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# Evaluating the Montreal Cognitive Assessment (MoCA) and the Mini Mental State Exam (MMSE) for Cognitive Impairment Post Stroke: A Validation Study against the Cognistat

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## Abstract

**Objective.** To identify the better of two commonly used screening tools for detecting probable cognitive impairment in stroke patients in a large regional rehabilitation hospital (Parkwood Hospital, London, Ontario). This was a validation study of the Mini-Mental State Exam (MMSE) and the Montreal Cognitive Assessment (MoCA), using the Cognistat, as the criterion or 'gold standard'. It was hypothesized that the MoCA is a superior screening instrument to the MMSE for the detection of cognitive impairment in stroke patients.

**Methods.** The MMSE and the MoCA were administered by occupational therapists and the Cognistat was administered by the student investigator. A second Cognistat was administered by two occupational therapists for the reliability sub-study. Age was abstracted in a chart review and patients were asked their level of education. ROC curves, sensitivity, specificity, positive and negative predictive values and positive likelihood ratios were analyzed. Intraclass correlation coefficients and kappa statistics were also calculated.

**Results and Conclusion.** The MMSE and the MoCA have relative strengths and weaknesses. The MoCA had a slightly better diagnostic accuracy than the MMSE and demonstrated to be the more sensitive tool. These results should be viewed with some caution due to the use of the Cognistat as the gold standard.



**Keywords:** MoCA, MMSE, Cognistat, cognitive impairment, post-stroke, validity, reliability

## Dedication

I dedicate this thesis to my loving parents, Maureen and Michael Friedman who have encouraged and fully supported me each step of the way.

## Acknowledgments

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## List of Abbreviations

AUC – Area Under the Curve

CI – Cognitive Impairment

Conf I – Confidence Interval

MCI – Mild Cognitive Impairment

MMSE – Mini Mental State Exam

MoCA – Montreal Cognitive Assessment

ROC – Receiver Operator Characteristics

SD – Standard Deviation

# Chapter 1

## Purpose and Objectives

Purpose

Post-stroke cognitive impairment (CI) is frequent but remains underdiagnosed and carries a poor prognosis (Godefroy et al., 2011). Post-stroke CI includes reduced mental speed, neglect, attention deficits, aphasia, apraxia, and memory impairments (Godefroy et al., 2011); (Nokleby et al 2008). Some form of cognitive impairment "is observed in 40 to 70% of patients and the severity of the impairment meets the criteria for dementia in half of the cases" (Godefroy et al., 2011). Identifying CI in stroke patients initially is facilitated by the use of an accurate screening tool. It is important that individuals who have suffered a stroke and who screen positive for CI are then assessed to confirm the level of impairment and provide direction for appropriate treatment. Treatment is designed to prevent further cognitive decline and/or provide rehabilitation to improve cognition. The Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA) are two commonly employed screening instruments for detecting CI after stroke. In the rehabilitation of stroke patients the most accurate tool should be used to screen for CI leading then to further assessment and treatment. Early detection of cognitive impairment is essential in facilitating the prevention of further cognitive decline as well as directing cognitive rehabilitation.

Objective

The main objective of this study was to identify the better of two commonly used screening tools for detecting probable CI in stroke patients admitted to a large regional rehabilitation hospital (Parkwood Hospital, London, Ontario). This was a validation study of the MMSE and the MoCA, using the Cognistat, as the criterion or 'gold standard'. It was hypothesized that the MoCA is a superior screening instrument to the MMSE for the detection of cognitive impairment in stroke patients. The rational for the hypothesis stems from a review of literature. The MoCA has been demonstrated to be a more effective tool in the detection of cognitive impairment compared to the MMSE in several populations including those with Parkinson's disease, cerebral small vessels disease, cardiovascular disease as well as in Alzheimer's Disease and dementia.

# Chapter 2

# Literature Review

## 2.1 Screening and the Validity of Screening Tests

The term screening, as used in this thesis, is defined as the administration of tests to 'sort out apparently well persons who probably have a disease [or impairment] from those who probably do not'. A screening test is not intended to be diagnostic." (Porta, 2008:224; parentheses added.) There are two rationales for screening for CI in stroke patients. First, it is known that CI after stroke is common, but there are insufficient resources to provide full clinical assessments for all patients. Second, screening is part of secondary prevention, where a major focus is to improve outcomes through early detection and prompt initiation of therapy.

Although screening tests are not diagnostic, both screening and diagnostic tests are evaluated using a common set of epidemiologic methods. One major question is the validity of the test when judged against a criterion or 'gold standard'. Four basic statistics used to evaluate a screening test are sensitivity, specificity, positive predictive value, and negative predictive value. Two additional statistics that are extensions of the above are the Area Under the Curve (AUC) and the Likelihood Ratio. These are explained and defined in Chapter 4 - Methods.

Two commonly used screening tests for CI in stroke patients are the Mini- Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA). These are described in the following sections.

## 2.2 The Mini- Mental State Examination (MMSE)

The Mini- Mental State Examination (MMSE) was designed by Folstein, Folstein and McHugh in 1975) was designed in 1975 by Marshal Folstein to provide a standardized, brief and practical assessment of cognitive status in geriatric patients. It is used as a brief screening tool for cognitive impairment and does not identify specific disorders (Crum, Anthony, Bassett, & Folstein, 1993). It concentrates only on the cognitive aspects of mental functions and excludes questions on mood, abnormal mental experiences as well as the form of thinking (Folstein, Folstein & McHugh.,1975). The MMSE has been used with different cultural and ethnic subgroups and has been translated into several different languages (Crum et al., 1993). A modified version has also been created for the hearing impaired (Crum et al., 1993).

The MMSE is easily administered and requires only 5- 10 minutes to complete depending on the impairment of the individual. The MMSE includes 30 items grouped into five categories: orientation, registration, attention and calculation, recall and language. The test is divided into two sections; the first requires verbal responses to orientation, memory and attention questions. The second requires naming, reading and writing and the ability to follow verbal and written commands, write a sentence and copy

a polygon (Folstein, Folstein & McHugh.,1975). A copy of the William Molloy version of the MMSE is not included in the appendix due to copyright.

The MMSE is scored out of 30 possible points with higher scores indicating higher functioning. However, there has been considerable discussion over scoring and cutoff points. The most widely used cutoff is a score of less than 24 (Folstein et al 2001). Several studies have suggested that different cutoff scores are needed for different populations, age and education levels (Lopez, Charter, Mostafavi, Nibut, & Smith, 2005). In a study conducted by Tombaugh and McIntyre (1992), cutoff levels were determined depending on the severity of the CI: a score of greater than or equal to 24 indicated no impairment, a score of 18 to 23 indicated mild impairment and a score of less than 17 indicated severe impairment. In a 2001 study by Folstein and colleagues, the following cutoffs were determined: greater than or equal to 27 is normal, 21 to 26 is mild impairment, 11 to 20 is moderate impairment and less than or equal to 10 is severe impairment. Cutoff points were also established depending on educational level because a single cutoff point may miss cases among more educated people and cause false positives among those with less education. In a study by Crum et al. (1993) with a sample size of over 1800 participants, normative data were obtained. MMSE scores were found to be related both to age and educational level. Across increasing levels of education, the MMSE score increased and the range of scores narrowed with a median score of 29 for those 18 to 24 years of age, down to 25 for those 80 years of age and older (Crum et al., 1993). The median score was 29 for individuals with at least nine years of education, 26 for those with 5 to 8 years and 22 for those with 0 to 4 years of education (Crum et al.,

1993). The greatest variability was seen in the lowest educational groups and the oldest ages. In a similar study by Grigoletto and colleagues (1999) scores were inversely proportional to age and increased with increasing level of education. When scoring the test, it is important to use normative data to locate an individual patient's MMSE score within the percentile distribution shown for that patient's age and educational level, which in turn provides a method of comparison that takes into account age and education (Crum et al., 1993).

To distinguish between the effects of dementia and the influences of age and education on MMSE score, Monsch and colleagues (1995) studied a group of healthy older adults and found a significant influence of both age and education on MMSE scores ($p=0.006$). They also investigated the validity of the MMSE in a clinical setting ($n=120$, 50 healthy controls and 70 dementia patients). They produced a ROC curve and determined that a cutoff score of less than 26/30 generated a maximum sensitivity and specificity of 74% and 98% respectively. A second ROC curve was created with scores adjusted for age and education and resulted in a similar optimal cutoff score of less than 26/30 with a sensitivity of 74% and a specificity of 100% (Monsch et al., 1995); positive predictive value was 100% and negative predictive value 79% (Monsch et al., 1995).

Spering and colleagues (2012) attempted to validate the MMSE in a group of ethnically diverse, highly educated individuals. They determined that in this sample, a cutoff score of 27 provided better estimates of diagnostic accuracy than the original cutoff score of 24. With a cutoff score of 24, the MMSE yielded a sensitivity and

specificity of 58% and 98% respectively. A cutoff score of 27 resulted in a sensitivity and specificity of 79% and 90% respectively (Spering et al., 2012). O'Bryant and colleagues (2008) found similar results in a sample of predominantly white individuals. Therefore there was an improvement in diagnostic accuracy with higher cutoff scores in a sample of ethnically diverse participants with high levels of education (16 or more years) (Spering et al., 2012). Interestingly, this study also found that the sensitivity and specificity varied between ethnic groups. This study provides a range of cutoff scores for different ethnic and linguistic groups so that appropriate cutoff scores can be used for a given setting (Spering et al., 2012)

A meta-analysis by Mitchell (2009) of 34 studies examined the diagnostic accuracy of the MMSE in distinguishing between individuals with dementia and healthy subjects, mild cognitive impairment (MCI) versus healthy subjects and dementia versus MCI. They found that the MMSE was best at confirming suspected diagnosis in specialist settings and was modestly effective at ruling out dementia in these settings. In non-clinical settings, the MMSE was most effective at ruling out dementia.

The MMSE has known limitations. As previously mentioned, the ideal cut-off varies according to age and education as 12% of the variance in MMSE scores can be due to age and education alone (Mitchell, 2009). Even after adjustment, the accuracy is lower in those with less education (Mitchell, 2009). Many older adults have chronic conditions and disabilities such as arthritis or motor impairments that may affect their ability to complete certain items on the MMSE such as folding a paper in half and placing it on the

floor or holding a pencil to complete a sentence or to draw a figure (Pangman, Sloan, & Guse, 2000). There is a floor effect in patients with advanced dementia, and in those with little education or in non-English speaking groups, and a ceiling effect for those with mild disease, no disease and for those with high cognitive functioning or high education (Mitchell, 2009). Other disadvantages of the MMSE include difficulty identifying MCI and difficulty in recording change in cases of severe dementia. Furthermore, age, education, cultural and socioeconomic background can cause a considerable bias in the MMSE scores (Harefuah, 2006).

Although the MMSE is the most widely used screening tool for cognitive CI many difficulties in detecting change in cognition have been reported, the greatest being the lack of sensitivity in identifying small changes in CI. Individuals who meet the criteria for MCI can score in the normal range on the MMSE demonstrating that it cannot accurately distinguish MCI from normal (Nasreddine et al., 2005). The MMSE has been shown to be insensitive to conditions associated with frontal-executive and subcortical dysfunction and to milder forms of cognitive impairment (Pendlebury, Cuthbertson, Welch, Mehta, & Rothwell, 2010).

## 2.3 The Montreal Cognitive Assessment (MoCA)

The Montreal Cognitive Assessment (MoCA), a screening tool developed by Nasreddine and colleagues (2005) was designed to be used by clinicians in the detection of CI. It was developed to screen patients who present with cognitive complaints but still perform in the normal range on the MMSE. The MoCA has been shown to be useful for the detection of mild stages of CI while the MMSE has been shown to be superior for more advanced stages of cognitive impairment (Nasreddine et al., 2005). The tasks tested in the MoCA are more similar to those seen in a typical neuropsychological testing battery when compared with those included in the MMSE (Waldron-Perrine & Axelrod, 2012).

The MoCA, like the MMSE takes approximately 10 minutes to complete, has a total of 30 possible points and takes 1 minute to score. The test is divided into eight domains: visuospacial/executive function, naming, memory, attention, language, abstraction and orientation. Visuospacial abilities are assessed using a clock drawing task and copying a three dimensional cube. Executive functions are assessed using an alternation task drawing a line from a number to a letter in ascending order. Naming is assessed using three animals (lion, camel, rhinoceros). By repeating a list of digits in forward and backwards order, a target detection task, as well as a serial subtraction task, attention abilities are evaluated. Language is assessed through repetition of two syntactically complex sentences and a fluency task. Abstraction is evaluated using a

similarity task. Lastly, orientation to time and place is evaluated. A copy of the MoCA can be found in Appendix A.

Nasreddine and colleagues (2005) conducted a validation study for the MoCA in a community and an academic centre setting. Ninety-four patients met the clinical criteria for MCI, 93 had mild Alzheimer Disease and 90 were healthy elderly controls. Clinical diagnosis was made using neuropsychological evaluation as the gold standard. Both the MoCA and the MMSE were administered to all participants. Using a cutoff score of 26, a mean educational level of 13 years and a one-point educational correction for those with less than or equal to 12 years of education, the MMSE had a sensitivity of 18% in detecting MCI whereas the MoCA detected 90% of MCI participants (Nasreddine et al., 2005). In the group with mild Alzheimer Disease, sensitivity was 78% and 100% for the MMSE and the MoCA respectively (Nasreddine et al., 2005) while the specificity for both tools was excellent at 100% for the MMSE and 87% for the MoCA. The MoCA places more emphasis on tasks of frontal executive functioning and attention than the MMSE, which may make it more sensitive in detecting CI (Smith, Gildeh, & Holmes, 2007).

The differences between groups, (MCI, Alzheimer Disease and healthy older adults) were much more pronounced using the MoCA than the MMSE. The mean score of the MCI participants fell within the normal range on the MMSE but in the abnormal range on the MoCA (Nasreddine et al., 2005). The majority of the MCI participants and some mild Alzheimer participants had MMSE scores in the normal range. However, few MCI participants and no Alzheimer participants scored in the normal range on the MoCA

(Nasreddine et al., 2005). Seventy-three percent of MCI participants scored in the abnormal range on the MoCA but in the normal range on the MMSE (Nasreddine et al., 2005).

In a similar study conducted by Smith and colleagues (2007), MoCA was prospectively validated in a memory clinic in the United Kingdom with a sample of 26 patients. MoCA had superior sensitivity than the MMSE in identifying MCI and dementia but specificity was only 50%. However, the results of this study sample may not be generalizable to a larger population because the study took place in a memory clinic where CI would be expected to be very common. Other limitations include a small sample size and a short follow up period of 6 months. In a recent study, Larner (2012) assessed the MoCA compared with the MMSE in a memory clinic setting. Standard clinical diagnostic criteria (DSM-IV) were used to diagnose dementia and MCI. The MoCA was found to be more sensitive than the MMSE, 97% vs. 65% respectively but less specific, 60% vs. 89% respectively (Larner, 2012). The MoCA had better diagnostic accuracy than the MMSE with an area under the curve of 0.91 versus 0.83 (Larner, 2012).

Paul and colleagues (2011) examined the relationships between MoCA scores and regional brain volumes determined by Magnetic Resonance Imaging (MRI) in 111 older adults (ages 51-85) who were enrolled in a study on cognitive aging. A subset of 69 participants underwent MRI. Modest (r= 0.27) correlations were found between individual subscales of the MoCA and neuroimaging variables including volume of total

frontal gray matter, total hippocampus, weighted subcortical hyperintensities and total brain volume (Paul et al., 2011). The total MoCA score did not significantly correlate with any of the neuroimaging measures but a trend was seen between total MoCA score and total subcortical hyperintensities (r= -0.26) (Paul et al., 2011). Total MMSE scores did not significantly correlate with any of the neuroimaging indices (Paul et al., 2011). However, individual domain scores on the MoCA correlated with many of the neuroimaging indices. Larger brain volume significantly correlated with better performance on the visuospacial/executive, attention and learning domains (Paul et al., 2011).

In a recent study by Rossetti et al. 2011, normative MoCA data was stratified by age and education in a large (n=2653), ethically diverse population-based sample. As expected, they found that participants with more education had higher MoCA scores. MoCA scores decreased only slightly with age among those with greater than 12 years of education and more so in those with less education (Rossetti, Lacritz, Cullum, & Weiner, 2011). Even with the one point education increase, the majority of the participants scored below the cutoff of less than 26, indicating that this cutoff and the one point increase may not be appropriate (Rossetti et al., 2011). High failure rates were seen on certain items such as drawing a cube, delayed free recall, sentence repetition, placement of clock hands, abstraction and verbal fluency. In addition, overall mean total scores were lower than previously published normative data would suggest (mean= 23.36, SD= 3.99) (Rossetti et al., 2011). This suggests that caution is required when interpreting MoCA scores and demographic factors such as age and education also need to be considered.

Using the MoCA to determine whether a patient is cognitively impaired requires that scores should be evaluated in comparison to other individuals of a similar background as opposed to a defined cutoff score (not unlike the MMSE) (Waldron-Perrine & Axelrod, 2012).

Given that it is still unclear whether the published cutoff score of 26 is appropriate across populations, Waldron-Perrine and Axelrod (2012), attempted to determine optimal cutoff scores on the MoCA compared with a neurological battery (including the MMSE) administered by a psychologist. Subjects included 185 veterans (95% male) at an urban-based Veteran's Affairs hospital on the basis of referral from their physician (referrals included mental health, neurology and in-house extended care facility (van Gorp et al., 1999). The MoCA demonstrated adequate sensitivity, specificity and overall classification rates in predicting impairment compared to all neuropsychological testing variables. However, the optimal cutoff score to detect impairment was less than or equal to 20 which is considerably lower than the published cutoff score of 26.

Freitas and colleagues (2012) analyzed the influence of sociodemographic factors (age, sex, educational level, marital and employment status, geographic region) and health variables (subjective memory complaints by the participant and evaluated memory complaints, depressive symptoms and family history of dementia) on the participants' MoCA scores. This study was conducted in a community-based sample of volunteers who were recruited at national health and social security services in all geographic regions of the Portuguese mainland (Freitas, Simoes, Alves, & Santana, 2012). They

found that age and educational level significantly influenced the MoCA score, accounting for 49% of the variance (Freitas et al., 2012). In this study, gender, marital and employment status as well as whether individuals lived in urban or rural areas had no effect on the MoCA scores. Similar results were found regarding health variables on MoCA scores. There was no significant association between family history of dementia or memory complaints on MoCA score (Freitas et al., 2012). However, depressive symptoms and subjective memory complaints of the participant had significant negative correlations with the MoCA scores and these variables also showed a significant intercorrelation (Freitas et al., 2012).

### 2.4 The MoCA versus the MMSE in Stroke Patients

The MMSE and the MoCA have been compared in several studies identifying cognitive deficits in patients with Parkinson's disease (Dalrymple-Alford et al., 2010; Hoops et al., 2009; Zadikoff et al., 2008), cerebral small vessel disease (Wong et al., 2009), as well as cardiovascular disease (McLennan, Mathias, Brennan, & Stewart, 2011), where the MoCA was found to be a more sensitive tool in detecting cognitive impairment compared to the MMSE. The MMSE has been criticized as being an insufficient screening test for patients with vascular cognitive impairment because of its lack of sensitivity to visuospatial and executive function deficits (Ihara, Okamoto, & Takahashi, 2012). However, few studies have been performed that assess the validity of the MoCA and the MMSE in stroke patient populations; none have utilized a stroke rehabilitation population.

Pendlebury and colleagues (2010) compared the MoCA and the MMSE in a population-based study of transient ischemic attack (TIA) and stroke patients (n = 413). The MoCA identified substantially more cognitive deficits than the MMSE in these patients (Pendlebury et al., 2010). Using a cutoff score of ≥ 27, 58% of patients with a normal MMSE had an abnormal MoCA. The MoCA differentiated well between different levels of cognitive ability, whereas over half the patients with MMSE scores ≥ 27 were designated as cognitively impaired using the MoCA. This echoes the findings of the original MoCA study by Nasreddine and colleagues (2005). However, a major limitation in this study was that sensitivity and specificity for these screening tools could not be determined because of the lack of a gold standard. Dong and colleagues (2010), tested whether the MoCA was more sensitive than the MMSE for detecting CI in a population of 100 sub-acute stroke patients in Singapore. They also reported the MoCA to be more sensitive than the MMSE in screening for CI in this population; however, there was no gold standard. In addition, three Singapore versions of the MoCA were used with modifications that had not been validated (Dong et al., 2010). Blake and colleagues (2002), screened 112 stroke patients recruited from a previous randomized control trial for CI on the MMSE and a variety of other screening tools (not including the MoCA). Overall, the MMSE was determined to not be a useful screening tool in detecting CI using the cutoff point of <24 with 88% specificity and 62% sensitivity (Blake, McKinney, Treece, Lee, & Lincoln, 2002).

In a sample of 95 stroke patients, Godefroy and colleagues (2011) assessed the ability of the MoCA and the MMSE to detect post-stroke cognitive impairment using a

neuropsychological battery as the gold standard. Using the published cutoff score of 26, the MoCA demonstrated high sensitivity (0.94) but low specificity (0.42) when compared to the gold standard. The inverse was found for the MMSE with a sensitivity of 0.66 and a specificity of 0.97 (Godefroy et al., 2011). The areas under the curve for both the MoCA and the MMSE were greater than 0.88 suggesting that both tests had a similar ability to detect post-stroke cognitive impairment (Godefroy et al., 2011). Age and education adjusted test scores were also computed. The adjusted MMSE and MoCA scores were less than or equal to 24 and less than or equal to 20 (much lower than the published cutoff score) respectively. For the MMSE, the adjusted sensitivity was 0.7 and the adjusted specificity was 0.97. The adjusted MoCA scores had a sensitivity and specificity of 66% and 90% respectively (Godefroy et al., 2011). These results differed from those of previous studies, as the MoCA proved to be no more sensitive than the MMSE when screening for cognitive impairment when adjusted cutoff scores were used. This was unanticipated as MoCA better tests executive function and psychomotor speed, which are frequently impaired in patients with stroke (Godefroy et al., 2011).

A recent study by Pendlebury and colleagues (2012) suggests that the MoCA cutoff of less than 26 for MCI is derived from a memory clinic population and may not be entirely appropriate for use with individuals who have suffered a stroke or have evidence of cerebrovascular disease. The authors examined the relation between the MoCA, the MMSE and another test, the Addenbrooke's Cognitive Examination-Revised (ACER-R) at one or more years after a transient ischemic attack or stroke, for the detection of MCI. MCI was identified utilizing a neuropsychological battery

recommended in the National Institute of Neurological Disorders and Stroke- Canadian Stroke Network Vascular Cognitive Impairment Harmonization Standards working group. They found no difference in age, education level and sex distribution between patients with stroke or TIA; however, when compared to those with TIA, the stroke patients had lower mean MMSE, MoCA, ACE-R and memory scores (Pendlebury, Mariz, Bull, Mehta, & Rothwell, 2012a). Furthermore, out of 91 stroke and TIA participants who completed the battery, 42% had MCI (Pendlebury, Mariz, Bull, Mehta, & Rothwell, 2012a). Sensitivity (77%) and specificity (83%) for MCI were optimal with a MoCA cutoff score of less than 25 with a positive and negative predictive value of 0.64 and 0.87 respectively (Pendlebury, Mariz, Bull, Mehta, & Rothwell, 2012b). The sensitivity and specificity for the MMSE were 77% and 81% respectively with a positive predictive value of 0.75 and a negative predictive value of 0.82; however, these optimal values where reached with a cutoff score of less than 29 (Pendlebury, Mariz, Bull, Mehta, & Rothwell, 2012b).

Toglia and colleagues (2011) compared the ability of the MoCA and the MMSE to classify stroke patients as cognitively impaired on an acute inpatient rehabilitation unit. Using a cutoff score of 27 (higher than the published cutoff by Folstein) on the MMSE and 26 on the MoCA, the MoCA classified more patients as cognitively impaired than the MMSE, 89% verses 63% respectively (Toglia et al., 2011). The sensitivity and specificity of these tools were not determined. These authors also examined the relationship between each test and discharge functional status. Functional status was measured using the motor subscale of the FIM instrument (mFIM) and the motor relative functional efficiency

(mRFE) scores. Results indicate that the MoCA was marginally more strongly associated with discharge functional status than the MMSE ($r=0.4$; $P< 0.01$ and $r=0.3$; $P>0.05$ respectively) (Toglia et al 2011). In addition, the MoCA visuoexecutive sub-score was the strongest predictor of functional status (Toglia et al 2011).

In a similar study, Schweizer and colleagues (2012) examined how MoCA and MMSE scores related to cognitive impairment against several other neurocognitive tests and their association with the ability to return to work in a population of aneurysmal subarachnoid hemorrhage patients (n=32). They found that 42% of the patients were impaired on the MoCA and none were impaired on the MMSE. The MMSE failed to detect cognitive impairment in any domain (Schweizer, Al-Khindi, & Macdonald, 2012). The MoCA, unlike the MMSE, correlated with neurocognitive test performance, suggesting that the MoCA can be used as a proxy for neurocognitive assessment if the latter is not feasible (Schweizer et al., 2012). Superior performance on the animal naming and abstraction subtests of the MoCA score were associated with return to work following an aneurysmal subarachnoid hemorrhage; however, more research is needed to address this issue (Schweizer et al., 2012).

## 2.5 The Cognistat

Cognitive status examinations usually provide a global score, and to be useful at the bedside they are brief, have a structured format and they originate from traditional mental status examinations (Kiernan, Mueller, Langston, & Van Dyke, 1987). However, these examinations have several limitations such as high false- negative rates and the

reliance on a global score may not be accurate. In contrast, there are long batteries of cognitive testing that require several hours to administer, are tiring for the patients, are impractical for routine use at the bedside and are expensive (Kiernan et al., 1987). The Cognistat, previously known as the Neurobehavioural Cognitive Status Examination developed by Kiernan and colleagues (1987), independently assesses multiple domains of cognitive functioning and thereby provides a differentiated profile of the patient's cognitive status. The scoring system was designed so that successful performance in several cognitive domains does not obscure deficits in others (Macaulay, Battista, Lebby, & Mueller, 2003). This tool takes approximately 20- 40 minutes to complete depending on the level of impairment and takes about 2 minutes for the administrator to score.

The Cognistat begins with an assessment of consciousness to determine if the patient is alert or impaired as this can affect test performance (Kiernan et al., 1987). Level of consciousness is rated by observation. The Cognistat then assesses cognition using independent tests to evaluate seven major cognitive ability areas: orientation, attention, language (fluency, comprehension, repetition and naming), construction, memory, calculation and reasoning (similarities and judgment). There are a total of 10 independent scores.

The Cognistat follows a 'screen and metric' approach. With the exception of the memory and orientation tests, the tests all begin with a screen item that is more difficult and if the patient passes the screen then the skill is considered intact and no further testing of that skill is required (Kiernan et al., 1987). If the patient fails the screen, then the metric is administered which consists of a series of questions of graded difficulty

(Kiernan et al., 1987). A copy of the Cognistat is not included in the appendix due to copyright.

The screen for the attention domain is to repeat a six digit sequence and the metric is to repeat digit sequences that increase in difficulty. Language is assessed in four areas; fluency, comprehension, repetition and naming. Fluency is assessed by showing the patient a picture of a fishing scene and recording the patient's description. No points are given for this section, and it is evaluated qualitatively with attention to word finding difficulties (Kiernan et al., 1987). In the screen for the attention domain, the patient follows a three-step command, and if they fail, they are asked to follow a series of commands. To test repetition, the patient is asked to repeat a complex sentence for the screen and if they fail they must repeat a series of phrases that are increasingly difficult for the metric. To assess the construction domain, the patient is asked to draw two figures from memory after a 10 second study period. If they fail this task, the patient is given the metric which requires the construction of 3 mosaic patterns using 4 tiles out of 8. To test memory, the patient is asked at the beginning of the test to repeat and remember four words that they will need to know later on in the examination. Approximately 10- 15 minutes later, after an interference task consisting of the language and construction domains, the patients is asked to recall the four words. Next, the screen for the calculation domain is assessed by asking the patient to multiply 5 by 13. If failed, the metric involves four simpler arithmetic questions involving addition, subtraction and division. The reasoning domain is divided into similarity tasks and judgment tasks. To assess similarities, the patient is asked in what way are two items alike, for example

painting and music. If the patient fails this screen, they are then presented with four more word pairs in which the similarity is progressively more difficult to identify (Kiernan et al., 1987). To assess judgment, the patient is asked questions in the form of "What would you do if…" The patient is asked one scenario for the screen and if they fail, they are asked three additional questions for the metric.

The creators of the Cognistat collected normative data on 60 subjects who were volunteers from their medical centers. They were divided into two groups: young (n=30, ages 20 to 39) and old (n=30, ages 40 to 66). There was very little variability among these subjects on any of the domains and no significant difference was found between the two age groups (Kiernan et al., 1987). They also provide standardization data for geriatric (n=59, ages 70 to 92) and neurosurgical patient (n=30, mean age 54.2 years) populations. The geriatric sample were volunteers who had no history of medical or psychiatric conditions and had not received any psychiatric drugs (Kiernan et al., 1987). The mean test scores fell within the normal range established by the young and old groups, however, the mean scores in construction, memory and similarities were significantly lower thereby resulting in a broader range of normal functioning in the geriatric population (Kiernan et al., 1987). The neurosurgical patients had brain lesions (for example stroke, brain tumor, etc.) and their scores were all significantly lower than those of the geriatric group except for the judgment section (Kiernan et al., 1987).

Kiernan and colleagues (1987) address a few issues of reliability and validity with the Cognistat. As the Cognistat was designed to focus on the degree of impairment and

does not discriminate average from superior performance, the range of scores within the normal healthy population is very small (Kiernan et al., 1987). Healthy subjects perform almost perfectly on all domains and, because of this ceiling effect, test-retest studies in normal populations would not be relevant (Kiernan et al., 1987). Kiernan and colleagues (1987) suggested a split-half reliability study; however; this is also not practical as the Cognistat has too few items.

In a validation study, Drane and Osato (1997) examined the ability of the Cognistat to accurately distinguish between healthy elderly residents in a retirement center and patients with dementia in a nursing home. The nursing home patients were diagnosed with dementia as defined by DSM-III-R criteria. The Cognistat demonstrated 100% sensitivity by identifying cognitive impairment in all of the patients diagnosed with dementia but the specificity was only 30% therefore there was a high rate (70%) of false positives among the healthy controls (Drane & Osato, 1997). However, the sample size was very small (n=20). Drane and Osato (199) found that the largest group differences were between the memory and construction domains. It was explained that by expanding the normal range for elderly adults the specificity of the Cognistat would improve (Drane & Osato, 1997; Macaulay et al., 2003). It was also noted that a possible reason for the differences in the memory score may be due to the screen and metric approach as this procedure leads to variations in the duration of the overall stimulus retention interval (Drane & Osato, 1997). Those who successfully completed the screen had shorter retention time, less distractions and less fatigue.

Macaulay and colleagues (2003) established age-corrected norms for the older adult population (age 60 to 85). There were 123 participants who were recruited from several organizations such as senior centers, retirement groups and low income and elderly housing. Comparisons of test performance across several age groups (60-64, 65-69, 70- 74, 75-79 and 80-84) were made. The results suggested the need for age specific profiles. Results show a different pattern of change for memory functioning across age groups (Macaulay et al., 2003). They suggest an extension of the normal range of functioning on the memory domain for individuals in the 65-69 and 70-74 year- old age groups and a further extension for those in the 75-79 and 80 84 year-old age groups (Macaulay et al., 2003). Harris and colleagues (1990) in an earlier study found similar results. Results from this study supported extending the normal range for normal healthy people over the age of 65 on the construction, memory and reasoning domains however, the sample size was very small (Harris et al., 1990).

Nokleby and colleagues (2008) assessed the concurrent validity of three screening tests; the Cognistat, the Screening Instrument for Neuropsychological Impairments in Stroke (SINS) and the Clock drawing test in 49 stroke patients in a stroke rehabilitation setting. The Norwegian standard battery of neuropsychological assessment was used as the gold standard. Sensitivity in detecting deficits in any domain was 82% for the Cognistat composite score, 71% for the SINS composite score and 63% for the Clock Drawing Test (Nokleby et al, 2008). The Cognistat memory subtest performed best as an indicator of memory problems. For the detection of any cognitive deficit, the Cognistat composite score had the best sensitivity (Nokleby et al, 2008). They also explored a

composite Cognistat language score, comprising the results of the comprehension, repetition and naming subtests. The composite score performed better than the three language subtests alone with an AUC of 82% (Nokleby et al, 2008).

A study by Schwamm and colleagues (1987) was designed to determined whether the Cognistat was a more sensitive tool in the detection of cognitive impairment when compared with the MMSE in 30 patients with documented brain lesions. The Cognistat proved to be more sensitive than the MMSE; the MMSE had a false negative rate of 43% versus the Cognistat with a false negative rate of 7%. In another study by Van Gorp and colleagues (1999), the sensitivity and specificity of the MMSE, the Mattis Dementia Rating Scale (MDRS) and the Cognistat were compared in a sample of Alzheimer's disease patients (n=22), vascular dementia patients (n=19) as well as normal healthy elderly individuals (n=12). Subjects with Alzheimer's disease met criteria as defined by the National Institute of Neurological and Communication Disorders. Patients with vascular dementia met DSM-III-R criteria. With the published cutoff score of 23, the MMSE had a sensitivity of 71%, 100% specificity and an overall accuracy of 77% (van Gorp et al., 1999). However, with a cutoff score of 26 the overall accuracy increased to 98% and sensitivity also increased to 98% and the specificity remained at 100% (van Gorp et al., 1999). The sensitivity of the Cognistat ranged from 33% in the attention subtest to 88% in the memory subtest (van Gorp et al., 1999). The memory subtest was the only subtest that had less than 100 specificity (83%) (van Gorp et al., 1999). The memory and construction subtests resulted in the highest accuracy (86% and 80% respectively) suggesting good classification rates (van Gorp et al., 1999). Since the

Cognistat manual presents different profiles for patients with Alzheimer's disease and for those with vascular dementia, van Gorp and colleagues (1999) compared the mean profile configuration of the Cognistat subscales for these two patient groups. Both 100% of the controls and 100% of the dementia patients were successfully classified as impaired or unimpaired (van Gorp et al., 1999). However, within the dementia groups the Cognistat subtest scores correctly classified 67% of the Alzheimer's disease subjects and 75% of the vascular dementia subjects (van Gorp et al., 1999). Therefore, the Cognistat subtest score pattern did not differentiate between Alzheimer's disease and vascular dementia.

Mysiw and colleagues (1989) administered the Cognistat and the MMSE to 38 stroke patients before inpatient rehabilitation to determine the extent to which the scores predict rehabilitation outcome. Results demonstrated that the Cognistat was a more sensitive indicator of impairment than the other tool especially in the orientation and memory subtests (Mysiw et al., 1989). Toedter and colleagues (1995) conducted a study to determine whether reliable responses to standardized psychological measures including the Cognistat could be obtained in a group of 106 stroke patients in a rehabilitation hospital. Interestingly, the results demonstrated that the Cognistat was predictive for those stroke rehabilitation patients who had very low likelihood of being able to respond consistently and failed to identify those who would respond in a reliable manner (Toedter et al., 1995).

The Cognistat was chosen as the "gold standard" for the present study for a variety of reasons. As previously mentioned, the Cognistat independently assesses

multiple domains of cognitive functioning, providing a differentiated profile of the patient's cognitive status like a neuropsychological battery. However, the batteries are long and tiring and require a neuropsychological specialist to administer, which can also be costly. For these practical reasons, the Cognistat was used in place of a truly definitive 'gold standard', to provide a standardized criterion for the comparative evaluation of the MMSE and MoCA.

Several studies have compared the Cognistat to the definitive gold standard for cognitive impairment, the neuropsychological battery. Karzmark (1997) examined the validity of the Cognistat using a comprehensive neuropsychological assessment as the gold standard in a sample of 50 outpatient referrals to the neuropsychological assessment service of a general medical hospital. The sensitivity and specificity of the Cognistat was 74% and 86% respectively (Karzmar, 1997). However, the sensitivity of the individual subtests ranged from 20% to 48% and the specificity of the individual subtests ranged from 64% to 97% respectively (Karzmar, 1997). This suggests that the results of the Cognistat depend highly on the severity and the nature of the sample assessed and the criterion used (Karzmar, 1997). In summary, a review of literature found the Cognistat has demonstrated to be a highly sensitive tool; however, its validity has yet to be tested in a stroke inpatient rehabilitation population.

# Chapter 3

## Objectives and Hypothesis

General Objective

To evaluate two screening tools for cognitive impairment in stroke patients in a rehabilitation setting.

Specific Objective

To conduct a validation study of the MMSE and the MoCA using the Cognistat as the criterion or 'gold standard'.

Hypothesis

It is hypothesized that the MoCA is a superior screening instrument to the MMSE for the detection of cognitive impairment in stroke patients. The rational for the hypothesis stems from a review of literature. The MoCA has been demonstrated to be a more effective tool in the detection of cognitive impairment compared to the MMSE in several populations including those with Parkinson's disease, cerebral small vessel disease, cardiovascular disease as well as in Alzheimer's disease and dementia.

# Chapter 4

# Methods

*Ethics Approval:* This study was approved by The University of Western Ontario Health Sciences Research Ethics Board. Please see Appendix D for approval certificate.

Initial REB approval was granted from August 24, 2011 to October 31, 2011. An extension was requested, and approved effective November 29, 2011. Some patients were recruited between October 31 and November 29 according to the originally approved protocol. The REB was subsequently informed of this issue.

## 4.1 Subjects

*Initial Eligibility Criteria:* Individuals admitted to the stroke rehabilitation inpatient unit at Parkwood Hospital, London, Ontario, between August 2011 and March 2012 who were between 18 and 97 years of age. Patients admitted to the stroke rehabilitation unit as a rule must have experienced a recent stroke with subsequent disability, be able to learn, have definable rehabilitation goals and be able to participate physically in the rehabilitation program.

*Exclusion Criteria:* Individuals who were aphasic, dysphasic, or who had severe visual or hearing limitations were excluded from the study as the scores on each of the tests may be affected. These limitations were initially screened for by the physicians obtaining consent. If this was missed, the occupational therapists assigned to the patient informed the student investigator of the patient's condition. Patients who were unable to speak or read English were also excluded.

4.2 Sample Size

The sample size of 88 was calculated using the statistical program G* Power 3.1.2. A Chi-Square Goodness of Fit test was performed with 1 degree of freedom. Cohen's (1992) medium effect size of 0.3 was used and it is defined as an effect size that represents an effect likely to be visible to the naked eye of an observer. Therefore for clinical use, this is the value at which we will detect a difference. Cohen's effect sizes are widely used.

4.3 Recruitment

Dr. Robert Teasell or Dr. John Clement, members of the patient's health care team, first contacted the potential participants (all patients who met inclusion and exclusion criteria) to recruit them. The patients then received a Letter of Information and a Consent Form (Please see Appendix C). The study began once the patients were fully informed about the study and consent was obtained.

4.4 Measures

The measures used in the present study were reviewed in Chapter 2. Some of the following material repeats those earlier descriptions.

*The MMSE*

The MMSE is easily administered and requires 5- 10 minutes to complete depending on the impairment of the individual. The MMSE includes 30 items grouped into 5 categories: orientation, registration, attention and calculation, recall and language. The test is divided into two sections; the first requires verbal responses to orientation, memory

and attention questions. The second requires naming, reading and writing and the ability follow verbal and written commands, write a sentence and copy a polygon (Folstein & Folstein, 1975). The MMSE is scored out of 30 possible points and all points can be summed up quickly by the administrator. The score places the patient on a scale of cognitive function.

*The MoCA*

The MoCA, like the MMSE takes approximately 10 minutes to complete, has a total of 30 possible points and takes 1 minute to score. The test is divided into eight domains: visuospatial/executive function, naming, memory, attention, language, abstraction, delayed recall and orientation. Visuospatial abilities are assessed using a clock drawing task and to copy a three dimensional cube. Executive functions are assessed using an alternation task drawing a line from a number to a letter in ascending order. Naming is assessed using three very common animals (lion, camel, rhinoceros). By repeating a list of digits in forward and backwards order, a target detection task, as well as a serial subtraction task, attention abilities are evaluated. Language is assessed via repetition of two syntactically complex sentences and a fluency task. Abstraction is evaluated using a similarity task. Lastly, orientation to time and place is evaluated.

*The Cognistat*

The Cognistat, previously known as the Neurobehavioural Cognitive Status Examination, begins with an assessment of consciousness, attention and orientation. Then, it assesses cognition using independent tests to evaluate five major cognitive ability areas: language, construction, memory, calculation and reasoning (Kiernan et al., 1987). With the exception of the memory and orientation tests, the tests all begin with a screen item that

is more difficult. If the patient passes the screen then the skill is considered intact and no further testing of that skill is required (Kiernan et al., 1987). If the patient fails the screen, then the metric is administered which consists of a series of questions of graded difficulty (Kiernan et al., 1987). An important advantage of the Cognistat is that it independently assesses multiple domains of cognitive functioning and thereby provides the clinician with a differentiated profile of the patient's cognitive status (Kiernan et al., 1987). This tool takes approximately 20- 40 minutes to complete depending on the level of impairment and takes about 2 minutes for the administrator to score.

## 4.5 Data Collection

### *MoCA and MMSE*

For each patient, an occupational therapist administered both the MoCA and the MMSE consecutively. The occupational therapists recorded which of the two tests they administered in order to ensure that they were administering them in alternating order across patients. These screening tools were administered by the occupational therapist that was assigned to the patient during their therapeutic stay in the stroke rehabilitation unit. Published cutoff scores of 24 and 26 were used to establish cognitive impairment with the MMSE and the MoCA respectively. The screening tools took approximately 10 minutes each to complete.

### *Cognistat*

The Cognistat was then administered by the student investigator as soon after the two screening tests as possible, preferably the following day. An inter-rater reliability

sub-study was conducted in order to ensure the reliability of the test administration by the student investigator. Two of the occupational therapists administered the Cognistat in addition to the student investigator on 20 patients. For half of the patients the student investigator administered the Cognistat first and for the second half the occupational therapists administered it first. The patients were aware of the additional testing which was explained in the Letter of Information. The second Cognistat was performed within the same week as the first. The screen and metric approach was not used in this study (this will be discussed in Chapter 6- Discussion). A patient was deemed cognitively impaired if they scored in the impaired region in one or more domains on the Cognistat. A Cognistat composite score out of 82 possible points was also calculated by summing the scores of each individual domain. The Cognistat took an additional 20 minutes to complete although the timing varied depending on the patient's level of impairment.

As the student investigator was not a trained clinician, she initially observed the occupational therapists administer the Cognistat on several patients. Once she felt comfortable, the student investigator administered the tool under the supervision of an occupational therapist. The occupational therapist then decided when she was prepared for test administration.

After the student investigator received the original copy of the first two Cognistats from the reliability sub-study administered by the occupational therapists, she noticed that some of the scoring did not follow the precise instructions from the Cognistat manual. When this was detected the student investigator met with the occupational

therapists and went through the instruction manual and scoring for each domain on the Cognistat so that the test would be scored as accurately as possible.

Each test was administered in a private quiet room on the stroke rehabilitation unit to ensure that there were no distractions for the patient as well as to provide a comfortable testing environment. During testing, if the patient required, they were permitted to take a break before beginning the next test. Once all three tests were administered, the student investigator asked the patients their level of completed education. The side and location of the stroke as well as medication history was obtained through chart review and was recorded given that these factors had potential to explain some of the patient variance in performing the tests. Data input was in Microsoft Office Excel 2003 and data analysis was conducted using SPSS 20.0 (IBM Corporation, 2011) and SISA (Uitenbroek, 1997), an on-line software program.

4.6 Statistical Measures

The following statistical measures were calculated using SISA at http://www.quantitativeskills.com/sisa/statistics/diagnos.htm. Please refer to Figure 1 for the labeling of cells from the 2 x 2 table.

*Sensitivity* - 'the probability of correctly diagnosing a diseased person (case) or the probability that any given case will be identified by the test' (Porta, 2008) (p.227).

Sensitivity = a / a + c

*Specificity* - 'the probability that a person without the disease (noncase) will be correctly identified as nondiseased by the test' (Porta, 2008) (p.227). Specificity = d/ b + d

*Positive Predictive Value (PPV)* - 'the probability that a person with a positive test result is a true positive (does have the disease)' (Porta, 2008) (p.191). PPV= a / a + b

*Negative Predictive Value (NPV)* - 'the probability that a person with a negative test result is a true negative (does not have the disease)' (Porta, 2008) (p.191). NPV= d / c + d

*Positive Likelihood Ratio* – 'For a positive result, the likelihood ratio equals the ratio sensitivity/(1 – specificity)' (Porta, 2008) (p.145). It is 'the ratio of the proportion of diseased people with a positive test result (sensitivity) to the proportion of nondiseased people with a positive result (1 – specificity)' (Fletcher & Fletcher, 2005) (p.49). As a ratio statistic, the null value is equal to unity. For example, a test with both a sensitivity and a specificity of 50% (i.e. a random coin toss) would have an LR of 1.0, whereas an almost perfect test with both a sensitivity and specificity of 99% would have an LR of 99. While a negative likelihood ratio can also be calculated for a negative test result, for brevity in this thesis the term 'likelihood ratio' denotes the positive LR.

*95% Confidence Interval* – an interval estimate can be calculated to gauge the precision of each of the above point estimates. For example, for an estimate of sensitivity, the 95% CI indicates that we can be 95% certain that the true sensitivity of the test in the population falls within the stated limits.

| | | **"True" Condition** | |
|---|---|---|---|
| | | Present | Absent |
| **Test Result** | + | A | B |
| | - | C | D |

**Figure 1.** Standard 2x2 table.

## 4.7 Data Analysis

### *Descriptive Statistics*

The database was created in SPSS 20.0 (IBM Corporation, 2011). This statistical software as well as SISA was used to carry out all data management and the calculation of descriptive statistics. Minimum, maximum, mean, standard deviation and frequencies were determined where appropriate for age, education, MMSE and MoCA scores, the Cognistat composite score and sex. If the patient had greater than 12 years of education (eg, college, university) they were coded as having 13 years of education. The mean, minimum and maximum scores on the Cognistat were also determined for the metrics for all domains. The frequency and percent passes and failures were also determined for all the screens on the Cognistat.

### *Validation Study*

Cognitive impairment on the MMSE and the MoCA was first determined using published cutoff scores of 24 and 26 for the MMSE and the MoCA respectively (M. F. Folstein, Robins, & Helzer, 1983; Nasreddine et al., 2005). Since these published cutoff scores may not be accurate in stroke patients, additional analyses were performed to refine the cutoff scores for both tests. Receiver Operator Characteristic (ROC) curves were generated to examine the ability of the MMSE and the MoCA to discriminate between impaired verses normal status compared to the gold standard, the Cognistat. A patient is deemed impaired if the score was in the impaired region in one or more domains and not impaired if there were no impairments in any domain on the Cognistat. The area under the curve, sensitivity, specificity, positive predictive value and negative

predictive value were calculated. Optimal cutoff points were determined using the coordinates of the ROC curve. The optimal cutoff points were those with maximum sensitivity and specificity. A second ROC curve was generated for the MMSE where the executive function domains were removed on the Cognistat and participants were re-evaluated as impaired or not impaired. This was done to provide a better comparison between the MMSE and the Cognistat as the MMSE does not measure executive function. This was not done for the MoCA as the MoCA does test executive function. Additional ROC curves were generated for both the MMSE and the MoCA using the criterion of *two* or more impaired domains on the Cognistat being necessary to be deemed cognitively impaired. This was to assure that the original criteria were not too stringent.

*Reliability Sub-Study*

Inter-rater reliability was calculated between the student investigator and the two occupational therapists for the Cognistat. The two occupational therapist were made into one group for the inter-rater reliability calculations. The intraclass correlation coefficient (ICC) was calculated for all metrics on the Cognistat as they are scored as continuous variables. The metrics include: orientation, attention, language comprehension, language repetition, language naming, language total score, construction, memory, calculation, reasoning similarities, reasoning judgment and total reasoning score. Fluency was not included as no score is given for the domain as previously mentioned. The ICC for the Cognistat composite score was also determined. The kappa statistic was determined for all the screens as they are binary variables (pass and fail). Every domain has a screen with the exception of orientation and memory.

# Chapter 5

## Results

Among 144 consecutive stroke patients admitted to Parkwood Hospital between August 2011 and April 2012, 76 (53%) met the inclusion criteria and completed the study (Figure 2). Sixty eight patients were excluded from the study; 44 were aphasic or dysphasic, 9 patients did not speak English and 4 patients refused participation. Eleven patients did not participate for other reasons such as early discharge, one patient had a recurring stroke and went to another hospital, a patient had narcolepsy and could not complete any of the tests, several patients felt too sick to continue and a patient was excluded due to missing data for the MoCA. Due to changes in hospital admission policy and time constraints, the original goal of a sample size of 88 was not reached.

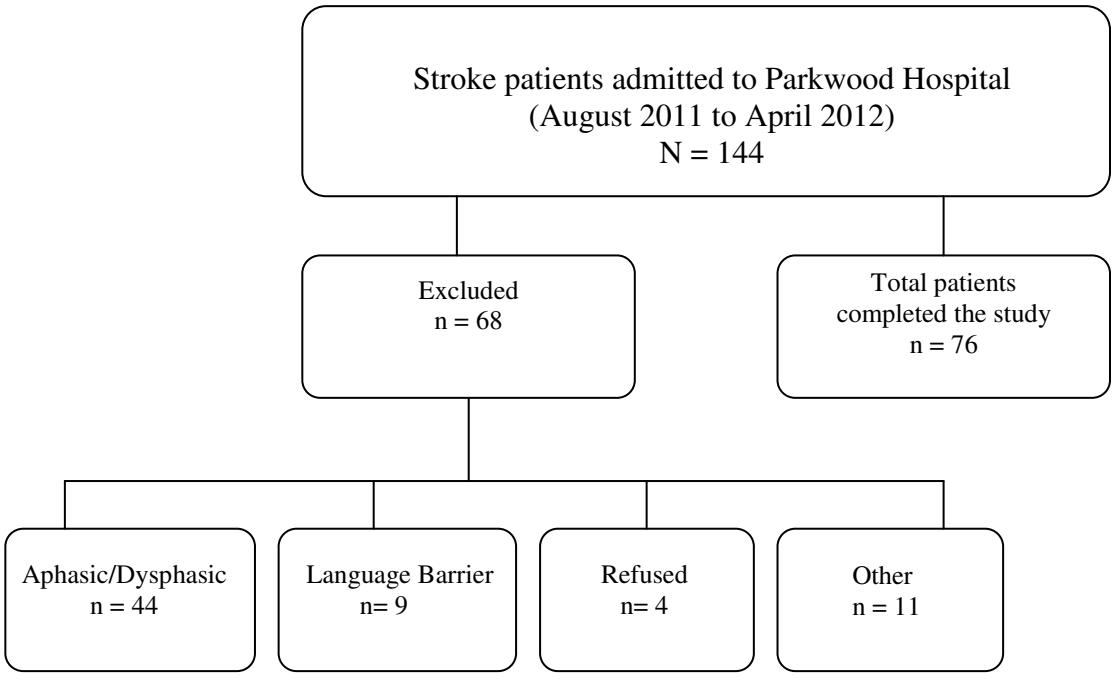


**Figure 2.** Study population flow chart.

5.1 Descriptive Statistics

Table 1 describes the sample of patients who met the inclusion criteria. The mean age of the study sample (n = 76) was 67.6 (SD 15.1) years. More than half of the patients were women (52.6%). The mean MMSE and MoCA scores for these patients was 26.47 (SD 3.4) and 20.88 (SD 5.3) respectively. The mean Cognistat composite score (the sum score of all domains) was 62.91 (SD 10.11) out of a possible 82 points.

**Table 1.** Descriptive statistics of the patients who met the inclusion criteria

| Variable | N | Minimum | Maximum | Mean | SD | Percent |
|---|---|---|---|---|---|---|
| Age | 76 | 18 | 97 | 67.58 | 15.08 | - |
| Education | 76 | 7 | 13 | 11.22 | 1.97 | - |
| MMSE | 76 | 15 | 30 | 26.47 | 3.41 | - |
| MoCA | 76 | 6 | 29 | 20.88 | 5.34 | - |
| Cognistat Composite Score | 76 | 37 | 78 | 62.91 | 10.11 | - |
| Sex: | | - | - | - | - | |
| Women | 40 | | | | | 52.6 |
| Men | 36 | | | | | 47.4 |

5.2 Validation Study

*The MMSE and the Cognistat*

Sensitivity and specificity were determined using the Cognistat as the gold standard. Cognitive impairment was defined as impairment in one or more domains on the Cognistat, for which 70 out of 76 patients (92%) tested positive. The MMSE exhibited specificity of 100% and sensitivity of 35.7% (Table 2). The positive and

negative predictive values were 100% and 11.8% respectively (Table 2). The 2x2 table is provided in Appendix B. The area under the ROC curve (Figure 3) was 0.81 (95% ConfI 0.69-0.93, p= 0.012) however, this is at an optimal cutoff of 29 (Figure 6A).

Since this cutoff score is very high, a second ROC curve (Figure 4) was generated for the MMSE where the executive function domains were removed on the Cognistat and participants were re-evaluated as impaired or not impaired. This was done to provide a better comparison between the MMSE and the Cognistat as the MMSE does not measure executive function. Results show that the AUC decreased to 0.76 (95% ConfI 0.63- 0.88, p= 0.005) and the cutoff score remained at 29 (Figure 6B).

A final ROC curve was produced using the criterion of two or more impaired domains on the Cognistat as cognitively impaired (Figure 7). Using this criterion, 55 (72%) patients tested positive for cognitive impairment and 21 tested negative. The MMSE exhibited excellent specificity (95.2%) and moderate sensitivity (43.6%). The positive and negative predictive values were 96% and 39.2% respectively with an increase in likelihood ratio to 9.16 (Table 3). The AUC was virtually unchanged at 0.82 (95% ConfI 0.72- 0.91, p=0.00).

*The MoCA and the Cognistat*

Like the MMSE, sensitivity and specificity were determined using the Cognistat as the gold standard where impairment was determined as impaired in one or more domains on the Cognistat. The MoCA demonstrated poor specificity (33.3%) and

excellent sensitivity (90%) (Table 2). The positive and negative predictive values were 94.0% and 22.2% respectively and the positive likelihood ratio was 1.35 (Table 2). The 2x2 table is provided in Appendix B. The area under the ROC curve (Figure 5) is 0.83 (95% ConfI 0.70- 0.95, p= 0.008) providing an optimal cutoff score of 26 (Figure 6C).

A final ROC curve was produced using the criterion of two or more impaired domains on the Cognistat as cognitively impaired (Figure 8). Using this criterion, 55 (72%) patients tested positive for cognitive impairment and 21 tested negative. The cutoff score remained at 26 and the AUC was 0.81 (95% CI 0.72- 0.91, p= 0.00) (Figure 8 and Figure 9). The MoCA exhibited poor specificity (19.1%) and excellent sensitivity (90.1%). The positive and negative predictive values were 74.6% and 44.4% respectively with a likelihood ratio of 1.12 (Table 3).

**Table 2.** The sensitivity, specificity, positive and negative predictive values and positive likelihood ratio for the MMSE and the MoCA with *one* or more impaired domains on the Cognistat. (95% ConfI).

| | Specificity | Sensitivity | NPV | PPV | Likelihood Ratio |
|---|---|---|---|---|---|
| MMSE | 100%<br>- | 35.71%<br>(0.21- 0.5) | 11.80%<br>(0.005- 0.23) | 100%<br>- | - |
| MoCA | 33.33%<br>(0.00- 0.81) | 90%<br>(0.81- 0.99) | 22.22%<br>(0.00- 0.57) | 94.03%<br>(0.87- 1.00) | 1.35<br>(0.65- 2.79) |

**Table 3.** The sensitivity, specificity, positive and negative predictive values and positive likelihood ratio for the MMSE and the MoCA with *two* or more impaired domains on the Cognistat. (95% CI).

| | Sensitivity | Specificity | PPV | NPV | Likelihood Ratio |
|---|---|---|---|---|---|
| MMSE | 95.23% (0.84- 1.07) | 43.64% (0.27- 0.6) | 39.22% (0.22- 0.56) | 96% (0.86- 1.06) | 1.69 (1.23- 2.33) |
| MoCA | 19.05% (-0.02- 0.41) | 90.1% (0.81- 1.01) | 44.44% (0.03- 0.86) | 74.6% (0.61- 0.88) | 2.1 (0.44-9.87) |

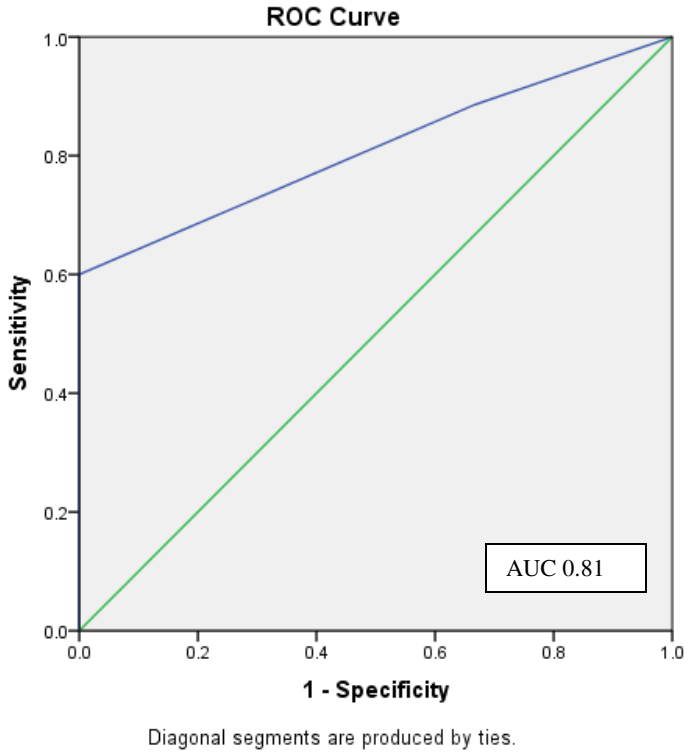


**Figure 3.** ROC curve for the MMSE with the Cognistat as the gold standard. AUC 0.81 (95% ConfI 0.69-0.93) and a cutoff scare of < 29 indicating CI.

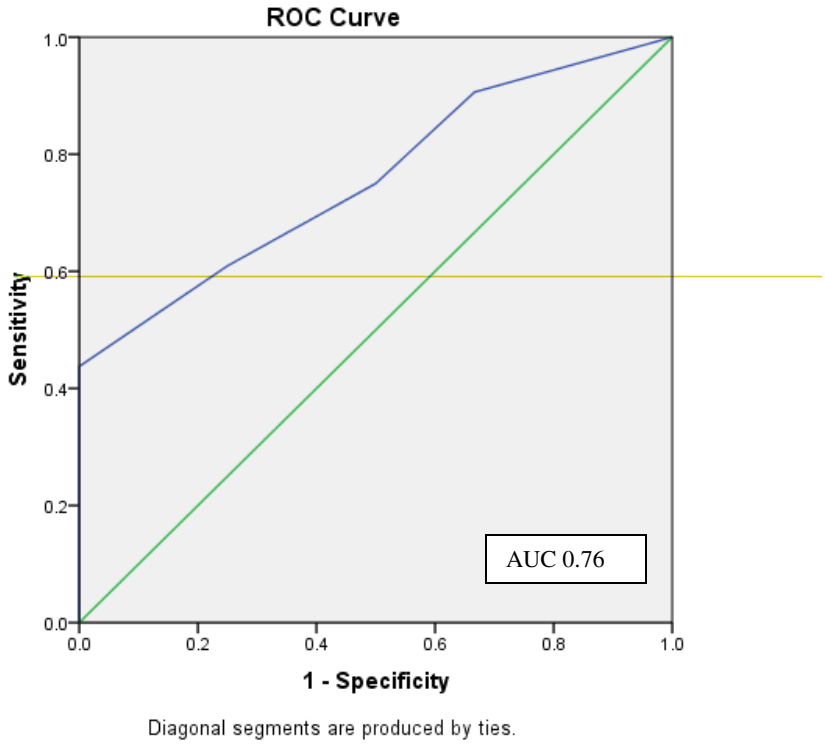


**Figure 4.** ROC curve for the MMSE with executive function removed on the Cognistat. AUC 0.76 (95% ConfI 0.63- 0.88) and a cutoff score of < 29 indicating CI.

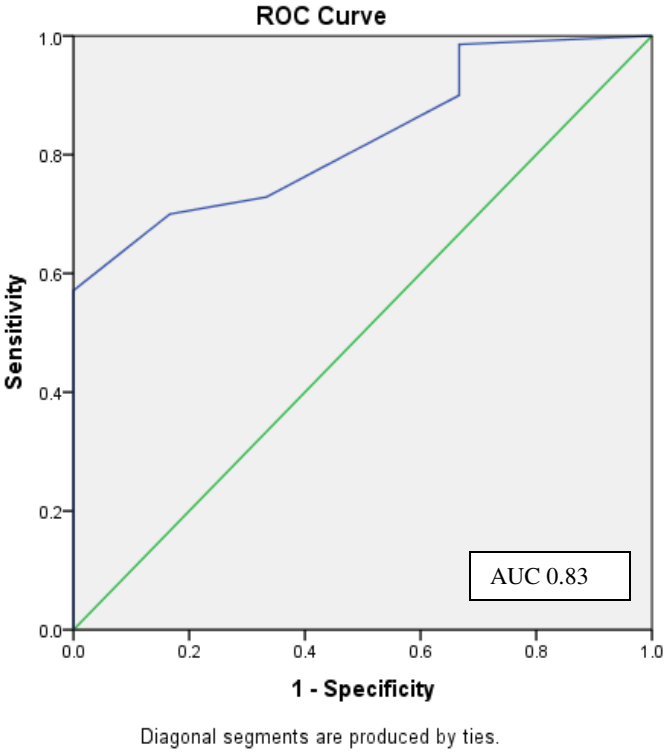


**Figure 5.** ROC curve for the MoCA with the Cognistat as the gold standard. AUC 0.83 (95% CI 0.70- 0.95) and a cutoff score of < 26 indicating CI.

**A)** Coordinates of the Curve

MMSE

| Positive if Less Than or Equal To[a] | Sensitivity | 1 - Specificity |
|---|---|---|
| 14.00 | .000 | .000 |
| 15.50 | .014 | .000 |
| 16.50 | .029 | .000 |
| 17.50 | .057 | .000 |
| 18.50 | .071 | .000 |
| 20.50 | .086 | .000 |
| 22.50 | .100 | .000 |
| 23.50 | .157 | .000 |
| 24.50 | .186 | .000 |
| 25.50 | .243 | .000 |
| 26.50 | .400 | .000 |
| 27.50 | .600 | .000 |
| 28.50 | .743 | .333 |
| 29.50 | .886 | .667 |
| 31.00 | 1.000 | 1.000 |

**B)** Coordinates of the Curve

MMSE

| Positive if Less Than or Equal To | Sensitivity | 1 - Specificity |
|---|---|---|
| 14.00 | .000 | .000 |
| 15.50 | .016 | .000 |
| 16.50 | .031 | .000 |
| 17.50 | .063 | .000 |
| 18.50 | .078 | .000 |
| 20.50 | .094 | .000 |
| 22.50 | .109 | .000 |
| 23.50 | .172 | .000 |
| 24.50 | .203 | .000 |
| 25.50 | .266 | .000 |
| 26.50 | .438 | .000 |
| 27.50 | .609 | .250 |
| 28.50 | .750 | .500 |
| 29.50 | .906 | .667 |
| 31.00 | 1.000 | 1.000 |

**C)** Coordinates of the Curve

MoCA

| Positive if Less Than or Equal To[a] | Sensitivity | 1 - Specificity |
|---|---|---|
| 5.00 | .000 | .000 |
| 7.00 | .014 | .000 |
| 8.50 | .043 | .000 |
| 10.00 | .071 | .000 |
| 11.50 | .086 | .000 |
| 12.50 | .100 | .000 |
| 14.50 | .114 | .000 |
| 16.50 | .171 | .000 |
| 17.50 | .229 | .000 |
| 18.50 | .329 | .000 |
| 19.50 | .429 | .000 |
| 20.50 | .457 | .000 |
| 21.50 | .543 | .000 |
| 22.50 | .571 | .000 |
| 23.50 | .700 | .167 |
| 24.50 | .729 | .333 |
| 25.50 | .814 | .500 |
| 26.50 | .900 | .667 |
| 27.50 | .957 | .667 |
| 28.50 | .986 | .667 |
| 30.00 | 1.000 | 1.000 |

**Figure 6.** The coordinates of the ROC curves for: A) the MMSE; B) the MMSE excluding the executive function domains on the Cognistat; C) the MoCA. One or more domains on the Cognistat indicate impairment.

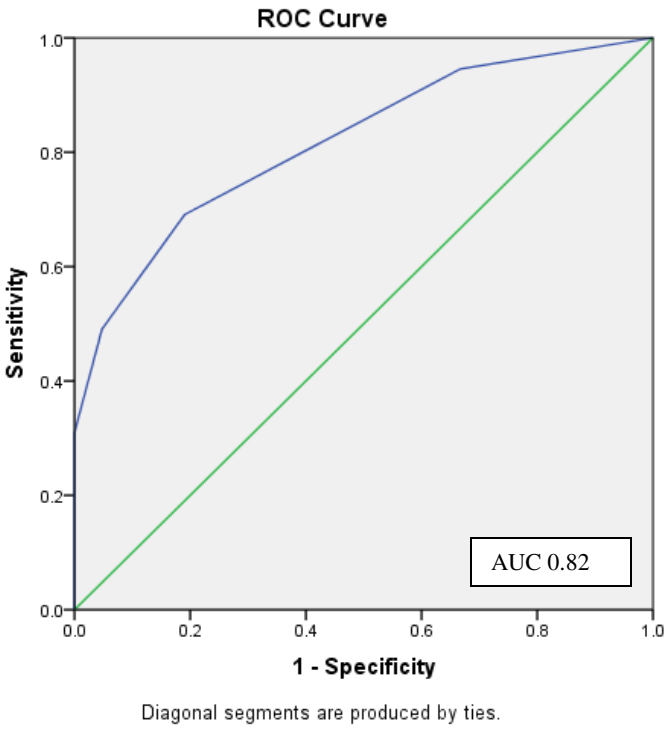


**Figure 7.** ROC curve for the MMSE when two or more domains are impaired on the Cognistat. AUC 0.82 (95% ConfI 0.72- 0.91) and a cutoff score of < 29 indicating CI.

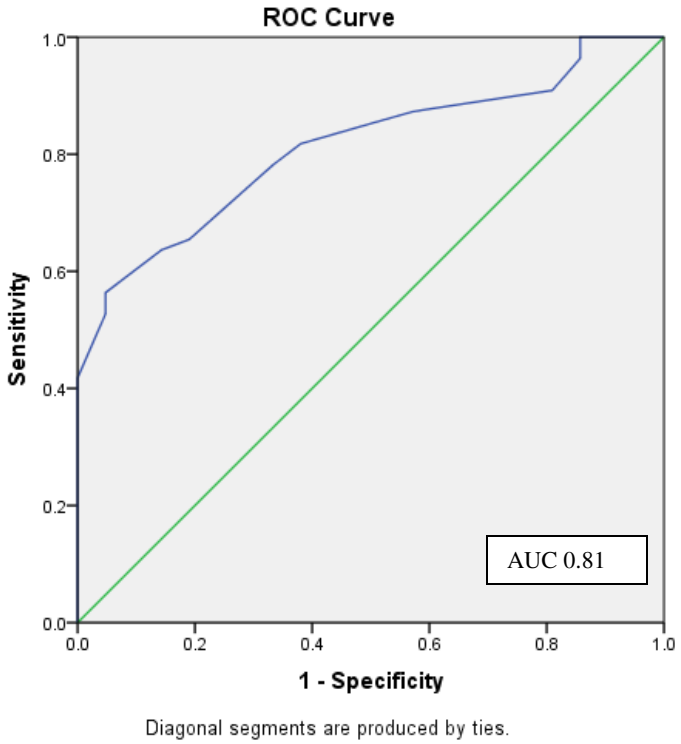


**Figure 8.** ROC curve for the MoCA when two or more domains on the Cognistat indicate impairment. AUC 0.81 (95% ConfI 0.72- 0.91) and a cutoff score of < 26 indicating CI.

**A)** Coordinates of the Curve

MMSE

| Positive if Less Than or Equal To | Sensitivity | 1 - Specificity |
|---|---|---|
| 14.00 | .000 | .000 |
| 15.50 | .018 | .000 |
| 16.50 | .036 | .000 |
| 17.50 | .073 | .000 |
| 18.50 | .091 | .000 |
| 20.50 | .109 | .000 |
| 22.50 | .127 | .000 |
| 23.50 | .200 | .000 |
| 24.50 | .236 | .000 |
| 25.50 | .309 | .000 |
| 26.50 | .491 | .048 |
| 27.50 | .691 | .190 |
| 28.50 | .818 | .429 |
| 29.50 | .945 | .667 |
| 31.00 | 1.000 | 1.000 |

**B)** Coordinates of the Curve

MoCA

| Positive if Less Than or Equal To | Sensitivity | 1 - Specificity |
|---|---|---|
| 5.00 | .000 | .000 |
| 7.00 | .018 | .000 |
| 8.50 | .055 | .000 |
| 10.00 | .091 | .000 |
| 11.50 | .109 | .000 |
| 12.50 | .127 | .000 |
| 14.50 | .145 | .000 |
| 16.50 | .218 | .000 |
| 17.50 | .291 | .000 |
| 18.50 | .418 | .000 |
| 19.50 | .527 | .048 |
| 20.50 | .564 | .048 |
| 21.50 | .636 | .143 |
| 22.50 | .655 | .190 |
| 23.50 | .782 | .333 |
| 24.50 | .818 | .381 |
| 25.50 | .873 | .571 |
| 26.50 | .909 | .810 |
| 27.50 | .964 | .857 |
| 28.50 | 1.000 | .857 |
| 30.00 | 1.000 | 1.000 |

**Figure 9.** The coordinates of the ROC curves for: A) the MMSE; B) the MoCA. Two or more domains on the Cognistat indicate impairment.

5.3 The Cognistat

Table 4 displays the minimum, maximum mean and standard deviation for all of the metric domains on the Cognistat. The mean score on the construction, memory and judgment domains are in the impaired region (Table 4). Table 5 displays the percent frequency of passes and failures in each of the screens on the Cognistat. The majority of patients did not pass 4 out of the 8 screens (language repetition, language naming, construction and reasoning judgment) (Table 5). The majority of the patients passed the remaining screens (attention, language comprehension, calculation and reasoning similarities) (Table 5).

**Table 4.** Descriptive statistics for each metric on the Cognistat.

| Domains | Minimum | Maximum | Mean | SD |
|---|---|---|---|---|
| Orientation | 3 | 12 | 10.66 | 2.02 |
| Attention | 3 | 8 | 6.74 | 1.37 |
| Language: | | | | |
| Comprehension | 3 | 6 | 5.21 | 0.82 |
| Repetition | 6 | 12 | 11.20 | 1.47 |
| Naming | 5 | 8 | 7.09 | 0.85 |
| Subtotal (language) | 17 | 26 | 23.53 | 2.32 |
| Construction | 0 | 6 | 2.92 | 1.90 |
| Memory | 0 | 12 | 6.84 | 3.04 |
| Calculation | 0 | 4 | 3.13 | 1.04 |
| Reasoning: | | | | |
| Similarities | 1 | 9 | 5.67 | 1.98 |
| Judgment | 0 | 6 | 3.62 | 1.41 |
| Subtotal (reasoning) | 1 | 14 | 9.28 | 2.85 |

**Table 5.** The frequency and percent of passes and failures on each screen on the Cognistat.

| Domains | Frequency passed (failed) | Percent passed (failed) |
|---|---|---|
| Attention | 66 (10) | 86.8 (13.2) |
| Language: | | |
| Comprehension | 58 (18) | 76.3 (23.7) |
| Repetition | 23 (53) | 30.3 (69.7) |
| Naming | 26 (50) | 34.2 (65.8) |
| Construction | 12 (64) | 15.8 (84.2) |
| Calculation | 41 (35) | 53.9 (46.1) |
| Reasoning: | | |
| Similarities | 42 (34) | 55.3 (44.7) |
| Judgment | 20 (56) | 26.3 (73.7) |

5.4 Reliability Sub-study

Substantial agreement for the raters was found for the metrics associated with the comprehension, repetition and memory domains of the Cognistat (Table 6). Almost perfect agreement was found for the remaining seven domains: naming, construction, calculation, similarities and judgment. The language total score and the reasoning total score also resulted in almost perfect agreement, ICC= 0.846 and ICC= 0.901 respectively. The strongest agreement for the raters was the composite score (the total score of all of the domains) which is 0.955. Agreement for the binary screens are low to moderate with the lowest agreement being the calculation domains and the strongest being the similarities screen in the reasoning domain (Table 6).

**Table 6.** Interrater reliability results for the metric and screen for every domain on the Cognistat.

| Cognistat Domains | ICC (metric) (95% ConfI) ($p < 0.001$) | kappa (screen) |
|---|---|---|
| Orientation | 0.920 (0.66- 0.94) | - |
| Attention | 0.878 (0.53- 0.91) | 0.419 (0.18- 2.30) |
| Language: | | |
| Comprehension | 0.734 (0.20- 0.81) | 0.432 (0.21- 1.94) |
| Repetition | 0.783 (0.29- 0.84) | 0.524 (0.21- 2.34) |
| Naming | 0.877 (0.53- 0.91) | 0.294 (0.22- 1.35) |
| Total Score | 0.846 (0.44- 0.88) | - |
| Construction | 0.898 (0.59- 0.92) | 0.692 (0.20- 3.35) |
| Memory | 0.787 (0.30- 0.84) | - |
| Calculation | 0.904 (0.61- 0.93) | 0.225 (0.22- 1.15) |
| Reasoning: | | |
| Similarities | 0.820 (0.38- 0.87) | 0.700 (0.15- 3.28) |
| Judgment | 0.894 (0.58- 0.92) | 0.483 (0.25- 2.20) |
| Total Score | 0.901 (0.60- 0.92) | - |
| Composite Score | 0.955 (0.80- 0.96) | - |

# Chapter 6

## Discussion

The primary aim of this study was identify the better of two commonly used screening tools for detecting probable cognitive impairment in stroke patients in a large regional rehabilitation hospital (Parkwood Hospital, London, Ontario). This was a comparative validation study of the MMSE and the MoCA, using the Cognistat, as the criterion or 'gold standard'.

Using the criterion for cognitive impairment that a patient with an impairment in one or more domains on the Cognistat is deemed cognitively impaired, the MMSE had 100% specificity, 35.7% sensitivity, 100% and 11.8% positive and negative predictive values respectively (Table 2). Using the same criterion for impairment on the Cognistat, the MoCA had a specificity of 33.3% and a sensitivity of 90%, positive and negative predictive values of 93.03% and 22.22% respectively, and a positive likelihood ratio of 1.35 (Table 2).

It is noteworthy that the performance of the two instruments were essentially mirror images of one another; whereas the MMSE had high specificity and low sensitivity, the opposite was true for the MoCA. In the original article by Nasreddine et al 2005, the MMSE had a poor sensitivity of 18% and the MoCA had 90% sensitivity in the detection of MCI. In the Alzheimer's disease group the MMSE had a sensitivity of 78% and the MoCA a sensitivity of 100% (Nasreddine et al., 2005). Both tests had excellent specificity, 100% and 87% for the MMSE and the MoCA respectively

(Nasreddine et al., 2005). Similar results were shown in another study by Larner and colleagues (2012) where the MoCA was found to be more sensitive than the MMSE, 97% vs. 65% respectively but less specific, 60% vs. 89% respectively (Larner, 2012). The MMSE is known to have poor sensitivity and the MoCA is known to be a sensitive tool, yet the present results demonstrate 100% sensitivity for the MMSE and 33.3% sensitivity when the Cognistat is used as the gold standard.

## 6.1 The MMSE and the Cognistat

In Figure 3, the ROC curve (AUC = 0.81) shows an optimal cutoff score on the MMSE of 29 which is much higher than the published cutoff score of 24. There are many possible explanations for this result. Several difficulties in detecting change in cognition have been reported when using the MMSE, the greatest being the lack of sensitivity in identifying small changes in CI. Individuals who meet the criteria (as defined by Peterson et al 2001) for mild cognitive impairment (MCI) can score in the normal range on the MMSE demonstrating that it cannot accurately distinguish MCI from normal (Nasreddine et al., 2005). A ceiling effect occurs in those with mild disease (Mitchell, 2009). As well, there is a floor effect in patients with advanced dementia, in those with little education or in non-English speaking groups (Mitchell, 2009). The MMSE has been shown to be insensitive to conditions associated with frontal-executive and subcortical dysfunction and to milder forms of cognitive impairment (Pendlebury et al., 2010). Since the MMSE does not test executive function, a second ROC curve was generated for the MMSE where the executive function domains were removed on the Cognistat and participants were re-evaluated as impaired or not impaired. This was done

to provide a better comparison between the MMSE and the Cognistat as the MMSE does not measure executive function. However, results show that the AUC decreased to 0.76 and the cutoff score remained at 29.

Another possible explanation is out of the total sample of 76 patients, 70 scored positive for cognitive impairment on the Cognistat. This high positive rate was not anticipated. Using the Cognistat as the 'gold standard' could explain these results. It is possible that the MMSE is not sensitive enough or the Cognistat is too sensitive. There is also the issue of the administration of the Cognistat which will be further discussed in the limitation section. The criterion for cognitive impairment is impairment in one or more domains on the Cognistat. This threshold might be too low. In a study by van Gorp and colleagues (1999), the sensitivity and specificity of the Cognistat was assessed in patients with Alzheimer's disease and vascular dementia using DSM-III-R criteria as well as neuroimaging. Implementing the decision rule requiring one or more domains to be impaired to classify a patient as impaired resulted in a sensitivity of 100% and a specificity of 83% (van Gorp et al., 1999). Using a more stringent requirement of two or more subscales to be impaired reduced the test sensitivity slightly to 94% but increased the specificity to 100% (van Gorp et al., 1999). In a study by Osato and colleagues (1993) in a different patient cohort, a cutpoint of two or more impaired subtests best discriminated between the patient groups. Because of these results, the student investigator of the present study re-analyzed the results using the rule of *two* or more domains on the Cognistat to classify a patient as cognitively impaired. This resulted in a sensitivity of 95.2%, specificity of 43.6%, a positive and negative predictive value of

39.2% and 96% respectively and a likelihood ratio of 1.7 (Table 3). This also increased the AUC to 0.82 (Figure 4) however, the cutoff value remained at 29.

The total sample size of this study was 76. The estimated sample size requirement of 88 was not reached due to hospital admissions changes that occurred near the end of the data collection process that were beyond the control of the student investigator. While a sample of 88 would have produced narrower confidence intervals, there is no reason to believe that the evaluation statistics would be dramatically different if an additional 12 patients were recruited using the same inclusion and exclusion criteria. As with any sample, the results of the present study could be due to chance sampling variability. The confidence intervals show the range in the point estimates that would be expected under repeated random sampling. In addition, as with other health constructs that are not definitively observable, such as depression and quality of life, definitions of a 'gold standard' will be subject to theoretical differences in addition to advances in our understanding of underlying pathological mechanisms and the technology to detect them.

## 6.2 The MoCA and the Cognistat

In Figure 5, the ROC curve (AUC 0.83) shows an optimal cutoff score on the MoCA of 26 which is the same as the published cutoff score. As with the MMSE, an additional ROC curve was generated where those with two or more domains were deemed cognitively impaired on the Cognistat. The optimal cutoff remained at 26 and there was a slight decrease in the AUC to 0.81 (Figure 8). However, the specificity decreased to 19.1%, the sensitivity remained at 90%, the positive predictive value was

74.6%, the negative predictive value was 44.4% and the likelihood ratio of 1.12 (Table 3).

Overall, the results are in accord with the hypothesis; the MoCA is a superior screening instrument to the MMSE for the detection of cognitive impairment in stroke patients. The sensitivity of the MoCA was higher than that of the MMSE and the MoCA had a slightly better diagnostic accuracy than the MMSE with an area under the curve of 0.83 versus 0.81. These results are similar to those discussed in the Literature Review. However, these results should be viewed with some caution due to the use of the Cognistat as the gold standard.

6.3 The Cognistat

Table 5 displays the mean score of the metrics for all domains. The construction, memory and judgment domains revealed mean scores in the impaired range. This is not surprising. When administering the Cognistat, it was obvious that the majority of people greatly struggled with the construction domain. Although the instructions were clearly stated in the manual that subjects are to use four tiles to complete the structure, many of the patients attempted using more than four tiles. The greatest amount of difficulty was the third figure. Many of the patients seemed confused as to which tiles they should use. Memory was another domain that the majority of patients struggled with. Most patients scored in the impaired range, with only 18 patients scoring in the normal range for memory. When I was going over each patient's score for each domain to determine if they met the criteria of impaired in one or more domains, the majority of patients were

deemed impaired because they failed the memory domain. In the judgment domain patients were asked “What would you do if…” in three different situations and each question was scored out of two. The majority of patients did not receive full points as they only partially answered. Also, some of the marking criteria were a little stringent. For example when asked “ What would you do if you came home and found a broken pipe was flooding the kitchen” several of the women responded “ Call my husband” or “Call my son” but the answer worth full marks was to turn the water off and the answer worth one mark was to call the plumber. In such cases I did not reward the patient any points.

Table 6 displays the percent frequency of passes and failures in each of the screens on the Cognistat. The majority of patients did not pass 4 out of the 8 screens (Language repetition, language naming, construction and reasoning judgment) (Table 6). For the language repetition screen, the patients were required to repeat a long difficult sentence after the test administrator. Although most patients passed the metric for the language naming domain, many of the patients found the screen to be difficult. They were shown a pen and were required to name that object and all of its parts including the top, the cap, the clip and the point/nib. The majority of patients were not able to name the “clip” however; they knew its function and responded “it is the part that goes on your shirt”. This raises the question whether this is a cognitive impairment issue or a language finding issue. When naming the cap, several patients responded that it was a lid, but the manual states that “cap” is the only acceptable response. For the construction screen, the patients were given 10 seconds to study two figures, and then had to draw the two figures

from memory. Most patients were not able to remember either of the figures and some were able to draw only the easier of the two. For the judgment screen patients were asked "What would you do if you were stranded in the Denver airport with only one dollar in your pocket?" The only acceptable answer was to make a phone call and wire money. Many patients only responded "Make a phone call". These scoring rules may be too stringent. I believe that if the patient made a phone call, the person on the other end of the line might have suggested wiring money or they would have helped out in some other way.

## 6.4 Validity and the Cognistat

The Cognistat has generally demonstrated poor specificity in prior research (Karzmark, 1997). The reason for this is unclear but the test has been characterized as "excessively sensitive to the presence of cognitive dysfunction (low specificity/ high false positive rate)" (Karzmark, 1997). The sensitivity and specificity are relative to the comparison standard and the characteristics of the population under consideration (Karzmark, 1997). In this study by Karzmark (1997), the sensitivity and specificity of the Cognistat were evaluated using a neuropsychological battery as the gold standard in an outpatient population who were referred to the neuropsychological consultation service at a hospital. The sensitivity and specificity of the Cognistat (composite score) were 74% and 86% respectively. However, the sensitivity and specificity of the individual subtests ranged from 0.20 to 0.49 and 0.64 to 0.97 respectively. Karzmark et al (1997) suggest that loss of sensitivity would be consistent with application of the test to less neurologically impaired individuals. Changes in test sensitivity and specificity can be

affected by changing the definition of the criterion measures, the cutoff scores used for the predictor and the nature of the study sample (Karzmark, 1997).

When both the screen and the entire metric sequence were administered to a patient sample, researchers found that the number of persons passing the screen but going onto the metric was unacceptably high (high false positive rates) and it was concluded that it is best to administer the entire metric sequence to all subjects (Drane et al., 2003) Therefore the screen and metric approach was abandoned in this current study. As mentioned in the Literature Review, the Drane and colleagues (1997) study showed the screen and metric approach leads to procedural variability by creating differences in the delay period involved in the memory domain. Patients who fail the screens have to complete more items than those who do not which also create differences in the distracter items that must be completed (Drane et al., 2003). Distracter items are the items that are administered between the time the patient is given the four words and is asked to remember them for later on in the examination and the time in which they are asked to recall the four words. The distracter items include the language, repetition and construction domains. In addition, those who tend to perform poorly on the exam, actually end up with a longer period of delay and more intervening subtests as distractions (Drane et al., 2003). Administering all items in each domain leads to a more standardized period of delay for the recall of the four words for the memory domain. As false negatives have been associated with the use of the screen items, Drane and colleagues (2003) thought that by administering the entire Cognistat the false negative rate would decrease. Therefore, in his study, a Composite Score, the sum of all metric

scores out of a possible 82 points was calculated. The validity of the Composite Score construct is supported by a factor analytic study by Engelhart and colleagues (1999). The Composite Score makes it possible to evaluate the overall severity of cognitive dysfunction and allows one to more directly compare the general neurocognitive functioning of individual patients. Drane and colleagues (2003) determined normative data for a healthy sample of older adults (n=108) ranging from 60 to 96 years old. The Composite Score based upon the original normative data sample is 77.6 for the old group (mean age 51 years) and 74.9 for the geriatric group (mean age 78 years) (Kierman et al., 1987). In the sample population in the Drane et al 2003 study, the Composite Score was comparably lower (73 and 69.2). In the present study with the mean age of 67.6 years, the mean composite score was 62.9. The results suggest that by administering the entire screen and metric it is likely to result in a lower Composite Score which is more reliable due to administering more items per subtest (Drane et al., 2003).

6.5 Reliability Sub-study

An inter-rater reliability sub-study was conducted in order to evaluate the reliability of the test administration by student investigator. Two of the occupational therapists at Parkwood Hospital in London, Ontario administered the Cognistat for a second time on 20 patients. For half of the patients the student investigator administered the Cognistat first and for the second half, the occupational therapists administered it first in order to avoid bias. The results showed excellent interrater reliability in the metrics in all domains on the Cognistat. Reliability ranged from 0.73 to 0.96 (Table 7). However, the interrater reliability for the binary screens was not as strong and ranged from 0. 23 to

0.7 (Table 7). The scores between raters could be different for a few reasons. Although the student investigator first observed the occupational therapists administer the Cognistat before she administered it on the patients, the occupational therapists were not experienced using this tool. It is possible that the occupational therapists were not comfortable using the Cognistat until they had practice with the first few patients.

## 6.6 Limitations

There are a few limitations to this study. The first drawback is that although a sample size calculation was performed and recruitment reached 86% of the target, in the 2x2 tables, there were small cells which are statistically problematic. In general, estimates based on small numbers of observations are less reliable than those based on larger ones. In addition, although the student investigator and the occupational therapists tried to ensure that all three cognitive impairment tools were administered within the same week, it was very difficult. Patients were too tired and canceled their appointment and it was rescheduled as soon as possible, sometimes not until later the following week. Scheduling was also difficult as the patient's day was already filled with other therapy and the cognitive screening was then scheduled as soon as possible. Another limitation that might have introduced a potential source of error variance is the clinical expertise of the occupational therapists. The occupational therapists were not trained in administering the Cognistat however, they were very comfortable administering the MoCA and the MMSE as these tools are used on a daily basis in the stroke unit at Parkwood Hospital. This was noted earlier in the study. After the student investigator received the original copy of the first two Cognistats from the reliability sub-study administered by the

occupational therapists, she noticed that some of the scoring did not follow the precise instructions from the Cognistat manual. When this was detected the student investigator met with the occupational therapists and went through the instruction manual and scoring of each domain. Lastly, it is not known whether these patients were representative of all stroke patients. The results are valid for all eligible patients seen in a major stroke rehabilitation facility over a 9 month period. However, inevitably there will be variations over time in the cognitive abilities of succeeding cohorts of stroke patients. Thus, differences between those seen here and published in the literature could be partly explained by chance sampling variability.

6.7 Clinical Application and Future Research

The Cognistat is a tool that has been used at Parkwood Hospital. The current findings suggest that more research is needed in determining appropriate screens for cognitive impairment post-stroke, as well as more research on the use of the Cognistat as a "gold standard". If funding permitted, the methodology in this study might have been strengthened by use of expert clinician diagnosis as the gold standard (e.g., a neuropsychological assessment).

It is clear that the majority of stroke patients are left cognitively impaired. It is necessary that when a patient tests positive for cognitive impairment on a screening tool, the clinicians provide the necessary steps such as further assessment that leads to proper treatment to prevent further cognitive decline and/or to provide rehabilitation to improve cognition. The Canadian Best Practice Recommendations for Stroke Care suggest that all patients with stroke should be screened for cognitive impairment and that persons who

are detected as having cognitive impairment on a screening test should receive additional cognitive assessment. McClure and colleagues (2012) set out to determine whether care in an Ontario inpatient stroke rehabilitation program in Southwestern Ontario, Canada was following these recommendations. From 123 stroke inpatients, 82.9% of patients were screened using a formal cognitive screening tool and 77% scored below the threshold for cognitive impairment (McClure et al, 2012). From those scored as impaired, only three patients were referred for a comprehensive cognitive assessment (McClure et al., 2012).

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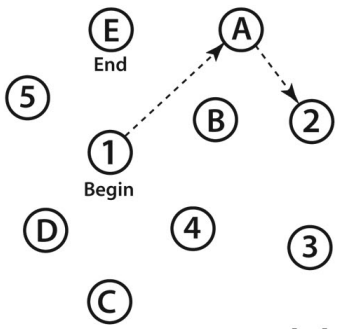
# Appendices

# Appendix A: The MoCA

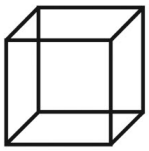
**MONTREAL COGNITIVE ASSESSMENT (MOCA)**
Version 7.1 Original Version

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

**VISUOSPATIAL / EXECUTIVE** — POINTS




Copy cube



[ ] [ ]

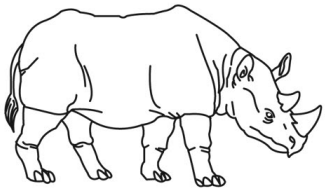
Draw CLOCK (Ten past eleven) ( 3 points )

[ ] Contour [ ] Numbers [ ] Hands

__/5

**NAMING**

[ ]



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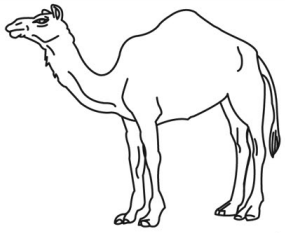

[ ]

__/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

© Z.Nasreddine MD www.mocatest.org Normal ≥ 26 / 30

TOTAL __/30

Add 1 point if ≤ 12 yr edu

Administered by: _____

## Appendix B: 2x2 Tables

0 = disease (CI) absent

1 = desease (CI) present

| | | Cognistat | | Total |
|---|---|---|---|---|
| | | 1 | 0 | |
| MMSE | 1 | 25 | 0 | 25 |
| | 0 | 45 | 6 | 51 |
| Total | | 70 | 6 | 76 |

a) MMSE – impaired in one or more domains on the Cognistat

| | | Cognistat | | Total |
|---|---|---|---|---|
| | | 1 | 0 | |
| MoCA | 1 | 63 | 4 | 67 |
| | 0 | 7 | 2 | 9 |
| Total | | 70 | 6 | 76 |

b) MoCA- impaired in one or more domains on the Cognistat

| | | Cognistat | | Total |
|---|---|---|---|---|
| | | 1 | 0 | |
| MMSE | 1 | 24 | 1 | 25 |
| | 0 | 31 | 20 | 51 |
| Total | | 21 | 55 | 76 |

c) MMSE- impaired in two or more domains on the Cognistat

| | | Cognistat | | Total |
|---|---|---|---|---|
| | | 1 | 0 | |
| MoCa | 1 | 50 | 17 | 67 |
| | 0 | 5 | 4 | 9 |
| Total | | 55 | 21 | 76 |

d) MoCA- impaired in two or more domains on the Cognistat

# Appendix C- Letter of Information and Consent Form

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**Letter of Information**

May 25, 2011

**Title of Project:** The Evaluation of the Montreal Cognitive Assessment (MoCA) and the Mini-Mental State Exam (MMSE) for Cognitive Impairment Post Stroke: A Validation Study against the Cognistat.

Dear Participant,

You are being invited to participate in a research study looking at the detection of cognitive impairment post stroke. The purpose of this letter is to provide you with the information you require to make an informed decision on participating in this research.

**Principle Investigators:**

| |
|---|
| |

**Purpose of Study:**
You have been invited to take part in a research study designed to evaluate the ability of two cognitive screening tools to detect cognitive impairment in stroke patients. Detection of cognitive impairment (CI) in stroke patients requires the use of an accurate screening tool. Early detection of cognitive impairment is essential in directing treatment to prevent further cognitive decline and improve current cognitive impairment. It is important that stroke rehabilitation patients screened for CI and score in the impaired range can then be adequately diagnosed and receive the proper treatment. The purpose of this study is to identify the screening tool that best detects cognitive impairment in stroke patients in a rehabilitation hospital. Two commonly used screening tools are being assessed in this

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**Participant initials**

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study, the Montreal Cognitive Assessment (MoCA) and the Mini-Mental State Exam (MMSE) along with the Cognistat, a "gold standard" assessment test.
We are recruiting 88 patients who have had a stroke and are being admitted to Parkwood Hospital for rehabilitation. If participant is identified as cognitively impaired proper treatment can then be provided.

**Procedure:**
The MoCA or the MMSE and sometimes both, are administered as part of routine care as screening tests. For this study, you will be required to complete the MoCA and the MMSE as well as an additional test, the Cognistat. The Cognistat is being used because it is considered a 'gold standard' test for the evaluation of the MoCA and the MMSE. Each test will be taken consecutively and each test will only be taken once. An occupational therapist will administer the MMSE and the MoCA. The student investigator will then administer the Cognistat.

1. The MoCA is a series of questions that requires verbal and written responses. The test will take 5-10 minutes to complete. Your responses will be recorded.
2. The MMSE is a series of questions that requires verbal and written responses. The test will take 5-10 minutes to complete. Your responses will be recorded.
3. Cognistat a slightly more extensive series of questions that requires verbal and written responses. The test will take approximately 20 minutes to complete. Your responses will be recorded. In order to assess inter- rater reliability, forty six participants will be asked to complete this test a second time and this time it will be administered by an occupational therapist.

Once the tests have been completed, you will be asked the year in which you were born as well your level of education (elementary, high school and years post graduate school).

**Time Commitment:**
The maximum time requirement for these tests is estimated to be a total of 40 minutes.

**Location of Research:**
This study will be conducted at Parkwood Hospital.

**Personal Benefits of Participation:**
This testing is to ensure cognitive problems after a stroke are adequately diagnosed and treated.
A potential benefit to the patient population being studied, the most effective tool will be utilized to detect cognitive impairment so that impairment in future stroke patients will

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no longer go undetected. Treatment can then be provided when necessary. Participation in the study may be of no direct benefit to you.

**Risks:**
There are no known risks involved in the participation of this study.

**Stopping the Session:**
If you become fatigued or overwhelmed with the questioning, you will have the opportunity to take a break before going on to the next screening test.

**Changing Your Mind about Participation:**
You may withdraw from this study at any time without penalty. To do so, indicate this to the researcher or one of the research assistants.
Participation in this study is voluntary. You may refuse to participate, refuse to answer any questions or withdraw from the study at any time with no effect on your future care. The decision to participate or not to participate is solely up to you. There are no alternatives to this study.
Your participation will require only one session. You will not be contacted for further study and your personal information will not be retained for future use. No compensation will be provided for participation in this study.

**Confidentiality:**
To ensure the confidentiality of individuals' data, each participant will be identified by a participant identification code known only to the principal investigators. You will not be identified in any reports or publications. Only group-level statistics will be reported. Once data analysis is complete, data will be destroyed.

The results of this study may be published in a peer reviewed journal. If you wish to receive a copy of these results please write your name and contact information on a separated sheet of paper and return it to the studies investigator.

Representatives of the University of Western Ontario Health Sciences Research Ethics Board may contact you or require access to your study-related records to monitor the conduct of the research.

**Contact Information:**
If you have any questions about the study at any time, please contact either Dr. Robert Teasell at [redacted], Dr. Mark Speechley at the

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Schulich

[redacted]

**Concerns about Your Participation:**
If you have any comments or concerns resulting from your participation in this study, you may contact Dr. David Hill, Scientific Director, Lawson Health Research a[redacted] You may keep this copy of the Information Letter as well as a copy of the Consent Form.

By signing the consent form, you are not waiving your legal rights or releasing the investigators or involved institutions from their legal and professional responsibilities.

We look forward to hearing from you, and wish to thank you again for your time and participation.

Yours sincerely,

Lauren Friedman

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**CONSENT FORM**

I agree to take part in a research study being conducted by Dr. Robert Teasell, Dr. Mark Speechley and Lauren Friedman of the Department of Epidemiology and Biostatistics at the University of Western Ontario.

I have read the letter of information, have had the nature of the study explained to me and I agree to participate. All questions have been answered to my satisfaction.

Name of Participant (please print) _____ Signature of Participant _____

Date _____

Name of Person obtaining consent _____ Signature _____

Date _____

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**Participant initials**

# Appendix D- HSREB Approval Forms

Use of Human Participants - Ethics Approval Notice

**Principal Investigator:** Dr. Robert Teasell
**Review Number:** 18099
**Review Level:** Full Board
**Approved Local Adult Participants:** 88
**Approved Local Minor Participants:** 0
**Protocol Title:** The Evaluation of the MoCA and the MMSE for Cognitive Impairment Post Stroke: A Validation Study against Cognistat
**Department & Institution:** Physical Medicine & Rehab,St. Joseph's Health Care London
**Sponsor:** Canadian Stroke Network

**Ethics Approval Date:** August 24, 2011 **Expiry Date:** October 31, 2011

**Documents Reviewed & Approved & Documents Received for Information:**

| Document Name | Comments | Version Date |
|---|---|---|
| UWO Protocol | | |
| Letter of Information & Consent | | |

This is to notify you that the University of Western Ontario Health Sciences Research Ethics Board (HSREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced study on the approval date noted above. The membership of this HSREB also complies with the membership requirements for REB's as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the UWO Updated Approval Request form.

Member of the HSREB that are named as investigators in research studies, or declare a conflict of interest, do not participate in discussions related to, nor vote on, such studies when they are presented to the HSREB.

The Chair of the HSREB is Dr. Joseph Gilbert. The UWO HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Sign

**Ethics Officer to Contact for Further Information**

| | | |
|---|---|---|
| X Janice Sutherland (jsutherl@uwo.ca) | Grace Kelly (grace.kelly@uwo.ca) | Shantel Walcott (swalcot@uwo.ca) |

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Research Western

**Use of Human Participants - Ethics Approval Notice**

**Principal Investigator:** Dr. Robert Teasell
**Review Number:** 18099
**Review Level:** Delegated
**Approved Local Adult Participants:** 88
**Approved Local Minor Participants:** 0
**Protocol Title:** The Evaluation of the MoCA and the MMSE for Cognitive Impairment Post Stroke: A Validation Study against Cognistat
**Department & Institution:** Physical Medicine & Rehab, St. Joseph's Health Care London
**Sponsor:** Canadian Stroke Network

**Ethics Approval Date:** November 29, 2011 **Expiry Date:** March 31, 2012
**Documents Reviewed & Approved & Documents Received for Information:**

| Document Name | Comments | Version Date |
|---|---|---|
| Revised Study End Date | | |

This is to notify you that The University of Western Ontario Research Ethics Board for Health Sciences Research Involving Human Subjects (HSREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced revision(s) or amendment(s) on the approval date noted above. The membership of this REB also complies with the membership requirements for REB's as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the UWO Updated Approval Request Form.

Members of the HSREB who are named as investigators in research studies, or declare a conflict of interest, do not participate in discussion related to, nor vote on, such studies when they are presented to the HSREB.

The Chair of the HSREB is Dr. Joseph Gilbert. The UWO HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Signature

**Ethics Officer to Contact for Further Information**

| | | |
|---|---|---|
| Janice Sutherland (jsutherl@uwo.ca) | Grace Kelly (grace.kelly@uwo.ca) | Shantel Walcott (swalcot@uwo.ca) |

*This is an official document. Please retain the original in your files.*

| Patient ID | Name | Room # | Chart # | Age | Sex | Education | Side of stroke |
|---|---|---|---|---|---|---|---|
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**Apendix E- Data Collection Form**

# Curriculum Vitae

| | |
|---|---|
| **Name** | Lauren E. Friedman |
| **Post-secondary Education and Degrees** | The University of Western Ontario<br>London, Ontario, Canada<br>2005-2009 B.H.Sc. |
| | The University of Western Ontario<br>London, Ontario, Canada<br>2010-2012 M.Sc. |
| **Honours and Awards** | Schulich Graduate Scholarship<br>2010-2011, 2011-2012 |

**Publications**

***Poster Presentations***

**Friedman L**, Meyer MJ, Donaldson S, Leci EP, Teasell R. Oral Care Protocols in a Stroke Rehabilitation Inpatient Population. West GTA Stroke Network Symposium. Mississauga, Ontario, February 16, 2012.

**Friedman L**, Meyer MJ, Donaldson S, Leci EP, Teasell R. Oral Care Protocols in a Stroke Rehabilitation Inpatient Population. GTA Rehab Network Best Practices Day 2012. Toronto, Ontario, February 27, 2012.