COWAT-S	Controls	7.5(3.8)	7.6(4.0)	7.6(3.9)	0.1	0.899
	MCI	4.0(2.7)	5.9(3.9)	5.4(3.7)	1.4	0.157
	Dementia	4.0(0)	5.7(2.9)	5.5(2.8)	0.4	0.659
COWAT ANIMAL	Controls	11.8(4.1)	11.9(4.2)	11.9(4.1)	0.04	0.966
	MCI	9.3(4.2)	7.8(3.8)	8.1(3.8)	0.8	0.431
	Dementia	3.0(0)	7.0(4.5)	6.5(4.4)	0.883	0.377
DIGIT SYMBOL 90secs	Controls	26.8(11.3)	25.4(10.3)	25.8(10.6)	0.6	0.553
	MCI	17.7(10.1)	20.7(6.6)	20.0(7.5)	0.8	0.447
	Dementia	10.0(0)	13.3(7.1)	12.9(6.7)	0.4	0.826
DIGIT SYMBOL 120secs	Controls	34.6(15.7)	30.5(15.9)	31.9(15.9)	1.0	0.326
	MCI	22.0(12.1)	26.5(8.8)	25.5(9.6)	1.1	0.291
	Dementia	14.0(0)	13.3(7.1)	12.9(6.7)	0.2	0.826

[a] Mann-Whitney U Test

*Significance p<.05

Table 6: Test by Education

Tests	Group	Mean (SD) 8-11 (n=87)	12 (n=20)	>12 (n=10)	Total (N=117)	K[a]	p value
CDT	Controls	8.8(1.8)	8.6(2.1)	8.5(1.4)	8.7(1.6)	0.5	0.765
	MCI	8.5(2.0)	8.5(2.3)		8.5(2.0)	0.8	0.687
	Dementia	6.1(3.1)		8.5(0.7)	6.7(2.9)	0.4	0.550
LURIA SCORE	Controls	2.4(1.4)	2.9(1.3)	2.5(1.8)	2.5(1.4)	1.3	0.517
	MCI	2.1(1.4)	3.2(1.8)		2.3(1.5)	1.5	0.224
	Dementia	1.8(1.9)		2.0(2.8)	1.9(2.0)	0.0	1.00
TMT-A	Controls	69.2(28.0)	80.9(67.0)	63.9(31.5)	70.8(38.0)	0.8	0.681
	MCI	84.9(33.4)	72.7(18.5)		82.4(31.1)	0.5	0.468
	Dementia	86.8(33.4)		84.5(31.8)	86.3(30.7)	0.1	0.739
TMT-B	Controls	159.4(71.6)	157.6(82.9)	116.9(45.7)	154.6(71.8)	3.1	0.217
	MCI	202.0(75.7)	167.7(63.9)		195.1(73.8)	1.1	0.300
	Dementia	304.5(259.7)		247.0(25.5)	290.1(221.3)	0.4	0.505
COWAT-F	Controls	6.7(3.9)	6.3(3.0)	8.0(4.8)	6.8(3.8)	0.5	0.792
	MCI	4.5(2.2)	5.0(5.6)		4.6(3.1)	0.2	0.656
	Dementia	5.2(2.1)		5.0(5.7)	5.1(2.8)	0.0	1.00
COWAT-A	Controls	3.9(3.0)	5.1(2.9)	4.6(3.3)	4.2(3.0)	2.8	0.249
	MCI	2.7(1.8)	4.2(4.8)		3.0(2.7)	0.01	0.916
	Dementia	4.2(2.1)		2.5(3.5)	3.8(2.4)	0.7	0.399
COWAT-S	Controls	7.3(4.2)	8.6(2.8)	7.4(3.4)	7.6(3.9)	1.8	0.406
	MCI	4.8(2.2)	7.8(6.9)		5.4(3.7)	0.1	0.733
	Dementia	5.2(2.8)		6.5(3.5)	5.5(2.8)	0.5	0.500
COWAT ANIMAL	Controls	11.2(3.6)	13.4(4.9)	14.0(4.7)	11.9(4.1)	5.1	0.077
	MCI	7.1(2.9)	12.2(4.6)		8.1(3.8)	5.9	0.015
	Dementia	5.2(4.1)		10.5(3.5)	6.5(4.4)	2.3	0.129
DIGIT SYMBOL 90secs	Controls	24.4(9.7)	28.7(11.0)	31.3(14.4)	25.8(10.6)	5.3	0.072
	MCI	19.7(7.5)	21.2(8.1)		20.0(7.5)	0.1	0.736
	Dementia	12.5(7.8)		14.0(1.4)	12.9(6.7)	1.8	0.180
DIGIT SYMBOL 120secs	Controls	29.3(15.5)	37.9(14.3)	39.3(17.8)	31.9(15.9)	6.4	0.040*
	MCI	25.0(9.4)	27.3(11.3)		25.5(9.6)	0.2	0.640
	Dementia	12.0(14.1)		19.5(0.7)	13.9(12.4)	1.8	0.180

[a] Kruskall Wallis Independent Samples Test

*Significance p<.05

7.7 Paper 6

Sensitivity and Specificity of neuropsychological tests for Dementia and Mild Cognitive Impairment in a sample of residential elderly in South Africa

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Abstract

Background

Neuropsychological tests can successfully distinguish between healthy elderly persons and those with clinically significant cognitive impairment. A battery of neuropsychological tests was evaluated for their discriminant validity of cognitive impairment in a group of elderly persons in Durban, South Africa.

Methods

A sample of 117 English-speaking participants of different race groups (nine with dementia, 30 with mild cognitive impairment [MCI] and 78 controls) from a group of residential homes for the elderly was administered a battery of 11 neuropsychological tests. Kruskal-Wallis tests were used to compare performance of controls with the two diagnostic groups. Sensitivity and Specificity of the tests for dementia and MCI were determined using Receiver Operating Characteristic (ROC) Analysis.

Results

Most tests were able to discriminate between participants with dementia, MCI and controls ($p<.05$). Areas Under the Curve (AUC) values for dementia vs non-dementia ranged from .519 for the Digit Span (forward) to .828 for the Digit Symbol (90s) with 14 of the 29 scores achieving significance ($p<.05$). AUC values for MCI ranged from .754 for COWAT-animal to .507 for the RCF copy; 17 of the 29 scores achieving significance ($p<.05$).

Conclusions

Several measures from the neuropsychological battery had discriminant validity for the differential diagnosis of cognitive disturbances in the elderly. Further studies are needed to assess the effect of culture and language on the appropriateness of the tests for different populations.

Keywords: Area under curve (AUC), dementia, diagnostic accuracy, discriminant validity, mild cognitive impairment (MCI), neuropsychological tests.

Background

A growing number of people are surviving into old age (Department of Social Development, 2009), with an associated predicted increase in the prevalence of dementia (Prince et al., 2013) resulting in a call for the condition to be regarded as a global health priority (World Health Organization, 2012). This highlights the need for the accurate detection and characterization of cognitive deficits in order to distinguish normal age-associated cognitive deficits from those due to Mild Cognitive Impairment (MCI), a pre-dementia stage, and dementia. However, up to 80% of cases remain undiagnosed (Weimer & Sager, 2009) even though there is a considerable fiscal, clinical and social burden posed by Alzheimer's Disease (AD) (Alzheimer's Association, 2012). Delaying the progression from MCI to dementia by even one year, through the successful management of MCI, has been shown to result in significant cost savings (R. C. Petersen et al., 2001). Economic evaluation of the value of early recognition and diagnosis of cognitive impairment confirms that, despite significant initial costs, it is cost-effective and has health benefits when compared to treatment in the absence of early assessment (Getsios, Blume, Ishak, Maclaine, & Hernandez, 2012). Early recognition and diagnosis are however dependent on the availability of suitable and valid assessment measures. The absence of reliable, universally acceptable biological and radiological markers for dementia necessitate the reliance on clinical assessments for a diagnosis (Robillard, 2007), supported by a multidisciplinary approach to the assessment of cognitive disturbances (Verhey et al., 1993).

Neuropsychological testing is an important component of a clinically integrative approach to assessing cognitive impairment in the elderly. Neuropsychological testing could be purposively applied to distinguish age-related cognitive deficits from those due to MCI or dementia (Jacova, Kertesz, Blair, Fisk, & Feldman, 2007; Salmon & Bondi, 2009). Although

there is no generally accepted battery of tests for MCI, deficits in various cognitive domains have been identified with neuropsychological tests (Grundman et al., 2004; Kramer et al., 2006; Seo et al., 2010). Complementing clinical and radiological diagnostic evidence, the use of neuropsychological tests allow for the qualitative and quantitative assessment of specific cognitive domains, and is superior to brief cognitive tools whose floor and ceiling effects threaten their validity (Jacova et al., 2007; Salmon & Bondi, 2009). Neuropsychological tests have been shown to have high accuracy in differentiating cognitively normal elderly from those with mild or advanced dementia (Seo et al., 2010; Welsh, Butters, Hughes, Mohs, & Heyman, 1991), with sensitivities exceeding 80% and specificities in excess of 90% being reported (Cahn et al., 1995; Swearer, O'Donnell, Kane, Hoople, & Lavoie, 1998). The aim of this paper is to determine the sensitivity and specificity of a battery of neuropsychological tests in a sample of elderly persons living in a residential setting.

Methods

This study was part of a larger study on dementia, conducted in 2010-2011, on residents in a group of homes for the elderly (total of 1 371 residents), in Durban, KwaZulu-Natal Province, South Africa. The homes are administered by a non-governmental organisation (NGO) and cater for those needing frail care, assisted living and independent living for people aged 60 years and older. Inclusion criteria for the larger study were: residents who were 60 years and older, a minimum of eight years of formal schooling, the ability to speak, read and write in English, and the ability to give written, informed consent. Exclusion criteria were: residents with severe physical, mental or sensory handicaps that precluded their engagement in the assessment procedures. Permission to conduct the study was obtained from the Biomedical Research Ethics Committee (BREC) of the University of KwaZulu-Natal, with residents providing written, informed consent to participate. The research was completed in compliance with the Helsinki Declaration (World Medical Association, 2001).

The study consisted of three stages of cognitive assessments conducted sequentially at the participants' residences, namely, general screening (stage 1), clinical assessment (stage 2) and neuropsychological test screening (stage 3). Details of stages one and two are described fully elsewhere(Ramlall, Chipps, Bhigjee, & Pillay, 2013; Ramlall, Chipps, Pillay, & Bhigjee, 2013). In the third stage, participants from stage 2 were administered a neuropsychological battery of tests. The neuropsychological assessments were administered by clinical psychologists who were blind to the participants' performances on the screening measures used in stage 1 as well as their clinical diagnostic status (stage 2). Two participants died during the study and 20 either refused or were unavailable to participate. One person was unable to complete any of the neuropsychological tests and was excluded from the dataset. Participants were classified into groups with 'Dementia' or 'MCI' according to specific criteria(Ramlall, Chipps, Pillay, et al., 2013). Dementia was diagnosed using the Diagnostic and Statistical Manual of Mental Disorders 4th Edition-Text Revised (DSM IV-TR). Criteria A and B for Alzheimer's and Vascular Dementia were applied to assign a general diagnosis of dementia without reference to aetiology. MCI was diagnosed using the criteria contained in the Report of the International Working Group on Mild Cognitive Impairment (Winblad et al., 2004).

Participants

One hundred and seventeen participants, who completed the neuropsychological battery of tests, were included in this study. Of these, nine were diagnosed with Dementia and 30 with MCI. The 78 participants who did not meet the criteria for MCI or for dementia represented the control group. Of the 30 cases of MCI, 14 (46.7%) were classified as amnestic MCI single domain (aMCIsd), seven (23.3%) were classified as non-amnestic MCI single domain

(naMCIsd), and nine (30%) were classified as amnestic MCI multiple domain (naMCImd). None was classified as amnestic MCI, multi-domain (aMCImd).

Tests administered

The following eleven tests were administered in English in a single session at the participants' residences: Rey Auditory Verbal Learning Test (RAVLT)(Lezak, Howieson, & Loring, 2004; Strauss, Sherman, & Spreen, 2006); Digit Span (Wechsler, 1997) and Digit Symbol (Wechsler, 1997); Controlled Oral Word Association Test (COWAT-FAS and Animal) (Lezak et al., 2004); Short Story Comprehension and Recall (a South African adaptation of the Cowboy Story, 'A Farmer from Transkei')(Lezak et al., 2004); the Token Test (Short version)(De Renzi & Vignolo, 1962; Lezak et al., 2004); Rey Complex Figure (RCF)(Lezak et al., 2004); Trail Making Test A and B (TMT A and B)(Lezak et al., 2004; Reitan, 1955; Strauss et al., 2006); the Clock Drawing Test (Freedman et al., 1994) (the free-drawing version with the '10 past 11' time setting instruction used the Rouleau's 10-point scoring system) (Rouleau, Salmon, & Butters, 1996; Rouleau, Salmon, Butters, Kennedy, & McGuire, 1992); the Luria Hand Sequence (Lezak et al., 2004; Weiner, Hynan, Rossetti, & Falkowski, 2011) and the Mazes Tests (Lezak et al., 2004).

Statistical Analysis

Data were analysed using IBM SPSS® v21.0 (IBM Corp, 2012). MedCalc® v12.5.0 (MedCalc Software, 2012) was used for the Random Operating Curve (ROC) analysis. Descriptive statistics were calculated for demographic variables,and mean neuropsychological scores were calculated for each of the groups. Between-group comparisons were undertaken using non-parametric Kruskal-Wallis Tests and Chi-square Tests (including Fisher Exact Tests where appropriate). For all cognitive tests, differences

were tested using non-parametric Kruskall-Wallis tests and 95% confidence intervals were calculated. After establishing the discriminant validity of these tests for MCI and Dementia, ROC analyses were used to summarise the diagnostic accuracy of the tests on all possible cut-off scores, giving equal weighting to sensitivity and specificity. This allowed comparison of the discriminatory validity and diagnostic accuracy of the different cognitive tests (Ritchie & Fuhrer, 1992)'(Kukull et al., 1994), and the ranking of the sensitivities and specificities of the various tests. ROC curves and the sensitivities and specificities were produced for each of the tests for Dementia (n=9) compared with the performance of non-dementia participants (Controls + MCI; n=108). Similar comparisons were done between MCI (n=30) and Controls (n=78). For each test measure, the area under the curve (AUC) was calculated with 95% confidence intervals. Optimal cut-off scores (Youden Index) and associated sensitivity and specificity values were generated for each test for dementia and MCI respectively. Swets' interpretation of AUC scores were used in this study: 0.5=non-informative; 0.5<AUC$\leq$ O.7 = less accurate; 0.7< AUC $\leq$ 0.9 = moderately accurate; 0.9<AUC<1 = highly accurate and the perfect test has an AUC = 1 (Swets, 1988). For those tests where the area beneath the curve was significant, we selected the cut-off score on each one that gave the optimum sensitivity to cases, balanced against the optimum specificity for the comparator group.

Results

Demographics

Of the 117 participants, there were 55 (47.0%) Whites, 35 (29.9%) Coloureds, 23 (19.7%) Asians and 4 (3.4%) Blacks. Their mean age was 74.2 (±7.5) years, with most participants being female (82, 70.1%). The average years of education was 10.1 (±2.2), with 87 (74.4%) reporting 8-11 years of formal education, 20 (17.1%) with 12 years and 10 (8.5%) with more

than 12 years of formal schooling. English was the first language for 103 (88.0%) of the participants, followed by Afrikaans 6(5.1%), isiZulu 4(3.4%), and other languages 4(3.4%). There was a significant difference between the three diagnostic groups by race and age (Table 1), with the mean age of control group being lower than that of MCI and Dementia groups. The mean age of MCI participants was older than control group but younger than those with Dementia.

Table 1: Demographic data per diagnostic group

Demographics	**Controls (n=78)**	**MCI (n=30)**	**Dementia (n=9)**	**Statistic**	***P***
Race (%)				X^2=12.5	.015*
Asian	18 (23.1%)	5 (16.7%)	0 (0%)		
Black	2 (2.6%)	1 (3.3%)	1 (11.1%)		
Coloured	22 (28.2%)	13 (43.3%)	0 (0%)		
White	36 (46.2%)	11 (36.7%)	8 (88.9%)		
Gender (%)				X^2=2.6	.260
Female	51 (65.4%)	23 (76.7%)	8 (88.9%)		

Male	27 (34.6%)	7 (23.3%)	1 (11.1%)		
Age (years)	72.1 ± 6.7	76.4 ± 8.4	79.0 ± 7.5	*K*=10.1	.006*
Education (years)	10.3 ± 2.2	9.3 ± 1.6	10.1 ± 2.2	*K* =5.8	.055

Age and Years of Education were compared using Independent Samples Kruskal-Wallis Tests. Gender and Race was compared using Pearson Chi-square Tests and Fisher Exact Tests where appropriate. *Significance level set as p< .05 and 95% Confidence Intervals.

Neuropsychological test performance of participants

The performance of the control group and the two diagnostic groups on the various neuropsychological tests for are presented in Table 2.

Table 2: Mean test scores per diagnostic group

Test	**Control Mean (95% CI) (n=78)**	**MCI Mean(95% CI) (n=30)**	**Dementia Mean(95% CI) (n=9)**	**Statistic**	***P***
RAVLT Trial I	4.8 (4.4-5.2)	4.2 (3.4 – 4.9)	3.3 (1.9 – 4.8)	*K* =6.6	.037*
RAVLT Trial II	6.8 (6.2-7.4)	5.8 (5.1-6.6)	4.6 (3.4-5.7)	*K* =10.2	.006*
RAVLT Trial III	7.9 (7.3-8.5)	6.9 (5.9-7.8)	5.2 (4.0-6.5)	*K* =11.2	.004*
RAVLT Trial IV	8.6 (8.0-9.3)	7.0 (6.1-8.0)	5.6 (3.8-7.3)	*K* =14.2	.001*
RAVLT Trial V	9.1 (8.5-9.8)	7.7 (6.7-8.8)	5.4 (3.6-7.30)	*K* =14.5	.001*
RAVLT Trials I-V	37.3 (34.8-39.8)	31.6 (27.6-35.6)	24.1 (18.8-29.5)	*K* =15.4	<.001*
RAVLT Immediate	6.6 (5.8-7.5)	5.5 (4.4-6.7)	3.1 (0.9-5.3)	*K* =9.6	.008*

Recall					
RAVLT 20 Minute Recall	6.0 (5.1-6.0)	5.0 (3.9-6.1)	2.6 (0.5-4.70)	*K* =6.9	.032*
Digit Span forward	9.0(8.5-9.5)	7.8(7.0-8.6)	8.4(7.0-9.9)	*K* =5.9	.052
Digit Span backward	5.0(4.6-5.5)	4.2(3.6-4.9)	3.8(2.9-4.7)	*K* =7.2	.028*
Digit Span total	14.0(13.2-14.9)	12.2(10.9-13.5)	12.2(10.0-14.5)	*K* =5.4	.066
Digit Symbol 90s	25.9(23.5-28.2)	20.0(17.2-22.8)	12.9(7.3-18.5)	*K* =17.0	<.001*
Digit Symbol 120s	31.9(28.3-35.5)	25.5(21.9-29.1)	13.9(3.5-24.3)	*K* =13.4	.001*
COWAT –F	6.8(5.9-7.7)	4.6(3.4-5.7)	5.1(2.8-7.5)	*K* =9.3	.010*
COWAT-A	4.2(3.5-4.9)	3.0(2.0-4.0)	3.8(1.8-5.7)	*K* =4.5	.102
COWAT-S	7.6(6.7-8.4)	5.4(4.1-6.8)*	5.5(3.2-7.8)	*K* =9.1	.011*
COWAT FAS Total	18.5(16.4-20.7)	12.4(9.5-15.4)	14.4(8.6-20.1)	*K* =12.2	.002*
COWAT-Animal	11.9(10.9-12.8)	8.1(6.7-9.6)	6.5(2.8-10.2)	*K* =22.2	<.001*
Narrative Recall	8.1(7.0-9.2)	7.1(5.9-8.3)	4.4(1.4-7.5)	*K* =6.2	.045*
Narrative Delayed Recall	6.8(5.8-7.9)	5.8(4.4-7.3)	3.6(0.3-6.8)	*K* =4.8	.090
Token Test	162.7(159.2-166.2)	153.0(143.9-162.1)	147.1(124.5-169.7)	*K* =5.5	.064
RCF Copy	30.7(29.2-32.2)	40.4(19.1-61.7)	21.2(12.6-29.7)	*K* =8.2	.017*
RCF Recall	13.5(11.8-15.3)	10.7(8.7-12.7)	7.7(2.3-13.1)	*K* =7.1	.028*
RCF Delayed	14.1(12.5-15.8)	11.0(8.9-13.2)	6.3(0.7-11.9)	*K* =11.6	.003*
Clock Drawing	8.7(8.4-9.1)	8.5(7.7-9.3)	6.7(4.5-8.9)	*K* =6.1	.047*
Luria Hand Sequence	2.5(2.2-2.8)	2.3(1.8-2.9)	1.9(0.2-3.5)	*K* =1.3	.530
TMT A	70.8(62.2-79.4)	82.4(70.8-4.1)	86.3(60.6-11.9)	*K* =8.4	.015*
TMT B	154.6(138.2-171.0)	195.1(167.6-222.6)	290.1(105.1-475.1)	*K* =10.4	.005*
Maze Total	385.1(344.1-426.1)	521.7(440.7-602.7)	571.1(312.3-830.0)	*K* =10.5	.005*

Tests were compared using Independent Samples Kruskal-Wallis Tests. *Significance level set as p< .05 and 95% Confidence Intervals. RAVLT=Rey Auditory Verbal Learning Test, COWAT= Controlled Oral Word Association Test, RCF=Rey Complex Figure, TMT= Trail Making Test

With the exception of the Digit Span (forward), Digit Span total, COWAT-A, Narrative Memory Test (delayed recall), Token Test and the Luria Hand Sequence Test, there were significant mean differences on all other tests in the three groups (see Table 2). The mean score on most tests demonstrated a progressive declining pattern in cognitive performance from the control group to MCI to dementia subjects. The exceptions to this pattern were on Digit Span total (where no difference in mean scores between MCI (12.2) and dementia (12.2), p=.066,) and the COWAT group (where the mean dementia group scores were

slightly better than the MCI group scores, namely COWAT-F (5.5 vs 4.6, p=.010), COWAT-A (3.8 vs 3.0, p=.102), COWAT-S (5.5 vs 5.4, p=.011) and COWAT-total (14.4 vs 12.4, p=.002)). Similarly, for the RCF (copy), the MCI score (40.4) was better than those of the controls (30.7), p=.017. Across the three classification categories, the differences in score means of the RAVLT (total), Digit Symbol (90s), and COWAT (animal category) were highly significant, with p values of <.001.

All tests were further analysed to determine their ability to discriminate participants with dementia from those without dementia, and those with MCI from the controls.

Sensitivity and Specificity of Tests: Dementia vs non-Dementia

Using ROC curves to measure how well the tests separates those with (dementia) from those without dementia (includes MCI and control groups), 15 of the 29 scores achieved significant (p<.05) AUC (Table 3). AUCs ranged from .828 for the Digit Symbol (90s) to .709 for the RCF (recall). A significance of p<.001 were demonstrated on the RAVLT Trial II (.753), RAVLT Trial III (.775), RAVLT Trial V (.812), RAVLT Total (0.805), RAVLT immediate recall (.770), RAVLT 20 minute recall (.741), Digit Symbol 90s (.828), Digit Symbol 120s (.804) and RCF copy (.783). The tests with non-significant discriminatory capacity included those that assessed attention (Digit Span), language (COWAT FAS total; Narrative Memory Test (delayed recall); Token Test) and executive functions (Luria Hand Sequence Test, TMT, Mazes).

Table 3: Summary of ROC analysis with cut-off scores for Dementia group (n=9) and Control group (n=108)

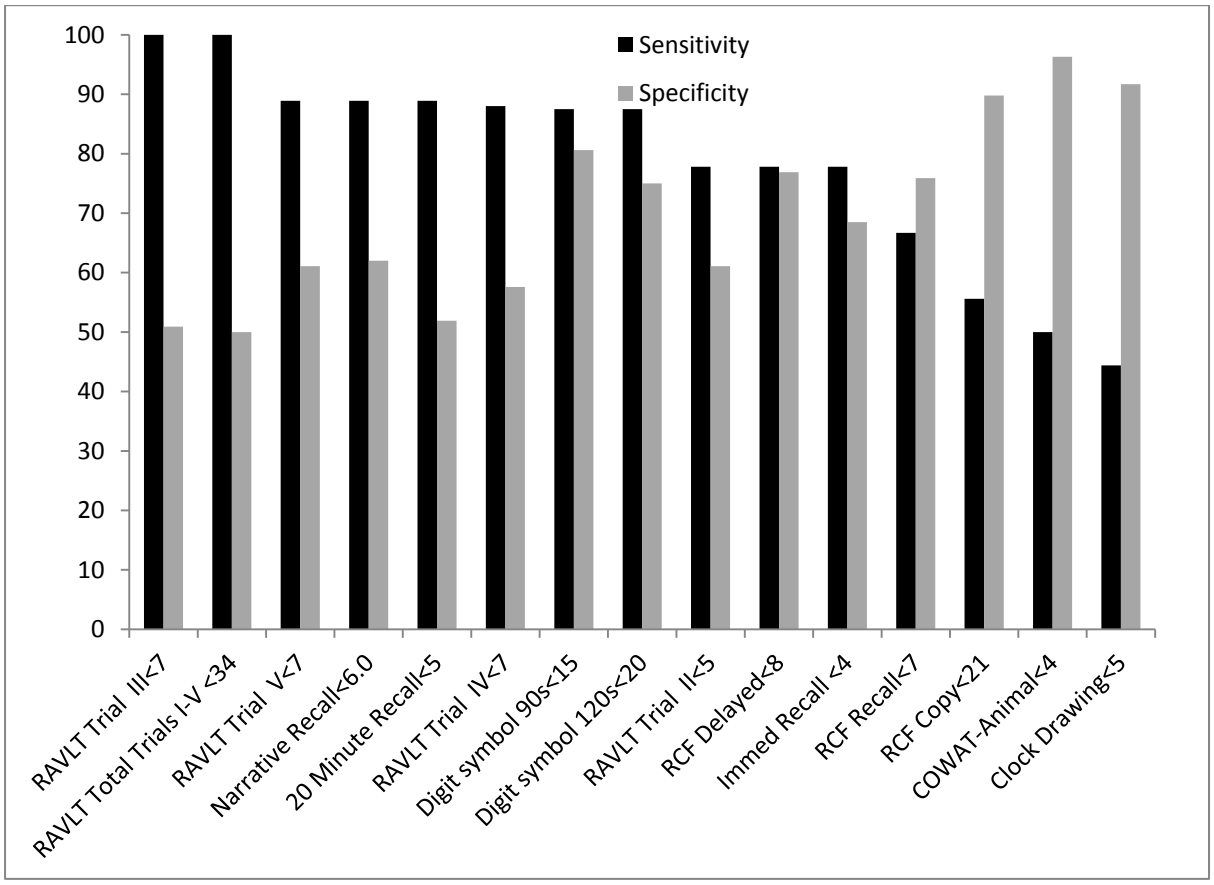
Test	AUC (95%CI)	P-Value	Cut-off	Sensitivity	Specificity
RAVLT Trial I	.670 (.577-.754)	.095	≤2	44.4	88.9
RAVLT Trial II	.753 (.665-.828)	<.001*	≤5	77.8	61.1
RAVLT Trial III	.775 (.688-.847)	<.001*	≤7	100	50.9
RAVLT Trial IV	.757 (.669-.832)	<.001*	≤7	88.0	57.6
RAVLT Trial V	.812 (.729-.878)	<.001*	≤7	88.9	61.1
RAVLT Total Trials I-V	.805(.721-.872)	<.001*	≤34	100	50.0
RAVLT Immediate	.770(.683-.842)	<.001*	≤4	77.8	68.5

Recall					
RAVLT 20 Minute Recall	.741(.652-.817)	<.001*	≤5	88.9	51.9
Digit span forward	.519(.424,.612)	.835	≥8	66.7	53.7
Digit span backward	.646(.552-.732)	.094	≤5	100.0	24.1
Digit span total	.549(.454-.641)	.600	≤15	100.0	25.0
Digit symbol 90s	.828(.746-.891)	<.001*	≤15	87.5	80.6
Digit symbol 120s	.804(.720-.872)	<.001*	≤20	87.5	75.0
COWAT –F	.561(.466,.654)	.557	≤4	50.0	56.4
COWAT-A	.530(.434-.624)	.787	>4	50.0	69.2
COWAT-S	.595(.500-.685)	.308	≤9	100	26.9
COWAT Total	.552(.456-.644)	.622	≤23	100	20.4
COWAT-Animal	.763(.675-.837)	.017*	≤4	50.0	96.3
Narrative Recall	.736(.646-.813)	.011*	≤6.0	88.9	62.0
Narrative Delayed Recall	.693(.601-.775)	.050	≤0,	44.4	88.0
Token Test Total	.650(.557-.736)	.180	≥162	77.8	63.0
RCF Copy	.783(.698-854)	<.001*	≤21	55.6	89.8
RCF Recall	.709(.618-.790)	.039*	≤7	66.7	75.9
RCF Delayed	.781(.696-.852)	.005*	≤8	77.8	76.9
Clock Drawing	.732(.642,.810)	.012*	≤5	44.4	91.7
Luria hand sequence	.600(.505-.690)	.448	≤1	50.0	75.0
TMT A	.669(.575-.754)	.141	>72	75.0	62.6
TMT B	.669(.575-.754)	.143	>210	62.5	76.4
Maze Total	.641(.546-.728)	.130	>329	100.0	34.3

*Significance level set as p< .05 and 95% Confidence Intervals. RAVLT=Rey Auditory Verbal Learning Test, COWAT= Controlled Oral Word Association Test, RCF=Rey Complex Figure, TMT= Trail Making Test

Fifteen scores that significantly discriminated between subjects with dementia and without dementia were further considered, based on recommended cut-off scores that yielded the optimum balance between sensitivity and specificity (Figure 1). Although the RAVLT Trial III and the RAVLT Total had the best discriminatory sensitivity (100%, cut off scores <7 and <34 respectively), this was at the expense of their specificities, which were 50.0% and 50.9% respectively. The most balanced test was the Digit Symbol, with a sensitivity of 87.5% and specificities of 80.6% at 90s and 75.0% at 120s. (cut-off scores of <15 and <20 respectively).

Figure 1: Optimal Sensitivity, Specificity and cut-off scores for significant tests for Dementia



RAVLT=Rey Auditory Verbal Learning Test, COWAT= Controlled Oral Word Association Test, RCF=Rey Complex Figure, TMT= Trail Making Test

Sensitivity and Specificity of Tests: MCI vs controls

ROC curves were used to determine how well the tests predicted participants with MCI from those without MCI. Seventeen of the 29 scores achieved a significant AUC ($p<.05$) -see Table 3. AUCs ranged from .621 to .754, with significance levels of $p<.001$ on the Digit Symbol (90s), COWAT (F), COWAT (Total), and COWAT (animal).

No significance for MCI was found on the RAVLT Trial I, RAVLT (immediate and 20 minute recall), Narrative Memory (recall), Token Test, RCF, Clock Drawing Test and Luria Hand Sequence Test.

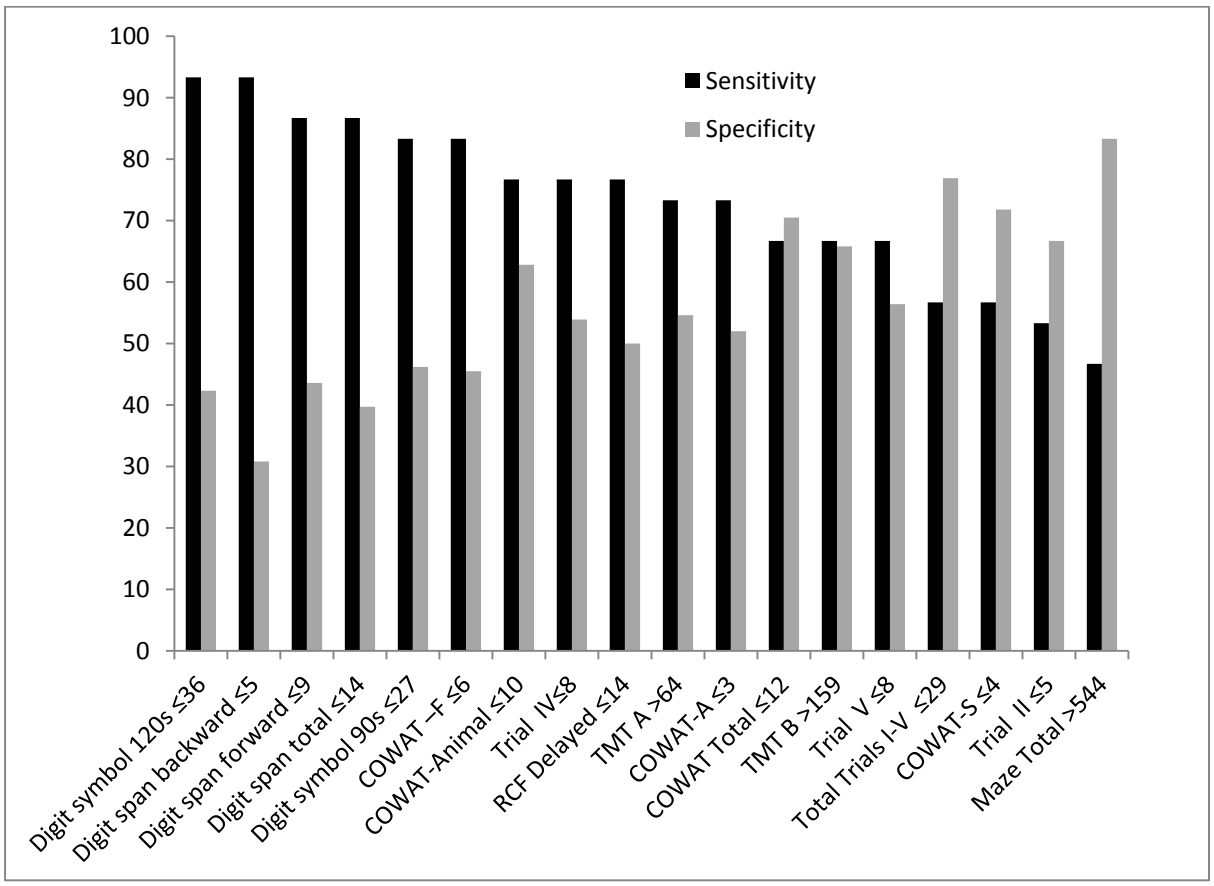
Table 4: Summary of ROC analysis with cut-off score for MCI (n=30) and Controls (n=78)

Test Parameter	AUC (95%CI)	P-Value	Cut-off	Sensitivity	Specificity
RAVLT Trial I	.618 (.519-.709)	.061	≤4	70.0	53.9
RAVLT Trial II	.621 (.523-.713)	.037*	≤5	53.3	66.7
RAVLT Trial III	.618 (.520-.710)	.051	≤7	63.3	56.4
RAVLT Trial IV	.671 (.574-.759)	.002*	≤8	76.7	53.9
RAVLT Trial V	.639 (.541-.729)	.019*	≤8	66.7	56.4
RAVLT Total Trials I-V	.657 (.559-.745)	.009*	≤29	56.7	76.9
RAVLT Immediate Recall	.599 (.501-.692)	.097	≤7	76.7	42.3
RAVLT 20 Minute Recall	.568 (.470-.663)	.229	≤7	86.7	37.2
Digit span forward	.646 (.549-.736)	.011*	≤9	86.7	43.6
Digit span backward	.635 (.537-.726)	.014*	≤5	93.3	30.8
Digit span total	.638 (.540-.728)	.016*	≤14	86.7	39.7
Digit symbol 90s	.677 (.580-.764)	<.001*	≤27	83.3	46.2
Digit symbol 120s	.649 (.551-.738)	.005*	≤36	93.3	42.3
COWAT –F	.685 (.588-.771)	<.001*	≤6	83.3	45. 5
COWAT-A	.631 (.532-.722)	.027*	≤3	73.3	52.0
COWAT-S	.676 (.579-.763)	.002*	≤4	56.7	71.8
COWAT Total	.714 (.619-.797)	<.001*	≤12	66.7	70.5
COWAT-Animal	.754 (.662-.832)	<.001*	≤10	76.7	62.8
Narrative Recall	.557 (.459-.653)	.307	≤12	96.7	23.1
Narrative Delayed Recall	.566 (.467-.661)	.251	≤8	80.0	39.7
Token Test Total	.611 (.512-.703)	.089	≤156	46.7	79.5
RCF Copy	.507 (.409-.604)	.918	>28	73.3	21.8
RCF Recall	.603 (.505-.696)	.062	≤13	76.7	46.1
RCF Delayed	.631 (.533-.722)	.023*	≤14	76.7	50.0
Clock Drawing	.506 (.408-.604)	.922	≤5	16.7	94.9
Luria hand sequence	.537 (.438-.633)	.547	≤3	80.0	28.2
TMT A	.655 (.557-.744)	.006	>64	73.3	54.6
TMT B	.679 (.581-.766)	.001*	>159	66.7	65.8
Maze Total	.685 (.588-.771)	.002*	>544	46.7	83.3

*Significance level set as p< .05 and 95% Confidence Intervals. RAVLT=Rey Auditory Verbal Learning Test, COWAT= Controlled Oral Word Association Test, RCF=Rey Complex Figure, TMT= Trail Making Test

Seventeen of the test scores that significantly discriminated those with MCI from those without were included in an analysis of recommended cut-off scores that yielded the optimum balance between sensitivity and specificity (Figure 2). The highest sensitivity reported was 93.3%, which was for Digit Span (backwards) and Digit Symbol (120s) at cut off scores of ≤5 and ≤36 respectively, with the highest specificity being 83.3% (Mazes Total) at a cut off score of >544. The most balanced sub-test score, the RCF (delayed recall), had a sensitivity of 77.8% and specificity of 76.9%, at a cut off score of ≤14.

Figure 2: Optimal Sensitivity, Specificity and cut-off scores for significant tests for MCI



RAVLT=Rey Auditory Verbal Learning Test, COWAT= Controlled Oral Word Association Test, RCF=Rey Complex Figure, TMT= Trail Making Test

Discussion

This study sought to determine the sensitivity and specificity of a battery of neuropsychological tests in elderly participants from a residential setting who were diagnosed with MCI and dementia. With the exception of recall on the Narrative Memory Test and the Token Test, all the tests were able to significantly discriminate between controls and those with clinically significant cognitive impairment (Dementia or MCI). The Token Test was found to be of little value, in keeping with previous research which found that the Token Test ceiling effects limited its utility (De Jager, Hogervorst, Combrinck, & Budge, 2003). While the tests used in this study have been widely researched, to our knowledge, this is the first time that their diagnostic discriminability was evaluated in a heterogeneous elderly South African population. The findings of this study are discussed in terms of screening for overall cognitive decline, screening for dementia and screening for MCI.

Screening for overall pathological cognitive decline

The Clock Drawing Test has been described as the ideal cognitive screening test due to its ease of administration and scoring, its ability to assess a range of cognitive abilities and good psychometric properties (Royall, Cordes, & Polk, 1998; Schramm et al., 2002; Shulman, 2000). While it has shown good correlation with the Mini-Mental State Examination (MMSE) (r=0.5) (Shulman, 2000), it has also shown moderate sensitivity and specificity in detecting executive dysfunction in patients who have a normal MMSE (Juby, Tench, & Baker, 2002). In this study, the Clock-drawing Test, with an AUC of 0.732, supports its utility as a dementia assessment (Mendez, Ala, & Underwood, 1992; Rouleau et al., 1992; Royall et al., 1998) and confirms earlier findings in differentiating normal

from pathological cognitive decline (Cahn et al., 1996; Tuokko, Hadjistavropoulos, Miller, & Beattie, 1992). However, the sensitivity of 44.4% in this study is much lower than the mean of 85% reported in the literature for dementia screening. The specificity of 91.7% obtained in our study compares favourably with the specificity of 85% reported in the literature (Shulman, 2000). The data support the conclusion that the Clock Drawing Test has value for screening moderate to severe cognitive impairment but is 'relatively poor' at detecting milder forms of cognitive impairment (Nishiwaki et al., 2004).

Screening for Dementia

Memory disturbances is one of the commonest cognitive complaints in the elderly and can be attributed to the normal decline associated with ageing or to dementia (Morris, Worsley, & Maththews, 2000). While there is a range of tests available for assessing memory, the RAVLT is a brief test of memory function that is easy to administer (Rosenberg, Ryan, & Prifitera, 1984) and sensitive to encoding, storage and retrieval of memory (Mitrushina et al., 1994). In this study, the RAVLT demonstrated both discriminant and diagnostic accuracy for identifying dementia, thus confirming its utility in diagnosing the disorder. With the exception of the trial 1 on the RAVLT, all the RAVLT sub-test measures displayed significance at $p<.001$. This finding is consistent with previous studies showing that the RAVLT is useful in distinguishing participants with dementia from those in the control group (Estevez-Gonzalez, Kulisevsky, Boltes, Otermin, & Garcia-Sanchez, 2003a; Mitrushina et al., 1994; M. C. Tierney, Snow, Szalai, Fisher, & Zorzitto, 1996). Some studies have also shown that the RAVLT is useful in distinguishing normal participants and those with dementia associated with Alzheimer's Disease and Vascular dementia (Baillon et al., 2003; Brewster, McDowell, Moineddin, &

Tierney, 2012; Estevez-Gonzalez, Kulisevsky, Boltes, Otermin, & Garcia-Sanchez, 2003b), and that the RAVLT is also able to predict the conversion to dementia in those individuals with subjective memory complaints (SMC)(Estevez-Gonzalez et al., 2003b) and MCI (Hart, Kwentus, Wade, & Hamer, 1987).

The Digit Symbol Test, which measures attention and working memory, also displayed a significance of $p<.001$ for participants with dementia compared to those in the control group. Digit Span was non-significant for dementia. These findings suggest that the memory deficits evident by the RAVLT scores may be attributable to storage and retrieval difficulties. The Digit Symbol Test is more demanding of attention and concentration consistent with the graded deterioration of cognitive functions in dementia. The mean scores on the Digit Symbol (90 secs) in the study were lower than those reported by Hart et al. (25.8 vs 43.7 for control group and 12.9 vs 25.1 for dementia group, respectively). As education level is reported to affect performance on the Digit Symbol Test (F. Ostrosky-Solis, 2004; Feggy Ostrosky-Solis & Lozano, 2006), the finding in our study may be attributed to the lower mean education level of participants compared to Hart et al (Hart et al., 1987).

Another test to display significance at $p<.001$, in differentiating between participants with dementia compared to those in the control group, was the RCF (including both the recall and delayed components of this test). This finding is similar to other studies that showed that the RCF was able to distinguish patients with Alzheimer's disease and Vascular Dementia from those in the control group (Cherrier, Mendez, Dave, & Perryman, 1999), and to show greater impairment in Alzheimer's disease patients than in those with closed head injuries (Bigler, Rosa, Schultz, Hall, & Harris, 1989).

On the COWAT, semantic fluency ('animal' category) displayed diagnostic significance for dementia (p=.017.), whereas phonological fluency (FAS) did not. These findings are consistent with other South African studies (Roos et al., 2010). The superiority of semantic fluency over other verbal fluency measures has been shown in the study by Monsch et al, where category fluency had a sensitivity of 100% and specificity of 92.5% for Alzheimer's disease vs those in the normal control group(Monsch et al., 1992). Semantic categories of a Chinese version of verbal fluency test was also significant in differentiating between control and dementia groups (Chiu et al., 1997).The utility of verbal fluency in discriminating between Alzheimer's disease and healthy controls was confirmed in a meta-analysis showing that the former group were significantly more impaired on semantic fluency than phonemic fluency (Henry, Crawford, & Phillips, 2004). The animal category has a test-retest reliability of .68 (Harrison, Buxton, Husain, & Wise, 2000) and being simple to administer and interpret, can be valuable as a screening and or diagnostic measure for use in low income country settings.

In a 10-year follow-up study, the RAVLT (delayed recall) and the Digit Symbol Test were significant predictors of incident dementia (sensitivity 78% and specificity 72%). The five-year prediction for these tests, together with the Wechsler Memory Scale Information subtest and animal fluency, had a sensitivity of 75% and specificity of 74% for dementia (M.C. Tierney, Moineddin, & McDowell, 2010).

Although the TMT is a popular neuropsychological test and is included in most test batteries, in this study the TMT did not significantly discriminate dementia from non-dementia participants. However this finding may be due to us employing a non-clinical

sample in this study as neuropsychological tests are considered to be less accurate in community samples (Cahn et al., 1995).

Screening for MCI

MCI is widely regarded as an intermediate stage between Alzheimer's disease and normal ageing, and has a heterogeneous cognitive profile (Nordlund, Rolstad, Hellstrom, Sjogren, & Wallin, 2005; R. C. Petersen, 2004). This diversity corresponds to the diagnostic sub-categories of MCI that are distinguished by amnestic and non-amnestic subtypes, with single or multi-domain involvement of other functional areas (R.C. Petersen, 2004). It is therefore recommended that an extensive range of domains be covered when assessing for MCI, including language, memory, executive functions and attention (Grundman et al., 2004; Kramer et al., 2006; R.C. Petersen, Smith, & Waring, 1999; Sachdev et al., 2012). The Goteborg MCI study found that MCI subjects performed worse than controls on five cognitive domains: speed and attention, memory and learning, visuospatial, language and executive functions (Nordlund et al., 2005), a trend also reflected in our study. Several tests displayed significant diagnostic accuracy for MCI, such as, Digit Symbol (90 secs), COWAT F, FAS Total and animal category, and the TMT-B, which were all significant at $p<.001$, with sensitivities ranging from 83.3% to 66.7% and lower specificities ranging from 70.5% to 45.5%. Our findings showed a similarity to the Goteborg MCI study with significantly low scores on memory, attention and working memory, visuospatial and executive functions. Our findings therefore validate MCI as a distinct clinical entity that is distinguishable, with neuropsychological testing, from age-related and dementia–associated cognitive decline.

Compared to the profile of tests that were significant for dementia, the language tests (COWAT FAS, total and animal) and the working memory/attention tests (Digit Span) showed little overlap, suggesting that in this sample at least, that MCI and dementia may represent different clinical entities rather than MCI being a milder or earlier stage of dementia.

Limitations of Study

The small number of dementia cases limits the generalizability of our findings. Also, our sample did not represent all race groups adequately, and in view of the confounding effects of culture on test performance, they should be further researched in a sample with a larger number of Black African participants. Although the ability to speak English was required for eligibility to participate in the study, the confounding effects of language cannot be excluded as English was not the first language of all participants. Further, the discriminatory capacity of the tests for dementia may have been diminished by the inclusion of MCI participants in the comparison group, inflating the mean test scores of the 'non-dementia' group.

Conclusion

The present study supports the view that neuropsychological tests can be effectively used to screen for and/or discriminate between early and later stages of cognitive impairment in the elderly. However, in line with the Jacova 2007 evidence-based review, it is recommended that neuropsychological tests should not be used alone for diagnostic purposes. They should be (1) part of a clinically integrative process, (2) used selectively to aid in distinguishing normal age-related cognition from MCI and early dementia, (3) for the differential diagnosis

of cognitive impairment and (4) possibly assessing the risk of progression from MCI to dementia [10].

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Author's contributions

SR conceived of the study, and participated in its design and coordination, analysed the data and wrote the manuscript. JC participated in its design, performed the statistical analyses and co-wrote the paper. BJP participated in the design of the study, analysis of the data and editing. AIB participated in the design of the study and editing. All authors read and approved the final manuscript.

CHAPTER 8

DISCUSSION, LIMITATIONS AND CONCLUSIONS

8.1 Introduction

In this concluding chapter, the main findings and conclusions of the research study are reviewed, key contributions to the field are highlighted, limitations and weaknesses are addressed, recommendations are made, and priority areas for future research are identified.

8.2 Main Findings and Contributions to the Field

The main aim of the study was to evaluate the performance and utility of a set of screening measures and a neuropsychological battery of tests for dementia screening in a heterogeneous local population.

The objectives of the study were:

1. To establish the utility and validity of subjective measures, objective measures and an informant questionnaire in screening for dementia.

   Papers: Paper 1 (Chapter 4) and Paper 3 (Chapter 6)

2. To establish whether combining screening measures would increase their sensitivity in screening for dementia.

   Paper: Paper 3 (Chapter 6).

3. To establish the optimal cut-off points for identifying dementia on the various screening measures and neuropsychological tests.

Papers: Paper 3 and Paper 5 (Chapter 6 and Chapter 7).

4. To establish the utility and validity of a neuropsychological battery of tests for the diagnosis of dementia in the South African context.

   Paper: Paper 5 (Chapter 7).

The focus was on evaluating screening measures that would be suitable for clinical settings (as opposed to research platforms) and relevant to the local public health services infrastructure. In evaluating the clinical usefulness of these measures for local use, cost and ease of administration are important considerations due to the resource constraints (human, specialists and health-care) experienced locally. The summary is presented with regard to the four main objectives of the study and should be read in conjunction with the relevant discussions in the four main papers.

8.2.1 To Establish the Utility and Validity of Subjective Measures, Objective Measures and an Informant Questionnaire in Screening for Dementia.

In planning to address the increase in the elderly population and the expected increase in disease burden due to cognitive impairment, the need to identify suitable and effective screening measures for local use was identified. A range of measures was assessed to evaluate which measures would be most appropriate. Assessment of their utility was based on the influence of education, and demographic variables on their performance as well as their sensitivity and specificity for dementia.

a. Education and demographic variables

In the screening sample of 302, the mean number of years of formal education was 10.4 years, with the Asians and Black groups having significantly lower means. This impacted on the MMSE scores, with a significant association between low education and lower scores. Black participants scored significantly lower than their White counterparts. However, caution must be exercised in interpreting this information as the number of Black participants was lower than that of other race groups.

As highlighted in the literature review, education has been shown to be the most important non-biological correlate of cognitive performance, with formal education being the most crucial variable in cognitive test scores (Ostrosky-Solis 2004). Lower MMSE scores were significantly associated with race ($p<.001$), and MMSE screen positives had significantly lower education than screen negatives ($p<0.001$). The education effects were not however evident in the SIS, which contains a subset of the MMSE items, suggesting that certain items are more dependent on skills acquired through the formal education process. Education effects were not significantly associated with the presence of SMC ($p=.613$), SMCC ($p=.368$) or SMRS ($p=.753$), and DECO($p=.807$) test scores. Our data therefore confirm the education effects on objective tests of cognition.

CDT scores were not significantly influenced by years of education ($K=0.8$, $p=0.687$). The education effects were observed despite all participants having a minimum of eight years of formal education, confirming the benefits of greater numbers of years of formal education on cognition, consistent with cognitive reserve theory(Stern

2003). Logistic regression testing of the MMSE revealed that for every additional year of education, participants were 0.71 times less likely to be classified as cognitively impaired using the MMSE. In considering the effect of education on individual items within the MMSE, significant associations existed with the following five items: geographical orientation (K=8.1, p=.017), recommended (K=22.3, p=.001) and alternate attention/concentration (K=7.3, p=.026), repetition (K=7.3, p=.026) and construction items (K=13.5, p=.001). These findings highlight the need for the careful choice of psychometric tools, especially when working with populations where education levels differ due to racial, ethnic or socio-economic differences.

b. Race

Ensuring culture-fairness in the South African context is necessary for both professional and political reasons. Race was found to significantly impact on MMSE (p<.001), SIS (p=.041), SMRS (p=.002), but not CDT scores (p=.968). The presence of SMC was not associated with race (p=.123), but SMCC was significantly associated with race (p=.003).Although the MMSE is the most widely used and researched tool in the world, the results obtained in our study suggests caution in its widespread use in the absence of further research, and adaptation for use in all race groups. There were significant differences for the race groups in the recommended attention/concentration item score (the Black group scoring lower - *K*=23.0, p<.001) but not for the alternate item score (*K*=3.6, p=.315). The mean score for Black participants on the recommended item was 1.7±1.5 compared to a mean score of 4.8±0.7 on the alternate item (W=2.6, p=.011). In the whole sample, MMSE scores were significantly associated with both the recommended (p=.014) and alternate

(p=.004) items for attention /concentration but, in view of the significant differences in performance due to race and the stronger association of the alternate item, the latter is recommended for local use.

There was also significant differential item functioning on several of other MMSE test items between race groups. Black participants scored consistently lower than other race groups on three of the orientation items (*K*=9.3, *p*=.025; *K*=9.3, *p*=.025; *K*=16.3, *p*=.001), as well as on the attention/concentration (*K*=23.0, *p*=.000), naming (*K*=10.7, *p*=.014), repetition (*K*=21.4, *p*=.001), comprehension of verbal (*K*=17,0, *p*=.001) and written command (*K*=12.7, *p*=.005) items. Black participants' total score on the MMSE was significantly lower than other race groups, and there was also a significant differential item performance on several MMSE items that resulted in their lower scores.

The elderly participants of this study would have been schooled during the apartheid era, when educational opportunities were particularly discrepant among the various race groups. A significant association between race and years of education (p<.001) was confirmed. However, this does not necessarily convey information about the quality of the education received. Quality of education is increasingly recognised as an important factor in evaluating the relationship between education status and risk for dementia (Manly, Jacobs et al. 2000).

c. Sensitivity and Specificity of Screening Measures

SMCs (p=.002) and SMCCs (p<.001), which are both subjective measures, and the MMSE (p=.010) and CDT (p=.009), which are both objective measures, displayed significant ability to discriminate between controls, MCI and dementia participants, with AUC values exceeding .700. The informant questionnaire, the DECO, failed to show significant discriminative ability between controls, MCI and dementia participants (p=.301) and a sensitivity of 50% for dementia. This could possibly be attributed to the fact that informants were not residing with the participants, hence rendering their observations less accurate. This could also explain the discrepancy in our findings with that of Lenger (1996) in whose study, participants were community-dwelling.

The presence of an SMCC carried a sensitivity of 90.9% and a NPV of 98.3% for dementia, suggesting that this would be a useful screening tool to 'rule out' dementia. Furthermore, as there are no associated costs for its use, and it has extremely modest administration and scoring/interpretation requirements, it lends itself well to application in our low-resourced, busy primary health clinics (PHC).

Our findings suggest that a cut-off score of $\leq$24 be applied locally to achieve an optimum balance of 81.8% sensitivity and 66.7% specificity. Its NPV of 96.1% at the cut-off score of $\leq$23 also identifies it as a useful tool to rule out a diagnosis of dementia. However, given the significant education and race effects on its performance, caution must be applied in its application and interpretation of scores, especially in Blacks. Staff have to be trained to administer and interpret the MMSE,

whose length of administration may pose a challenge for busy, under-staffed PHCs. The copyright cost implications also limit its widespread use in low-resourced settings.

Although the CDT requires minimal training to administer, scoring requires skill. It displayed a relatively low sensitivity of 44.4% at a cut-off score of ≤6, and raising the cut-off score to ≤9 would improve its sensitivity to 80%. Despite its limitations, it has minimal administration costs and its visual nature makes it easy to record and monitor deterioration. It is also a powerful communication tool for caregivers and can probably be better understood than abstract numerical test scores.

8.2.2 To Establish whether Combining Screening Measures Would Increase their Sensitivity in Screening for Dementia.

Combining measures in parallel or sequentially can address the challenges of the 'trade-off' between sensitivity and specificity (Flicker, Logiudice et al. 1997; Mackinnon A 1998; Herman, Gill et al. 2002). The SMCC (a single domain measure) and MMSE (a multi-domain measure) were combined in four different ways and tested for improvements in accuracy of screening for dementia, compared to the use of the MMSE or SMCC alone: *Sequential combination*, *compensatory combination*, c*onjunctive combination*, p*robability combination*.

By combining tests that evaluate complementary functions, their discriminant validity can be improved. The combination of the SMCC and MMSE, using the logistic regression model, provides the best discrimination (AUC>.80). However, its application in clinical settings is impractical, as the calculated scores are arbitrary values that do not share the attributes of the scales of the tests being combined(Mackinnon A 1998). Of the remaining three

combination methods, conjunctive and compensatory combinations added minimal value to the predictive validity of the MMSE of SMCC alone, but sequential screening, as described earlier, improved the sensitivity of the MMSE and the specificity of the SMCC, and may be the most practical and predictive approach in the local setting.

8.2.3 To Establish the Optimal Cut-Off Points for Identifying Dementia on the Various Screening Measures and Neuropsychological Tests.

Using ROC analyses and the Youden index, optimum cut-off scores were determined for the local population for the screening tools (paper 3) and the neuropsychological battery of tests for dementia. For the screening instruments, cut-off scores were presented for achieving optimum sensitivity (80%), optimum specificity (80%) or an optimum sensitivity and specificity. In addition, data is presented for MCI screening.

Similarly, age, gender, race and education-specific norms for cognitively normal elderly, as well as those with a diagnosis of dementia or MCI, were presented for the neuropsychological tests. Optimum cut-off scores for dementia and MCI are presented in paper 4.

8.2.4 To Establish The Utility and Validity of a Neuropsychological Battery of Tests for the Diagnosis of Dementia in the South African Context.

Fifteen of the neuropsychological test scores significantly ($p<.05$) discriminated dementia from non-dementia participants. In addition, the tests and subtests achieving $p<.001$ were: the RAVLT II (.753), RAVLT III (.775), RAVLT V (.812), RAVLT-total (0.805), RAVLT-immediate recall (.770), RAVLT -20 minute recall (.741), Digit Symbol 90s (.828), Digit Symbol 120s

(.804) and RCF copy (.783). The tests with non-significant discriminatory capacity included those that assessed attention (Digit Span), language (COWAT/FAS (total); Narrative Memory Test (delayed recall); Token Test) and executive functions (Luria, TMT, Maze). Based on our findings, the following tests would be useful and sensitive in identifying individuals with dementia: Rey Auditory Verbal Learning Test, Controlled Oral Word Association Test (in particular the animal naming), Rey Complex Figure, Trail Making Test, Clock Drawing Test, Narrative Memory Test (recall) and Digit Symbol.

a. MCI

Although not an original objectives of the study, data was collated for MCI screening and neuropsychological testing, as there is increasing focus on the pre-clinical stages of dementia (Albert, DeKosky et al. 2011; Sperling, Aisen et al. 2011). In the absence of a cure for (Alzheimer's) dementia, and the recognition that Alzheimer pathology is detectable decades before symptoms manifest clinically(Morris 2005), clinical focus on MCI recognition affords patients and clinicians to institute preventive and supportive measures earlier in the disease stage. The SMRS and DECO, with AUC values of .729 and .833 respectively for distinguishing MCI from controls, are worthy of further study. These tests did not display significant utility, as screening tools for dementia suggesting that MCI has a distinct clinical profile dissimilar to that of dementia.

Several neuropsychological test measures displayed discriminability between MCI and controls, indicating that applying different cut-off scores can assist clinicians in identifying individuals with MCI as opposed to dementia. The following tests would be useful in a battery of tests intended to identify individuals with MCI: Rey Auditory

Verbal Learning Test, Controlled Oral Word Association Test, Rey Complex Figure, Trail Making Test, Mazes, Digit symbol and Digit span.

With the exception of the Digit symbol (120s) and COWAT (animal) measures, none of the remaining neuropsychological test measures were significantly associated with level of education. Seven measures were significantly associated with race, with Blacks scoring the lowest. Application and interpretation of these tests should be done with reference to appropriate norms.

b. Sensitivity and Specificity of Neuropsychological Tests

Of the 11 neuropsychological tests evaluated, sensitivities for dementia ranged from 44.4% to 100%; specificity ranged from 20.4% to 96.3%.With few exceptions, the tests are sensitive for the diagnosis of dementia.

c. An algorithm for assessment and referral of cognitive impairment in local public health settings

Based on the findings in this study, the following screening algorithm is proposed for addressing cognitive impairment in the elderly (Figure 8.1). A primary health-care level focussed dementia intervention strategy is necessary in a country such as SA, with fewer than ten geriatricians and fewer than five specialists in geriatric psychiatry, and there are few memory clinics, most of which are urban and tertiary-hospital based. A primary-level approach to screening is necessary to reach the large number of potential referrals, especially those residing in rural areas (Kalula and Petros 2011). However, in keeping with the United States Preventative Services Task Force

(Boustani, Peterson et al. 2003) recommendations and a recent UK systematic review(Alzheimer's Association 2013), population screening for dementia is not recommended. The Alzheimer's Association recommends medical evaluation at the first signs of memory problems(Alzheimer's Association 2013). Our proposed model is in keeping with this recommendation as screening would be focused on those presenting with subjective memory problems.

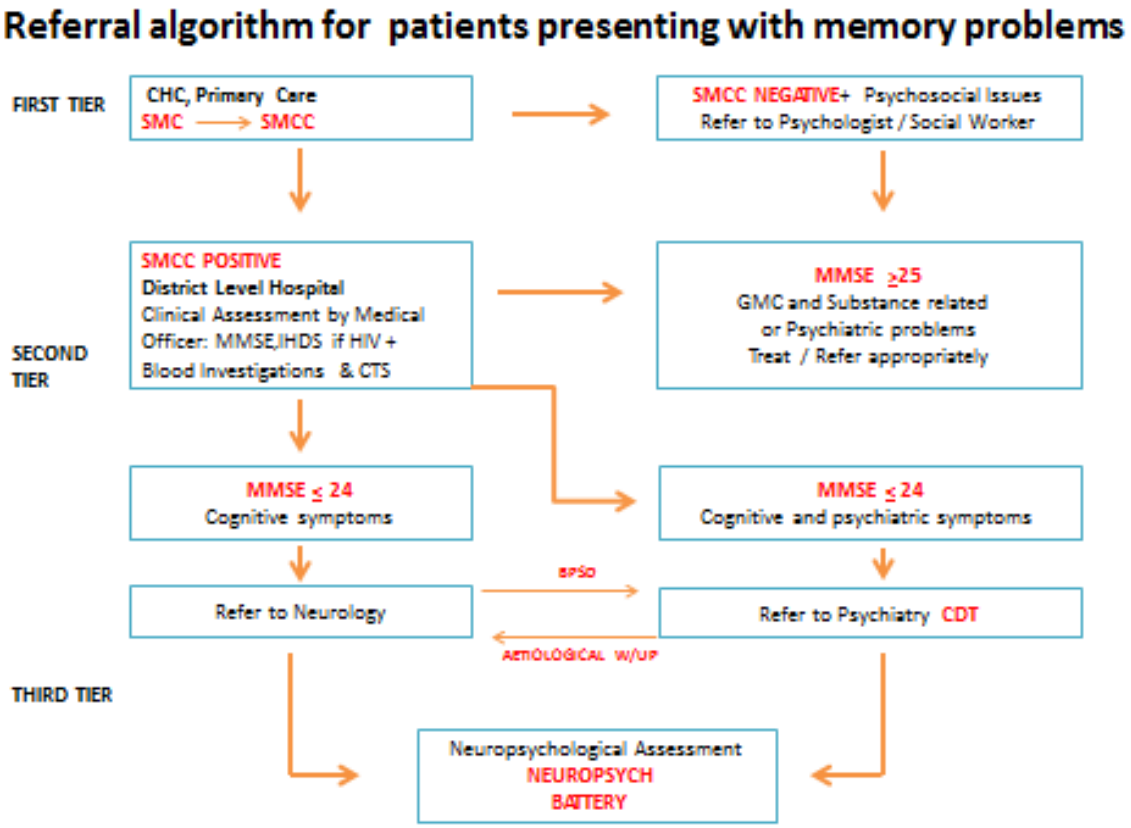

Figure 1: Referral algorithm for cognitive screening

NB. The IHDS was not evaluated in this study

Based on the findings of this study, the following screening model is proposed:

PHC: Nurse-administered Subjective Memory Complaints (SMCC) questionnaire (Table 8.1) to elderly patients. This simple measure will correctly identify 90.9% of individuals who have dementia. This approach is supported by the findings of four studies presented at the 2013 Alzheimer's Association conference citing increasing evidence that self-reported memory or cognitive problems are a potentially valid early clinical marker of brain and cognitive changes that may indicate AD(Alzheimer's Association 2013). Screen positives would then be referred to a district hospital where the MMSE could be administered.

Table 8: Subjective memory complaint screening questions

Subjective Memory Complaint (SMCC) Items
1. Difficulty remembering things that had happened in the last few days?
2. Difficulty remembering the names of common objects?
3. Difficulty remembering where you left your belongings?
4. Difficulty remembering the names of people you have known for a long time?
5. Difficulty remembering the names of people who you had met within the last week?
6. Difficulty finding your way around your home?
7. Difficulty finding your way around other places (e.g. Shopping centre/home of a friend/relative/church)?

Those screening positive on the MMSE using a cut-off score of $\leq$24 would require evaluation for medical causes of cognitive impairment. For those screening negative, depression and other psychiatric or social contributory factors can be excluded. In MMSE screen positives, where no treatable or contributory medical cause can be established, referral to specialist neurologist for further diagnostic evaluation is indicated. Those who have co-morbid behavioural and psychiatric symptoms, treatment by psychiatrists may be necessary before further neurological assessment can be undertaken. At specialist level, the

clock drawing test can be administered as a preliminary cognitive screening tool. At a cut-off score of ≤9, a sensitivity of 80% can be achieved, and a specificity of 80.9% is achieved using a cut-off score of ≤6. A more comprehensive neuropsychological battery of tests can be administered to define the profile of neurocognitive deficits, which can then assist in confirming a diagnosis, determining the likely aetiology (vascular, Alzheimer, fronto-temporal) and severity of the dementia.

8.2 Limitations of the Study

Within the individual papers, specific limitations and weaknesses have been stated.

While the study is valuable in profiling the cognitive status of a local group of elderly residents, the data generated must be interpreted with caution, and a number of limitations are acknowledged.

a. Study population

The ideal sample for a study of this nature would have been community-dwelling elderly. This would have represented a more naturalistic setting. Our use of participants living in a residential setting has potential biases. Many reasons underlie the decision of elderly individuals and their families to opt for residential living. These include financial, social and health reasons. The challenges and burden associated with living with an individual with cognitive impairment has been shown to increase the likelihood of institutionalisation (Boustani, Peterson et al. 2003); conversely, the loneliness and isolation of living apart from family is also known to impact negatively on mental health and can therefore be a risk factor for cognitive decline (Fillit, Butler et al. 2002; Williams, Plassman et al. 2010).

b. Sampling

Ideally, a stratified sample, equally representative of all race groups, would have enabled comparisons to be made between race groups. Unfortunately, all race groups were not equally represented in the population, with very low numbers of Black residents being compounded by a low level of education, resulting in their failure to meet inclusion criteria. The sample size was small. Although the initial sample screened (n=302) was calculated as being optimal to generate sufficient numbers of participants with dementia, the estimated prevalence of dementia in this sample was much lower than the conservative estimate of 25%. This resulted in low statistical power.

The sample was not equally representative of all racial groups, nor was it demographically representative of the racial profile of South Africa. This was due in part to the varying use of old age residences by different race groups for cultural and economic reasons. This resulted in limited ability to compare differences based on race, and the results are therefore not generalizable. Analysis of data along racial lines is necessary in a study of this nature, as the prevalence of dementia and performance on screening and neuropsychological tests are influenced by racial and ethnic variables. Accurate epidemiological and validity data are therefore reliant on racial characterisation of participants.

Exclusion criteria precluded the participation of those with severe cognitive impairment, thus potentially biasing the prevalence figures obtained. We were not able to corroborate data obtained from participants. It was also not practical to obtain collateral information from informants who resided apart from the participants. These limited our

ability to stage or sub-type the dementia cases and self-reported data on symptoms and functional status should ideally be confirmed.

Accessibility to the residents also proved a challenge. Sampling initially commenced with a random selection of residents, generated electronically from the residential database. This proved to be extremely time-consuming, and resulted in a very low yield of residents who agreed to participate and met the inclusion criteria. It was then decided to revert to convenience sampling which entailed approaching every resident in each building systematically according to residential door numbers until the desired number of participants was attained. It is noteworthy that several buildings had to be revisited due to the numbers of residents who were not present during the first round of visits. The number of contactable informants was very low, which hindered the interpretation of the DECO's performance as a screening tool.

c. Language and cultural factors

In a multiracial, multi-linguistic setting, the choice of language is a challenge. To obviate some of the confounding effects of language differences between investigators and participants, it was decided to conduct the study in English only and to restrict participation to those who were proficient in speaking, reading and writing English. This was necessitated also by the use of screening instruments that were available in English and were not validated in the local languages. Almost 90% of the participants in stage 1 used English as the first language. This however does not eliminate the many potential biases due to language and cultural factors that can influence performance on psychometric instruments, as discussed in the literature review.

d. Choice of instruments

As discussed in the literature review, choosing suitable, valid and culture-fair instruments remains a challenge in a setting where dementia has not been much researched and where cost factors preclude large-scale epidemiological and validation studies.

e. Time lag between assessments

The total duration of the data collection spanned eight months. Each of the three stages had to be completed prior to the commencement of the next stage as subsamples from the preceding stage formed the sample for the next stage. Hence, sensitivities and specificities of the screening instruments were based on diagnoses made one to two months later. While there could theoretically have been deterioration in the cognitive status of participants in this interval, we do not believe that this would have substantially impacted on the data. A similar lag existed between clinical assessments and neuropsychological testing.

f. Clinical sample sizes

The number of cases of dementia identified was lower than expected. This could be a true reflection of the prevalence or a result of the exclusion criteria applied.

8.3 Recommendations for Future Research and Practice

The results of this research highlight the need for on-going research into cognitive measures that are valid and culture fair across all racial groups, and that are not significantly

influenced by the education level of individuals. The following recommendations are made as a result of this study:

- Cultural adaptation of the MMSE: this is indicated for administration to Black individuals.
- The use of the alternate attention/concentration item locally: this could reduce false labelling of individuals as being impaired cognitively
- Use the MMSE: translate it into local official languages and validate if this has not been done.
- Determine the utility and validity of subjective memory complaints for dementia screening: this should be replicated in prospective longitudinal studies to determine their predictive validity
- Explore the utility and validity of functional assessments (ADL and IADL) for dementia screening: this is recommended for the local setting. Functional assessments have the potential to obviate many of the cultural biases, language and educational challenges associated with existing psychometric instruments, and their use has minimum cost and administration requirements. Prospective longitudinal studies can be used to determine their predictive validity would be useful.
- Regarding the neuropsychological battery there should be a replication of our findings in larger and more demographically representative samples is necessary. Suitable alternative tests need to be researched to replace those that were not significantly discriminating of participants with and without cognitive impairment viz. the Token and Narrative Memory Tests and the Luria Hand Sequence Test.

8.4 Conclusion

The study provides a useful platform for future local research into cognitive disorders in the elderly. It serves to confirm the effects of age, gender, race and education levels on performance on both cognitive screening and neuropsychological tests. It also highlights the importance of establishing test norms for local populations and defining optimum cut-off scores for cognitive assessment tools. Despite its limitations, the findings have the potential to impact on local clinical services related to dementia:

- Clinical policy guidelines on screening: The findings provide local data on the utility and validity of different types of screening and neuropsychological tests. Further, their applicability at different levels of care can provide a useful framework for the implementation of a screening policy framework. The findings of the influence of race and education level, in particular, have important implications for health care workers' interpretation of psychometric test results.
- Referral policy: The performance of the various assessment measures provides a framework for the development of a referral policy. This is particularly relevant in the local setting where there is a shortage of mental health professionals; appropriate referrals will ensure optimum utilization of limited human resources.
- Increasing knowledge and awareness of dementia and cognitive impairment in the elderly: Locally relevant data will stimulate awareness and knowledge both among community members and the medical fraternity about the importance of dementia.
- Teaching and training: The local data on the performance of screening and neuropsychological tests for dementia can be integrated into the teaching and training of health and para-medical health workers.

- Advocacy: The availability of local clinical data will hopefully encourage community and health-worker advocacy movements to increase awareness of dementia and promote its early recognition and comprehensive treatment.

Future research needs to focus on the replication of the findings on larger, demographically representative samples at a community level and to validate the tools in local ethnic languages.

8.5 References

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APPENDICES

Appendix 1: Glossary

Term	Description
Age associated cognitive decline (AACD)	The concept of mild impairments in multiple cognitive domains but not of sufficient severity to constitute the diagnosis of dementia.
Age associated memory impairment (AAMI)	The concept of increasing memory impairment with age. References memory function in the elderly cohort to young normal adult subjects.
Dementia	A disturbance characterized by impairment in short and long-term memory, associated with impairment in abstract thinking, impaired judgment, other disturbances of higher cortical functioning or personality change. The disturbance is severe enough to interfere significantly with work or usual social activities or relationships with others.
Informant screening measure	Assessments based on the observations of caregivers or family-members
Mild cognitive impairment (MCI)	Characterized by memory impairment, without impairment in daily functioning; the transitional stage normal ageing and early dementia.
Multi-domain screening measures	Assessments based on performance in more than one cognitive domain e.g. memory, executive function, language and visuospatial skills
Objective screening measures	Assessments based on participant's performance on administered cognitive tasks
Single-domain screening measures	Assessments based on performance in one cognitive domain e.g. memory or executive function
Subjective memory complaints/impairment (SMC/SMI)	Subjective reports of memory disturbances of patients with no reference to objective findings.
Subjective screening measures	Assessment based on self-reports of participants

Appendix 2: Abbreviations

Abbreviation	Description
AD	Alzheimer's Disease
AUC	Area Under Curve
COWAT	Controlled Oral Word Association Test
CDT	Clock Drawing Test
CR	Cognitive Reserve
CT	Computerized Tomography
DECO	Deterioration Cognitive Observee
DSM	Diagnostic and Statistical Manual
GDS	Geriatric Depression Scale
NINCDS ADRDA	National Institute of Neurologic, Communicative Disorders and Stroke Alzheimer's Disease and Related Disorders Association
MCI	Mild Cognitive Impairment
MMSE	Mini Mental State Examination
MRI	Magnetic Resonance Imageing
MSE	Mental state examination
RAVLT	Rey Auditory Verbal Learning Test
ROC	Receiver Operating Characteristic
R(O)CF	Rey (Osterreith) Complex Figure
SIS	Six Item Screener
SMC	Subjective Memory Complaint
SMCC	Subjective Memory Complaint-Clinical
SMI	Subjective Memory Impairment
SMRS	Subjective Memory Rating Scale
TMT	Trail Making Test
VAD	Vascular Dementia
WHO	World Health Organization

Appendix 3: Approval Letters African Journal of Psychiatry

From: Christopher Szabo [mailto:Christopher.Szabo@wits.ac.za]
Sent: 18 February 2013 11:25 AM
To: Suvira Ramlall
Subject: African Journal of Psychiatry

Dear Dr Ramlall, this serves to confirm that the following paper – with yourself as first author - has been accepted for publication in the *African Journal of Psychiatry:*

Mild Cognitive Impairment and Dementia in a heterogeneous elderly population: prevalence and risk profile

Yours sincerely,

Christopher P. Szabo

Editor-in-Chief

African Journal of Psychiatry

www.ajop.co.za

From: Christopher Szabo [Christopher.Szabo@wits.ac.za]
Sent: 14 February 2013 11:57 AM
To: Suvira Ramlall
Subject: African Journal of Psychiatry

Dear Dr Ramlall, this serves to confirm that the following paper – with yourself as first author - has been accepted for publication in the *African Journal of Psychiatry:*

Screening a heterogeneous elderly South African population for cognitive impairment: The utility and performance of the Mini-Mental State Examination, Six Item Screener, Subjective Memory Rating Scale and Deterioration Cognitive Observee

Yours sincerely,

Christopher P. Szabo

Editor-in-Chief

African Journal of Psychiatry

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Appendix 4: Additional data: Depression and Dementia

Background

A significant association has been shown between depression and memory impairment (Burt, Zembar et al. 1995) with documented cognitive impairments in geriatric depression(Kramer-Ginsberg, Greenwald et al. 1999). Depression and dementia are prevalent in the elderly and their frequent co-existence suggests that they share complex associations with each other (Chen, Ganguli et al. 1999; Steffens and Potter 2008) either as early manifestation of dementia(Chen.P. and Ganguli M 1999) or a risk factor for its development(Jorm 2001; Ownby, Crocco et al. 2006). Disorders of affect are important in relation to AD because they are potentially treatable, may be indicative of sub-types of AD and impact on caregiver stress(Burns 1991).

Twenty five to fifty per cent of patients with dementia are also depressed (Olin, Katz et al. 2002; Sadock, Sadock et al. 2003; Zubenko, Zubenko et al. 2003). However studies consistently bear out that the prevalence of depressive symptoms is much greater than the prevalence of syndromes of depression as defined by the DSM(Ballard, Neill et al. 2000). Prevalence figures for major depression in the elderly vary considerably (1%-27.1%) based on the population (community, nursing homes, primary care) as well as the diagnostic method used(Mulsant and Ganguli 1999; Teresi, Abrams et al. 2001; McDougall, Matthews et al. 2007).

Major depression occurs in 11.5% of mild and 10% of moderate AD but only in 4.5% of severe AD(Lopez, Gonzalez et al. 1995). The declining prevalence with increasing dementia severity may be related to the declining insight of patients as the dementia progresses, as well as increasing difficulty in eliciting depressive symptoms in the face of advanced cognitive impairment.

Several key brain regions have been implicated in depression, with abnormalities detected on both structural and functional imaging (Steffens, Payne et al. 2002; Steffens DC 2007; Butters, Klunk et al. 2008; Grool, Gerritsen et al. 2013). In a population-based sample of elderly who had depression but no dementia, late-life depression was associated with

smaller total brain and hippocampal volumes and increased white matter hyper-intensities; depression scores were not associated with these pathological findings but were associated with antidepressant use(Geerlings, Brickman et al. 2012).

Depression in patients with dementia has been shown to lead to accelerated cognitive deterioration, irrespective of gender and education levels; this suggests that depression exerts its own adverse impact on cognition (Rapp, Schnaider-Beeri et al. 2011). The influence of depression on cognition may be mediated by neurobiological pathways (Dwivedi, Rizavi et al. 2003; Taylor, Steffens et al. 2003), vascular mechanisms (Steffens, Taylor et al. 2003) or add to the pathology underlying AD(Rapp, Schnaider-Beeri et al. 2006; Rapp, Schnaider-Beeri et al. 2008; Sun, Steffens et al. 2008). Byers and Yaffe provide a comprehensive literature review of the putative neuropathological links between depression and dementia in the elderly, implicating vascular disease, the cortisol hippocampal pathway, amyloid plaque formation, inflammatory and nerve growth factors. The prevalence of depression is greater in vascular dementia (6%-45%) as opposed to AD (10-20%)(Ballard, Neill et al. 2000) and may be related to the different underlying pathophysiological pathways implicated in the two dementia subtypes.

The question of whether depression is a risk factor for dementia has been the topic of much research. A systematic review of case-control and cohort studies conducted by da Silva et al concluded that , while depression may be a prodrome or a risk factor for the development of dementia in the elderly, mood disorders(both depression and bipolar disorder) confer increased risk for dementia (da Silva, Goncalves-Pereira et al. 2013).The literature is divided regarding the effect of depression treatment on the trajectory of cognitive decline in dementia. In light of the multifactorial pathways linking depression and dementia in the elderly, a combined treatment regime is recommended (Byers and Yaffe 2011).

Given the complex relationship between depression and cognitive impairment, a determination of mood status is essential when evaluating the cognitive status of the elderly. Based on current evidence, there are no screening measures that are sufficiently valid for distinguishing between depression, MCI and dementia in a clinical setting, especially when depression and cognitive impairment occur together (Steffens, Potter et al.

2007). Limitations in screening approaches may necessitate comprehensive assessment in complex cases where differential diagnosis is important to treatment planning(Potter and Steffens 2007).

The Geriatric Depression Scale (GDS 30) was specifically created and validated as a self-report tool for the elderly(Yesavage, Brink et al. 1982) and has a sensitivity of 84% and a specificity of 95% at a cut score of 11 and greater(Montorio and Izal 1996). Subsequently the GDS 15 was validated with sensitivity and specificity values of 97.0% and 54.8% respectively at a cut score of 5 and greater(Sheikh and Yesavage 1986; Almeida and Almeida 1999; Aikman and Oehlert 2000). Using a cut-off score of $\geq$ 4, a sensitivity of 100% and specificity of 69.1% has been reported (Rait, Burns et al. 1999)Its use in demented persons is not recommended as it requires the ability to recall affective status for the preceding week (Burke, Houston et al. 1989).The GDS is not valid in demented populations(Montorio and Izal 1996)

Cognitive evaluations should be accompanied by mood assessments in order to exclude depression as a cause or contributory factor. The Geriatric Depression Scale (GDS) was administered as a screening measure for depression in the screening stage of the study. Although this was not one of the objectives of the study, a summary of the data pertaining to the performance of the GDS is presented below as it does have local relevance especially for dementia screening initiatives.

Method

During stage 1 of this study, as reported in chapter 3, the GDS was administered together with the cognitive screening tests to 302 participants.
In stage 2 of the study, 140 participants were administered the Mini-International Neuropsychiatric Interview (M.I.N.I.)**(**Depression)(Sheehan, Lecrubier et al. 1998).

Results

Using the GDS to screen for depression:

A total of 301 participants completed the GDS30. The average GDS score was 8.6 ± 6.5[SR1] (median 7, range 0-29). The total GDS score was significantly associated with race (mean scores of 15.0, 9.4, 8.0 and 8.4 were obtained for Black, Coloured, White and Asian participants respectively; p=.021). The GDS scores were not significantly associated with age groups (p=.829), gender (p=.051) or level of education (p=.099).Using the 30 and the 15 item GDS respectively and standard cut off scores of >11 and >5 respectively, a total of 100 (33.2%) and 95 (31.6%) participants screened positive for depression respectively. The presence of depression (>11 score in GDS30) was not significantly associated with race (p=.08), age (p=.253); gender (p=.127) or education (p=.486).

GDS performance in comparison to other cognitive screening tests evaluated

There was poor correlation between GDS and MMSE scores (r=0.145) and GDS and SMRS scores (r=0.3).However, there was a significant association between being depressed (≥11) and having a subjective memory complaint (SMC), with 64/100 (64%) people who were depressed reporting a SMC; and 64/140 (45.7%) of participants with SMC being depressed on the GDS (Fisher Exact X^2=9.9, p=.006).

GDS30 vs GDS15

There was a good correlation between the GDS 30 vs GDS 15 (r=.93) with 86.3% of the variation explained by the correlation. In testing whether the GDS15 using a standard cut-off of ≥ **5** could be used to predict depression as measured by the GDS30, a sensitivity of 84% and specificity of 95% was obtained.

Clinical assessment of depression

Thirteen cases (9.3%) of major depression (current) were identified; 25 (17.9%) participants had a history of depression. The demographic profile of those with depression is as follows:

12 females and 1 male; 4 Asian, 2 Black, 3 Coloured and 4 White and only 1 with >12 years of education. Average age 69.1 (sd 6.5). Depression was diagnosed in one of the 11 participants who were diagnosed with dementia (9.1 %); 2 of the 38 MCI participants(5.3 %) and 10 of the 81 controls (12.3%); p=.646. Hence there is not a significant association between depression and cognitive impairment (dementia or MCI).The sensitivity and specificity of the GDS for Major Depression was 61.5% (31.6-86%) and 67.2% (58.9-75.4%) respectively.

NB. The GDS was administered at least 3 months prior to the clinical diagnosis (gold standard) of depression.

Discussion

The prevalence of depression in our screened sample (33.2% with GDS 30 and 31.6% with GDS15) and clinically diagnosed sample (9.3%) are in keeping with figures reported in the literature. However the association between cognitive impairment and depression is not born out in our study where there was not a significant association between cognitive impairment (dementia and MCI) and depression. The GDS is the most extensively used self-report questionnaire for depression in the elderly. It has shown good correlations with a clinical diagnosis of depression and this is supported by our findings.

There is a suggestion that race may influence scores on the GDS as a difference in the prevalence(Keyes, Barnes et al. 2011) and nature of symptoms of depression(Ayalon and Young 2003) between American Whites and Blacks has been reported. While Blacks scored significantly higher on the GDS, this did not translate into an increase in screen positives. The GDS has also been shown to be reliable and valid across age, gender and ethnicity groups in an Asian population (Nyunt, Fones et al. 2009).

While GDS depression has been found to be significantly more severe with increasing age and female gender (Osborn, Fletcher et al. 2002; Gautam and Houde 2011)and illiteracy (Gautam and Houde 2011); these associations were not evident in our study. There was a poor correlation between GDS and MMSE scores in our sample. This finding is in keeping

with a recent study which found the GDS to be valid in elderly with low MMSE scores (Conradsson, Rosendahl et al. 2013) and other studies which found no correlation between the scores on the two instruments (Arkin and Mahendra 2001; Begg, Richardson et al. 2006).In our sample, the two versions of the GDS were well correlated and consistent with other studies(Alden, Austin et al. 1989).

Conclusion

Our data on the GDS support the use of both the GDS 30 and GDS 15 in our local population without significant influence on its performance due to race, age, gender, level of education and MMSE scores.

Appendix 5: TAFTA Letter of Approval

TAFTA

80 Aliwal Street,
Durban, 4001

PO Box 2983,
Durban, 4000

Tel: (031) 3323721
Fax: (031) 3378787

2 April 2009

Dr Suvira Ramlall
Principle Specialist Psychiatrist
King George V Hospital
Department of Psychiatry

Dear Dr Ramlall

It was good to meet with you. Thank you for your clear description of the type and extend of your intended research topic.

I am convinced that the end result will be most beneficial.

This letter serves to confirm that TAFTA gives its consent to you conducting this study within our organization. Please be assured that we will offer whatever help and support you may require during your time with us.

Kind regards

Margie Smith

Margie Smith
CEO - TAFTA

The Associations
for the Aged
Fund Raising Number
NPO 002093

Appendix 6: Letter of Approval: Biomedical Research Ethics Committee

UNIVERSITY OF
KWAZULU-NATAL

RESEARCH OFFICE
BIOMEDICAL RESEARCH ETHICS ADMINISTRATION
Westville Campus
Govan Mbeki Building
Private Bag X 54001
Durban
4000
KwaZulu-Natal, SOUTH AFRICA
Tel: 27 31 2604769 - Fax: 27 31 2604609
Email: BREC@ukzn.ac.za
Website: http://research.ukzn.ac.za/ResearchEthics/BiomedicalResearchEthics.aspx

07 June 2010

Dr Suvira Ramlall
PO Box 65810
Reservoir Hills
Durban
4090

Dear Dr Ramlall

PROTOCOL: Screening for and diagnosing dementia in an elderly residential home population. REF: BF200/09.

The Biomedical Research Ethics Committee (BREC) has considered the abovementioned application.

The study was approved by a quorate meeting of BREC on 13 October 2009 pending appropriate responses to queries raised. Your responses received by BREC on 03 June 2010 to queries raised on 23 February 2010 have been noted by a sub-committee of the Biomedical Research Ethics Committee. The conditions have now been met and the study is given full ethics approval and may begin as from 07 June 2010.

This approval is valid for one year from 07 June 2010. To ensure uninterrupted approval of this study beyond the approval expiry date, an application for recertification must be submitted to BREC on the appropriate BREC form 2-3 months before the expiry date.

Any amendments to this study, unless urgently required to ensure safety of participants, must be approved by BREC prior to implementation.

Your acceptance of this approval denotes your compliance with South African National Research Ethics Guidelines (2004), South African National Good Clinical Practice Guidelines (2006) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at http://research.ukzn.ac.za/ResearchEthics11415.aspx.
BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRP) Federal-wide Assurance (FWA 678).

Appendix 7: Payment for use of MMSE

121214342GTT4694_27585401

CUSTOMER ADVICE

2012/12/14

UNIVERSITY OF KWAZULU NAT
UNIVERSITY ROAD CHILTERN HILLS
WESTVILLE
DURBAN
4001

CIB:OIB OPS HUB

OUTWARD TELETRANSMISSION

REFERENCE NO 121214 5426 :: 4694

BENEFICIARY	PSYCHOLOGICAL ASSESSMENT RESOURCES	
BENEFICIARY BANK		
PAYING BANK	STANCHART NEW YORK	
VALUE DATE	2012/12/14	
PRINCIPAL AMOUNT	USD 398.64	
EXCHANGE RATE	8.78570000	
SETTLEMENT AMOUNT	ZAR 3502.33	
TOTAL AMOUNT PAID	ZAR 3565.33	

BANK CHARGES

COMMISSION	ZAR	63.00
TRANSMISSION	ZAR	0.00
SUNDRIES	ZAR	0.00
TOTAL CHARGES	ZAR	63.00

CUSTOMER ACCOUNT NO 5426 0 005 308 216 8
CUSTOMER REFERENCE 51388784

THANK YOU FOR YOUR CUSTOM

Appendix 8: DECO Questionnaire

	Better or about the same	Not as well	Much worse
1. Does he/she remember as well as before which day and which month it is?			
2. When he/she goes out of the house, does he/she know the way as well as before?			
3. Have there been changes in his/her ability to remember her own address or telephone number?			
4. In the house, does he/she remember as well as before where are things usually kept?			
5. And when an object isn't in its usual place, is he/she capable of finding it again?			
6. In comparison with a year ago, how well is he/she able to use household appliances (washing machine,?			
7. Has his/her ability to dress or undress changed at all?			
8. How well does he/she manage his/her money, for example doing the shopping?			
9. Apart from difficulties due to physical problems, has there been a reduction in his/her activity level?			
10. How well can he/she follow a story on television, in a Book or told by someone?			
11. And writing letters for business or to friends, does he/she do this as well as a year ago?			
12. How does he/she recall a conversation you have had with him/her a few days ago? Has this changed over the past year?			
13. if you remind him/her of this conversation, does he/she still have difficulty remembering it in comparison with a year ago?			
14. Does he/she forget what he/she wanted to say in the middle of a conversation? Has this changed over the past year?			
15. In a conversation, does he/she sometimes have difficulty finding the right word?			
16. In comparison with a year ago, how well does he/she recognize the faces of people he/she knows well?			
17. And how well does he/she remember the names of these people?			
18. In comparison with a year ago, how well does he/she remember other details concerning people he/she knows well: where they live, what they do?			
19. Over the past year, have there been changes in his/her ability to remember what has happened recently?			

Appendix 9: Subjective Memory Rating Scale- SMRS

ITEM	DEFINITELY IMPROVED 1	SLIGHTLY IMPROVED 2	NO CHANGE 3	SLIGHTLY DETERIORATED 4	DEFINITELY DETERIORATED 5
NAMES					
FACES					
NAMES OF FRIENDS/RELATIVES					
APPOINTMENTS					
TIME					

In the past 10 or 20 years, do you think?

1. Your ability to remember the names of people you have just met has changed?
2. Your ability to remember the faces of people you have just met has changed?
3. Your ability to remember the names of close friends or relatives has changed?
4. Your ability to remember appointments correctly has changed?
5. Your ability to judge the passage of time and guessing the time of day without looking at a clock or the sun has changed?"

The instrument is scored on a Likert scale: definitely improved =1; slightly improved= 2; no change = 3; slightly deteriorated=4; definitely deteriorated=5.

Appendix 10: Geriatric Depression Scale (GDS)

1. Are you basically satisfied with your life?
2. Have you dropped many of your activities and interests?
3. Do you feel that your life is empty?
4. Do you often get bored?
5. Are you hopeful about the future?
6. Are you bothered by thoughts you can't get out of your head?
7. Are you in good spirits most of the time?
8. Are you afraid that something bad is going to happen to you?
9. Do you feel happy most of the time?
10. Do you often feel helpless?
11. Do you often get restless and fidgety?
12. Do you prefer to stay at home, rather than going out and doing new things?
13. Do you frequently worry about the future?
14. Do you feel you have more problems with memory than most?
15. Do you think it is wonderful to be alive now?
16. Do you often feel downhearted and blue?
17. Do you feel pretty worthless the way you are now?
18. Do you worry a lot about the past?
19. Do you find life very exciting?
20. Is it hard for you to get started on new projects?
21. Do you feel full of energy?
22. Do you feel that your situation is hopeless?
23. Do you think that most people are better off than you are?
24. Do you frequently get upset over little things?
25. Do you frequently feel like crying?
26. Do you have trouble concentrating?
27. Do you enjoy getting up in the morning?
28. Do you prefer to avoid social gatherings?
29. Is it easy for you to make decisions?
30. Is your mind as clear as it used to be?

Original scoring for the scale: one point for each of these answers. Cutoff: normal 0-9, mild depressives 10-19, severe depressives 20-30.

The psychometric properties of the tests are reported in Table 1.

Geriatric Depression Scale.A complex relationship exists between symptoms of depression and dementia. The 30-item GDS will be used to screen for dementia. Statistical analysis will be conducted to assess if the 15-item version, validated overseas, is equally sensitive as the 30-item version. . A score of 11/30 will be used to be indicative of the presence of depression, which correlates with the following scoring system for the GDS:

0-10 = Not depressed ;11-20= Mild depression; 21-30= Severe depression

The 15 items that constitute the 15-item GDS were scored as below.

0-4 No depression' 5-10 Suggestive of mild depression; 11+ Suggestive of severe depression

Appendix 11: Clinical Data Sheet

STUDY NO.

CLINICAL DATA SHEET

1. Name: _____
2. Residence: _____
3. Room No.: _____
4. Telephone: _____
5. Age: _____
6. DOB: _____
7. Gender: M ☐ F ☐
8. Race: A ☐ C ☐ I ☐ W ☐
9. Residential Status: Assisted ☐ Independent ☐
10. Lives: Alone ☐ With Partner/Spouse ☐ Communal ☐
11. Income: State Pension ☐ Private Pension ☐ Family ☐ Other ☐
12. Highest Standard Passed: _____
13. Tertiary Education Y ☐ N ☐
14. Current Employment Status: Retired ☐ Part-Time Voluntary ☐
    Part Time ☐ Full-Time Voluntary ☐
    Full Time Paid ☐
15. Home Language: _____
16. English Proficiency: Speak Y ☐ N ☐ Read Y ☐ N ☐ Write Y ☐ N ☐
17. Marital Status: Single ☐ Married ☐ Divorced ☐
    Separated ☐ Widowed ☐ Living Together ☐

SUBJECTIVE MEMORY ASSESSMENT

Over the last year, have you experienced any of the following?

18. Difficulty at least once a week remembering things that had happened in the last few days? Y N

19. Difficulty at least once a week remembering the names of common objects? Y N

20. Difficulty at least once a week remembering where you left your belongings? Y N

21. Difficulty at least once a week remembering the names of people you have known for a long time? Y N

22. Difficulty at least once a week remembering the names of people who you had met within the last week? Y N

23. Difficulty at least once a week finding your way around your home? Y N

24. Difficulty at least once a week finding your way around other places (such as the shopping centre/home of a friend/relative/church etc)? Y N

IF 'NO' TO ITEMS 18-24, GO TO NO.28
IF 'YES' TO ANY ITEM 18-24 GO TO NO. 25

25. Was the onset: Gradual ☐ Sudden ☐ Unclear ☐

26. If SUDDEN, was there a precipitating event? Y N

(a) If YES, specify…….....

27. Have the memory difficulties been: Stable ☐
Gradual worsening ☐
Deteriorating stepwise ☐
Other ☐

Aphasia

28. At least once a week do you have difficulty finding the right words when you speak? Y N

29. At least once a week do you find it difficult to understand what people are saying? Y N

30. At least once a week do other people have difficulty understanding you when you speak? Y N

Agnosia

31. At least once a week do you have difficulty recognizing objects? Y N

32. At least once a week do you find it difficult to know what to do with certain items? Y N

Executive functioning

33. At least once a week do you feel you cannot cope when you have many things to do at the same time? Y N

Symptoms suggestive of Dementia with Lewy bodies (DLB)

34. Do you see things which others are unable to see (clarify that these are visual hallucinations)? Y N

35. Do you experience difficulties with your concentration, e.g. reading books, watching TV or when knitting? Y N

36. Do you find that there are some days that your concentration is better than others? Y N

37. Are you experiencing any of the following symptoms?

a. stiffness (rigidity) Y N b. shaking limbs or head (tremors) Y N

c. feeling slowed down in your movements, speech or thinking Y N

MEDICAL HISTORY

Have you ever had to see a doctor for any of the following reasons?

38.	Heart attack	Y N	39.	IHD/Angina	Y N
40.	High blood pressure	Y N	41.	High cholesterol	Y N
42.	Blackouts	Y N	43.	Bouts of confusion	Y N
44.	Head injury	Y N	45.	Falls	Y N
46.	Frequent headaches	Y N	47.	Diabetes Mellitus	Y N
48.	Stroke	Y N	49.	Epilepsy	Y N
			49a.	If yes, age of onset _____	
50.	Depression	Y N			

51. Other psychiatric conditions:_____

52. How many operations have you had?_____

(a) Reasons:

_____

53. No. of hospitalizations: _____

54. For which of the above medical conditions are you currently receiving treatment? (list the numbers of the conditions as above)_____

MEDICATION HISTORY

55. Are you currently on medication? Y N

If 'NO', go to No. 62

56. Medication details available from resident. Y N

57. Medication details obtained from bottle/packets. Y N

58. Medication details not available. Y N

59. List of current medications including OTC, HERBAL VITAMINS ETC, and its duration of use.

MEDICATION	DAYS	WEEKS	MONTHS	YEARS

60. No. of prescription drugs= _____

61 No. of non-prescription drugs= _____

SUBSTANCE USE HISTORY

		If yes, please complete below			
Have you ever used any of the following:	**Y / N**	**Current or Past**	**Frequency per day**	**Number of Years of use**	**Pattern of consumption**
62.Cigarettes	Y N	a. Current Past	b.	c.	d. Social Regular
63.Cigars	Y N	a. Current Past	b.	c.	d. Social Regular
64.Pipe	Y N	a. Current Past	b.	c.	d. Social Regular
65.Chew tobacco	Y N	a. Current Past	b.	c.	d. Social Regular
66. Snuff	Y N	a. Current Past	b.	c.	d. Social Regular
67. Alcohol	Y N	a. Current Past	b.	c.	d. Social Regular

FAMILY HISTORY

Do you have a PARENT, SIBLING OR CHILD who has been diagnosed with any of the following conditions?

CONDITION	**Yes No**	**Parent**	**Sibling**	**Child**
68. Heart attack		a)	b)	c)
69. Stroke		a)	b)	c)
70. Hypertension		a)	b)	c)
71. Diabetes Mellitus		a)	b)	c)
72. Parkinson's disease		a)	b)	c)
73. Cancer		a)	b)	c)
74. Dementia		a)	b)	c)
75. Depression		a)	b)	c)
76. Other mental illnesses		a)	b)	c)

SOCIAL ACTIVITIES

Do you engage in any of the following and if so, how frequently?

ACTIVITY	**Never**	**At least once a week**	**At least once a month**	**At least once in 3 months**
77. Going to the hairdresser/barber				
78. Exercise class				
79. Dancing				
80. Attend a social club				
81. Go to the cinema				
82. Visit family/be visited by family				
83. Visit friends/be visited by friends				
84. Attend religious services				
85. Other (reading, puzzles, sport etc specify)				

MENTAL STATE ASSESSMENT

COGNITIVE ASSESSMENT

IMMEDIATE MEMORY:

Registration

Repeat these three words after I say them once: house, fish, ball.

House	**Correct…..1**
	Incorrect…..0
Fish	**Correct…..1**
	Incorrect…..0
Ball	**Correct…..1**
	Incorrect…..0

86. No of items immediately recalled: 0

1

2

3

(repeat up to 5 times until resident has successfully said the 3 words)

87. Number of attempts _____

Good, now remember these words and I will ask you to repeat them later.

Attention, Concentration and Calculation

88. List the days of the week starting from Sunday. **Correct…..1**

Incorrect…..0

89. List the days of the week backward starting from Sunday. **Correct…..1**

Incorrect…..0

90. If you had R20 and bought groceries for R17, how much change would you get?

Correct…..1

Incorrect…..0

91. How much change would you get if you spent R2,50 on milk and paid with a R5 coin.

Correct…..1

Incorrect…..0

SHORT TERM MEMORY:

Recall

List the three items I asked you to remember earlier.

92. No of items recalled:

0
1
2
3

Retrieval of recent information:

93. Who is the President of SA?

Correct…..1

Incorrect…..0

94. What international sporting event was held in SA in June/July this year?

Correct…..1

Incorrect…..0

Retrieval of remote information

95. Which year did SA have its first democratic election?

Correct…..1

Incorrect…..0

96. Who was SA's first democratically elected President?

Correct…..1

Incorrect…..0

ORIENTATION TO PLACE

97. Name of this residence/home

Correct…..1

Incorrect…..0

98. What street is this residence/home on?

Correct…..1

Incorrect…..0

99. Name the city in which we live

Correct…..1

Incorrect…..0

100. Name the province in which we live

Correct…..1

Incorrect…..0

ORIENTATION TO TIME

101. What day of the week is it **Correct…..1**

Incorrect…..0

102. What month is it **Correct…..1**

Incorrect…..0

103. What year is it **Correct…..1**

Incorrect…..0

104. What season is it **Correct…..1**

Incorrect…..0

(acceptable spring or summer)

LANGUAGE

Comprehension: Motor response

105. Nod your head Correct….1 Incorrect ……0

106. Touch your knee Correct….1 Incorrect ……0

107. Point first to the ceiling and then to the window Correct….1 Incorrect ……0

Naming objects

108. Pen Correct….1 Incorrect ……0

109. Cell-phone/phone Correct….1 Incorrect ……0

110. Watch Correct….1 Incorrect ……0

Repetition

111. Fall Correct….1 Incorrect ……0

112. Aeroplane Correct….1 Incorrect ……0

113. The queen lives in a castle Correct….1 Incorrect ……0

114. The dog ate the bone Correct….1 Incorrect ……0

Reading Comprehension:

115. OPEN YOUR MOUTH Correct….1 Incorrect ……0

116. RAISE YOUR HANDS ABOVE YOUR HEAD Correct….1 Incorrect ……0

PRAXIS

Constructional-COPY FIGURES

117. Intersecting circles Correct….1 Incorrect ……0

118. Spiral Correct….1 Incorrect ……0

Writing- write a full sentence.

119. Grammatically correct meaningful sentence (ignore spelling errors) Y N

Without talking show me how you would:

120. Hammer a nail Correct….1 Incorrect ……0

121. Comb your hair Correct….1 Incorrect ……0

122. Wave goodbye Correct….1 Incorrect ……0

123. Blow a candle Correct….1 Incorrect ……0

Executive functions

Abstract-Similarities-

124. Orange/apple Correct….1 (fruit, can be eaten, round etc)
Incorrect ……0

125. Fork/knife Correct….1 (cutlery, made of steel, used to eat etc)
Incorrect ……0

126. Salt/pepper Correct….1 (condiments, can be eaten, powder form etc)
Incorrect ……0

Abstract thinking:

127. Too many cooks spoil the broth. Correct….1(Where there are too many people trying to do something, they make a mess of it)
Incorrect ……0

128. A stitch in time saves nine. Correct….1 (It is better to spend a little time to deal with problems or act right now than wait. If you wait until late, things will get worse, and it will take much longer to deal with them.)
Incorrect ……0

Judgment

You need to cross a road and there is no robot, pedestrian crossing or traffic officer. How would you get across safely? If the test taker says that they never cross the road by themselves (e.g. they are in a wheelchair or their eyesight is poor), then ask them the question again but modify as follows:

"What would anyone who wanted to cross the road have to do to get across safely?"

Examples of Correct Responses	**Examples of Incorrect Responses**
I would look for traffic.	Just go across.
Look left and right.	Put my hand up so the traffic knows I want to cross.
Check the cars.	Go to the corner and cross.
Check that it's clear.	Run as fast as I can.
Go across when there is nothing coming.	Cross when the walk sign is green.
Go across quickly but without running	Cross at the crossing.
Cross to the middle of the road and then look again to make sure there was no traffic before going right across.	Just put my head down and go.
Keep looking for traffic while crossing.	I wouldn't go across.
Ask for help	Wave at the cars so they can see me.
Wait till I could cross with some other people.	
Be careful.	

129. Judgment intact [Y] [N]

DEPRESSION ASSESSMENT-MINI

A. MAJOR DEPRESSIVE EPISODE

(➡ MEANS : GO TO THE DIAGNOSTIC BOXES, CIRCLE **NO** IN ALL DIAGNOSTIC BOXES, AND MOVE TO THE NEXT MODULE)

A1	a	Were you ever depressed or down, most of the day, nearly every day, for two weeks?	NO	YES
		IF NO, CODE NO TO **A1b**: IF **YES** ASK:		
	b	For the past two weeks, were you depressed or down, most of the day, nearly every day?	NO	YES
A2	a	Were you ever much less interested in most things or much less able to enjoy the things you used to enjoy most of the time, for two weeks?	NO	YES
		IF NO, CODE NO TO **A2b**: IF **YES** ASK:		
	b	In the past two weeks, were you much less interested in most things or much less able to enjoy the things you used to enjoy, most of the time?	NO	YES
			➡	
		IS **A1a** OR **A2a** CODED **YES**?	NO	YES

A3 IF **A1b** OR **A2b** = **YES**: EXPLORE THE **CURRENT** AND THE MOST SYMPTOMATIC **PAST** EPISODE, OTHERWISE
IF **A1b** AND **A2b** = **NO**: EXPLORE ONLY THE MOST SYMPTOMATIC **PAST** EPISODE

Over that two week period, when you felt depressed or uninterested:

		Past 2 Weeks		Past Episode	
a	Was your appetite decreased or increased nearly every day? Did your weight decrease or increase without trying intentionally (i.e., by ±5% of body weight or ±8 lb or ± 3.5 kg, for a 160 lb/70 kg person in a month)? IF **YES** TO EITHER, CODE **YES**.	NO	YES	NO	YES
b	Did you have trouble sleeping nearly every night (difficulty falling asleep, waking up in the middle of the night, early morning wakening or sleeping excessively)?	NO	YES	NO	YES
c	Did you talk or move more slowly than normal or were you fidgety, restless or having trouble sitting still almost every day?	NO	YES	NO	YES
d	Did you feel tired or without energy almost every day?	NO	YES	NO	YES
e	Did you feel worthless or guilty almost every day?	NO	YES	NO	YES
	IF **YES**, ASK FOR EXAMPLES. THE EXAMPLES ARE CONSISTENT WITH A DELUSIONAL IDEA. Current Episode ❒ No ❒ Yes Past Episode ❒ No ❒ Yes				
f	Did you have difficulty concentrating or making decisions almost every day?	NO	YES	NO	YES
g	Did you repeatedly consider hurting yourself, feel suicidal, or wish that you were dead? Did you attempt suicide or plan a suicide? IF **YES** TO EITHER, CODE **YES**.	NO	YES	NO	YES
A4	Did these symptoms cause significant problems at home, at work, socially, at school or in some other important way?	NO	YES	NO	YES

A5 In between 2 episodes of depression, did you ever have an interval of at least 2 months, without any significant depression or any significant loss of interest? NO YES

ARE **5** OR MORE ANSWERS (**A1-A3**) CODED **YES** AND IS **A4** CODED YES FOR THAT TIME FRAME?

SPECIFY IF THE EPISODE IS CURRENT AND / OR PAST.

IF **A5** IS CODED **YES,** CODE **YES** FOR RECURRENT.

NO	**YES**
MAJOR DEPRESSIVE EPISODE	
CURRENT	❒
PAST	❒
RECURRENT	❒

A6 a How many episodes of depression did you have in your lifetime? ____

Between each episode there must be at least 2 months without any significant depression.

130. MDD CURRENT= Y N

131. MDD PAST= Y N

132. NO. OF SUBSYNDROMAL SYMPTOMS _____

FUNCTIONAL ASSESSMENT

Can you still perform the following activities on your own? (If unable to perform function clarify if due to physical illness like arthritis, stroke etc and mark as N/A=4) 1=Still able to do independently 2= Requires assistance 3= Does not know 4= Not applicable eg never drove a vehicle

	ADL/IADL	1	2	3	4
133	Bathing with sponge, bath, or shower				
134	Dressing				
135	Using toilet				
136	Getting in and out of bed/chair				
137	Bladder control				
138	Bowel control				
139	Eating				
140	Use the telephone (look up numbers, dial, answer)				
141	Travel alone using public transportation				
142	Drive a vehicle				
143	Prepare a meal				
144	Housework-cleaning flat/room				
145	Operate washing machine				
146	Operate television				
147	Operate radio				
148	Operate microwave oven				
149	Medication use (Preparing and taking correct dose)				
150	Shop for food or clothes (regardless of transport)				
151	Manage your money (banking, pays bills, ATM)				

OBSERVATIONS ON MENTAL STATE(Y/N)

152	Self neglect		165	Slow speech	
153	Un co-operative		166	Poverty of speech	
154	Suspicious		167	Rambling/incoherent	
155	Hostile/irritable		168	Slurred speech	
156	silly/bizarre		169	Perseveration	
157	Psychomotor retarded		170	Lack of insight	
158	Psychomotor agitated		171	Clouded consciousness	
159	Anxious/fearful		172	Peculiar use of terms	
160	Depressed		173	Speaks to self	
161	Labile mood		174	Impaired attention	
162	Flat affect		175	Fluctuating consciousness	
163	Hallucinating		176	Hypochondria cal/somatic	
164	Rapid speech		177	Echolalia	

PHYSICAL ASSESSMENT

178	Systolic BP	Y	N
179	Diastolic BP	Y	N
180	Respiratory signs(creps, rhonchi, dyspnoea)	Y	N
181	Hemiparesis	Y	N
182	Gait abnormality	Y	N
183	Rigidity	Y	N
184	Tremors	Y	N
185	Bradykinesia	Y	N
186	Glabellar tap (>5 abnormal)	Y	N
187	Snout	Y	N
188	Palmomental	Y	N
189	Grasp	Y	N
190	Visual problems	Y	N
191	Wears glasses/contact lenses	Y	N
192	Hearing problems	Y	N
193	Wears hearing aid	Y	N
194	Uses walking aid	Y	N

MODIFIED HACHINSKI SCALE

Abrupt onset	2
Stepwise deterioration	1
Somatic complaints	1
History or presence of hypertension	1
History of strokes	2
Focal neurological symptoms	2
Focal neurological signs	2
Total	11

≥5 = vascular dementia

195. MODIFIED HACHINSKI ISCHAEMIC SCORE =

Name of Psychiatrist_____

Date of assessment_____

196**.Comments**

_____

_____

_____

_____

_____

_____

197. Will resident be willing to have blood tests if indicated by assessment? Y N

198. Will resident be willing to have a CT without contrast if indicated by assessment? Y N

199. If yes to 198, will resident require transport to central town to have CT? Y N

200. If yes to 198, contact telephone number/person if resident has no telephone

_____

_____

_____

FINAL ASSESSMENT BY PANEL

201**.** SMC (yes to any item 18-24) Y N

202. COGNITIVELY IMPAIRED (memory + aphasia and/or apraxia and/or executive functioning) Y N

203. FUNCTIONALLY IMPAIRED (unable to perform at least 2 functions that previously could, impairment not due to physical illness) Y N

204. DELIRIOUS (clouded consciousness, poor attention, fluctuating level of consciousness) Y N

205. DEMENTIA (Yes to 202 and 203; No to 204) Y N

206. MCI

Y	N