Is the Montreal Cognitive Assessment a suitable replacement for Mini Mental Status Examination in the detection of clinical cognitive deterioration?

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Attestation of Authorship

"I hereby declare that this submission is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person (except where explicitly defined in the acknowledgements), nor any material which to a substantial extent has been submitted for the award of any other degree or diploma of a university or other institution of higher learning."

7/01/15

Linda Moses Date

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To those who cannot be thanked enough,

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My family who I have missed so very much during this time

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My children, who remain my greatest work

Abstract

Background: Once situated within a care facility or acute hospital, cognitive impairment may be overlooked by the clinician. Early identification and intervention is critical not only in ameliorating symptoms but also in delaying or potentially arresting further cognitive decline. The Mini Mental State Exam (MMSE) has been the cognitive assessment tool of choice; however it is no longer freely available. The consistent use of a brief screening tool with similar or superior qualities, such as the Montreal Cognitive Assessment (MoCA) tool, is needed.

Aim: To validate the utility of MoCA as a suitable alternative to MMSE in the detection of cognitive impairment.

Methods: The PICO model was deployed to structure the research question and to guide the research design. Literature review was deemed to be an appropriate method for the purposes of this inquiry; articles retrieved were evaluated for inclusion using the critical skills analysis programme (CASP).

Results: Sensitivity and specificity are pivotal to identifying the validity of a cognitive assessment tool, with the use of cut off scores critical to these values. MoCA was more sensitive than MMSE in the detection of cognitive impairment and this was particularly evident in the case of mild cognitive impairment where persons test as 'normal' using the MMSE but are identified as cognitively impaired using MoCA.

Conclusion: Early intervention is key in extending quality of life for persons with cognitive impairment. Thus it was determined that MoCA is a valid brief cognitive assessment instrument and can be recommended for use by healthcare professionals in the early detection of mild cognitive decline.

Chapter 1: Introduction

Individuals suffering from the behavioural and psychological symptoms associated with cognitive impairment are not always afforded the care they need when their level of dependency is not correctly matched to the level of care they require within a residential care setting. Cognitive impairment leads to situations where staff are unable to maintain an individual's safety secondary to wandering, poor memory or lack of insight. Staff in care facilities also struggle to prevent resident's dignity from becoming compromised as would occur when individuals impaired in regulation of conduct used public spaces to perform undressing and hygiene procedures or toileting. As further examples, they may intrude into private spaces, relocate the personal property of others or openly engage in verbal and physical assault. In essence these behaviours place individuals at risk of self-harm or pose a risk to others and they are distressing not only for the individual concerned but for all involved in their care.

Older adults are a vulnerable population and at the time they enter into residential care they are likely to have at least one chronic condition which is often accompanied by multiple comorbidities and may include cognitive impairment (Boyd et al., 2008).

Cognitive impairment is a subtle insidious condition which affects a significant number of individuals as they age and currently there is no process in place to routinely screen for impairment prior to an individual's admission to a care facility. There is also no consistency in utilisation of a cognitive screening instrument and this potentially impedes the transfer of generalizable information between clinicians. It seems appropriate that routine cognitive screening practices be put into place and, ideally, a validated cognitive assessment tool be used to enable the transfer of generalizable information. The purpose of this dissertation is to explore two commonly used cognitive

assessment tools to identify their suitability for use by nurses in residential care facilities.

Cognitive impairment; the situation in New Zealand

In response to a call from the World Health Organisation [WHO] to give public health priority to dementia (WHO, 2012) each New Zealand District Health Board [DHB] was given additional annual funding ring-fenced with the mandate to develop clear pathways for people with dementia in order to maximise wellbeing and ensure they are supported to be as independent as possible. Collaboration between the Ministry of Health [MOH] and DHB's has resulted in New Zealand's Framework for Dementia Care (MOH, 2013). The aim of the framework is to ensure clear guidelines for dementia pathway development ensuring that the individual with dementia has access to services as early as possible and that these continue to end of life. The Framework advocates early identification of cognitive decline as a priority and any individual with known risk factors should be offered routine monitoring including an assessment if cognitive impairment is suspected. Another framework requirement is that health services "develop a standardised assessment process that is culturally sensitive, comprehensive and follows the National Institute for Health and Clinical Excellence [NICE] clinical guideline 42, using a validated assessment tool" (National Institute for Health and Clinical Excellence, 2006, p. 16). The NICE clinical guideline 42 (2006) names MMSE (see Appendix B) as a standardised instrument for use in formal cognitive assessment. In contrast, the New Zealand Framework for Dementia Care (2013) identifies MoCA (see Appendix C) as a validated tool for clinical cognitive assessment, stating that it meets good practice criteria.

In aged care facilities nurses are able to play a key role in improving the situation for individuals with deteriorating cognition through use of a brief cognitive screening tool.

The results of a cognitive assessment could be used to support an application for clinical review potentially culminating in improved case management through the application of relevant interventions. The choice of tools to explore was a result of my working within a single DHB in Auckland. The residential care facility where I was working when this project began utilised the MMSE to assess cognition and the DHB within which the residential care facility is located utilised MoCA. Because of the ongoing discourse regarding which cognitive assessment tool was superior, MMSE or MoCA, the PICO model was engaged and applied to the identified problem in order to arrive at a research question and an appropriate research design to enable resolution. This process will be described in detail but in brief, the research problem identified was a need for nursing to be able to utilise a valid brief cognitive instrument in order to detect clinical cognitive deterioration and direct appropriate care. The research question arrived at was "Is the Montreal Cognitive Assessment a suitable replacement for Mini Mental Status Examination in the detection of clinical cognitive deterioration?" At this point a literature review using the critical skills appraisal programme was deemed a valid methodology.

Chapter 2: Background

The purpose of this project is to establish whether MoCA is a suitable tool to replace MMSE in the detection of cognitive impairment. A reliable and validated brief cognitive screening tool is necessary for use in the early identification of cognitive decline in older aged individuals living within New Zealand's' residential aged care setting.

Population of Interest

One criterion for government funded admission into New Zealand residential aged care is that individuals are aged 65 years and over, therefore cognitively impaired individuals within this age group are of interest for this project. Within the residential care setting there will be individuals who were cognitively intact on admission and who exhibit symptoms suggestive of cognitive impairment. Early recognition is important as the individual can then be facilitated to live well and meet challenges in order that well-being is maximised (MOH, 2013). The governmental drive for early intervention is promoted by many factors including recognition that 50% of persons with mild cognitive impairment will convert to dementia (NICE, 2006).

Early diagnosis of cognitive impairment also facilitates the identification of underlying medical conditions. Sometimes treating underlying conditions can result in reversal of symptoms and/or delay the progression of the condition to dementia. For example vascular causes of cognitive decline can be treated to prevent further deterioration. Alternatively, dementia specific medications such as Donepezil can be administered, which when given early enough can delay dementia, affording the person with dementia and their family time to put in place any legal or financial planning as well as establishing advanced care directives (Chen, Leung, & Chen, 2011). Psychosocial, occupational and physical interventions can be facilitated in a timely manner; not only

does this serve to assist individuals and their families, but can also result in a delay of cognitive decline and prevention of other adverse events (WHO, 2012). In order that the population within the studies reviewed are aligned with those for whom the problem statement was initiated it is desirable to review studies of older aged cognitively impaired individuals who are situated within a residential care setting. Should studies not include all elements of the population of interest then quality analysis of the studies highlighting the relevance of explicit findings in relation to the local population will be important. For example, it is feasible that the care setting from which a population is sampled may prove irrelevant to the findings.

Interventions of Interest

One intervention enabling early identification of cognitive difficulty and which forms the backbone of this project is cognitive assessment screening. This literature review will seek to understand the similarities and differences between the two selected cognitive instruments, MMSE and MoCA. The aim is to establish whether one instrument demonstrates better diagnostic utility in the detection of cognitive impairment. It is therefore important to confirm those traits desirable in a suitable cognitive screening instrument in order to provide reference points for the critique.

According to Larner (2013) the ideal cognitive assessment instrument would be capable of being administered in 15 minutes or less by any clinician. It should test cognition in the domains of visuo-spatial skill and executive function, memory, language, attention and orientation. It should require use of minimal resource, be reliable, and possess test-retest and inter-rater validity as well as being able to detect cognitive disorder. Tests should be easy to interpret and should include clear cut off scores (Larner, 2013).

I begin the literature review in examining what Folstein, Folstein and McHugh (1975) write about the cognitive screener that they developed, MMSE and in what Nasreddine

et al (2005) write about their cognitive screening instrument, MoCA. Review of each tool will facilitate the comparison of one tool with the other as well as providing context when comparing what is known about each tool in relation to information uncovered secondary to the literature review.

Mini Mental State Examination (MMSE)

MMSE was designed to provide a simple, scored and brief tool with which to screen cognitive status while also capable of being administered within 5 to 10 minutes (Folstein et al., 1975). The developers did not intend that MMSE replace a complete clinical appraisal nor be a stand-alone tool upon which a diagnosis could be made. An "accurate diagnosis including appraisal of the significance of cognitive disabilities uncovered in MMSE depend on the evidence provided by a full psychiatric history and pertinent laboratory data" (p. 195).

The developers claimed that MMSE provided a reliable and valid quantitative measure of cognitive function for use in discriminating between those individuals with cognitive disturbances from those with none. A main finding in scoring was that the mean score for "normal" was 27.6; this score agreed with the "clinical opinion of the presence of cognitive difficulties" (Folstein et al., 1975, p. 192). MMSE was said to be ideal for initial and serial measurements and could demonstrate a decline or improvement in cognitive status over time and with treatment. Folstein et al (p. 195) found MMSE "makes more objective what is commonly a vague and subjective impression of cognitive disability during the assessment of a patient. MMSE has become one of the most commonly used brief measures of cognitive status worldwide.

Licensing of MMSE

During the course of this literature review it was uncovered that there exist copyright issues with MMSE and this is perhaps the reason why the DHB no longer uses this tool.

Unless the test is able to be administered from memory, a license must be purchased from www.parinc.com. There may be some protection afforded under the "fair use law" in certain non-profit situations such as research, but this only applies to limited and unspecified parts of the tool (Newman & Feldman, 2011). It seems that information relating to copyright is as yet, largely unknown; copyright is not consistently reported in even the most recently published research. Certainly within the residential care facility where I worked, MMSE was administered without knowledge that copyright was being breached. Copyright issues alone will suffice to ensure many seek to utilise an alternate, suitable and valid brief cognitive screening tool.

The Montreal Cognitive Assessment (MoCA)

Nasreddine et al (2005) developed the MoCA which aimed to support physicians in the detection of mild cognitive impairment (MCI) and which was capable of being administered within ten minutes. Originally designed to test across ten cognitive domains which were generally found to be defective in persons with MCI, the current MoCA tests performance in eight cognitive domains. At the time of its development, no other screening tools were able to reliably and quickly distinguish MCI in individuals from a population of normal controls. Nasreddine et al recommend a cut off score of 26 where those who score 26 or more would be "extremely unlikely to meet clinical and neuropsychological criteria for MCI even after extensive evaluation" (p. 698). Education was noted to correlate with poorer MoCA performance in those persons with ≤12 years of education and to correct for this potentially confounding factor, it was recommended 1 point is added to a person's total score if that score is <30 and the individual had ≤12 years of education.

Nasreddine et al claim MoCA is a "simple stand-alone cognitive screening tool with superior sensitivity" (2005, p. 698). The reasons for the superior sensitivity using

MoCA are inherent in the design; memory testing in MoCA involves “more words, fewer learning trials and a longer delay before recall” (p. 698). Unlike MMSE, MoCA incorporates more numerous and demanding tasks assessing executive function, higher level language ability and complex visuospatial processing, which can be impaired in persons with MCI.

Neuropsychological Battery

Comprehensive neuropsychological battery (NP battery) is suggested to be the gold standard in cognitive testing; however, a paucity of specific information became apparent. I have concluded that an NP battery can consist of a number of individual tests selected to specifically assess performance in various cognitive domains and this will be discussed further when evaluating the literature review findings.

Chapter 3: Research design

In meeting criteria assessing an individual's dependence or in being deemed to have an irreversible condition, older aged people admitted into residential aged care can be said to constitute a vulnerable population. When they become cognitively impaired or their existing impairment deteriorates they clearly become a group in need of strong advocacy in order to assist them to obtain access to relevant services. As nurses we are well placed to note changes in an individual's cognitive status, but do not always have access to a designated tool by which the relevant and vital information pertaining to the deterioration is easily collated for communication to other health professionals. As described in the introduction, the purpose of this research project is to identify a brief cognitive assessment tool capable of validating clinical deterioration in cognitive impairment. In reviewing available literature a plethora of available cognitive measurement instruments became evident; however, the most commonly used tools within clinical practice locally are the MMSE and MoCA.

Step One: Identifying a focus-based question

The first stage in evidence based healthcare is the 'translation of uncertainty to an answerable question' (Pearson, Wiechula, Court, & Lockwood, 2005, p. 208). A research question is defined as an 'explicit query about a problem or issue that can be challenged, examined and analysed and that will yield useful new information' (Wood & Ross-Kerr, 2010) . The specific clinical issue at hand was that nurses need to be able to utilise a valid cognitive assessment tool in order to detect cognitive impairment in a residential care population of older aged individuals. The first step was to formulate a focussed clinical question based on the specific clinical issue. Questions are the "driving force behind evidence based practice and the most challenging aspect is to identify an answerable question" (Davies, 2011, p. 75). A decision was made to structure the research question using the PICO model.

Developed by Richardson, Wilson, Nishikawa and Hayward (1995), the PICO model provides a framework within which a research question can be structured. The elements of PICO are patient population (P), an intervention or independent variable (I), comparison (C), the dependent variables or outcome of interest (O). This paper focusses on older individuals identified as those aged 65 years of age and over (P). The intervention being studied comprises cognitive assessment (I) and specifically comparing an individual's performance using MMSE and MoCA (C). The outcome is to distinguish whether the MoCA is a suitable replacement tool for MMSE in detecting cognitive impairment. Therefore the focus based question for this evidence based literature review is, "Is the Montreal Cognitive Assessment a suitable replacement for Mini Mental Status Examination in the detection of clinical cognitive deterioration?"

Step Two: Conducting a literature search

Trainor & Graue (2014) write that "theory gleaned from extant literature informs the research question and purpose as well as the design and analysis" (page 114). Literature review is the second stage of evidence based healthcare and involves the "systematic retrieval of the best evidence available" (Pearson et al., 2005, p. 208). To locate literature which would assist in answering the identified PICO, specific databases, search terms and limits were used. These are summarised in Table 1. An English language literature search was undertaken and databases searched included Wiley online library, Medline via PubMed, Academic search premier via Ebsco Host, Academic research library via ProQuest, the Cochrane library via Ovid, Evidence based medicine via Ovid and Summon online portal via AUT library. Primary search terms used were 'MMSE' and 'MoCA', secondary search terms used were "superior" and "comparison." Limits used included those articles which were published within scholarly or peer reviewed journals and available in full English text.

Study selection

Articles identified from the electronic searches were then manually reviewed to identify those that were not applicable and identify duplicates. Inclusion criteria included articles with a main focus on comparison between MMSE and MoCA. Potential articles were selected by title and abstract, and where deemed relevant the full article was retrieved. An in depth article review was then conducted to evaluate content in relation to the validity of each cognitive assessment tool in relation to the other. Research articles were manually searched including reference lists for further relevant articles not located through databases, a practice endorsed by the New Zealand Guidelines Group (2001). Exclusion criteria included articles with a main focus on a different condition, the use of a cognitive assessment tool other than MMSE or MoCA, not constituting a comparison study, not focussing on the detection of cognitive impairment, written in another language (despite limiting the search to English) and not available for retrieval (no full text availability or too new to be available for downloading).

In total 508 articles were identified in the early searching phase and of these 495 articles were excluded based on overwhelming broadness to the research topic or where the data was unlikely to be extrapolated into the residential care setting, see table 1 . A total of 13 documents were included for review and the researcher moved to the third step in the process.

Table 1: Literature Search

This table shows the gross numbers of articles retrieved through searching using the key words and in applying the limiters described. The total remaining following exclusion criterion application are shown and the overall total of articles selected for inclusion in the literature review is 13. Key to search terms: (a) MMSE (b) MoCA (c) superior (d) comparison

Database	Search terms	Limiters	Number of articles			
	Keyword		Gross	Less duplicate	Less Not applicable	Net total
Summon	(a) + (b)	Full text, English	736	Not done	Not done	Not done
	(a) + (b) + (c)	scholarly, journal	201	Not done	Not done	Not done
	(a) + (b) + (d)		472	Not done	Not done	Not done
Total number of Summon articles considered – overwhelming number to screen, not used			0	0	0	0
Wiley Online Library	(a) + (b)	Full text, English	41	2	39	0
	(a) + (b) + (c)		24	0	24	0
	(a) + (b) + (d)		38	0	38	0
Total number of Wiley Online Library articles considered			103	2	101	0
Academic Research Library	(a) + (b)	Full text, English	51	7	42	2
	(a) + (b) + (c)		22	10	12	0
Via ProQuest	(a) + (b) + (d)	Peer reviewed	41	16	25	0
Total number of Academic Research Library articles considered			114	33	79	2
MEDLINE via PubMed	(a) + (b)	Full text, English	180	56	121	3
	(a) + (b) + (c)		30	14	16	0
	(a) + (b) + (d)		30	18	10	2
Total number of MEDLINE articles considered			240	88	147	5
CINAHL Plus with full text via	(a) + (b)	Full text, English	9	0	6	3
EBSCO	(a) + (b) + (c)		0	0	0	0
	(a) + (b) + (d)	Peer reviewed	2	2	0	0
Total number of CINAHL articles considered			11	2	6	3
Academic Search Premier via EBSCO	(a) + (b)	Full text	30	0	27	3
	(a) + (b) + (c)		4	4	0	0
	(a) + (b) + (d)	Scholarly	6	6	0	0
Total number of Academic Search Premier articles considered			40	10	27	3
Total number of articles considered			**508**	**135**	**360**	**13**

Step Three: Critical appraisal

The third stage in evidence based healthcare is critical appraisal of the evidence for validity (Pearson et al., 2005) and this occurs through evaluating the rigour of the study design and methods, in identifying the findings and considering the relevance of the findings to the research question.

Quality assessment (CASP)

The Critical Appraisal Skills Programme tool provides the framework for critique in this literature review. Developed during 1993 in Oxford by Dr Amanda Burls, CASP provides a basis to ensure appraised research is reliable, relevant and unbiased (Singh, 2013). There are different tools for each of the study designs: randomised controlled trials (RCT's), systematic reviews, qualitative, case control, diagnostic, cohort, economic evaluation and clinical prediction rule (CASP, 2013).

CASP enables a sound approach to evidence based assessment with the primary goal being to establish validity within a study for review. Each CASP tool is comprised of three sections which in combination establish study validity; the first section is internal validity or rigour of the tool, the second section evaluates the results of the study and the third requires consideration of the results and their application to practice.

Each section of a CASP tool provides prompts which facilitate the researcher in ensuring all important factors are considered when evaluating studies. CASP provides the analysis framework and can be seen in Appendix A. Use of CASP facilitates the independent evaluation of each article allowing themes to become apparent. Identified themes can then be explored in relation to whether MoCA is a valid cognitive assessment tool for the detection of cognitive impairment such that it can be used in place of the MMSE. CASP analysis of the literature reviewed is presented in table 2.

Table 2: CASP analysis

This table shows the CASP analysis for each of the articles reviewed.

Title of study reviewed: A comparison of the MMSE to the MoCA in identifying cognitive deficits in Parkinson's disease Authors and publication date: Zadikoff et al., 2008	
CASP Questions	Findings
Did the study address a clearly focussed issue?	Issue: presence of dementia is an absolute contraindication to deep brain stimulation therefore early recognition of cognitive impairment in PD important. Population: Canadian individuals with PD, mean age 65 years. There were 62 males and 26 females
What method was used to answer their question?	Method: Prospective cross sectional comparison study Study Aim: To determine whether MoCA is more sensitive than MMSE in detecting MCI in individuals with PD
Were the cases/controls recruited in an acceptable way?	No controls. Power calculation used to determine sample size Sample 88 individuals with Parkinson's disease referred to movement disorder clinic Cases defined as idiopathic PD of ≥ 5 years duration, but no standard clinical reference criteria applied
Was bias considered?	Measurements not validated against 'gold standard' neuropsychological testing therefore identified that there may be no certainty that lower MoCA scores are meaningful
What confounding factors have been accommodated for?	Individuals excluded when 'significant' depression present Global level of education information provided and adjustments were made but there is no specific detail about what the adjustment consisted of. "After adjusting for education more subjects scored < 26 on MoCA (43%) than on MMSE" (Zadikoff, 2008, p. 298). Other potentially confounding factors such as age, gender, socioeconomic, cultural background seem to have been overlooked.
What are the results of this study?	Study abandoned early secondary to resource issues Limitation was identified that the cut off score used has not been validated for use in this population Authors note that a longitudinal study is necessary to determine whether MoCA scores are predictors of future decline in this population Authors report that MoCA is less prone to ceiling effects than MMSE
Do you believe the results?	36% of subjects who scored > 25 MMSE had score < 26 MoCA; P = <0.0001 However, not all variables taken into account and it seems the study was discontinued at an undeclared stage therefore total impact unclear
Do the results fit locally?	Results fit locally although it is unclear to what extent the different setting may impact locally i.e. movement disorder clinic population.
Do these results fit with other available evidence?	These results fit with those of other studies; Domain errors using MoCA are reported as occurring in attention, visuospatial and executive function, which is consistent. MoCA was less prone to ceiling effect than MMSE. May be useful to note that this study was likely to have been occurring at the time of MoCA assessment tool publication i.e. 2005, given that this study has a publication date of 2008. Therefore early study results are already indicating the possibility that MoCA is more sensitive than MMSE in the detection of MCI

Study reviewed: Validity of the MoCA and the MMSE in the detection of MCI and dementia in Parkinson disease Authors and publication date: Hoops et al., 2009	
CASP Questions	Findings
Did the study address a clearly focussed issue?	Issue: Concern for the high prevalence (80%) of PD dementia, with impairment not meeting criteria for dementia i.e. MCI occurring in 20-30% of individuals with PD. Population: 132 American individuals with PD; mean age 65.1 years, 75.8% male, 94.7% white, PD duration 5.5 years, 16.5 years education
What method was used to answer their question?	Method: Longitudinal design cohort study using convenience sampling within 2 movement disorder clinics Study aim: To determine whether MoCA is more sensitive than MMSE in detecting MCI in individuals with PD
Were the cases/controls recruited in an acceptable way?	Precisely defined population; demographic and clinical characteristic are listed Power calculation used to determine sample size. 132 individuals with Parkinson's disease referred to movement disorder clinic recruited. Cases defined as idiopathic PD against established criteria; all cases are mild to moderate PD and MCI determined against modified Petersen's criteria. Exclusions include those who had deep brain stimulation within previous 6 months and those with diagnosis of dementia and data when the neuropsychological battery was not completed within 6 months of MoCA and MMSE.
Was bias considered?	There is no use of a control group and the authors' state there was no intention to compare the cognitive functioning of PD individuals with non PD individuals. It is stated that MCI and PDD criteria were applied by an "investigator blinded to the MoCA and MMSE results" (p 1738). Noted 5 of the 7 authors have declared conflict of interest.
What confounding factors have been accommodated for?	Subjects were administered 15 item geriatric depression scale to determine severity of depression symptomatology. Subjects were encouraged to take routine medications to ensure they were assessed during optimised functioning. Adjustments were made to control for age, gender and educational level although the specific details are not provided. Almost 10% of subjects were unable to discriminate colour during Stroop colour test; for any incomplete testing where total point omitted ≤ 3 points, prorated scoring was admitted.
What are the results of this study?	Psychometric properties for the detection of any cognitive disorder were similar with a 95% confidence interval 0.79 for MoCA and 0.76 for MMSE. However, MoCA is superior as a screening instrument in detecting MCI or dementia in individuals with PD and this was evidenced with greater specificity at the optimal screening cut off and MoCA produced a larger range of scores than MMSE; MoCA specificity 0.53, 64% accurately diagnosed; range of scores 12 – 30 or 19 points vs. MMSE specificity 0.38, 54% correctly diagnosed; range of scores 22 – 30 or 9 points.
Do you believe the results?	Relatively low sample population and no matched control group who do not have PD. Participants predominantly well-educated male and white therefore findings may not be generalizable Cube copying was extracted and rescored for use in the NP battery and this could have been a potential limitation in the NP battery
Do the results fit locally?	Detail regarding the population studied is largely relative to the local population (According to Alzheimer NZ (2008) the prevalence of cognitive impairment in New Zealand is not predominantly male). It is unclear to what extent a movement disorder clinic population, i.e. different setting, may impact locally
Do these results fit with other available evidence?	These results reflect those of other studies; MoCA found more sensitive than MMSE in the detection of MCI. Domain errors reported as occurring in attention, language, delayed recall, visuospatial and executive function and orientation

Title of study reviewed: Comparison of the Folstein MMSE to the MoCA as a cognitive screening tool in an inpatient rehabilitation setting Authors and publication date: Aggarwal & Kean., 2010	
CASP Questions	Findings
Did the study address a clearly focussed issue?	Issue: Identification of MCI in patients admitted for rehabilitation important as impairment may impact on their ability to effectively/actively participate. Population: 50 Australian individuals, 42% with primary neurological diagnoses. Mean age 71.7 years, 31 male and 19 female
What method was used to answer their question?	Method: Described by authors as Longitudinal study sampling an Australian inpatient rehabilitation setting. No power calculation given. Study aim: The primary aim is to determine the correlation between MMSE and MoCA scores in individual patients with the secondary aim being to determine whether MoCA more suitable for use in detecting MCI in comparison to the MMSE
Were the cases/controls recruited in an acceptable way?	Cases are poorly defined with no standard reference for clinical criteria, no prevalence data available to analyse whether the sample are representative of the defined population. No power calculation is used to determine sample size. Sample size of 50 individuals is small and the period reported for recruitment i.e. 6 months arguably not indicative of a longitudinal design. Medically unstable subjects and those with aphasia or non-English speaking were excluded from the study as was one individual with dementia
Was bias considered?	No indication that bias has been considered
What confounding factors have been accommodated for?	Authors have indicated a 3 day wait occurred between admission and psychometric testing to allow time for patients to settle into an unfamiliar environment; I suggest this not a sufficient time frame within which to expect older individuals are 'settled.' The authors acknowledge that age, gender, level of education and socioeconomic status influence MMSE and also inpatient populations are more difficult to assess secondary to the interplay of "current physical illness, deconditioning, increased anxiety, noise and distractions" (Aggarwal, 2010, p. 41). There is no adjustment made to control for these factors within the study design.
What are the results of this study?	MMSE was found to perform poorly as a screening instrument for MCI and a marked ceiling effect in MMSE with 20% achieving a perfect score as compared to 7% using MoCA. "Pearson's correlation coefficient reflecting the degree of linear relationship between the MMSE score and the MoCA score was poor at 0.695" (Aggarwal, 2010, p. 40).
Do you believe the results?	Small sample population and no matched control group Participant population poorly defined, identified confounding factors not accommodated. Little or no evidence supports the finding that MMSE is not as sensitive to detecting MCI compared to MoCA. I suggest the study findings should not be used in isolation in order that "MoCA be used over the widely used MMSE" (Aggarwal, 2010, p. 41).
Do the results fit locally?	I perceive marked limitations within this study and therefore do not equate the results with local fit.
Do these results fit with other available evidence?	I perceive marked limitations within this study and therefore do not feel the results elicit meaningful comparison

Title of study reviewed: Is MOCA superior to the MMSE to detect post stroke cognitive impairment. Authors and publication date: Godefroy et al., 2010	
CASP Questions	Findings
Did the study address a clearly focussed issue?	Issue: "Post stroke cognitive impairment is frequent, remains underdiagnosed and results in poor prognosis" (Godefroy, 2011, p. 1712). Population: cerebral infarct or haemorrhage patients within a French Hospital. Mean age 68.2 years, 60 out of 95 participants were male.
What method was used to answer their question?	Method: Longitudinal cohort study over 6 month timeframe; case and controls for education age effect only. Study aim: To test the hypothesis that MoCA is more sensitive than MMSE in detecting cognitive impairment in a population of sub-acute stroke patients
Were the cases/controls recruited in an acceptable way?	Consecutive admissions were recruited. The population was precisely defined using standard clinical reference criteria. No power calculation was given; however, there were a total sample of 95 acute stroke patients referred to movement disorder clinic. Individuals with severe general and neurological conditions which would preclude neuropsychological testing as well as those individuals who did not provide consent were excluded. Detail regarding recruitment of controls not given
Was bias considered?	MoCA and MMSE performed in a counterbalanced order and with a mean stroke interval of 6.6 days to control for potential order effect All patients administered MoCA and MMSE and those scoring ≥ 23 using MMSE were also administered a NP battery. Research funded through centre National pour la Recherche Scientifique.
What confounding factors have been accommodated for?	The presence of depression was considered but it is unclear whether this was controlled for in any manner. Age and education were given as confounding factors which were controlled for through the refining of cut off scores. The authors state that there was no evidence supporting the recommended cut scores for MoCA which need to be "refined in a large sample representative of the general population" (Godefroy, 2011, p. 1715). In using the refined cut off score they found that sensitivity of MMSE was improved at the cost of MMSE specificity and conversely, the specificity of MoCA was improved at the cost of MoCA.
What are the results of this study?	The main finding of this study is that when adjusted cut off scores are used MoCA is not more sensitive than MMSE for screening of cognitive deficit. Both tests had discriminant validity to identify impaired and non-impaired subjects; 95% confidence interval of 0.818 to 0.949 for MMSE and 0.832 to 0.956 for MoCA. The presence of cognitive impairment was associated with "age, more severe neurological deficit, higher depression scores, left sided stroke and poor outcome" (Godefroy, 2011, p. 1714).
Do you believe the results?	Using published norms patients were less frequently impaired when using MMSE than when using MoCA which fits well with the results of other studies. Discriminant validity of each test is reinforced through comparison with neuropsychological battery, although unclear whether this can be relied on given that not all subjects were NP tested. I feel the authors have not considered the effect of using a younger population to determine the effects of age and education using linear regression analysis and on which they have based the altered cut off scores. The alteration quite obviously leads to different results and the concept of cut off scores becomes undermined to such an extent they appear arbitrary as opposed to scientific, are the new results potentially invalidated as an outcome of this process?
Do the results fit locally?	The population studied and results would be relative to the local population when published norms have led to use of the cut off score. It is not clear how the setting, in this instance an acute hospital would affect outcome within a residential care setting.
Do these results fit with other available evidence?	These results do reflect those of other studies ONLY when considering results in which published norms have been used as cut off score.

Title of study reviewed: Underestimation of cognitive impairment by MMSE versus the MoCA in patients with transient ischaemic attack (TIA) and stroke Authors and publication date: Pendlebury et al, 2010	
CASP Questions	Findings
Did the study address a clearly focussed issue?	Issue: The MMSE has been found insensitive to mild cognitive impairment, MoCA may detect cognitive deficit in patients with cerebrovascular disease. Population: 80 patients drawn from the Oxford vascular study at either a 6 month or 5 year follow up visit post TIA or stroke.
What method was used to answer their question?	Method: Longitudinal cohort study Study Aim: To determine the validity of MoCA versus MMSE in a population of individuals with cerebrovascular disease and in whom frontal lobe deficits may be prominent.
Were the cases/controls recruited in an acceptable way?	493 patients were enrolled at either their 6 month or 5 year follow up visit following TIA or stroke; a power calculation is given. 80 were excluded secondary to aphasia or presence of dementia, a small number were unable to operate their dominant hand. Non testable patients were predominantly older and more likely to have had a previous cerebrovascular event. More stroke patients were excluded than TIA.
Was bias considered?	Limitation reported by authors through an inability to determine sensitivity and specificity of the MoCA in the detection of cognitive impairment as formal NP testing was not performed. Heterogeneity is considered secondary to the application of the tests by different investigators and testing at differing stages in the patient's condition i.e. 6 months post stroke and then again at 5 years post stroke. The authors neglect to recognise that order effect should have been considered as they routinely administered MMSE at the start of each patient appointment and MoCA administered at the end of each 30 minute appointment.
What confounding factors have been accommodated for?	Examination occurred at the end of the appointment which may affect test performance and therefore results, secondary to fatigue. The authors assert that some prospective subjects were too old to test, those with dysphasia and dementia were also excluded. The authors state that results were similar between older and younger individuals and results also seemingly not affected through differing levels of education.
What are the results of this study?	The authors assert that they have identified that MoCA detects more cognitive deficits than MMSE in a population of cerebrovascular patients.
Do you believe the results?	Results are credible despite limited information available in how results were reached; 58% of patients with normal MMSE had an abnormal MoCA score and these patients were more dependent as measured by Rankin scale. This is an important finding with potential to impact within all clinical settings
Do the results fit locally?	Older individuals mean age of 69.9 years in both cohorts combined i.e. 6 month and 5 year follow ups; community dwelling population assumed
Do these results fit with other available evidence?	These results are well aligned with the findings in other studies reviewed. Note: a cut off score of ≥ 27 on MMSE and < 26 on MoCA was the point at which cognitive impairment was identified within this study.

Title of study reviewed: The MoCA and the MMSE as screening instruments for cognitive impairment: Item analyses and threshold scores Authors and publication date: Damian et al., 2011	
CASP Questions	Findings
Did the study address a clearly focussed issue?	Issue: MoCA has been studied in a number of different clinical populations but not all studies have included NP battery as a reference standard Population: 135 subjects, 89 cognitively normal and 46 cognitively impaired. "Mean age, years of education, prevalence of subjects with less than 12 years education and prevalence of movement disorders did not differ substantially between the two groups" (Damian, 2011, p. 128).
What method was used to answer their question?	Method: Longitudinal cohort study Study Aim: To perform an item analysis of the MoCA compared to the MMSE in the prediction of cognitive impairment and to examine the characteristics of different MoCA threshold scores. Threshold scores is used as an alternate term meaning cut off scores
Were the cases/controls recruited in an acceptable way?	Cross sectional study, no controls recruited from within an American brain and body donation programme where enrolled individuals undergo annual standardised examination including physical and neurological exam, neuropsychological assessment and evaluation by a movement disorder specialist – cases are precisely defined although diagnoses not operationalised against standard clinical criteria
Was bias considered?	MMSE administered first then MoCA, usually on the same day followed up with NP battery with all test being completed within one month.
What confounding factors have been accommodated for?	Individuals were assessed for depression but it is not clear whether adjustments were made or significantly depressed individuals excluded for example. Age, gender, level of education and the presence of any movement disorder are considered, however, no adjustments appear to have been made
What are the results of this study?	Confirmation through discriminant validity compared to NP battery that the MoCA tasks are not all of equal predictive value, the task to name unfamiliar animals was found to have a ceiling effect (too easy) while the 5 word recall task was found to have a flooring effect (too hard). Receiver operating characteristic (ROC) demonstrated that for any cut off score selected for MMSE, there was a cut off score for MoCA that yielded both higher sensitivity and specificity (Damian, 2011, p. 128).
Do you believe the results?	The authors offer sample homogeneity as a potential limitation of this study, however, the results appear credible
Do the results fit locally?	The population studied here may not be reflective of the local population. It is unclear to what extent the recruitment setting may impact locally and there is no information on either conditions which individuals may have nor comorbidities
Do these results fit with other available evidence?	Given that the study results demonstrate superior sensitivity of MoCA compared to that of MMSE in the detection of cognitive impairment, the results fit with those of other studies

Title of study reviewed: The MMSE and MoCA in individuals with mild sub-acute stroke: relationship to functional outcome Authors and publication date: Toglia et al., 2011	
CASP Questions	Findings
Did the study address a clearly focussed issue?	Issue: Cognitive impairment is known to adversely affect functional outcome post stroke and little is known about the impact of MCI. Population: 72 American post-stroke rehabilitation inpatients, median 8 days post-stroke, 13 haemorrhagic and 59 ischaemic strokes, 34 males and 38 females, mean age 70 years, predominantly white 52/72
What method was used to answer their question?	Method: Retrospective cohort study Study Aim: To determine and compare MoCA and MMSE global and sub scores in detecting cognitive impairment in individuals with mild stroke. Authors hypothesised that MoCA would correctly classify more patients as cognitively impaired and be highly correlated to functional status at time of discharge
Were the cases/controls recruited in an acceptable way?	Recruits with a primary diagnosis of stroke were retrospectively analysed Population is well defined as stroke and functional status were operationalised against standard criteria
Was bias considered?	The measures are not validated against standard NP criterion and there are no controls
Confounding factors that are accommodated for?	Participant group consisted of primarily white individuals with high level of education for which an adjustment is made. No other confounding factors are considered
What are the results of this study?	Individuals with "severe strokes or moderate to severe cognitive and language impairment were exclude due to priori criteria" (Toglia, 2011, p. 796). Authors identify a limitation secondary to not utilising the NP battery in the study design; "only with such a criterion standard can true sensitivity of the MoCA for detecting cognitive impairment can be ascertained" (Toglia, 2011, p. 797).
Do you believe the results?	The MMSE was less sensitive in classifying cognitive impairment than MoCA and this represents a consistent finding Domain findings are aligned with those identified in the literature and include delayed recall, visuoexecutive and verbal fluency are the most impaired tasks in MoCA and in MMSE delayed recall resulted in the lowest sub-score. Patients performed similarly in orientation and serial subtraction using both tests
Do the results fit locally?	The results are likely to fit with the local population. It is unclear to what extent an inpatient rehabilitation population may impact locally
Do these results fit with other available evidence?	These results reflect those of other studies: 67% of individuals, who scored at or above the cut off score of 27 on the MMSE, were found to be cognitively impaired using MoCA.

Title of study reviewed: Screening for MCI in patients with heart failure: MoCA versus MMSE Authors and publication date: Cameron et al., 2012	
CASP Questions	Findings
Did the study address a clearly focussed issue?	Issue: Individual's with congestive heart failure (CHF) have a 62% increased risk to develop cognitive impairment than those individuals without CHF Population: 93 Australian inpatients with CHF. A power calculation was made to determine sample size. Demographics include mean age of 70 years, 77% had completed ≤ 12 years of education, 39 participants lived alone and 44 participants had functional deficits. 71% male
What method was used to answer their question?	Method: Participants were opportunistically recruited from within an existing cross-sectional observational study and this study uses a cross sectional cohort methodology. Study Aim: To compare the performance of MoCA to that of MMSE in the detection of MCI in patients with congestive heart failure.
Were the cases/controls recruited in an acceptable way?	Participants were referred from a CHF management programme. Diagnosis of CHF was operationalised against standard clinical criteria. Exclusions were made on the basis of pre-existing neurocognitive issues, usually resides within residential care, inability to answer questions secondary to language barriers or visual acuity
Was bias considered?	Order of MMSE and MoCA administration was randomly assigned to control for order effect. 30 individuals who met study eligibility declined to participate predominantly due to priori criteria. There is no control group. Authors indicate that the measurements were not validated against 'gold standard' neuropsychological testing therefore MoCA may have over-identified impairment
What confounding factors have been accommodated for?	Only 25 participants were not depressed but no indication if this was controlled for or depressed subjects excluded Age, gender, education and cultural background have also been considered as potentially confounding factors, however, there have been adjustments made to control for these effects in the study design Individuals with poor vision or hearing were excluded from the study
What are the results of this study?	Main finding is that MoCA is more clinically effective than MMSE in the detection of MCI in a individual's with CHF. Using a cut off score of <26 for MoCA and <27 cut off score for MMSE, there were statistically more individuals classified as impaired
Do you believe the results?	The results bear strong correlation to those of other studies and demonstrate strong statistical reliability. The study provides strong evidence for the validity of MoCA as a suitable tool to classify MCI in this patient population
Do the results fit locally?	The results are relative to the local population and, although reflective of an acute inpatient sample, are likely to be generalizable to other settings.
Do these results fit with other available evidence?	These results reinforce those found in other studies

Title of study reviewed: The MoCA is superior to the MMSE in detecting patients at higher risk of dementia Authors and publication date: Dong et al, 2012	
CASP Questions	Findings
Did the study address a clearly focussed issue?	Issue: presence of dementia is an absolute contraindication to deep brain stimulation therefore early recognition of cognitive impairment in PD important Population: 230 Singaporean memory clinic recruits; mean age 72.7 years, 103 males and 127 females, mean 6.1 years education
What method was used to answer their question?	Method: Prospective study recruiting consecutive new patients attending a memory clinic over a 26 month period Study Aim: To examine the discriminant validity of the MoCA and the MMSE in detecting patients with cognitive impairment within a memory clinic population. Exclusions were made if people were visually or hearing impaired, presence of manifest psychiatric disease, or had moderate to severe depression as determined by geriatric depression scale (GDS), incomplete investigation were also excluded. All participants were administered the MoCA, MMSE, GDS and a formal comprehensive NP test covering 7 cognitive domains and administered by trained researched psychologists, though the process is not clear i.e. temporal lapse between tests and whether controlled for order effects.
Were the cases/controls recruited in an acceptable way?	Cohort, no controls. The cases are precisely defined using standard clinical diagnostic criteria applied using DSM-IV for dementia and Petersen's criteria for MCI. Additionally Petersen's diagnostic algorithm was applied to categorise MCI into 4 subgroups; amnestic MCI multiple domain, Amnestic MCI single domain, non-amnestic MCI multi domain, non-amnestic MCI single domain.
Was bias considered?	Measurements are validated against 'gold standard' neuropsychological testing therefore scores are meaningful. Depression measured using the Geriatric Depression Scale
Confounding factors that are accommodated for?	Individuals excluded when moderately to severe depression present. Age and education were considered as potentially confounding factors "There were no significant differences in gender and ethnic groups distributions across diagnostic groups" (Dong, 2012, p. 1752).
What are the results of this study?	MoCA superior to the MMSE in the detection of cognitive impairment and patients with "lower MoCA scores should receive a more comprehensive neuropsychological evaluation" (Dong, 2012, p. 1754). Limitation identified that results may not be generalizable to the community where people are less likely to be as impaired as memory clinic population. Discriminant validity of age and education adjusted scores was not conducted. High internal consistency in demonstrated in MoCA, $\alpha = 0.96$. Total MoCA and total MMSE scores indicate good convergent validity; at $r\,(230) = 0.93$, $p < 0.01$
Do you believe the results?	The results appear credible, however the authors have indicated that their findings may vary from those in other studies secondary to the use of different NP batteries to define cognitive status, different comparison methods used to determine the discriminant validity between the MoCA and the MMSE, different populations – they have included all presentations to a memory clinic as opposed to carefully selected participants
Do the results fit locally?	It is unclear to what extent or whether the Singaporean version of MoCA may have affected values and how this may correlate with results in the local population. It is not clear whether the results from a memory service study are generalizable to the local population
Do these results fit with other available evidence?	These results reinforce those found in other studies. It is unclear to what extent or whether the Singaporean version of MoCA may have affected values and how this may correlate with results in the local population

Title of study reviewed: Differences in cognitive profile between TIA, Stroke and Elderly Memory research subjects: A comparison of the MMSE and MoCA Authors and publication date: Pendlebury et al., 2012	
CASP Questions	Findings
Did the study address a clearly focussed issue?	Issue: cognitive impairment, greater than that expected for age, is associated with increased risk of dementia in patients with cerebrovascular disease Population: Patients from Oxford vascular study were compared to those in the Oxford Project To Investigate Memory and Aging study (OPTIMA) United Kingdom study. TIA and stroke operationalised using WHO criteria
What method was used to answer their question?	Method: Longitudinal cohort study Study Aim: To compare the performance of MMSE and MoCA in TIA and stroke patients; expecting a pattern of vascular cognitive impairment in cerebrovascular patient cohort (attention and executive function) and memory deficit in the memory research cohort
Were the cases/controls recruited in an acceptable way?	Sample consisted of 107 memory research subjects, 46% male and older with mean age of 76 years and higher level of education than cerebrovascular cohort. There were 363 cerebrovascular subjects, 53% male. Exclusions included those subjects moderately to severely cognitively impaired, an inability to use the dominant arm and aphasia. Consecutive cerebrovascular patients were administered MMSE and MoCA ≥ 6 months following the index event and on consecutive memory research patients. A cut off score of ≥ 27 on MMSE was an indicator for normal cognitive function and a score of < 26 on MoCA an indicator for impaired cognitive function.
Was bias considered?	I consider that bias may occur through the exclusion of subjects with MMSE <24 and secondary to study funding through various UK institutions.
Confounding factors that are accommodated for?	Age and education were controlled for through an adjustment; one point added when education level < 12 years, socioeconomic and cultural factors are not considered. The authors note that the Oxford vascular study and the OPTIMA study were two independent studies and therefore this may have resulted in subtle differences in administration of the tests, which may affect the results.
What are the results of this study?	The MoCA is demonstrated to be superior to the MMSE in the detection of cognitive impairment in both the memory research cohort and the cerebrovascular cohort
Do you believe the results?	The overall results are credible given they are well aligned with the findings in other studies but there exists no data which allows comparison between studies as a different comparison tool is used within this study and there are no sensitivity or specificity data
Do the results fit locally?	The results would fit within a residential care population
Do these results fit with other available evidence?	The global outcome is consistent with findings in other studies; MMSE insensitive to MCI 32 memory research cohort were normal scored using MMSE ≥ 27 and of these 31 were impaired using MoCA < 26

Title of study reviewed: Montreal Cognitive Assessment and Mini-Mental State Examination are both valid cognitive tools in stroke Authors and publication date: Cumming, Churilov, Linden & Bernhardt, 2012	
CASP Questions	Findings
Did the study address a clearly focussed issue?	Issue: Because of a reported high conversion rate of mild cognitive impairment to dementia, the researchers conducting this study wanted to be able to detect individuals with early cognitive impairment within a memory clinic population; MMSE testing in the domain of memory was limited. Population: Australian individuals mean age 72.1 years, 44 males and 16 females, mean 10.5 years of education
What method was used to answer their question?	Method: Prospective cross sectional study occurring over a 30 month period. Study Aim: To determine and compare the validity of MoCA and MMSE as screening tools for cognitive impairment after stroke.
Were the cases/controls recruited in an acceptable way?	Cohort, no controls. Sample 60 individuals with completed ischaemic or haemorrhagic stroke admitted to an Australian stroke unit; a power calculation was made to guide sample size. "Criterion standard classification of cognitive impairment was determined based on the NP battery" (Cumming et al., 2012, p.124). Exclusions were made on the basis of major visual, hearing or language impairment, unconscious on admission to hospital, youth; screening for recruitment took place during the acute phase.
Was bias considered?	NP battery conducted one week post initial MMSE and MoCA administration, which was conducted at 3 months post stroke by 2 psychology graduates trained in administration and scoring of the tools. NP battery conducted by a researcher blinded to the findings of the first testing session. Participants were screened for depression. MMSE/MoCA administered in counterbalanced order
What confounding factors have been accommodated for?	Site of cerebral insult was considered as potentially confounding; "mean screening tool score did not significantly differ by lesion side" (Cumming et al., 2012, p. 125). Some influence on predictive validity was noted in lesion side; "area under the curve higher in those with right hemisphere lesions than those with left" (Cumming et al., 2012, p. 125). Depression and anxiety were not significantly correlated with total score on the MMSE or MoCA; I assume, therefore, that adjustments were not made for this potentially confounding factor. Authors state both tools are subject to the effects of age and education though no indication given as to whether adjustments are made to control for these; I assume, therefore, that adjustments were not made for this potentially confounding factor.
What are the results of this study?	The authors indicate their main finding is that both MMSE and MoCA are "both good clinical indicators of cognition after stroke" (Cumming et al., 2012, p. 128). When using the optimal cut off scores (which are not provided) the MoCA correctly classified 43 of 60 patients as cognitively impaired and the MMSE correctly classified 37 of 60 patients. The authors write that agreement is higher for the MoCA 95% confidence interval 0.41 – 0.83 than for the MMSE 95% confidence interval 0.36 – 0.79
Do you believe the results?	The authors state " the most important quality in a screening tool is sensitivity, so as not to miss patients who need further assessment, and the MoCA had good sensitivity even at the mild end" (Cumming et al., 2012, p. 127). Despite this their main finding is that both tools are good clinical indicators of cognition; which I find perplexing
Do the results fit locally?	I am not convinced with the results of this study and therefore would not assess the results as being applicable to the local population
Do these results fit with other available evidence?	The results do not easily fit with those of other studies as different comparison methods are used to determine the discriminant validity between MMSE and MoCA. The resultant complexity ensures challenge in ascertaining whether the results of this study are aligned with those in other studies reviewed.

Title of Study reviewed: Comparative accuracies of two common screening instruments for classification of Alzheimer's disease, MCI, and healthy aging Authors and publication date: Roalf et al., 2013	
CASP Questions	Findings
Did the study address a clearly focussed issue?	Issue: There has been no previous study in which a brief screening instrument has been evaluated in differentiating MCI from AD Population: 321 subjects with Alzheimer's disease, 126 with MCI and 140 older adult controls with healthy cognition
What method was used to answer their question?	Method: Case control study, conducted in USA Study Aim: To compare the diagnostic accuracy and utility of the MMSE and the MoCA in the diagnosis of MCI and Alzheimer's disease in a clinical cohort
Were the cases/controls recruited in an acceptable way?	Very little information is provided regarding recruitment of case and controls excepting that they were a population recruited from a specialised memory centre and an unknown source for the control population, the authors state sample size is adequate but include no power calculation. Full diagnostic assessment was conducted including review of all available imaging, laboratory and psychometric data in order to enable a consensus diagnosis using established clinical criteria. All subjects were screened using MMSE, MoCA and an NP battery developed specifically for use in AD, known as Consortium to Establish a Registry for Alzheimer's Neuropsychologic Battery (CERAD-NB).
Was bias considered?	Authors suggest diagnostic decisions may have been influenced through there being no blinding to MMSE, CERAD-NB or DSRS during consensus diagnosis. The "impact of comorbid clinical factors such as depression were not considered but could impact the utility of some screening measures" (Roalf et al, p 535). Not considered as potential bias by the authors included the fact that while all participants received the MMSE and the MoCA, not all received the geriatric depression scale, the CERAD-NB and the dementia severity rating scale; this omission may well have introduced bias. The authors recognise that "the MoCA appears robust to depression symptoms within healthy cohorts" (Roalf, 2013, p. 535).
What confounding factors have been accommodated for?	The sample was well educated which poses challenges in generalizing to less well educated populations more. There were adjustments made for age, education and gender in the CERAD-NB but it is not known whether adjustments were also made to MoCA and MMSE. The diagnostic groups are noted to not have differences in race or ethnicity
What are the results of this study?	The MoCA is superior to MMSE as a cognitive screening tool and when used in combination with informant based rating of individuals functional status, overall diagnostic accuracy is improved.
Do you believe the results?	Dementia severity rating scale used to determine functional status, CERAD – NB provided age, education and gender adjusted scores, additionally, MMSE excluded from CERAD-NB total score. Area under curve measure used to determine diagnostic accuracy. The results appear credible
Do the results fit locally?	The results fit with the local population
Do these results fit with other available evidence?	The results are well aligned with those determined in other studies reviewed

Title of Study reviewed: Reliability, validity and optimal cut off score of the MoCA (Changsha version) in ischaemic cerebrovascular disease patients Hunan, China Authors and publication date: Tu et al., 2013	
CASP Questions	Findings
Did the study address a clearly focussed issue?	Issue: Cerebrovascular disease is the second most common cause of dementia, executive function and attention are two of the most sensitive domains for detecting vascular cognitive impairment; MMSE lacks items testing these two domains Population: 375 ischaemic cerebrovascular disease patients and 185 controls with no cerebral related disease
What method was used to answer their question?	Method: Case control study Study Aim: To examine the reliability and validity of the Changsha version of the MoCA compared to MMSE in ischaemic cerebrovascular disease patients
Were the cases/controls recruited in an acceptable way?	Cases were recruited from inpatient neurology and geriatric departments if they had previous history of an ischaemic cerebral event accompanied by absence of acute event within the preceding 3 months. Exclusions applied to those individuals with cognitive complaints secondary to brain disorders or medical or other conditions which may affect cognition. Controls were recruited as volunteers from the community and had no history of any cerebral related or cognitive complaint. The study was ethics approved and written consent was obtained. All subjects were administered MoCA, MMSE and NP; diagnoses were
Was bias considered?	Alluding to sample homogeneity, the authors suggest the sample size is relatively small and although no power calculation is provided, this is possibly true given China's population and that Hunan province is one of the largest areas within China. Two experienced clinicians made the cognitive diagnoses, each independent of the other and blinded to MoCA-CS and MMSE; all medical, psychometric and imaging material were considered and all subjects diagnoses were operationalised against standard clinical criteria
What confounding factors have been accommodated for?	Adjustments were made to control for the effect of education level; regression equations demonstrated that gender had no significant effect on raw MoCA scores. Age when evaluated across all groups indicated that older subjects performed more poorly than younger individuals whether they had normal cognition, VCI or vascular dementia (VaD).
What are the results of this study?	The MoCA-CS was found to have good reliability and validity; a suitable tool with which to screen for vascular cognitive impairment in populations of individuals with ischaemic cerebrovascular disease in Hunan province, China
Do you believe the results?	Test re-test and inter rater reliability statistics are employed using Pearson correlation coefficient. Area under the curve and Youden index are utilised to define the cut off score at which optimal differentiation occurs. Following identification using Youden index a cut off score of 26/27 for MoCA elicited sensitivity of 90% and specificity of 87%. I believe the results, as they are presented, are credible.
Do the results fit locally?	I don't believe that the results can be said to fit locally as they are drawn from a study wherein an almost untested translated version of the MoCA has been utilised and so the results may not be generalizable to local populations. Also of significance is that the education system in China is markedly different and so the adjustments made to accommodate this variable may have resulted in less meaningful scores; this affects the potential to generalise the results to other populations.
Do these results fit with other available evidence?	The overall result, that MoCA demonstrates good reliability and validity for discriminating VCI, is aligned with other studies.

Chapter 4: Data

Using the critical appraisal skills programme and the PICO model thirteen articles were critiqued to determine the validity and reliability of MMSE compared to the MoCA. The thirteen articles evaluated were comprised of eleven cross sectional and two case control studies.

Study designs

The studies consisted of eleven cohort studies and two case control studies. Cohort and case control studies are both examples of observational study designs used in quantitative research; the "researcher collects information on the characteristics, attributes or measurements of interest" (Healy & Devane, 2011, p. 32). Observational study designs are used to describe or compare and this project has reviewed comparative studies in which there is an attempt to quantify the relationship between two factors. The main focus of this project was to assess and quantify the relationship between the capacity of MMSE compared to the capacity of MoCA in the detection of cognitive impairment.

Cohort studies can be cross sectional in design meaning that the measurement of interest occurs at one point in time; there were three cross sectional studies. Cohort studies can also be longitudinal in design meaning that data is collected at several points in time; seven of the studies were longitudinal. Cohort studies can also be described as retrospective meaning that the study looks back in time to collect data about the measurement of interest (Healy & Devane, 2011); one study was conducted retrospectively. The findings of cohort studies provide information about associations between variables; the "strength and consistency of associations can be used to draw inferences about causation" (Healy & Devane, 2011, p. 36).

The strengths or advantages in cohort study design are that they can document progression of disease and measure incidence rates while allowing the study of multiple potential effects (Healy & Devane, 2011). Cohort studies also permit flexibility in the selection of variables to be evaluated and provide detail on risk factors. The weaknesses or disadvantages in cohort study design are that they can be expensive to conduct and have a potentially long duration for follow up which means that they can yield a high dropout rate. Healy and Devane (2011) maintain that cohort studies require a large sample size and this especially challenging in the case of rare disease. Also, it can be difficult to control for extraneous variables in cohort studies and it is possible exposure may be linked to unknown confounding factors. Healy and Devane (2011) find that blinding is not always achievable and exposure or practices can change over the study timeframe rendering the results irrelevant.

Case control studies examine individuals with a particular condition (cases) and compare them to individuals who do not have the condition (controls). Data is collected about the two groups of people and comparisons made to determine whether there are any characteristics which are contributing to the finding (Hoe & Hoare, 2012). In the two case control studies reviewed, data is collected about the capacity for MMSE and MoCA to detect cognitive impairment in individuals post stroke and in individuals known to have Alzheimer disease (AD) and compared to data collected about the capacity for MMSE and MoCA to detect cognitive impairment in healthy individuals. Historically case control studies have been thought inherently prone to bias and therefore considered less valid than cohort studies. However, a London based professor of epidemiology and biostatistics writes this is fallacious (Pearce, 1993). Case control studies are said to be “indispensable if the disease is rare or assessment of the exposure is expensive, and in situations where results are needed quickly” (Knol, Vandenbroucke, Scott, & Egger, 2008, p. 1073).

To improve rigour in study design, eligibility criteria should be standardised and any "diagnosis should be made by healthcare professionals with expertise in differential diagnosis using international standardised criteria" (NICE, 2006, p.21). International standardised criteria include DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, fourth edition; ICD-10, International Classification of Diseases, 10th revision; NINCDS/ADRDA, National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorders Association; NINDS-AIREN, Neuroepidemiology Branch of the National Institute of Neurological Disorders and Stroke Association Internationale pour la Recherche et l'Enseignement en Neurosciences (NICE, 2006). Within the articles reviewed for this project only one study utilised criterion from the above; Tu et al (2013) used NINDS-AIREN. Interesting to note is that NINCDS/ADRDA can only be utilised post mortem at autopsy and this makes its deployment somewhat less feasible than the others. Also of interest was an incidental finding that ICD-10 is utilised for clinical coding purposes within MOH New Zealand and it would be logical to assume that ICD-10 is preferred in the classification of diseases and related health problems within this country's health systems.

Study participants

The intent of this project as guided by PICO was to evaluate findings for relevance to individuals aged 65 years or over; 65 years of age is aligned with the criterion requirement relating to government funding of individuals into NZ aged residential care. The critique has identified age as a potential confounding factor for which adjustments have been deployed in the majority of articles; the older age groups have been shown to score less well in both MMSE and MoCA. It was identified that explicit criteria outlined for population for this project were not met. Most studies documented the mean age for their subjects and this ranged from 65.0 years within the Zadikoff et al research (2008) to 72.7 years within the control group of the Dong et al

research (2012). Where non-statistical information was provided the range of ages was as young as 47 to as old as 100. As a result of inclusion criteria within some studies, the age of individual participants may have been outside of the population of interest for this project. As an example, Toglia et al (2011) used inclusion criteria for their study which allowed inclusion of individuals >18 years of age. I assume that the inclusion criteria in relation to age as used by Toglia et al was opportunistic in that it likely reflects admission criteria to the stroke inpatient bed within the facilities where sampling for the study occurred. However, as the focus of this project is cognitive impairment and vascular cognitive impairment is strongly associated with stroke, an incidental younger aged individual may not have confounded results. Additionally, although cognitive impairment mainly affects older individuals, it is thought the onset of up to 10% of all cases occurs before 65 years of age (WHO, 2012).

There was no consistency in the presentation of data relating to gender; some studies reported gender as a percentage of the total number of individuals studied while others provided pure numerical detail. However, overall the data revealed a higher incidence of male subjects which is not reflective of the local population; prevalence for dementia in NZ individuals aged 74 years and over is predominantly female (Alzheimers, 2008). There was a paucity of information indicating the relevance of gender to the data findings or discussion.

Data for education is mostly given as a mean number of years and this data ranges from as little as ≤2 years (Tu et al, 2013) to 16.4 years. Education has also been found to be a potentially confounding factor; individuals with low level of education have been found to score less well than those with higher number of year's education and a scoring adjustment is made in many studies. In New Zealand the proportion of adults with secondary school qualifications has shown an increase of 14% since 1991; 76.2% are found to have a secondary school level of education in the most recent census

(Statistics New Zealand, 2013). However, this may not reflect the educational level in the local population as a higher level of education was not as necessary historically, certainly among our oldest old population, to allow them entry to paid employment as it is in contemporary society.

In line with PICO, the intervention of interest is the MMSE and the MoCA cognitive assessment tools and in particular a focus on comparing the reliability and validity of each respective cognitive assessment tool in relation to the detection of cognitive impairment. All participants were administered both MMSE and MoCA in all the studies reviewed; therefore all articles provide findings in relation to each cognitive assessment tool's ability to detect cognitive impairment and this should facilitate comparison. Additional comparison is offered in six of the studies through the use of the 'gold standard' approach where performance is also rated in comparison to the findings of a comprehensive neuropsychological battery (Cumming, Churilov, Linden & Bernhardt, 2012; Damian et al, 2011; Godefroy et al, 2011; Hoops et al, 2009; Roalf et al, 2013; Tu et al, 2013). Outcome is represented statistically in most studies and varying statistical procedures have been applied to the data. Differences in study design and statistics deployed result in some difficulties with regard to interpreting the data and this is enlarged upon within the discussion chapter.

Thirteen studies were subject to CASP analysis. The CASP tables provide a snapshot of each study itemising the research problem and the purpose of the study. Brief information is provided around each author's consideration for bias and how this was mitigated. Study results are presented and confirmation made as to whether the results have been found credible and whether they are in alignment with all studies reviewed. Finally a consideration is made as to whether the results would benefit the local population, see Table 2.

Table 3, represents salient findings of the review which are extrapolated for address within the discussion; clustering of the data within a table facilitates comparison across all the studies. This figure provides a snapshot regarding demographic detail of study participants and lists statistical methods deployed in meta-analyses where relevant. Where comprehensive neuropsychological testing has occurred within a study, a list is provided regarding the items deployed when these have been identified. Finally where diagnostic criteria have been operationalised, the criteria are listed. This data has been graphically presented as it has bearing as to whether or not the findings of the study are validated and this is discussed within the following chapter.

Table 3: Study Comparison

This table allows identification of varying statistical procedures used to quantify cognitive impairment as well as demographic data of participants, whether standard criterion were used to operationalise diagnoses and which if any domain subtests were deployed.

Authors & year, sample size, Diagnostic criteria established	Age, gender and level of education	Meta-analysis; statistics used	Neuropsychological (NP) battery; cognitive domains tested
Zadikoff et al, 2008 Sample size: 88 Diagnostic criteria established: No	Age; Mean 65 Gender; 62 males 26 females Education; Not given	Power calculation	Not used
Hoops et al, 2009 Sample size: 72 Diagnostic criteria established: Modified Petersen's for MCI. Movement disorder society task force recommended diagnostic criteria for probable PDD; operationalised criteria for cognitive deficits Unified Parkinson's disease rating scale (UPDRS)	Age; Mean 65.1 Gender; 75.8 % male 24.2 % female Education; Mean 16.4 years	Power calculation Confidence interval (CI) Sensitivity and specificity Between group comparisons	Depression. 4 cognitive domains; memory, attention, executive abilities and visuospatial. Of particular interest the cube copying was extracted from MoCA and rescored to evaluate visuospatial cognitive domain performance
Aggarwal & Kean, 2010. Sample size: 50 Diagnostic criteria not established	Average age 71.7 Range 31 to 98 Gender; 31 male and 19 female Education Mean 11.7 years	Pearson's coefficient	Not used
Godefroy et al, 2010 Sample size: 95 Diagnostic criteria established; National Institute of Health Stroke Scale. Significant impairment on battery defined by impairment in at least 2 of the cognitive domains which corresponded to the 5% level. Patients categorised as cognitively impaired when the comprehensive battery impaired or MMSE <23	Cases, Mean 68.2 years Controls, Mean 62.4 years Gender; Cases, 60 male and 35 female Controls, 21 male and 51 female Education level only given for controls; Primary n = 27 Secondary n = 29 High school n = 16	Receiver operator characteristics (ROC) and area under the curve (AUC) used to examine the ability of MoCA and MMSE to discriminate between cognitively impaired and normal cognitive status Optimal cut off scores determined using Youden index. Linear regression analyses Sensitivity and specificity	Depression, anxiety and general intelligence efficiency 5 cognitive domains; Language, visuo-constructive, working and long term memory, action speed and executive functions Prestroke dementia assessed using 4 items of the instrumental activities of daily living scale and cut off scores validated in the Personnes Agees QUID (PAQUID) study

Authors & year, sample size, Diagnostic criteria established	Age, gender and level of education	Meta-analysis; statistics used	Neuropsychological (NP) battery; cognitive domains tested
Pendlebury et al, 2010 Sample size: 41 Diagnostic criteria established: Normal cognition identified with use of cut off score ≥27 using MMSE. Impaired cognition identified with use of cut off score < 26 using MoCA.	Age; mean 69.9 Gender; Female 49% Education; Not given	T tests applied to continuous variables and Fisher exact test applied to categorical variables to compare between tested and untested patients. Mean score Z score Z score rank Percent score Spearman correlation Rankin score	Not used and authors state "determination of the specificity and sensitivity of the MoCA for cognitive impairment could not be made because formal NP testing not performed" (Pendlebury, Cuthbertson, Welch, Mehta, & Rothwell, 2010, p. 1293).
Damian et al, 2011 Sample size: 135 subjects, 89 cognitively normal and 46 cognitively impaired Diagnostic criteria established: No. A Neurologist determined individuals as cognitively normal or abnormal based on the neuropsychological test outcome. Individuals were assessed by a movement disorder specialist. At a consensus conference attended by the study physician, neuropsychologist, nurse, and study coordinator, the underlying neurological and movement diagnoses were established	Age ranges from 46 to 100 Mean age impaired cognition = 79.4 Mean age normal cognition = 77.7 Gender; 28% with impaired cognition are female 58% with normal cognition are female Education; cognitively impaired = 15.5 years cognitively normal = 15.2 years Range from 10 to 23 years	Persson's $\chi 2$ test used to determine and compare prevalence and mean of characteristics of both impaired and cognitively normal group. Diagnostic accuracy of each screening test – MoCA and MMSE was evaluated using ROC and AUC. Youden index was used to determine optimal cut off scores. The relationship between cognitive impairment and each item was analysed using logistic regression. Bayes rule was used to calculate predictive value because sample prevalence of cognitive impairment was higher than the population prevalence secondary to the recruitment process for body and organ donation	Mattis dementia rating scale. NP battery included the following; WMSR Logical Memory, Rey Auditory Verbal Learning Test, Brief Visual Memory Test-Revised, Facial Recognition Test, Token Test, Category Fluency (animals and vegetables), Controlled Oral Word Association Test (CFL), Boston Naming Test-2, WMS-R Digit Span, Trail Making Tests A and B, Stroop, WAIS-III Similarities, WAIS-R Digit Symbol, Clock Drawing Test, Judgment of Line Orientation, WAIS-III Block Design, WAIS-III Vocabulary, WAIS-III Information and the WRAT-3 Reading subtest. Additionally, WAIS-III Information and Vocabulary and WRAT-3 reading provided estimates of premorbid abilities

Authors & year, sample size, Diagnostic criteria established	Age, gender and level of education	Meta-analysis; statistics used	Neuropsychological (NP) battery; cognitive domains tested
Toglia et al, 2011 Sample size: 72 Diagnostic criteria established: National Institutes of Health Stroke Scale score administered by physiatrists. FIM assessed within 72 hours of admission and again within 72 hours of discharge and was rated by the rehabilitation team all of whom hold accreditation with the uniform data system for medical rehabilitation Cut off score of <26 used to indicate cognitive impairment using MoCA MMSE is tested at cut off scores ranging from 25 to 27 despite noting that cut off score of <27 recommended for highly educated individuals	Mean age; 70 Gender; 34 male and 38 female Education Mean; 14.9 years	Frequency distribution and percentages calculated for categorical variables Means, medians and standard deviations (SD) calculated for continuous variables Differences between independent groups evaluated through the use of chi-square, 2-sample t or Mann-Whitney tests Wilcoxon signed rank test used to compare the difference between median MoCA and MMSE score for the same patient Spearman rank correlation coefficients evaluated the association between MoCA and MMSE scores and discharge motor relative functional efficiency and motor subscale of the functional independence measure (FIM)	Not conducted
Cameron et al, 2012 Sample size: 93 Diagnostic criteria established: CHF diagnosed in accordance with clinical criteria from Australian best practice guidelines	Age; Mean 70 Gender; 71% male Education; 77% ≤ 12 year	Kappa coefficient examines the level of agreement between scores suggestive of MCI $\chi 2$ test Z scores P values Odds ratio Continuous data presented as mean standard deviation	Authors indicate that the measurements were not validated against 'gold standard' neuropsychological testing therefore MoCA may have over-identified impairment

Authors & year, sample size, Diagnostic criteria established	Age, gender and level of education	Meta-analysis; statistics used	Neuropsychological (NP) battery; cognitive domains tested
Pendlebury et al, 2012 Sample size: 207 stroke, 156 TIA, 107 memory Diagnostic criteria established: TIA and Stroke identified using WHO criteria Cut off score of ≥ 27 MMSE indicated normal cognitive function Cut off score of <26 MoCA indicated impaired cognitive function	Mean Age; Stroke 72 TIA 71 Memory research 76 Gender; Stroke 54% male TIA 53% male Memory research 46% male Education; Detail not given Stated that adjustment made to control for education effect where level <12 years	P values CI 95% Standard deviation Odds ratio Linear regression Adjustments made for age and education	Not conducted
Cumming et al, 2012 Sample size: 60 Diagnostic criteria established: Criterion standard classification of cognitive impairment was determined based on the NP battery NIHSS score	Mean Age; 72.1 Gender; 44 male and 16 female Education; Mean 10.5 years	$\chi 2$ ROC, AUC Confidence interval P values Z scores Chi-square Statistically referenced sample size Mann-Whitney *U*-tests Kappa coefficient Intraclass correlation coefficient (ICC) Concordance correlation coefficient (CCC) Positive and negative predictive values Sensitivity and specificity	Mood disorder checked at 3/12 using hospital anxiety and depression scale NP battery included testing in the cognitive domains of Visuospatial, Memory, Executive function, language, attention and visual neglect

Roalf et al, 2013 Sample size: AD 321, MCI 126, Healthy Control (HC) 140 Diagnostic criteria established: "consensus diagnosis was established using standardized clinical criteria for AD, MCI, or other neurologic or psychiatric conditions presenting with cognitive impairment" (p. 531).	Mean age; AD 75.69 MCI 72.29 HC 71.19 Gender; AD 199 female 122 male MCI 64 male 62 female HC 46 male 94 female Education; AD 13.33 years MCI 14.86 years HC15.91 years	Pearson $\chi 2$ ANOVA *t*-tests ROC, AUC Equipercentile equating Youden index Sensitivity and specificity	Geriatric depression scale CERAD-NB subtests are verbal fluency, Boston naming test, MMSE, word list learning, constructional praxis, word list delayed recall, wordlist savings, word list recognition, delayed constructional praxis savings, clock drawing
Tu et al, 2013 Sample size: 338 cases, 132 controls Diagnostic criteria established: MCI diagnostic criteria from international working group NINDS-AIREN criteria used to diagnose Vascular dementia	Mean Age control; 66.56 Mean age of cases; 66.63 to 73.15 Gender; Controls 68 male and 64 female Cases 186 males and 152 female Education range; ≤2 to >12 years An adjustment is made for educational level	$\chi 2$ ANOVA Kruskal-Wallis adjacent pairwise comparison Standard deviation Cronbach α – internal consistency Youden index ROC, AUC Confidence interval Pearson correlation coefficient for inter-rater reliability	Simplified intelligence quotient NP battery included 4 subtests of Wechsler adult intelligence scale- Chinese revised, 3 subtests of Wechsler memory scale – Chinese revised and the Stroop test. In "subjects with negative screens who cooperated well also completed the logical memory, 5 minute delayed logical memory and Stroop tests in order to collect more information regarding memory and executive function" (p. 28)

Summary of CASP analysis findings: Identification of themes

In alignment with the statement by Higgins and Green (2011) the focus of this project is "examining the relationship between some clinical characteristics of the studies reviewed and the size of the intervention effect rather than on obtaining a summary effect estimate across a series of studies" (page 301). Accordingly within this literature review themes such as sensitivity, specificity and cut off scores became evident and it was thought relevant they be explored as foundational components of the review. Initially individuals with dementia were thought to be the population of interest however there is a shift in current literature from dementia to cognitive impairment to the extent that an announcement is made that the term dementia is to be "replaced by major or minor neurocognitive disorder in the updated DSM-V due to be published late in 2013" (Sorbi et al., 2012, p. 1161).

Advances are progressing rapidly in the diagnosis and management of cognitive impairment and although many individuals with mild cognitive impairment will progress to dementia, with early intervention there is increased capacity to delay onset, ameliorate symptoms and in some cases, prevent deterioration. While earlier studies were focussed predominantly in the arena of Alzheimer's disease and other dementia subtypes, emerging studies have shifted focus to the validity of screening instruments in relation to identifying cognitive impairment in those at risk such as individuals with Parkinson's disease, cardiovascular disease and stroke. All are represented within the articles reviewed. The evolving focus is enabling critical relationships to be drawn between the cognitive domain of impairment and the underlying condition; this is underpinning greater understanding in regard to the reasons individuals with certain conditions display particular behaviours.

Larner (2013, p.225) writes that "cognitive impairment may occur in many neurological diseases." He points out that some cognitive assessment tools are designed to test for impairment in individuals with specific conditions, such as Multiple Sclerosis wherein

cognitive impairment is common. It appears that testing is now occurring to determine whether any particular instruments are more capable in detecting cognitive impairment when specific diagnoses are suspected, such as vascular dementia secondary to stroke (Larner, 2013). I believe this is visible in the studies reviewed where the populations include individual's with Parkinson disease, transient ischaemic attack and stroke.

Chapter 5: Discussion

The purpose of this literature review was to identify whether MoCA was a suitable alternative to use in the place of MMSE for the detection of cognitive impairment. The findings using CASP analysis uncovered several aspects which are significant to the interpretation of these two screening tests and will be discussed in this section.

Cognitive Domains

The cognitive domains which are thought significant to decisions around general cognition and which are tested in MMSE and/or MoCA include the visuospatial/executive, naming, attention, language, abstraction, delayed recall and orientation; unlike MMSE, MoCA tests all of these domains. MMSE does not test executive function or abstraction and there is considerable support in articles reviewed which suggests that visuospatial testing is virtually non-existent in MMSE as well.

Visuospatial/Executive Domain

The visuospatial and executive function domain is tested using three tasks; modified trail making, copying of the cube, and clock drawing in MoCA. Neither trail making nor clock drawing are used in MMSE. Instead, MMSE assesses visuo-motor function through copying of two intersected pentagons. Indeed, the studies indicate that the insensitivity of MMSE to MCI is strongly associated with the lack of testing in the domain of visuospatial and executive functioning. This ensures that MoCA is found superior to MMSE in its ability to detect cognitive impairment. Cameron et al (2013) found that 81% of the patients they studied demonstrated task errors in the executive function domain of MoCA which, as they highlighted, is not assessed in MMSE. This was supported in the findings of another study where it was suggested that lower scores obtained when measuring using MoCA are largely attributable to errors in visuospatial/executive and fluency items, not represented in MMSE (Toglia et al, 2011).

Naming Domain

In MoCA, the naming domain is tested using a "three item confrontation naming task with low familiarity animals" (Nasreddine et al., 2005, p. 697) a camel, lion and rhinoceros. Similarly, in MMSE this domain is tested through showing the subject a pencil and then a wristwatch and asking what they are called. Both MMSE and MoCA have been criticised for ceiling effect in this cognitive domain; the tasks are too easy (Damian et al., 2011; Pendlebury et al., 2012). However, Julayanont, Phillips, Chertkow and Nasreddine (2013) state that confounding factors may include those individuals with low education level or cultural unfamiliarity with the animals and this may explain low scoring in some populations. Another low scoring population are those individuals with Parkinson disease where pathology includes disrupted subcortico-frontal pathways. It is interesting to note that the naming of animals (MoCA) was more highly associated with primary visual cortex activation than the naming of tools (MMSE) which is associated with frontal and parietal lobe activation (Julayanont et al, 2013, p. 116).

Attention Domain

The attention cognitive domain is tested using three tasks; the digit span, the letter A tapping test and serial 7 subtractions using MoCA. Neither digit span nor the letter 'A' tapping test are used in MMSE. Instead MMSE assesses attention using only serial 7 subtractions. It seems logical therefore, that the lack of testing in this cognitive domain using MMSE results in the finding that MoCA has superiority over MMSE. For example, prominent attentional deficits are expected in individuals with a vascular pattern of cognitive impairment (Pendlebury et al., 2012, p. 49). Deficits in attention were also commonly found in individuals with right hemisphere lesions (Cumming et al, 2012). Previously it has proved difficult to determine inattention in right hemispheric stroke patients when using MMSE; this finding was thought to be clinically significant as it indicates a possibility that MoCA may help identify those patients with agnosia and inattention (Cumming et al, 2012).

Language Domain

The language domain is tested using five tasks; naming, sentence repetition, letter fluency, three stage command and copying a design using MMSE. Naming, three stage command and copying a design are used and scored, within the naming domain and the visuospatial/executive function domain using MoCA. Sentence repetition is also used in MoCA and additionally MoCA uses the letter 'F' fluency task. It is interesting to note that semantic fluency is substituted for letter fluency where the latter does not exist, as occurs in languages such as Korean and Chinese (Julayanont, Phillips, Chertkow, & Nasreddine, 2013, p. 118). In my opinion, where substitution of letter fluency for semantic fluency occurs, a confounding factor is introduced. In evaluating cognitive performance in this domain, the studies identified pro's and con's for both MMSE and MoCA as follows. MMSE was found to have a "propensity for relatively easy verbal item tasks that do not have the sensitivity to identify subtle language deficits" (Cameron, Worrall-Carter, Page, Stewart, & Ski, 2013, p. 257). Pendlebury et al (2010) also found the sentence repetition task using MMSE did not find task errors as frequently as the sentence repetition task using MoCA. It was suggested by Toglia et al (2011) that lower scores obtained when using MoCA are largely attributable to errors in visuospatial/executive function and fluency items; neither are represented in MMSE. Conversely, a secondary analysis performed to compare the agreement between MMSE and MoCA with the neuropsychological battery found MMSE had a "particularly pronounced agreement with the neuropsychological battery" in the language domain (Cumming et al, 2012, p.127). I suggest that an important consideration with regard to the secondary analysis is the tasks the authors incorporated into their neuropsychological battery to assess cognition in this domain; there is potential for the introduction of a confounding factor here.

Abstraction Domain

Abstraction is tested using one task twice; the subject is asked to state what similarity exists between two items presented to them using MoCA (the Wechsler similarities test). MMSE does not test cognitive function in this domain. Individuals with Alzheimer's disease (AD) and Huntington's disease perform poorly in this test and individuals with fronto-temporal dementia exhibit more task errors than individuals with AD (Julayanont et al., 2013). Performance decline in this test is a predictor for conversion of individuals to AD (Julayanont et al., 2013). One study reported that the individuals studied scored lowest in abstraction domain (Pendlebury et al., 2012).

Delayed Recall Domain

The delayed recall domain is tested using one task in both MMSE and MoCA. However, MoCA requires the subject to recall five words which are given to the subject and repeated once only at the time of registration and this task is not scored; the subject is asked to recall the five words after a 5 minute interval and the delayed recall task is scored. In contrast using MMSE, the subject is given three words at registration and the words are repeated until the subject is able to verify the ability to recall them and registration is scored; they are asked to repeat the words back to the assessor following a five minute interval and delayed recall is scored. In evaluating task performance using MMSE and MoCA subjects were found to score poorly in delayed recall.

Delayed recall of five items using MoCA was said to have a flooring effect; it was too hard and therefore a poor discriminator in more cognitively impaired individuals (Pendlebury et al., 2012). The study by Cameron et al (2013) found that 96% of patients scored poorly for this domain using MoCA in comparison to 75% who scored poorly in the same domain using MMSE. Additionally, MoCA provided an option to perform cued memory recall once the delayed recall task was completed and scored. It was suggested this may result in collecting more information regarding group differences (Pendlebury et al., 2012).

Julayanont (2013) raised an important consideration in identifying that individuals with AD are prone to perform poorly in the recall domain owing to semantic memory impairment; this can be further confounded through low education level and/or literacy ability. But of further concern was the statement that memory recall, language and executive functions were most frequently impaired tasks in those identified as cognitively impaired using MoCA; these domains are those needed for learning and the "development of self-care management skills" (Cameron et al., 2012, p. 258).

Orientation Domain

Tasks performed in the orientation domain are the same in both MMSE and MoCA to the extent that Cumming et al (2012) note that as "MoCA overlapped with identical items on MMSE" the items were tested only once (p. 123). An important finding for nurses working within the residential aged care setting is that performance in the domain of orientation is promoted as the "single best predictor of daily functions in individuals with dementia" (Julayanont et al., 2013, p. 119). Another finding worth noting was the only significant difference in task performance between a TIA population and a stroke population occurred in the cognitive domain of orientation and specifically temporal orientation (Pendlebury et al., 2012). Indeed temporal orientation has been found sensitive in the detection of individuals with dementia and in those with delirium and additionally, temporal orientation status can "predict overall cognitive decline over time" (Julayanont et al, 2013; p. 120).

Neuropsychological battery

The gold standard in cognitive testing is the comprehensive 'neuropsychological battery' (NP battery). The neuropsychological battery consists of a number of individual tests selected to specifically assess performance in various domains. There is, however, no one neuropsychological battery which is consistently used. Dong et al (2012) highlight that different "formal neuropsychological battery are used to define cognitive status" (p.1753), and that this accounts for differences in research findings across

studies. They go on to say that other studies used either "short NP batteries or isolated memory functioning subtests while we employed a more comprehensive NP evaluation which covers a wide range of cognitive domains." In addition, Roalf et al (2013) was concerned that neuropsychological (NP) testing was neither a time nor a cost efficient way in which to reliably differentiate MCI from dementia and advocated the use of brief cognitive screening tools under the proviso that established cut off scores and confidence intervals be validated.

This literature review has revealed there was no consistency in the use of NP battery, neither in the selection of individual cognitive domains for testing, nor in which of the available subtests were applied. As an example Hoops et al (2009) opportunistically extracted cube copying from the MoCA and utilised it to inform the evaluation of visuospatial domain within the comprehensive neuropsychological battery. This introduces potential bias to the NP battery used. Roalf et al (2013) utilised an NP battery known as the CERAD-NP which dictates and lists the subtests to be utilised thereby providing a platform which facilitates consistency and allows results to be generalized. However the CERAD-NP incorporates MMSE. Accordingly, would use of this particular NP therefore place users in potential breach of the copyright issues associated with MMSE? Moreover as MMSE has been found to lack sensitivity to MCI, CERAD-NP is likely to be equally unreliable in the detection of MCI. The aim of using a neuropsychological battery is to determine the discriminant validity of MMSE and MoCA, thus the use of CERAD-NP as the gold standard introduces bias.

There appears to be a plethora of available tests and some used in the studies reviewed within this project date back to 1958 (Stroop test). In light of the fact that deployment of a gold standard is so variable and that that NP battery are predominantly comprised of randomly assigned subtests, their use appears questionable in determining validity. Certainly it would appear that there is little value in correlating cognitive assessment test accuracy to a randomly constructed neuropsychological battery. This concern is

compounded when extracting sections of other psychometric tests for use within the NP battery administered. NP battery may be useful in verifying the discriminant validity in relation to specific domains. However, overall, the manner in which neuropsychological battery has been utilised within the studies reviewed here has served to further complicate an already complex process.

Clinician experience of functionality

MoCA takes almost twice as long to administer, 5 to 30 minutes compared to 4 to 12 minutes for MMSE's. It is also a tool which clinicians are not as familiar with. Despite this clinicians found MoCA preferable to the MMSE (Aggarwal & Kean, 2010). MoCA facilitated discussion with other clinicians, it provided more information than MMSE and the findings were easy to interpret (Aggarwal & Kean, 2010).

Ceiling effect

Ceiling effect is said to occur when performance of a task is too easy and the resultant scoring is high. MMSE was found more prone to ceiling effect than MoCA (Roalf et al, 2013; Pendlebury et al, 2012; Toglia et al, 2011; Pendlebury et al, 2010; Zadikoff, 2008). Pendlebury et al (2012) found MMSE displayed ceiling effect in the domains of naming, registration, reading and writing where scoring almost reached the maximum.

The screening test was prone to ceiling effect with selected populations, such as individuals with stroke when using MMSE (Toglia et al, 2011). The MMSE demonstrated a pronounced ceiling effect associated with the detection of cognitive impairment in individuals with Parkinson's disease (PD) (Zadikoff et al., 2008). Similarly, a marked ceiling effect was found in the MMSE for younger, well-educated individuals (Roalf et al, 2013). MoCA was not without ceiling effect. Ceiling effect was said to have occurred in the animal naming task of MoCA (Damian, 2011), with the authors concluding that the task was too easy. Cumming et al (2012) reminded clinicians that data which is skewed toward ceiling does not necessarily imply that the tool has less sensitivity than another.

Cut off score

Crawford, Whitnall, Robertson and Evans (2012) argue that cognitive screening tools offer an opportunity to detect the presence of cognitive impairment, although the results cannot be used to make a diagnosis of dementia. Screening tools can be judged by their ability to accurately distinguish between those individuals who have an element of cognitive impairment from those individuals who do not, and the distinguishing factor is based on 'cut off' scores. The validity of an instrument is evident in its sensitivity to detect cognitive impairment in an individual. Sensitivity denotes the probability that a cognitive assessment tool will correctly identify individuals who are cognitively impaired, whereas specificity is the ability of a cognitive assessment tool to categorically exclude a particular attribute in an individual (Wood, Guiliano, Bignell & Pritham, 2006). Both sensitivity and specificity are determined through the use of cut off scores which identify the score at or below which impairment is detected (Wood et al, 2006). However, cut off scores are neither consistently applied nor reported similarly which creates challenges when analysing data. Additionally, altering the cut off scores changes both sensitivity and specificity, potentially altering outcomes, which hampers the capacity to compare one study with another (Cumming et al., 2012; Damian et al., 2011; Dong et al., 2012; Godefroy et al., 2011; Hoops et al., 2009).

Table 4: Sensitivity and specificity values

This table demonstrates Mini Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) Sensitivity and Specificity totals for individual studies at cut off scores as specified. Highlighted figures indicate the highest result for that particular data set as given within each individual study.
Key: - indicates no data available

Sensitivity Totals				Specificity Totals			
	Hoops et al, 2009	Godefroy et al, 2010	Hawkins et al, 2014	Cut score	Hoops et al, 2009	Godefroy et al, 2010	Hawkins et al, 2014
25 MMSE	28	77	43	25 MMSE	96	87	87
MoCA	80	94	64	MoCA	64	35	40
26 MMSE	38	80	60	26 MMSE	88	77	75
MoCA	90	97	79	MoCA	53	19	26
27 MMSE	53	86	70	27 MMSE	83	61	66
MoCA	93	98	94	MoCA	59	16	11
28 MMSE	78	95	83	28 MMSE	63	39	49
MoCA	100	100	96	MoCA	22	13	-

In evaluating the articles a decision was made to extrapolate available data relating to sensitivity and specificity in order to graph it. This allowed for trends to become apparent and Table 4 confirms that MoCA sensitivity is greater than that found for MMSE within each study. The converse is also apparent; MMSE specificity is greater than that found for MoCA. It can also be seen that there is little alignment between the values for either sensitivity or specificity across the studies. I suspect that this is secondary to the use of different statistical procedures applied in quantifying the level of impairment. Larner (2013) writes that "highly sensitive tests, which are generally thought desirable for screening purposes, will ensure that early cases are not missed but at the risk of making false positive diagnoses" (p.4). It is clearly demonstrated that MoCA is highly sensitive and therefore more likely than MMSE to identify early cases of cognitive impairment. However, secondary to the lower specificity of MoCA it is more likely to result in false positive diagnoses. In my opinion this finding is positive

as the aim is to utilise an instrument solely for screening purposes within the residential care setting; the results will be considered indicative and support the request that further investigation be conducted.

Roalf et al (2013) identified that a statistical tool known as the Youden index can be used to determine the cut off score at which optimal differentiation occurs between groups and stated it maximised the trade-off between the two indicators, sensitivity and specificity. Youden index was used within several studies (Damian et al., 2011; Dong et al., 2012; Godefroy et al., 2011; Roalf et al., 2013; Tu et al., 2013). Damian et al (2011) cautions that the predictive value of the MoCA versus the MMSE changes with the prevalence of cognitive impairment in the population studied and this can be manipulated through changing the cut off score. Zadikoff et al (2008) acknowledged the need to consider a different cut off score in their study. Although they used the cut off score of < 26 for MCI, its appropriateness for accurately identifying MCI in PD populations has not been established.

Statistics are becoming increasingly commonplace in the determination of cut off scores and an example includes the use of a statistical application known as receiver operating characteristic (ROC) analysis. This technique was used by Damian et al (2011) to demonstrate that use of varying cut off scores alters the predictive value of results, improving sensitivity at the expense of specificity. Damian et al (2011) indicated their finding allowed them to state that MoCA is more appropriate for screening purposes within settings such as primary care and a cut off score of < 24 would result in superior predictive value in a memory clinic setting where there likely exists high prevalence for MCI. Cronbach alpha is another statistical tool used to determine the reliability of findings, with a result of .70 or less indicating an unacceptable level of reliability. In one study, Cronbach alpha result was .60 for MMSE which indicated that MMSE may not be reliable when subjects score at the

upper end of the continuum (Toglia et al, 2011). This finding is consistent with those of other studies (Godefroy et al, 2011; Aggarwal et al, 2010; Hoops et al, 2009).

Cut off scores appear to be influenced by education. One study found that while "MoCA includes a minor correction for lower education levels, MMSE does not and this may affect the diagnostic accuracy of MMSE" (Hoops et al., 2009, p. 1743). Similarly, when controlling for the confounding effect of age and level of education in a post-stroke inpatient population, the use of new cut off scores resulted in improved sensitivity to the detriment of specificity when using MMSE and improved specificity to the detriment of sensitivity when using MoCA (Godefroy et al., 2011). The relationship between cut off scores and education was not directly mentioned in other studies: rather it was stated that additional points should be added to total scores where education levels are low, although the data varied with regard to application. I close this statistical summary which noted that "meta-analytic studies of quantitative accuracy are still in their infancy" (Larner, 2013, p. 230).

Study populations

Common comorbidities were included in the literature review as they frequently exist alongside cognitive impairment. In a population of sub-acute post-stroke patients the tasks of visuoexecutive function, delayed recall and verbal fluency were found to be those most impaired using MoCA (Toglia et al, 2011). Toglia et al identified that delayed recall was the lowest scoring task using MMSE, however, when analysing the mean percentage score for delayed recall in MoCA compared to the mean percentage score for delayed recall scoring in MMSE it can be seen that MoCA is more likely to classify impairments. One study identified that the "presence of cognitive impairment was associated with age, more severe neurological deficit, higher depression score, left sided stroke and poor outcome" (Godefroy et al, 2010; p. 1714). Conversely, Toglia et al found "no significant differences in MoCA visuospatial/executive subsection or total scores with side of the lesion" (p. 796).

Parkinson Disease

Poor task performance has been noted in individuals with white matter hypersensitivities and those with Parkinson disease, although they are of different neuropathology, both have disrupted subcortical-frontal pathways (Julayanont et al., 2013). Individuals with PD score poorly in the cognitive domains of attention, visuospatial and executive functioning, naming and repetition; this is consistent with error common to PD (Zadikoff et al., 2008). In examining MoCA sub-scores, Hoops et al (2009) report individuals with Parkinson disease and MCI or dementia were found to have deficits in the domains of attention, language, delayed recall, visuospatial and executive function and orientation.

Establishing the presence of MCI

Dong et al (2012) tried to establish the discriminant validity of the MoCA in detecting multi domain MCI (md-MCI) as this is the most common cognitive phenotype immediately prior to dementia conversion in PD. 75% of patients with md-MCI were impaired in at least four domains. The most impaired domains were visual memory and verbal memory as well as visuospatial/executive function, language and attention In their 2012 study Dong et al confirmed previous assumptions that MoCA was more suitable than the MMSE because of its capacity to screen for deficits in these cognitive domains. It has “more visuospatial and executive function sub tests as well as more demanding recall items” (p. 1753).

Chapter 6: Conclusion

This project has been challenging secondary to rapidly evolving complexities within the field of assessment of cognitive impairment, as previously discussed. However, it has been possible to gain resolution to the research question. Through my involvement in working within residential care I was concerned that nurses lacked the availability of a brief cognitive assessment screening tool which was validated in the detection of cognitive impairment. There was inconsistency in the cognitive assessment tool of choice with many using MMSE and others using MoCA, which complicated transferral of information.

I therefore embarked on a literature review in order to determine whether MoCA was a suitable replacement for MMSE. There is a plethora of literature written about all aspects of cognitive impairment and the main driver appears to be a search for the 'holy grail'; an assessment instrument which is capable of reliably translating physical and psychological symptomatology onto a scale to validate cognitive status. The MMSE, which has been the most commonly deployed instrument, must now be purchased for use and is free for use only when administered from memory. This may underpin the recent proliferation in cognitive assessment instruments. While the validity of the copyright issue is debatable, it nevertheless provides a deterrent to its use and has also underpinned a proliferation of more recent alternative screening instruments. A senior occupational therapist working within the local DHB confirmed that the DHB had moved to using MoCA as the preferred brief cognitive assessment tool subsequent to the copyright implications in using MMSE (Thompson, M; personal communication 10/12/2014). Enlarging on this statement he added that cognitive assessment was most appropriate where poor performance impacted on the functional capacity of an individual; MoCA permitted more information to be obtained in relation to executive function than was revealed using MMSE and this factor also contributed to a preference for MoCA. He closed in commenting that the MoCA was both easily

and rapidly administered, cautioning that it was a screen and therefore only an 'indication' of cognitive difficulty. Further examination would be necessary to determine dementia or quantify cognitive status.

Current research appears to have changed focus and now seeks to examine the utility of a cognitive assessment tool in relation to conditions such as Parkinson's, stroke and congestive heart failure as opposed to its earlier focus in relation to Alzheimer's disease dementia and dementia of other causes. This trend is accompanied by an imperative for an early diagnosis of cognitive impairment which aims to alleviate symptomatology, optimise the treatment of underlying and coexisting conditions and in some cases to prevent the progression of MCI to dementia. Understanding cognitive decline in relation to conditions which lead to dementia may assist in precipitating early detection as well as afford opportunity to optimise treatment for underlying conditions and comorbidity.

Challenges were presented in analysis of the data because of the manner in which it is both applied and interpreted which leads to varied and questionable outcomes. The direction of future research, such as that being undertaken at present by Davis et al (2013) who aim to review the accuracy of several of the neuropsychological tests on behalf of the Cochrane diagnostic test accuracy reviews in dementia, will hopefully serve to provide much needed answers to an ever increasing number of questions.

The limitations identified with this project research design include the vast amount of research available, making it difficult for one individual to digest alone within the constraints of time apportioned to a dissertation. Therefore, pertinent articles may not have been included as a result of oversight. In limiting the literature reviewed to articles written in English, bias is introduced through the exclusion of relevant studies which may have added value, offered alternative data or reached different conclusions. Statistical data within articles has the potential to be misinterpreted, however

conclusions have largely been drawn from the overall descriptions of findings within each of the studies. Potentially incorrect statistical data interpretation would not change the finding that MoCA is not only a suitable replacement for MMSE but affords early identification of cognitive impairment because it exhibits superior sensitivity to that of MMSE.

The most consistent finding was that MoCA is found to be a more reliable cognitive assessment tool in the detection of cognitive impairment and superior to MMSE in the detection of mild cognitive impairment. Therefore, I do not hesitate to suggest that residential care in New Zealand adopt MoCA as the brief cognitive assessment screening tool of choice. This review has shown it to be of value in that it is a brief cognitive screener taking around 10 minutes to administer (Hoops et al., 2009; Narzarko, 2013; Nasreddine et al., 2005). It is convenient and accessible, available from the developer's website www.mocatest.org where it is able to be downloaded and printed ready for use by the assessor at no cost. It is reliable and has been validated in detecting cognitive impairment and in particular is superior in detecting MCI compared to MMSE. Therefore the results, when positive, can be used to generate further review of an individual for whom there is concern. This finding reinforces the statement made by Nasreddine et al (2005) that "use of MoCA should provide quick guidance for referral and further investigation of MCI" (page 698).

I would also recommend that routine cognitive screening of individuals at risk be considered. Such a programme would target individuals at high risk such as those who have a history of drug or alcohol dependence, history of a significant head injury, delirium, late onset anxiety or depression. Individuals reporting memory complaints should be considered for routine and interval screening to monitor for early cognitive disorder. Routine screening should be considered on admission to primary or secondary healthcare environments; in this way, a baseline quantification of cognition is ensured and decline can then be captured, measured and responded to proactively.

Routine screening would also align practice with the New Zealand Framework for Dementia Care (MOH, 2013).

Nurses are able to be skilled in administering the MoCA with "very little training" (Roalf et al., 2013, p. 530). Training for nurses would align with the New Zealand Framework for Dementia Care through ensuring "health practitioners have skills and knowledge in cognitive assessment and knowledge of dementia" (MOH, 2013, p.16). Nursing has continuity in service across 24 hours and 7 days per week, whether they are situated directly on site or available on call, and have an established rapport with individuals and their families. Therefore nursing is well placed to use skill, knowledge and critical observation in combination with MoCA to ensure strong advocacy for those who do not themselves, have a voice.

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Appendix A: CASP Tool Case Control Studies

11 questions to help you make sense of case control study

How to use this appraisal tool

Three broad issues need to be considered when appraising a case control study:

- **Are the results of the trial valid?** **(Section A)**
- **What are the results?** **(Section B)**
- **Will the results help locally?** **(Section C)**

The 11 questions on the following pages are designed to help you think about these issues systematically.
The first two questions are screening questions and can be answered quickly. If the answer to both is "yes", it is worth proceeding with the remaining questions.

There is some degree of overlap between the questions, you are asked to record a "yes", "no" or "can't tell" to most of the questions. A number of prompts are given after each question. These are designed to remind you why the question is important. Record your reasons for your answers in the spaces provided.

There will not be time in the small groups to answer them all in detail!

(A) Are the results of the study valid?

Screening Questions

1. Did the study address a clearly focused issue? ❒ Yes ❒ Can't tell ❒ No

HINT: A question can be focused in terms of

- The population studied
- The risk factors studied
- Whether the study tried to detect a beneficial or harmful effect?

---

2. Did the authors use an appropriate method to answer their question? ❒ Yes ❒ Can't tell ❒ No

HINT: Consider

- Is a case control study an appropriate way of Answering the question under the circumstances? (Is the outcome rare or harmful)
- Did it address the study question?

Is it worth continuing?

Detailed questions

3. Were the cases recruited in an acceptable way? ❒ Yes ❒ Can't tell ❒ No

HINT: We are looking for selection bias which might compromise validity of the findings

- Are the cases defined precisely?
- Were the cases representative of a defined population? (geographically and/or temporally?)
- Was there an established reliable system for selecting all the cases
- Are they incident or prevalent?
- Is there something special about the cases?
- Is the time frame of the study relevant to disease/exposure?
- Was there a sufficient number of cases selected?
- Was there a power calculation?

---

4. Were the controls selected in an acceptable way? ❒ Yes ❒ Can't tell ❒ No

HINT: We are looking for selection bias which might compromise The generalisibilty of the findings

- Were the controls representative of defined population (geographically and/or temporally)
- Was there something special about the controls?
- Was the non-response high? Could non-respondents be different in any way?
- Are they matched, population based or randomly selected?
- Was there a sufficient number of controls selected?

5. Was the exposure accurately measured to minimise bias? ❒ Yes ❒ Can't tell ❒ No

HINT: We are looking for measurement, recall or classification bias

- Was the exposure clearly defined and accurately measured?
- Did the authors use subjective or objective measurements?
- Do the measures truly reflect what they are supposed to measure? (Have they been validated?)
- Were the measurement methods similar in the cases and controls?
- Did the study incorporate blinding where feasible?
- Is the temporal relation correct? (Does the exposure of interest precede the outcome?)

---

6. (a) What confounding factors have the authors accounted for? **List:**

HINT: List the ones you think might be important, that The author missed.

- Genetic
- Environmental
- Socio-economic

(b) Have the authors taken account of the potential confounding factors in the design and/or in their analysis? ❒ Yes ❒ Can't tell ❒ No

HINT: Look for

- Restriction in design, and techniques e.g. modelling stratified-, regression-, or sensitivity analysis to correct, control or adjust for confounding factors

7. What are the results of this study?

HINT: Consider

- What are the bottom line results?
- Is the analysis appropriate to the design?
- How strong is the association between exposure and outcome (look at the odds ratio)?
- Are the results adjusted for confounding, and might confounding still explain the association?
- Has adjustment made a big difference to the OR?

(B) What are the results?

8. How precise are the results?

How precise is the estimate of risk?

HINT: Consider

- Size of the P-value
- Size of the confidence intervals
- Have the authors considered all the important variables?
- How was the effect of subjects refusing to participate evaluated?

---

9. Do you believe the results? ❒ Yes ❒ No

HINT: Consider

- Big effect is hard to ignore!
- Can it be due to chance, bias or confounding?
- Are the design and methods of this study sufficiently flawed to make the results unreliable?
- Consider Bradford Hills criteria (e.g. time sequence, dose-response gradient, strength, biological plausibility)

(C) Will the results help locally?

10. Can the results be applied to the local population?

❒ Yes ❒ Can't tell ❒ No

HINT: Consider whether

- The subjects covered in the study could be sufficiently different from your population to cause concern
- Your local setting is likely to differ much from that of the study
- Can you quantify the local benefits and harms?

---

11. Do the results of this study fit with other available evidence?

❒ Yes ❒ Can't tell ❒ No

HINT: Consider all the available evidence from RCT's, systematic reviews, cohort studies and case-control studies as well for consistency.

Remember

One observational study rarely provides sufficiently robust evidence to recommend changes to clinical practice or within health policy decision making.
However, for certain questions observational studies provide the only evidence.
Recommendations from observational studies are always stronger when supported by other evidence.

Appendix B: Mini Mental State Examination (MMSE)

Folstein, M., Folstein, S., & McHugh, P. (1975)

Patient.....
Examiner .....
Date .....

"MINI-MENTAL STATE"

Maximum Score	Score	
		ORIENTATION
5	( )	What is the (year) (season) (date) (day) (month)?
5	( )	Where are we: (state) (county) (town) (hospital) (floor).
		REGISTRATION
3	( )	Name 3 objects: 1 second to say each. Then ask the patient all 3 after you have said them. Give 1 point for each correct answer. Then repeat them until he learns all 3. Count trials and record. Trials
		ATTENTION AND CALCULATION
5	( )	Serial 7's. 1 point for each correct. Stop after 5 answers. Alternatively spell "world" backwards.
		RECALL
3	( )	Ask for the 3 objects repeated above. Give 1 point for each correct.
		LANGUAGE
9	( )	Name a pencil, and watch (2 points) Repeat the following "No ifs, ands or buts." (1 point) Follow a 3-stage command: "Take a paper in your right hand, fold it in half, and put it on the floor" (3 points) Read and obey the following: CLOSE YOUR EYES (1 point) Write a sentence (1 point) Copy design (1 point)
_____		Total score

ASSESS level of consciousness along a continuum———————————
Alert Drowsy Stupor Coma

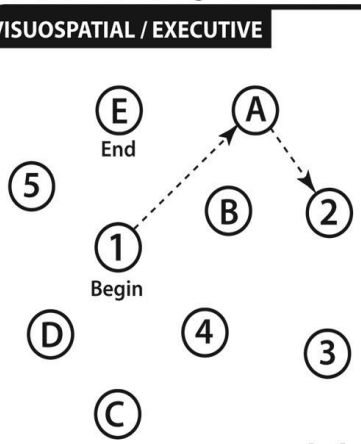
Appendix C: Montreal Cognitive Assessment (MoCA)

Nasreddine et al. (2005)

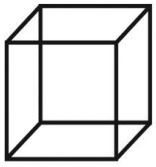
MONTREAL COGNITIVE ASSESSMENT (MOCA)
Version 7.1 Original Version

NAME :
Education : Date of birth :
Sex : DATE :

VISUOSPATIAL / EXECUTIVE



Copy cube



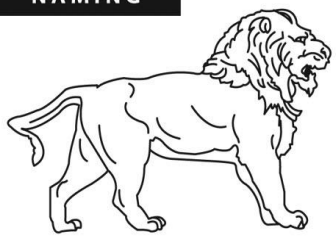
[ ] [ ]

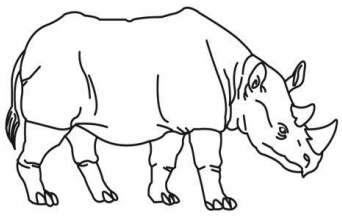
Draw CLOCK (Ten past eleven) (3 points)

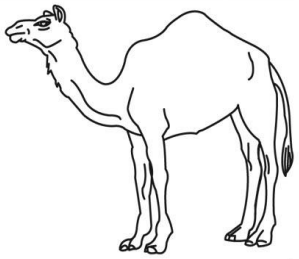
[ ] Contour [ ] Numbers [ ] Hands

POINTS __/5

NAMING







[ ] [ ] [ ] __/3

MEMORY Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION Read list of digits (1 digit/ sec.).

Subject has to repeat them in the forward order [ ] 2 1 8 5 4
Subject has to repeat them in the backward order [ ] 7 4 2 __/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors
[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B __/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65
4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt** __/3

LANGUAGE Repeat : I only know that John is the one to help today. [ ]
The cat always hid under the couch when dogs were in the room. [ ] __/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words) __/1

ABSTRACTION Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler __/2

DELAYED RECALL

	Has to recall words **WITH NO CUE**	FACE [ ]	VELVET [ ]	CHURCH [ ]	DAISY [ ]	RED [ ]	Points for UNCUED recall only
Optional	Category cue						
	Multiple choice cue						

__/5

ORIENTATION [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City __/6

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TOTAL __/30
Add 1 point if ≤ 12 yr edu

Administered by: _____