Identifying Predictors of Functional Outcome after Stroke:
Impact of Post-Stroke Depressive Symptoms, Obstructive Sleep Apnea
and Cognitive Impairment on Long-Term Body Function, Activity and
Participation

by

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Abstract

**Background:** Stroke impacts multiple levels of function. Few studies have examined the long-term impact of common post-stroke comorbidities, or examined multiple functional domains.

**Methods:** Baseline assessment of depression, apnea and cognition with 2-year follow-up assessment of functional outcome including: Body Function (MoCA), Activity (mRS) and Participation (RNLI).

**Results:** Long-term activity limitation was predicted by greater age (OR = 0.95), activity limitations (OR = 0.38) and cognitive impairment (OR = 1.28) at baseline. Body function impairment was predicted by greater age (OR = 0.96), fewer education years (OR = 1.19) and cognitive impairment (OR = 1.63). Participation restriction was predicted by activity limitations (OR = 0.48) and cognitive impairment (OR = 1.26). Of those with good mRS outcome, 54.4% were cognitively impaired and 51.6% had participation restrictions.

**Conclusion:** Baseline cognition predicts long-term deficits across functional domains. Assessment of post-stroke cognition and greater attention to multiple levels of functioning is warranted.
I would like to dedicate this work to

all those affected by stroke and their families
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Table of Contents

Acknowledgments.......................................................................................................................... iv
Contributions................................................................................................................................. v
List of Tables ................................................................................................................................. xi
List of Figures ............................................................................................................................... xii
List of Appendices ....................................................................................................................... xiii
Introduction: Impact & Burden of Stroke................................................................................... xiv
Chapter 1 Literature Review ......................................................................................................... 1

1.1 Stroke & Early Management ................................................................................................. 1

1.1.1 History of Stroke............................................................................................................... 1

1.1.2 Stroke ............................................................................................................................... 1

Classification & Etiology ............................................................................................................. 2

Signs & Symptoms ...................................................................................................................... 3

Diagnosis ...................................................................................................................................... 3

1.1.3 Interventions .................................................................................................................... 4

Acute Stroke Care ...................................................................................................................... 4

Rehabilitation ............................................................................................................................ 5

1.1.4 Early Adverse Events ...................................................................................................... 7

Stroke Recurrence ..................................................................................................................... 7

Comorbidities & Complications ................................................................................................. 7

1.1.5 Recovery ......................................................................................................................... 9

Neurological Recovery .............................................................................................................. 9

1.2 Defining Function ................................................................................................................ 12

1.2.1 WHO Levels of Functioning.......................................................................................... 12

1.3 Functional Recovery & Outcome after Stroke ................................................................... 15
1.3.1 Recovery in Body Function (Impairments) ...........................................................15
1.3.2 Recovery in Activity (Limitations) ........................................................................16
1.3.3 Recovery in Participation (Restrictions) ...............................................................18
1.3.4 Mechanism and Association of Neurological & Functional Recovery .................18
1.3.5 Functional Outcome after Stroke ...........................................................................18

1.4 Long-term Functioning ..............................................................................................21

1.4.1 The Concept of Recovery Plateau & Maintenance ................................................21
1.4.2 Long-Term Functional Outcome ...........................................................................22
1.4.3 Predictors of Long-Term Functional Outcome ......................................................22

1.5 Traditional Predictors of Functional Outcome ............................................................24

1.5.1 Age .........................................................................................................................24
1.5.2 Stroke Severity .......................................................................................................27
1.5.3 Short-Term Activity Limitations ...........................................................................29
1.5.4 Sex ..........................................................................................................................30

1.6 Potentially Modifiable Predictors of Functional Outcome ........................................31

1.6.1 Modifiability of Predictors .....................................................................................31
1.6.2 Depression ..............................................................................................................31
1.6.3 Obstructive Sleep Apnea ........................................................................................35
1.6.4 Cognitive Impairment ............................................................................................37
1.6.5 Social Factors .........................................................................................................40

Literature To Date ........................................................................................................43

Chapter 2 Research Aims and Hypotheses ....................................................................44

2.1 Aims ...........................................................................................................................44

2.2 Predictors of Functional Outcome .............................................................................44

2.2.1 Hypothesis 1: Traditional Predictors of Functional Outcome ...............................44
2.2.2 Hypothesis 2: Depression, Obstructive Sleep Apnea and Cognitive Impairment (DOC) Conditions as Predictors of Functional Outcome

2.3 Function Beyond Activity

2.3.1 Outcome in Physically Stable Patients

2.4 A Priori Exploratory Analysis

2.4.1 Frequency of Depression, OSA & Cognitive Impairment Treatment

2.4.2 Associations at Baseline and Follow-Up

Chapter 3

3.1 Ethics Approval

3.2 Study Design

3.3 Patient Population

3.3.1 Patient Selection: Exclusion & Inclusion Criteria

3.3.2 Sample Size Calculation and Power Estimates

3.4 Baseline Visit

3.4.1 Chart Abstraction

3.4.2 Depression, OSA & Cognition Screening

3.5 Follow-Up Assessment

3.5.1 Initial Contact

3.5.2 Outcome Measures

3.5.3 Supplementary Measures

3.6 Statistical Analyses

3.6.1 Descriptive Statistics

3.6.2 Multicollinearity

3.6.3 Univariate Analyses

3.6.4 Multivariate Analyses

3.6.5 Sub-Analysis
<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>Discussion</td>
<td>92</td>
</tr>
<tr>
<td></td>
<td>5.1 Predictions of Functional Outcome</td>
<td>92</td>
</tr>
<tr>
<td></td>
<td>5.1.1 Predictors of Activity Limitations</td>
<td>92</td>
</tr>
<tr>
<td></td>
<td>5.1.2 Predictors of Body Function Impairments</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td>5.1.3 Predictors of Participation Restrictions</td>
<td>96</td>
</tr>
<tr>
<td></td>
<td>5.1.4 Comparison of Established &amp; Exploratory Predictors</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td>5.1.5 Mechanisms of Depression &amp; Cognitive Impairment Post-Stroke</td>
<td>99</td>
</tr>
<tr>
<td></td>
<td>5.2 Multidimensionality of Function</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>5.3 Long-Term Outcomes</td>
<td>101</td>
</tr>
<tr>
<td></td>
<td>5.4 Strengths &amp; Limitations</td>
<td>102</td>
</tr>
<tr>
<td>6</td>
<td>Conclusion</td>
<td>104</td>
</tr>
<tr>
<td>7</td>
<td>Future Directions</td>
<td>106</td>
</tr>
<tr>
<td></td>
<td>7.1 Unexplained Variance</td>
<td>106</td>
</tr>
<tr>
<td></td>
<td>7.2 Neuroimaging Markers</td>
<td>106</td>
</tr>
<tr>
<td></td>
<td>7.3 Development &amp; Enhancement of Assessment Tools</td>
<td>107</td>
</tr>
<tr>
<td></td>
<td>7.4 Additional Components of Functioning</td>
<td>107</td>
</tr>
<tr>
<td></td>
<td>7.5 Depression, Obstructive Sleep Apnea and Cognitive Impairment Treatments</td>
<td>108</td>
</tr>
<tr>
<td></td>
<td>7.6 Clinical Impact</td>
<td>109</td>
</tr>
<tr>
<td></td>
<td>References</td>
<td>110</td>
</tr>
<tr>
<td></td>
<td>Appendices</td>
<td>138</td>
</tr>
</tbody>
</table>
List of Tables

Table 1.1: Previously Reported Associations between Predictors and Outcome .........................42
Table 3.1: Definition of Independent Variables ........................................................................51
Table 3.2: Definition of Dependent Variables ........................................................................58
Table 4.1: Baseline & Follow-Up Patient Characteristics ..........................................................64
Table 4.2: Comparison of Lost to Follow-Up, Declined & Enrolled Patient ..............................65
Table 4.3: Correlation between Independent Variables ..........................................................67
Table 4.4: Multicollinearity between Independent Variables ..................................................68
Table 4.5: Univariate & Multivariate Analyses: Basic Activity (mRs) ........................................75
Table 4.6: Univariate & Multivariate Analyses: Instrumental Activity (FAI) ............................78
Table 4.7: Univariate & Multivariate Analyses: Body Function (MoCA) ..................................80
Table 4.8: Univariate & Multivariate Analyses: Participation (RNLI) ......................................83
Table 4.9: Summary of Regression Analyses ..........................................................................86
List of Figures

Figure 1.1: Early Management of Stroke ................................................................. 11
Figure 1.2: Example WHO International Classification Framework for Stroke .......... 13
Figure 3.1: Patient Selection Process ........................................................................ 47
Figure 3.2: Sample Size Calculation ........................................................................... 49
Figure 3.3: Stroke Outcome Measures (Evidence Based Review of Stroke Rehabilitation) ..... 55
Figure 3.4: Outcome Measures Selected & Corresponding Level of Functioning ............ 57
Figure 4.1: Baseline and Follow-Up Modified Rankin Score Distribution ....................... 69
Figure 4.2: Baseline and Follow-Up Depression Risk .................................................... 71
Figure 4.3: Baseline and Follow-Up Obstructive Sleep Apnea Risk ................................. 72
Figure 4.4: Baseline and Follow-Up Cognitive Impairment Risk ..................................... 73
Figure 4.5: Activity/Global Functioning (mRS) Regression Model ROC Curve Including All Independent Variables ................................................................. 76
Figure 4.6: Activity/Global Functioning (mRS) Regression Model ROC Curve Including Only Age & Stroke Severity ........................................................................ 77
Figure 4.7: Body Function/Cognition (MoCA) Regression Model ROC Curve Including All Independent Variables ............................................................................ 81
Figure 4.8: Participation/Reintegration (RNLI) Regression Model ROC Curve Including All Independent Variables ................................................................. 84
Figure 4.9: Participation/Reintegration (RNLI) Regression Model ROC Curve Including Only Stroke Severity ................................................................. 85
List of Appendices

Appendix A: Comprehensive ICF Core Set for Stroke ................................................................. A1
Appendix B: DOC Screen ............................................................................................................. A13
Appendix C: Information Letter to Patients ................................................................................. A15
Appendix D: Follow-Up Telephone Script .................................................................................. A16
Appendix E: DOC Follow-Up Assessment Form ........................................................................ A17
Introduction: Impact & Burden of Stroke

One stroke occurs every 9 minutes in Canada, resulting in 62,000 strokes every year (Heart & Stroke Foundation of Canada, 2015). Of every 100 people who have a stroke, 15% die, 10% recovery completely and 75% are left with some extent of disability (Heart & Stroke Foundation of Ontario, 2008). Approximately 405,000 Canadians are currently living with effects of stroke (Krueger et al., 2015), making stroke the most common cause of complex disability (Adamson, Beswick, & Ebrahim, 2004). Stroke mortality is declining (Lackland et al., 2013) – 83% of those who have stroke and are able to make it to a hospital will now survive (Stroke Report 2015). However, as mortality declines and the population ages, the number of people living with the consequences of stroke is increasing. Between 2000 and 2012, there has been a substantial and rising increase in the number of stroke survivors living with the effects of stroke and by 2038, 726,000 individuals are expected to be living with the effects of stroke (Krueger et al., 2015). The impact of a stroke can be devastating and highly debilitating for survivors. Indeed, disability can be an outcome considered worse than death: majority of stroke patients surveyed by Hanger et al. (2000) said they would rather die than be severely disabled and some would even prefer death to minor disability. Those who survive the acute phase face chronic neurological deficits and functional limitations (Kelly-Hayes et al., 2003). Surprisingly, few studies have identified the impact of stroke on multiple functional domains. Most studies focus on physical disability, characterized by the WHO as limitations in activity. Others center on impairments in body function, a second domain considered central to function, and very few have examined restrictions in social roles and situations. The full range of functional deficits experienced by stroke survivors is thus not well characterized. Understanding the multifaceted nature of this disease is becoming increasingly important as advances in stroke prevention and acute stroke care reduce the likelihood of post-stroke mortality (Towfighi & Saver, 2011; Kapral et al., 2013) and increase the number of survivors suffering from impairments in body function, limitations in daily activities and restrictions in social roles and situations.
Chapter 1
Literature Review

1.1 Stroke & Early Management

1.1.1 History of Stroke

The clinical symptoms of a stroke were first observed and recorded by Hippocrates around 400 BCE (Nilsen, 2010; Caplan, 2004). Given that these visible symptoms were sudden and violent, Hippocrates originally labeled them as “apoplexy”, which means “struck with violence” (Storey & Pols, 2010). New etiological theories and pathophysiological discoveries have emerged since the Middle Ages, throughout the Renaissance Period and the 19th century (Nilsen, 2010). In the early 20th century, there was a shift in terminology from apoplexy to stroke and later, cerebrovascular accident (Storey & Pols, 2010). However, despite being recognized and studied for over 2400 years, our ability to alter the course of an acute stroke only actualized 20 years ago, with the discovery of first acute pharmacological treatment for stroke, recombinant tissue plasminogen activator (NINDS rt-PA Stroke Study Group, 1995). As Caplan (2004) put it, “this is the era of therapy”. Stroke is now considered both preventable and treatable, and disability is now considered malleable. Recovery and rehabilitation are newly active areas of research.

1.1.2 Stroke

An intricate vascular network continuously supplies nutrient and oxygen-rich blood to different parts of the brain to facilitate neuronal function. A stroke is a sudden loss of brain function due to a disruption in this blood supply (Heart & Stroke Foundation of Ontario, 2014). The World Health Organization defines stroke as “rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin” (Aho, 1980; WHO, 1978). In 2009, this definition was revised and an ischemic stroke was defined as “an infarction of central nervous system tissue”, visualized using imaging techniques (Easton et al., 2009). Strokes are categorized as either ischemic or hemorrhagic. While ischemic strokes result from blockage of blood flow and account for 80% of all strokes, hemorrhagic strokes are caused by ruptured blood vessels, are generally more severe and comprise approximately 20% of all strokes (Heart & Stroke
Foundation of Canada, 2016). The brain damage that follows a stroke depends largely on features of the stroke, such as type, location, size and laterality. These features also influence symptom manifestation, recovery and the extent of disability that follows.

**Classification & Etiology**

There are three types of brain ischemia and two types of haemorrhages (Caplan, 2016). Thrombosis, embolism and systemic hypoperfusion reduce arterial blood supply to the brain and are the main causes of ischemia. Thrombosis is a result of blood clot formation in the brain due to arterial wall disease (e.g. arteriosclerosis), while an embolism occurs when a blood clot travels to the brain from another part of the body (often the heart) and is lodged in an artery (American Heart Association, 2016). Atherosclerosis, vasoconstriction and arterial dissection are the most common causes of thrombosis in large vessels and atrial fibrillation is the most common cause of embolic stroke with a cardiac source (American Heart Association, 2016). When thrombosis or lipohyalinosis (i.e. vessel wall thickening) occurs in small vessels and causes ischemia, it is called a lacunar stroke (Caplan, 2016). Hypertension plays a significant role in such strokes (Filho, 2016; Fisher, 1982). The third most common cause of ischemic stroke is hypoperfusion, which results in a general reduction in blood flow to the brain and often causes ischemia in watershed regions. Unlike thrombotic and embolic strokes, which typically create focal injuries, systemic hypoperfusion causes diffuse damage (Caplan, 2016). If focal temporary cerebral ischemia does not result in infarction and only triggers brief neurologic dysfunction, it is characterized as a transient ischemic attack (Sacco et al., 2013; Easton et al., 2009). Thus, the presence of a focal cerebral, spinal or retinal infarction is needed to signify an ischemic stroke.

In contrast to ischemia, haemorrhages are a result of bleeding in or around the brain. Intracerebral haemorrhage (ICH) and subarachnoid haemorrhage (SAH) are the two main types of brain haemorrhages (American Heart Association, 2016). An ICH occurs when a blood vessel, usually a small artery, in the brain ruptures and leaks into the brain parenchyma and forms a hematoma (Caplan, 1992). Hypertension, trauma, ruptured aneurysm and arteriovenous malformations are the most common causes of ICH (Caplan, 1992). In contrast, SAH results from blood, typically from a ruptured aneurysm or vascular malformation, leaking into the subarachnoid space and entering the cerebrospinal fluid surrounding the brain (Singer et al.,
2016). Haemorrhages are extremely severe, associated with secondary injury, such as brain ischemia, and considered life-threatening if bleeding is not controlled.

**Signs & Symptoms**

The symptoms of a stroke depend on the insult location, size and type of stroke. Despite the large variability in symptoms, there are some common acute signs of a stroke: Facial droop, one-sided weakness or numbness, slurred speech (LR of $\geq 1$ finding=$5.5$; Goldstein & Simel, 2005). These signs are part of the Heart and Stroke Foundation’s new “FAST”—representing facial droop, arm weakness, slurred speech, and time to call 9-1-1—campaign to facilitate quicker identification of stroke symptoms and faster action to seek medical attention. Other symptoms can include sudden aphasia, loss of vision or double vision, numbness, reduction in level of consciousness, vertigo or headache. Most symptoms develop suddenly and may improve or worsen over time. Different symptoms may be associated with different types of stroke. For instance, headaches and loss of consciousness are typically associated with hemorrhagic strokes (Caplan, 2016). Similarly, language difficulties and unilateral motor and sensory symptoms may signify occlusion of anterior arteries whereas vertigo and bilateral motor and sensory signs may indicate posterior artery occlusions (Caplan, 2016). The National Institute of Health Stroke Scale (NIHSS) and the Canadian Neurological Scale (CNS) are assessment tools to evaluate and quantify the presence and severity of stroke signs and determine the severity of the stroke (Brott et al., 1989; Goldstein, Bertels & Davis, 1989; Cote et al., 1986, 1989). These tools measure neurological deficits and are able to capture the majority of stroke symptoms. However, certain stroke symptoms, such as vertigo, are not captured by these tools (Martin-Schild et al., 2011) and NIHSS has been found to be more sensitive to lesions in the left hemisphere (Fink et al., 2002).

Stroke severity assessed through symptom manifestation and quantified by the NIHSS or CNS is also an excellent predictor of patient outcomes (see 1.5.2).

**Diagnosis**

Timing is a critical factor in stroke interventions and thus, quick assessment and diagnosis is essential. An acute assessment typically involves obtaining a medical history, conducting a physical and neurological exam and obtaining a computerized tomography (CT) scan (American Stroke Association, 2016; Canadian Stroke Best Practice Recommendations, 2015). Stability of vital signs and concerns such as elevated blood pressure and fever are
addressed first (Filho, 2016). Patient history is then reviewed to aid a differential diagnosis of stroke. A physical and neurological examination is conducted next. The NIHSS score is obtained during the neurological examination. In most cases, a noncontract brain CT is used to determine whether the stroke is ischemic or haemorrhagic (Jauch et al., 2013; Wardlaw et al., 2004a). The neurological examination, patient history and imaging results all facilitate a presumptive diagnosis of stroke (Filho, 2016). A haemorrhagic stroke diagnosis can be made using a CT scan with high sensitivity (Hemphill et al., 2015). An ischemic infarct, however, may not be visible on CT very early and can only be detected with 66% (range, 20%-87%) sensitivity within 6 hours post-stroke (Wardlaw & Mielke, 2005). Early signs of brain infarction have been found to be associated with poor outcome (Wardlaw & Mielke, 2005). While a magnetic resonance imaging (MRI) is a better tool for early diagnosis of an ischemic stroke (Chalela et al., 2007), it is not commonly found in emergency room due to its greater cost and longer image acquisition time compared to CT (Wardlaw et al., 2004b). If no evidence of haemorrhage is found, eligibility for thrombolytic therapy and thrombectomy is determined.

After a presumptive diagnosis is determined and acute concerns are addressed, numerous diagnostic tests are required to confirm the diagnosis. Angiography, blood tests, carotid ultrasounds, holter monitoring and echocardiography are some common tests conducted to determine the underlying cause and establish and definite diagnosis (American Stroke Association, 2016; Filho, 2016).

1.1.3 Interventions

Acute stroke care and rehabilitation are commonly employed after a stroke to facilitate recovery. Acute interventions typically minimize neuronal damage and enable recovery of body function and accordingly, activity limitations. Rehabilitation interventions directly target functional recovery, typically on the body function and activity level. Both have the potential to alter the course of stroke recovery.

Acute Stroke Care

Intravenous thrombolytic therapy with alteplase (i.e. a tissue plasminogen activator (tPA)) and endovascular therapy (i.e. mechanical thrombectomy) are the two primary acute treatments for ischemic stroke. There are currently no acute interventions for intracerebral
haemorrhage. Only 2% to 5% of stroke patients are treated with tPA (Miller, Simpson & Silver, 2011b), primarily because majority of patients are unable to receive the treatment within 3 hours (Barber et al., 2001). Treatment with tPA within 4.5 hours of stroke onset has been associated with favourable activity (mRS) outcome at 3 months (Lees et al., 2010). Although tPA lowers the risk of short-term activity limitations, it has a neutral effect on survival (IST-3 Collaborative Group, 2013), does not lower the risk of stroke recurrence (Schmitz et al., 2014) and only one study has reported improvement in function and quality of life for up to 18 months (IST-3 Collaborative Group, 2013). A meta-analysis comparing endovascular therapy with mechanical thrombectomy to tPA concluded that endovascular therapy further improved activity (mRS score 0-2) at 90 days (Badhiwala et al., 2015) compared to standard medical care with tPA. However, very few patients receive tPA and fewer are eligible for thrombectomy, leaving majority of stroke patients without any acute intervention. Aspirin (i.e. antiplatelet therapy) initiation within 48 hours is also associated with reduced death or dependency between 10 days and 6 months, with a number needed to treat of 79 (Sandercock et al., 2014). While early recovery may benefit from such acute interventions, whether functional gains are sustained in the long-term remains unexplored.

Acute stroke unit care can also impact functional recovery: organized inpatient care in a specialized stroke unit significantly increases the odds of favourable activity outcome at 90 days (Stroke Unit Trialists’ Collaboration, 2013). Although the exact reason for improved outcomes is unknown, Evans et al. (2001) propose that interventions such as thrombolysis, early aspirin initiation, early mobilization and others, which could be vital in improving activity outcome, may be implemented more often in specialized stroke units. Differences in management could potentially explain improved outcomes in patients who receive stroke unit care compared to general wards patients. Like acute interventions, the sustainability of such short-term gains has not been studied extensively, with only one study reporting better outcomes at 10 years post-stroke in stroke patients treated in an acute and rehabilitation stroke unit (Indredavik, Bakke, Slørdahl, Rokseth, & Håheim, 1999).

**Rehabilitation**

Unlike neurological recovery, functional recovery, at least in terms of body function and activity, is believed to be modifiable for some patients, in the short-term, through rehabilitation
interventions. Post-stroke rehabilitation specifically aims to improve outcomes on the activity and body function levels of functioning.

Once a patient has medically stabilized after a stroke, assessment for rehabilitation should be conducted as soon as possible. The post-stroke rehabilitation panel suggests a framework for rehabilitation decisions (Gresham et al., 1997). Functional disability (in terms of activity and body function) and the ability to learn are considered the primary criteria for admission to an intensive rehabilitation program; physical endurance and ability to participate actively are also critical factors (Gresham et al., 1997). Ability to benefit from stroke rehabilitation is based primarily on initial disability (i.e. activity limitations) and age (Alexander, 1994), although other factors such as cognition and social situation may play a role in home discharge as well (Denti et al., 2008). Minimizing complications and body function impairments and maximizing activity are the primary goals of rehabilitation (Duncan et al., 2005). Patients who are risk of poor outcomes in these capacities must be promptly identified in order to obtain the maximum benefits of rehabilitation.

The timing and features of rehabilitation have been associated with improvements in body function and activities. A review by Cifu & Stewart (1999) established that initiation of rehabilitation within 3 and 30 days after stroke onset is associated with improved functional outcome. Recent evidence reinforces these findings, indicating a positive effect of early rehabilitation on activity at 3 months and body function (motor) at 3 and 12 months (Cumming et al., 2011). A critical review conducted in 1997 also reported a small effect of rehabilitation intensity on ADLs in the short-term (Kwakkel, Wagenaar, Koelman, Lankhorst, & Koetsier, 1997). Recent meta-analyses based on new data strengthen these finding (Cooke et al., 2010; Galvin et al., 2008), showing a small, positive effect of higher doses of therapy. However, in their review of the available evidence, Teasell & Hussein (2013) concluded that although a modest benefit of increased treatment intensity is observed, it is not maintained over time.

Current evidence suggests that the functional benefit of multidisciplinary, inpatient rehabilitation tends to dissipate by 8 to 12 months (Evans et al., 1995). Evans et al. (1995) propose that this lack of sustained benefit may be because patients do not continue to practice the skills they developed during rehabilitation after they return home, indicating the need for long-term home-based and outpatient rehabilitative strategies. Rehabilitation interventions applied in
the chronic phase (>6 months post-stroke) show positive functional benefit (Teasell et al., 2012), challenging the concept of a recovery plateau, reinforcing the importance of long-term rehabilitation and elucidating the possibility of further optimized recovery.

1.1.4 Early Adverse Events

Death, recurrent stroke and comorbid conditions are common adverse events following a stroke. Stroke has a global, overall one month case fatality of approximately 23%, with haemorrhages causing more deaths (ICH 42%; SAH 32%) than ischemic stroke (16%; Feigin, Lawes, Bennett, & Anderson, 2003). The risk of death after an ischemic stroke increases from 7% at 7 days to 14% at 30 days and further escalates to 53% at 5 years (Petty et al., 1998). Approximately two thirds of deaths within the first 30 days after stroke are due to the initial stroke, while the remaining deaths are due to other complications (e.g. pneumonia; Nedeltchev et al., 2010). For patients who survive, recurrent stroke and comorbid conditions have the potential to impact recovery by complicating acute care, delaying rehabilitation and possibly influencing outcome.

**Stroke Recurrence**

The risk of stroke recurrence is 3% at 30 days and increases to 26% at 5 years (Mohan et al., 2011). Recurrent stroke significantly increases case fatality (Hardie et al., 2004) and patients experience more activity limitations after recurrent stroke compared with the initial stroke (Hankey et al., 2007). Recurrent stroke has been associated with poor functional outcome on the activity level (mRS > 1) at 90 days (Wang & Wu, 2016) and affects basic activities even 3 years later. Recurrent stroke and concomitant chronic disabling disorders are the primary reasons for functional decline at 3 years (OR = 10.3; Pettersen, Dahl & Wyller, 2002). Given that recurrent strokes are a modifiable barrier to recovery and 80% of strokes can prevented with current treatments (Gorelick, 1995), secondary prevention strategies may aid maintenance of function gains “by reducing inpatient recidivism” (p.5, Salter, Campbell, Richardson, & Mehta, 2013; Goldberg & Berger, 1988).

**Comorbidities & Complications**

Post-stroke complications and comorbidities are common—between 59 to 95% of patients experience at least one complication (Langhorne et al., 2000; Johnston et al., 1998; Davenport et
Complications include neurological conditions (i.e. seizures), infections (i.e. pneumonia), falls and psychological conditions (i.e. depression; Langhorne et al., 2000). Most of these conditions develop within first few months after a stroke, pose a barrier to recovery and can be treated. At 3 months, serious medical events are associated with severe disability, even after accounting for stroke severity (Johnston et al., 1998). Johnston et al. propose numerous mechanisms that may explain the negative effect of post-stroke medical complications on outcome, including delayed rehabilitation, intensification of pre-stroke conditions, reduced motivation due to psychological conditions, lack of recognition of neurological worsening secondary to medical complications, and the possibility that medical complications may serve as an indicator for severe disability.

Although the high frequency of psychiatric, systemic, infectious and neurovascular comorbidities within 3 months of a stroke has been recognized, their independent impact on functional outcome in the long-term has not been well studied (Kissela et al., 2009). Pettersen et al. (2002) suggest that functional deterioration, in terms of activity, at 3 years is largely due to concomitant disabling disorders. However, comorbidities are often grouped or categorized together, using indexes such as the Carlson Comorbidity Index, disguising the influence of individual conditions on functional outcome. Certain conditions, such as pneumonia, occur early after a stroke, are well detected and managed and thus, may be less likely to affect outcomes in the long-term. Other conditions, such as depression and cognitive impairment, are less evident, often develop gradually, are under-assessed and under-treated and may be more likely to affect functioning (Swartz et al., 2016b). Latent and under-assessed post-stroke conditions may play a more significant role in long-term functioning compared to frequently encountered and manifest complications, and thus, evaluating the independent impact of different post-stroke comorbidities may provide an opportunity to specifically identify and target post-stroke conditions that may be more debilitating in the long-term. Depression, obstructive sleep apnea and cognitive impairment are three common post-stroke conditions that all under-assessed and under-treated and may play a significant role in long-term functioning. However, their independent impact on outcome is not well understood.
1.1.5 Recovery

Every stroke has unique features that independently or concurrently impact the course of recovery. Due to the large number of variables that influence its trajectory, recovery is a complex and dynamic process. Intrinsic recovery typically occurs in the weeks immediately following a stroke—after resolution of post-stroke edema—and is often altered by acute interventions and early adverse events. Once a stroke is complete, the brain responds to damage by initiating a series of mechanisms that result in neurological as well as functional recovery. Both these forms of recovery occur in two ways: (1) through restoration to pre-stroke conditions and (2) through compensation for damage (Levin, Kleim, & Wolf, 2009).

Neurological Recovery

Spontaneous neurological recovery is the natural return of brain function that is characterized by restoration of function in the damaged neural tissue and compensation for lost neural tissue through recruitment of new tissue (Teasell & Hussein, 2013; Levin et al., 2009). Spontaneous recovery often begins as soon as a stroke is complete. Processes such as reperfusion have been found to contribute to recovery in the acute phase, whereas CNS reorganization and neuronal plasticity is responsible for majority of the neurological recovery that takes place over the months following a stroke. Early improvements in neurological function occur as a result of restoration of brain function; resolution of the post-stroke edema and reperfusion of the ischemic penumbra are the key factors responsible for brain function restoration. Once restoration is complete, the brain adopts a compensation strategy, central nervous system (CNS) reorganization, to facilitate recovery (Dombovy, 1991; Nudo, 2003).

Given the variability in size and location of the lesion, type of stroke and patient characteristics, it is difficult to precisely delineate the process of long-term neurological recovery (Cramer, 2008). Despite this variability, functional magnetic resonance imaging (fMRI) studies have illustrated some common mechanisms of motor, sensation and language recovery by exploring brain activation patterns. Central nervous system reorganization during motor recovery typically involves local re-mapping in the primary motor cortex, recruitment of collateral pathways in the affected hemisphere and increased activity in the contralateral hemisphere (Johansen-Berg, 2007; Thirumala, Hier, & Patel, 2002). While initial recruitment of the contralateral hemisphere followed by renormalization of brain activity is an adaptive
compensation mechanism and associated with good recovery, prolonged recruitment of the contralateral hemisphere is maladaptive and indicates poor recovery (Joghasen-Berg, 2007; Jiang, Zhang, & Chopp, 2010). A similar pattern of brain activation—initial recruitment of the undamaged hemisphere—has been observed in patients with post-stroke aphasia (Belin et al., 1996). However, repossessing of language function by the left hemisphere and normalization of activity is required for a complete recovery (Kuest & Karbe, 2002; Winhuisen et al., 2005). Favourable outcomes after stroke are linked to renormalization of the brain activation (Crinion & Leff, 2007). Cramer (2008) maintains that “several lines of evidence suggest that final behavioral outcome at the end of the stroke recovery period is related to the degree of activity in primary cortex underlying the behavior under study” (p. 275).

Until recently, neurological impairments were considered difficult to treat through intervention because they involved manipulation of the brain itself (Teasell & Hussein, 2013; Demain, Wiles, Roberts, & McPherson, 2006). However, new acute stroke therapies and restorative therapies to minimize and reverse damage are now emerging and have the potential to change the course of recovery and improve final outcome.
Figure 1.1 Early Management of Stroke

Once a stroke is recognized and diagnosed, acute interventions, secondary stroke prevention strategies and rehabilitation interventions are implemented to aid recovery and reduce morbidity. However, the first three months following a stroke that are generally characterized by rapid recovery are also highly unstable. This is a high risk time for recurrent stroke events, myocardial infarctions, emergence of new complications or identification of new comorbid diseases. These adverse events both increase the chances of death during this time and deter recovery. Paradoxically, the first three months following a stroke are associated with a high risk of adverse events as well as significant improvements and gains in body function and activity. Thus, acute interventions, rehabilitation, intrinsic recovery and early adverse events all shape a survivors post-stroke trajectory and could potentially influence a patient’s eventual outcome.
1.2 Defining Function

Function is difficult to define, simply because it can be very subjective. Frattali (1998) proposes that “functional is that which allows an individual to participate meaningfully in the context of life activities as defined by that person’s society and culture” (p. 210). For one patient that might mean being able to walk and for another, it could imply being able to maintain a personal relationship. In an attempt to measure function for research and clinical purposes, the meaning of function was reduced to activities that are common to all individuals, basic activities of daily living (ADLs). Utilitarian measures (Holland & Thompson, 1998 as referenced in Frattali, 1998) such as the Barthel Index were developed in the 1960s to assess basic ADLs, continued to be used today and have shaped our current understanding of functional outcome. It was not until 1980 that the World Health Organization first introduced a framework to classify and define function beyond ADLs. Prior to this, functional outcome was considered synonymous with ADLs. To some extent, despite guidelines that capture the complex nature of functioning, our understanding of function is still limited to ADLs.

1.2.1 WHO Levels of Functioning

The WHO International Classification of Functioning originally published in 1980 categorized the consequences of a disease into 3 different dimensions: impairment, disability and handicap. In 2001, these 3 domains were renamed body function/structure, activity and participation (See Figure 1.2) to positively represent the 3 primary levels of human functioning respectively: the body, the whole person and the whole person in relation to his/her social context (WHO: 2001, 2002). Dysfunction on any of these levels is known as disability (WHO, 2002). The ICF embodies the shift in medicine science from a purely medical model to a biopsychosocial model of disease (WHO: 2002) and specifically in stroke, from a physical disability or ADL-focused perspective to a broader multi-dimensional view of functioning.

In addition to body function, activity and participation, a patient’s condition may also be influenced by environmental and personal factors. The activity and participation levels of functioning are most sensitive to environmental and personal factors (WHO: 2001, 2002). The
Figure 1.2: Example WHO International Classification Framework for Stroke

The WHO International Classification of Functioning categorizes the consequences of a disease into 3 different dimensions: body function/structure, activity and participation. A patient’s condition may also be influenced by environmental and personal factors. Dysfunction on any of the levels of functioning is known as disability.
WHO has a comprehensive list (i.e. ICF Core Set for stroke; Appendix A) of body function/structure impairments, activities limitations and participation restrictions that may result from stroke as well as environmental and personal factors that may play a role in shaping outcome. The 3 domains appear to fall on a continuum (Salter et al., 2013); body function impairments may result in activity limitations and activity limitation may bring about participation restrictions, but dysfunction can appear on any domain independently as well (Frattali, 1998). There is some overlap between domains and different domains may influence each other but each one represents a distinct level of functioning (WHO; 1980). Compared to other conditions, stroke affects more domains of functions and is the most common cause of complex disability (Adamson et al., 2004); the ICF Core Set for stroke is the largest compared to the other 12 most debilitating chronic conditions (Teasell & Hussein, 2013).

The WHO defines body function as “physiological functions of body systems (including psychological functions)” and dysfunction of this level is referred to as impairments (WHO, 2001). The brief ICF Core Set for stroke includes body functions such as consciousness functions, orientation functions, attention functions, memory functions, mental functions of language and muscle power functions (WHO Research Branch ICF Brief Core Set).

Activity and participation are grouped together in the ICF Core Set. Activity is “the execution of a task or action by an individual” and dysfunction on this level is labelled as a “limitation” (WHO, 2001); it is often categorized as either basic (i.e self-care) or instrumental (i.e. budgeting). Participation is “involvement in a life situation” and restrictions are problems on the participation level of functioning (WHO, 2001). The Core Set for stroke includes activities and participation such as speaking, walking, eating, community life, recreation and intimate relationships. Tasks such as eating and walking may be more relevant to the activity level of functioning, while basic interpersonal interactions and informal social relationships are more relevant to the participation domain. Together, this framework provides a clear depiction of all the domains of function that may be affected by stroke.
1.3 Functional Recovery & Outcome after Stroke

Recovery in physiological functions of body systems (body function) and execution of a task or action (activity) are the most dominant forms of functional improvements in the months immediately following a stroke. While the definition of function extends beyond these two levels of functioning (see 1.2), enhancement of body function and ability to manage basic activities of daily living (ADLs) are often considered synonymous with functional recovery immediately following a stroke. The definition of functional recovery currently lacks consensus and is often used vaguely to refer to one level of functioning (Levin et al., 2009). Body function and activity demonstrate significant changes in the months following a stroke and are thus, the most frequently evaluated and reported forms of functional changes in stroke recovery literature.

1.3.1 Recovery in Body Function (Impairments)

The most common acute impairment after a stroke is lower limb and upper limb motor deficit affecting 72.4% and 77.4% of patients respectively (Lawrence et al., 2001). Improvements in lower extremity function and ambulation typically occur in the first 6 months following a stroke. Skilbeck, Wade, and Hewer (1983) demonstrated that 71% of patients are independent in walking by 3 months, 81% by 6 months and 84% by 12 months. Other studies have reported similar frequencies of independent walking at 3 months, with results ranging between 64% and 71% (Jørgensen, Nakayama, Raaschou, & Olsen, 1995a; Wade, Wood, & Hewer, 1985). Peak walking function was achieved by 6 weeks in 80% of patients who were unable to walk on admission to the hospital in one study (Jorgensen et al., 1995a) and by 2 months in 88% of patients in another study (Andrews, Brocklehurst, Richards, & Laycock, 1981). By 11 weeks, 95% of patients have been found to reach their best walking function (Jorgensen et al., 1995a). Those who are able to walk on admission have been found to achieve peak walking function quicker (Jorgensen et al., 1995a) and overall, compared to those with severe deficits, patients with mild motor deficit at stroke onset are more than 10 times as likely to recover motor function (Bonita & Beaglehole, 1988). Generally, recovery progresses rapidly in the weeks following a stroke, peaks at 3 months and then, continues slowly up to 6 months and in some severe cases up to 1 or 1.5 years (Andrews et al., 1981).

Upper extremity function follows a similar pattern; recovery of arm function is concentrated in the first 3 months after stroke (Broeks, Lankhorst, Rumping, & Prevo. 1999;
Heller et al., 1987). However, whether upper extremity function recovers as fast as lower extremity function is often debated (Duncan et al., 1994). Severe arm paresis in the first month is associated with worse recovery of arm function (Krakauer, 2005) and if no observable movement or recordable finger grip is evident by 28 days, a patient is unlikely to recover useful function (Heller et al., 1987). Some studies suggest that recovery of useful function only occurs in approximately 40 to 50% of patients with significant initial arm paresis (Wade, Langton-Hewer, Wood, Skilbeck, & Ismail, 1983; Broeks et al., 1999) and recovery is typically slower in these patients. Nakayama, Jørgensen, Raaschou, and Olsen (1994) found that patients with mild upper-extremity paresis achieved peak function within 6 weeks, but patients with severe paresis needed 11 weeks to reach best function. Nonetheless, late recovery in arm function, beyond 16 weeks and up to 12 months, has been observed in some patients (Broeks et al., 1999; Skilbeck et al., 1983).

Somatosensory impairments, also common after stroke, typically reach maximal recovery within 4 to 6 months depending on the modality (Connell, Lincoln, & Radford, 2008). Unlike motor recovery, somatosensory recovery varies significantly between and within patients (Winward, Halligan, & Wade, 2007) and thus, the time course of recovery is difficult to delineate. Other common body function impairments include visual field defect, dysphagia, dysarthria, dysphasia, urinary incontinence, cognitive impairments (see 1.6.4) and impaired consciousness. Of all the impairments in body function, incontinence, coma, cognitive impairments, gaze paresis and dysphagia have been found to independently affect recovery in activity at 3 months (Lawrence et al., 2001).

1.3.2 Recovery in Activity (Limitations)

The ability to perform ADLs is highly dependent on improvements in body function, especially motor function. Recovery of lower limbs aids ambulation, while recovery of upper limbs supports feeding, bathing, grooming and dressing (Teasell & Hussein, 2013). Likewise, visual neglect may influence dressing and grooming. However, patients may learn to compensate for loss of body function and still be able to accomplish ADLs. For instance, feeding could be accomplished using the unaffected hand. Similar to neurological recovery and recovery in body function, recovery in activity is a product of restoration and compensation mechanisms.
The frequency of acute dependency is high, ranging from 68% to 75%, however it has been found to decrease by 3 months to 38% (Jørgensen, Nakayama, Raaschou, & Olsen, 1999; Kotila, Waltimo, Niemi, Laaksonen, & Lempinen, 1984; Dombovy, Sandok, & Basford, 1986). ADL recovery is concentrated in first 13 weeks after stroke onset for most patients in the presence of rehabilitation (Jorgensen et al., 1995b). However, stroke severity is an important determinant of the speed and extent of recovery function (Jorgensen et al., 1999). Jorgensen et al. (1995b) reported that patients with mild strokes reach their peak ADL function faster (9 weeks) compared to patients with severe strokes (20 weeks). Severe stroke patients also demonstrate the highest degree of variability in functional recovery, with some studies suggesting longer recovery periods for this group.

The extent of recovery in activity beyond 6 months is highly contested. Jorgensen et al., (1995b) propose that recovery should not be expected beyond 5 months even in severe cases; Only 1 in 25 of stroke patients experienced functional improvement beyond 3 months. Similarly, other studies have reported non-significant improvement between 3 and 6 months (Verheyden et al., 2007; Skilbeck et al., 1983). Yet, others have reported ADL recovery up to 2 years. Evidence of improvements between 6 months and 1 year and even up to 18 months has been noted (Andrews et al., 1981; Katz, Ford, Chinn, & Newill, 1966).

Given that recovery beyond 6 months only occurs in a small proportion of patients, recovery beyond this time point is rarely assessed. Few studies have examined long-term recovery and characteristics that could identify patients with the potential for long-term recovery are currently unclear. Skilbeck et al. (1983) also suggest the possibility that recovery is simply not detected beyond 6 months due to the “ceiling effect” of frequently used outcome assessments. The Barthel Index (BI) evaluates independence in basic activities of daily living on a scale of 0 to 100. By 6 months, a score of 95 or 100 on the BI is not uncommon and thus, the BI may not be sensitive to changes between 6 months and 1 year. They also suggest that recovery may not be evident beyond 6 months as improvements may be offset by other factors such as comorbidities that manifest over time (Skilbeck et al., 1983).

Based on current evidence, recovery occurs rapidly up to 3 months, then continues slowly and appears to peak within 6 months and may persist in small proportion of cases, typically severe stroke patients, for 1.5 years. Beyond this, recovery is believed to plateau and stabilize.
1.3.3 Recovery in Participation (Restrictions)

Few studies have explored recovery in participation. Desrosiers et al. (2006) explored changes in participation for up to 6 months after discharge from acute or rehabilitation and found that increase in participation occurred mainly over the first 3 months; however, Mayo, Wood-Dauphinee, Carlton, Durcan, & Carlton (2002) illustrated that even 6 months post-stroke, 65% of stroke patients experience restrictions in reintegration into community activity. Further research on recovery in overall participation as well as specific aspects of participation (e.g. leisure activities or social relationships) is needed and short-term as well as long-term studies are required to understand the trajectory of recovery in this domain of function.

1.3.4 Mechanism and Association of Neurological & Functional Recovery

Functional recovery typically shadows neurological recovery and occurs at a slower pace, following neurological recovery by 2 weeks on average (Jorgensen et al., 1995b). Impairments in body function are considered a manifestation of neurological deficits and are believed to lead to activity limitations, which are manifested by an inability to perform ADLs (Roth et al., 1998; WHO, 2001). Given this relationship, neurological recovery inherently facilitates functional recovery; renormalization of brain function allows body function and accordingly, activity to also return to normal. However, some improvements in function, both body function and activity, may be due compensation strategies instead of restoration of function. While restorative and compensation mechanisms are rarely differentiated when recovery is assessed, both are distinct mechanisms of recovery that together generate functional recovery. Patients often learn to adapt to their deficits by adopting new strategies to overcome the barriers posed by their deficits, allowing function to recover in the absence of neurological recovery. Similarly, patients may display complete neurological recovery on neuroimaging measures despite impairments in body function. Thus, neurological and functional recovery, which are associated with one another and typically improve simultaneously, may also evolve independently due to the complex mechanisms that govern their progress.

1.3.5 Functional Outcome after Stroke

Despite the large number of post-stroke functional outcome studies, almost all past studies have failed to acknowledge the complexity of the construct identified as function. Most studies have evaluated functional outcome only as the ability to carry out activities of daily
living, in spite of guidelines that define function as extending beyond activity limitations.

Functioning of the body as well as activity limitations have been studied to a much larger extent than life/role participation. Previous stroke research has focused primarily on understanding the impact of a stroke on the body in terms of impairments and the effect of those impairments on ADLs. A full neurological and body function recovery as well as independence in living may not be indicative of one’s ability to assimilate back into their environment (i.e. participation restrictions). Restrictions in participation may persist even after physical recovery is complete (Labi, Phillips, & Greshman, 1980). Stroke patients often feel isolated and depressed after a stroke, even after their recovery has stabilized (Hackett, Yapa, Parag, & Anderson, 2005b). These patients may have attained a full recovery in terms of activity but may still be experiencing difficulties in other domains of function and thus, may have a lower functional status than would be observed based only on an evaluation of disability in activities of daily living. Function at the level of participation is poorly understood and variables causing participation restrictions after stroke have not been well studied.

A systematic review of published acute stroke drug trials found that while most studies included death, impairment and activity measures, none assessed participation and only 1 evaluated quality of life (Duncan, Jorgensen, & Wade, 2000). A similar review with acute stroke trials from the Cochrane Stroke Group’s databases found similar results; only 2% of all trials included a measure of participation or quality of life. A recent review has also confirmed these findings using RCT up to 2005, observing only a slightly higher proportion of participation measures (< 6%; Salter, Foley, Jutai, & Teasell, 2007). The current lack of emphasis on post-stroke participation could partly be explained by two factors: (1) dearth of long-term outcome studies, and (2) lack of valid and reliable measurement tools. While improvements in body function and basic activities dominate the early phase of stroke recovery, integration into society typically occurs later in the course of recovery. Basic activities of daily living may be affected immediately after a stroke, but deficits in more complex activities may not be visible until a patient has attempted to return to normal living. Since most studies evaluate outcome at 90 days, long-term functioning, and accordingly participation, is less well understood. The lack of appropriate measure also makes assessment challenging. There is currently no consensus on how to measure participation (Andrenelli et al., 2015) and participation is a complex, multidimensional concept that may naturally be difficult to gauge. Yet, participation is arguably
the most important outcome for patients (Quinn, Dawson, Walters, & Lees, 2009) and more prevalent than activity limitations (Patel et al., 2006).

Studies assessing the frequency of long-term body function, activity and participation are limited. However, one study found that at 6 months post-stroke, 39% of patients reported activity limitations (on basic ADLs), 54% reported limitations in instrumental ADLs and 65% reported participation restrictions (Mayo et al., 2002). Another follow-up study reported that 26.1% and 26.3% of patients experience activity limitations in basic activities and 55% and 51% experience instrumental activity limitations at 1 and 3 years respectively (Patel et al., 2006). A 5-year follow-up study found 13% had severe activity limitations, 16% had moderate activity limitations, 37% were mildly disabled and 34% were independent in ADLs (Wilkinson et al., 1997). These findings have not been confirmed with further research.

Despite weak evidence, the current data hints that participation may be more restricted than other domains in the long-term. Depression, quality of life and social isolation are all common concerns for stroke survivors (Hannah, Lindholm, & Maisch, 2014; O’Brien et al., 2014) and yet, research on such outcomes is scarce. Patients are often more concerned about long-term prognosis and potential for recovery and yet, stroke research has primarily focuses on 3 month and 1 year outcomes (O’Brien et al., 2014). The need for multi-domain assessment and management of long-term stroke outcomes has been recognized (Feigin et al., 2010) but not yet implemented. Further evidence of participation restrictions in stroke patients may reinforce the significance of assessing multiple domains to obtain a holistic view of post-stroke function. Furthermore, identifying variables that result in unfavourable outcomes could facilitate the development of interventions that target multiple domains of functioning. Future research should include the domain of participation.
1.4 Long-term Functioning

1.4.1 The Concept of Recovery Plateau & Maintenance

The current lack of long-term follow-up studies impedes a clear understanding of recovery cessation and maintenance of functional gains. Demain et al. (2006) suggest that the “plateau” that is often observed and assumed to be permanent may perhaps be a temporary cessation in improvement. Neuromuscular adaptation to therapeutic exercise regimes may be misinterpreted as motor recovery plateau (Page, Sisto, Levine, & McGrath, 2004). Given that recovery is observed even in chronic stroke patients, Demain et al. (2006) propose that “appearance may not be a reliable indicator of the optimum limit to recovery” and that the instruments currently used to measure recovery further obscure plateau recognition. Without long-term follow-up studies and appropriate instruments, determining the point of recovery cessation is challenging.

Once recovery has stabilized however, functional status, in terms of body function and ADLs, has been found to remain stable for up to 3 years (Reutter-Bernays & Rentsch, 1993; Katz et al. 1966; Skilbeck et al., 1983; Teasell & Hussein, 2013). However, beyond 3 years, function appears to decline (Meyer et al., 2015; Pettersen et al., 2002). Deterioration becomes especially obvious and significant at 5 years. A long-term follow-up study by Meyer et al. uncovered that body function (i.e. motor) and activity limitations (i.e. ADLs) outcomes at 5 years are equivalent to 2 month outcomes, indicating a return to pre-recovery level of functioning. Recent long-term studies are now demonstrating that functional gains within the first 6 months after a stroke are not always maintained in the long-term (Meyer et al., 2015; Pettersen et al., 2002).

While the trajectory of post-stroke function is slowly becoming more precise, the primary factors that influence functional maintenance and decline are yet to be determined. Factors that typically inform peak and rate of recovery, such as age, may become less important in the long-term (Borucki, Volpe, & Reding, 1992). Other factors, such as comorbidities, may become increasingly significant in the long-term. Comorbid diseases have consistently been reported as the primary cause for functional decline (see 1.1.4; Pettersen et al., 2002, Reutter-Bernays & Rentsch, 1993; Borucki et al., 1992). Identification and treatment of these conditions could potentially deter functional decline.
1.4.2 Long-Term Functional Outcome

In most stroke clinical trials and prognostic studies, the primary outcome is usually measured at 90 days (Stroke Therapy Academic Industry Roundtable II (STAIR-II), 2001; Duncan et al., 2000) to reduce the confounding effects of new events or post-stroke comorbidities on clinical outcome. The early phase of stroke recovery is thus well characterized, with numerous studies elucidating the risk of death as well as the impairments and disabilities that occur during this period. However, long-term outcomes, which may be more relevant to a patient, are less well understood. In fact, the definition of “long-term” is also unclear and rather arbitrary—some studies report 3 month outcomes as long-term outcome (Konig et al., 2008), while other consider 3 year outcomes to be long-term (Pettersen et al., 2002).

Outcomes beyond 1 year have received less attention due to concerns regarding the effect of additional post-stroke events that may obscure the relationship between stroke and outcome. As time from stroke increases, multiple factors such as comorbidities and life situations may confound the association between stroke and outcome. However, comorbidities are an inevitable consequence of stroke, have the potential to impact the course of recovery and thus, should be considered when outcome is evaluated (see 1.1.4). The current lack of long-term functional outcome studies precludes our understanding of the long-term, patient-centred consequences of a stroke and the factors that influence it.

1.4.3 Predictors of Long-Term Functional Outcome

Given the complex nature of stroke recovery, several factors can affect a patient’s functional outcome. Numerous prognostic models have been developed to predict functioning after stroke. Typically, these models utilize baseline patient characteristics (a varying time points post-stroke) to predict activity at 3 months post-stroke. Predictors of functioning in the early stroke phase and even up to 1 year post-stroke are well studied, with several models confirming the predictive value of variables such as age and stroke severity.

Weimar, Ziegler, König, and Diener (2002) conducted a systematic literature search to identify all previously suggested independent prognostic factors for stroke outcome that could be assessed within the first 72 hours after admission. Age, stroke severity, activity limitations, gender, prior stroke, neurological complications, diabetes, fever, lenticulostriate infarction and
right and left arm paresis were all independent predictors for functional independence (activity limitations) at 100 days post stroke. Konig et al. (2008) also found that age and stroke severity within 6 hours post-stroke can accurately predict functional outcome at 3 months in 73% of patients. The ability of age and stroke severity to predict outcome particularly early—even within 6 hours—has been long-established by multiple studies (e.g. Weimar, König, Kraywinkel, Ziegler, & Diener, 2004; Adams et al., 1999; Knoflach, Ru, & Kiechl, 2012). While predictors of short-term (i.e. 3 months) activity limitations have been recognized, less is known about predictors of long-term functional outcome in multiple domains. More importantly, factors that have received the most research attention—age and stroke severity—are non-modifiable once a stroke is complete. Other potentially modifiable factors, such as post-stroke comorbidities and complications, may play a role as well, especially if they are left untreated in the long-term.
1.5 Traditional Predictors of Functional Outcome

1.5.1 Age

Age is typically considered a major predictor of outcome after a stroke and is commonly used in prognostic models. Advancing age is directly related to post-stroke mortality; 30-day post-stroke fatality rate increases from 9% in individuals between the ages of 65 and 74 to 13.1% in those between 74 and 84 and finally to 23% in those above the age of 85 years (Go et al., 2014, Heart Disease and Stroke Statistics). Three month mortality further demonstrates the impact of progressing age on stroke mortality, as 28% of patients over the age of 80 are dead within 90 days compared to 13% of patients under the age of the 80 years (Bentsen, Christensen, Christensen, & Christensen, 2014). Increasing age is, thus, is risk factor for poor outcome in terms of mortality.

The influence of age on functional outcome, however, is not as clear. During hospital stay, a 10-year increase in age results in a 3-point decrease in discharge BI and BI gain (Nakayama et al., 1994). Similarly, Knoflach et al. (2012) and Macciocchi, Diamond, Alves, & Mertz (1998) identified age as a predictor of activity limitations at 3 months. At 12 months post-stroke, 84% of those under the age of 65 are independent in ADLs compared to 52% of those over 65 years of age (Kotila et al., 1984). Knoflach et al. (2012) propose that “intact vascular compensation mechanisms and a more pronounced neuronal plasticity” may facilitate better recovery in younger patients.

However, Andrews, Brocklehurst, Richards, and Laycock (1984) found that in those who survived 1 year, there was no difference in ADL function between those aged 64 and younger, those between 65 and 74 years of age and those above the age of 75 years. The effect of age may also dependent on initial activity limitations; Black-Schaffer & Winston (2004) found that increasing age was associated with poorer functional gain in those with greater admission activity limitations but there was no relationship between age and outcome in patients with few activity limitations at admission. Similarly, Bagg, Pombo, and Hopman (2002) found that age alone accounted for only 3% of the variance in activity limitations at discharge from a 6-year long stroke rehabilitation program. The heterogeneity in outcome measures in functional outcome studies could potentially explain some of the inconsistencies in the literature (Black-Schaffer & Winston, 2004).
In a summary by Black-Schaffer & Winston (2004) of studies that evaluated the relationship of age to functional outcome after stroke, almost every study used a unique set of measures. Some used institutionalization as an outcome measure (e.g. Colantonio, Kasl, Ostfeld, & Berkman, 1996), others used change in Barthel Index (i.e. activity limitations; e.g. Macciocchi et al., 1998) and yet, others used speed of recovery (e.g. Nakayama et al., 1994) as an outcome. Even scores on a single scale can represent different outcomes. For instance, Functional Independence Measure (FIM) scores can be analyzed in multiple ways: discharge FIM, change in FIM (i.e. functional gain) and discharge Motor FIM (Bagg et al. 2002). In fact, Bagg et al. (2002) found that age significantly predicted total FIM scores—which include a motor (i.e. activity limitation) and cognitive (i.e. body function) component—as well as just motor FIM scores but did not predict FIM change at discharge from rehabilitation. Different outcome measures also capture different constructs. The BI only measures basic activities and focuses on motor functioning whereas FIM assesses additional domains such as social interaction and problem solving and evaluates motor as well as cognitive tasks. Differences in functional outcome due to age may be augmented when concepts such as cognitive abilities are included in outcome assessments and thus, multidimensional scales (ex. FIM) may offer different conclusions than scales that focus on specific domains such as motor disability (ex. BI). Recognizing the level of function being evaluated is important, as different domains of function may be associated with different predictors. The use of different instruments and outcomes obscures the true relationship between age and functional outcome.

Timing of assessments may also play a critical role. Most outcome assessments take place within 1 year of a stroke. Given that recovery is still taking place during this time and some patient may recover at different rates than others, especially due to age, early outcomes assessment may not represent optimal outcome. Greater independence in daily activities has been observed in younger patients at 2 weeks, however this difference in independence dissipates at 6 months (Andrews et al., 1984; Black-Schaffer & Winston, 2004). Andrew et al. suggest that age itself may not be a barrier to recovery. They propose that the same type of recovery should be expected regardless of age, if older patients do not die due to their disabilities. Older patients may be able to achieve the same level of activity as younger patients, but at a slower pace (Black-Schaffer & Winston, 2004). Andrews et al. (1984) note that “poor prognosis in elderly
must be seen in the context of long-term survivors” (p. 52). By allowing older patients to reach peak functioning before outcome is assessed, long-term studies can explore this suggestion.

Previous research also suggests that older patients may in fact have poor outcome compared to younger patients due to factors related to age, but not because of age itself. Poor outcomes observed in older patients may be due to limited use of diagnostic resources for older patients. An investigation by Carlo et al. (1999) indicated that patients over the age of 80 are less likely to have a Doppler examination, echocardiogram, angiography and brain imaging compared to those under the age of 80, despite having more severe acute disability. They suggest that the limited investigation may lead to limited interventions for older patients and thus, may partially explain the worse outcome observed in this population. A review by Luker et al. (2011) also found discrepancies in acute care for younger and older patients, with older patients generally receiving inferior care. The use of CT head scans and carotid imaging was found to be significantly lower in older patients compared to younger patients. Whether these factors play a major role in determining functional outcome is unknown.

Alternatively, other age-related factors, such as comorbidities, may be regulating function. Aside from stroke, age is a risk factor for many other medical conditions that are rarely included in prognostic models. Comorbidities such as cognitive impairment, which are more common in older patients, are associated with functional disability and institutionalization (Graham et al., 1997; Rockwood, Stolee, & McDowell, 1996; Pendlebury & Rothwell, 2009). Gauging cognitive ability may be especially crucial in older patients. In fact, it has been suggested that “the more carefully patients are matched for absence of comorbid medical problems and severity of neurological impairment, the less relevant age becomes as a factor in rehabilitation outcome” (Reding as cited in Granger, Hamilton, & Fiedler, 1992). Age also does not influence stability of functional gains in the absence of comorbid medical problems (Borucki et al., 1992). It is possible that comorbid conditions are responsible for the poorer functioning observed in older patients.

Further research on the impact of age on post-stroke body function and participation is also warranted. Previous research has primarily focused on ADLs and physical disability. The greater need for institutional care in older patients may indicate higher participation restrictions than activity limitations in this population (Andrews et al., 1984). One study has indicated that
age, along with comorbidities, affect and lower extremity coordinator, are predictors of social participation at 6 months and 2-4 years later (Desrosiers et al., 2006). However, given the large number of variables included in the model and the small sample size, the authors advise that this study was exploratory in nature. With a larger sample size and using multivariable analyses, Sturm et al. (2004) found that age was a predictor of participation at 2 years but Clarke, Black, Badley, Lawrence, and Williams (1999) found no effect of age at 1 year. Few other studies have also reported contradictory findings (Gadidi, Katz-Leurer, Carmeli, & Bornstein, 2011; Lo et al., 2008).

Younger stroke victims may also have participation restrictions without physical disability. In a long-term follow-up of young stroke survivors, only 42% of patients had returned to work (Kappelle et al., 1994). Such restrictions in younger patients were also observed by Knoflach et al. (2012) after ischemic stroke and by Rinkel and Algra (2011) after subarachnoid hemorrhagic stroke. These observations may be associated with mood and cognitive disturbances that may not be within the realm of constructs assessed by the modified Rankin or other ADL measures (Rinkel & Algra., 2011; Knoflach et al., 2012). The effect of age on participation may be altered by mood and cognition. Future research in this area is especially important given than participation restrictions might be more easily modifiable than physical disability.

1.5.2 Stroke Severity

Stroke severity has been established as a reliable way to predict both short term and long term post-stroke case-fatality (Andersen & Olsen, 2011) and discharge location (Bejot et al., 2012). Often assessed through a neurological assessment, functional assessment or neuroimaging data, stroke severity is also regularly incorporated into prognostic models of functional outcome, consistently found to have high predictive value and often considered the single most important predictor of outcome (Saver & Altman, 2012).

The National Institutes of Health Stroke Scale (NIHSS; Brott et al., 1989; Goldstein et al., 1989) is the most commonly used scale to evaluate stroke severity. It assesses levels of consciousness, gaze, vision, facial palsy, arm and leg strength, limb ataxia, sensory loss, best language, dysarthria, and extinction and inattention. Scores range from 0 to 42 and are stratified such that a score of 0 signifies no stroke, 1- 4 indicates minor stroke, 5- 15 indicates moderate stroke, 15-20 indicates moderate/severe stroke and 21- 42 suggests severe stroke. Other common
scales include the Canadian Neurological Scale (Cote et al., 1986, 1989) and the Scandinavian Stroke Scale (Scandinavia Stroke Study Group, 1985).

Baseline NIHSS score is one of the strongest predictors of disability at 3 months (Weimar et al., 2002). When assessed within 6 hours of an ischemic stroke onset, age and NIHSS score are able to correctly predict survival in 91.5% of patients and full functional recovery in 83.2% of patients after 3 months (Weimar et al., 2004). When assessed within 24 hours, the possibility of a favourable body function and activity outcome at 3 months decreases by 17% with every point increase in NIHSS score (Adams et al., 1999). A NIHSS score of 16 or higher indicates a high likelihood of severe activity limitations or death and a score of or below 6 predicts good recovery at 3 months (Adams et al., 1999). The prognostic value of the NIHSS, however, is highly time dependent (Saver & Altman, 2012). Stroke severity generally becomes increasingly predictive of 3-month functional outcome over time as deficits stabilize. Saver and Altman (2012) found that at 24 hours, NIHSS explained 51% of the variance in functional outcome, whereas at 90 days, NIHSS scores accounted for 76% of the variance in 3-month outcome.

Few studies have examined the ability of stroke severity to predict long-term function (Kwakkel & Kollen, 2013). When assessed within 9 days, the NIHSS is able to predict 6 month activity limitations with 72% accuracy (Kwakkel et al., 2010). Kissela et al. (2009) also found that stroke severity was associated with worse activity limitations at 4 years but this association was not significant in a multivariable model. Stroke severity has also been associated with activity limitations and motor body function at 2 months, 6 months and 5 years (Meyer et al., 2015). Further research is warranted to confirm these findings, to determine whether stroke severity is an independent predictor of long-term activity limitation in a multivariable model and to understand its impact on post-stroke participation.

Stroke infarct volume is also an indicator of stroke severity and has been associated functional deficits. A recent review illustrated that MRI lesion volume was correlated with body function (NIHSS) and activity (BI) within 6 months post-stroke (Schiemanck, Kwakkel, Post, Kappelle, & Prevo, 2006). When assessed using magnetic resonance diffusion-weighted imaging (MR DWI), smaller lesion volumes increased the likelihood of recovery compared to larger lesion volumes and a combination of clinical and MR DWI factors improved predictive power (Baird et al., 2001). White matter disease may also be contributing to functional ability. Kissela
et al. (2009) discovered that severe periventricular white matter disease (PVWMD) was related to activity limitations at 3 months and that “risk factors traditionally associated with poor outcome in univariable modeling became insignificant when PVWMD was included in multivariable models” (p. 534). There may be a role for imaging markers in prediction models, however given the limited availability and cost associated with imaging tools, including such variables in a prognostic model may limit generalizability.

1.5.3 Short-Term Activity Limitations

The Barthel Index and modified Rankin Scale are the two most common functional assessment scales (see 3.4.1). Like measures of neurological impairment, early activity limitations are also a proxy for stroke severity and short-term limitations are also associated with long-term activity limitations. Kwakkel & Kollen (2013) argue that because determining basic ADLs can be difficult if the patient is still bedridden, activity assessments within the first 3 days may underestimate longer-term activity. Nonetheless, Weimar et al. (2002) found that Rankin score (i.e. activity limitations) 48-72 hours after a stroke was a prognostic factor for functional independence at 100 days. ADL function at 30-days is also considered “valid proxy” for ADL function at 90-days (Rost et al., 2016). Activity limitations in the short-term may be a more important predictor of long-term activity limitations than stroke severity. Pre-stroke activity, post-stroke activity and 3-month activity limitations, along with prior stroke and infectious complications, were all significant predictors of 4 year activity limitations in a multivariable model (Kissela et al., 2009), whereas stroke severity was no longer significant when these variables were included. Meyer et al. (2015) also demonstrated that activity limitations and body function at 2 months and 5 years are equivalent. However, 5 year activity limitations were significantly greater than 6 month limitations, indicating a decline in functioning.

Activity limitations are also associated with lower levels of participation on admission to rehabilitation (Yang & Kong, 2013) as well as up to 4 years after stroke (Gadidi et al., 2011). At 2 years, stroke severity, activity limitations and mood are all associated with participation restrictions (D’Alisa, Baudo, Mauro, & Miscio, 2005). However, whether short-term activity limitations can predict long-term participation and body function remains unknown.
1.5.4 Sex

Sex may play an indirect role in long-term functional outcomes. Female sex has been
associated with worse outcomes (Kong, Tao, Hao, & Liu, 2009; Feigin et al., 2010). However,
based on a review of current literature, Gall, Tran, Martin, Blizzard, and Srikanth (2012)
maintain that the sex difference in activity limitations is greatly reduced after accounting for
other factors such as age and stroke severity. Participation restrictions studies show similar
findings, sex does not appear to independently predict restrictions when other predictors such as
age, activity limitations and mood are accounted for (Gall et al., 2012). Clark et al. (1999) found
that martial status may moderate the relationship between sex and participation restrictions after
stroke. Married men experienced less participation restrictions, whereas married women reported
greater restrictions, possibly due to the plentiful roles and responsibilities of married women
(Clark et al., 1999; Kandel et al., 1985). Depressive symptoms, which are more common in
females post-stroke (Herrmann, Black, Lawrence, Szekely, & Szalai, 1998) and also associated
with participation restrictions (Astrom, Adolfsson, & Asplund, 1993) may also be mediating this
relationship. Therefore, gender may influence functional outcome through its impact on other
key predictors.
1.6 Potentially Modifiable Predictors of Functional Outcome

1.6.1 Modifiability of Predictors

Long-term functional outcome after stroke is shaped by non-modifiable, partially modifiable and modifiable factors. Factors such as age, initial stroke severity, gender, race, and side of lesion are examples of non-modifiable factors once a stroke is complete. Some factors such as social support and education are partially modifiable and can be altered to some degree after a stroke. Yet, others can be easily targeted and theoretically modified; hypertension, diabetes, smoking, rehabilitation length, depression, sleep apnea, cognitive impairment and other post-stroke comorbidities are modifiable variables.

Given that non-modifiable factors (e.g. age and stroke severity) have been studied more extensively than modifiable factors, post-stroke disability is sometimes considered irreversible. Much of the variability in long-term outcomes, however, is not explained by non-modifiable factors. Recognition of modifiable factors, that may explain part of the variability, provides an opportunity for the development of focused interventions to improve post-stroke outcome. Hypertension, diabetes, smoking and atrial fibrillation are common, modifiable stroke risk factors (American Stroke Association, 2016) that are typically assessed and managed by stroke prevention clinics. However, depression, OSA and cognitive impairment are three are common post-stroke comorbidities (House et al., 1991; Gottlieb, Salagnik, Kipnis, & Brill, 2002; Joo et al., 2011; Tosun, Köktürk, Karataş, Çiftçi, & Sepici, 2008; Chan, Coutts, & Hanly, 2010; Black, 2011; Zinn, Bosworth, Hoenig, & Swartzwelder, 2007) that are under-assessed and overlooked despite being potentially modifiable. Treatment of these comorbidities has been found to enhance outcomes (Mikami et al., 2011; Ryan, Bayley, Green, Murray, & Bradley, 2011; Verdelho et al., 2012). Recognizing both, non-modifiable and modifiable, predictors as well as treating modifiable conditions may be best strategy to optimize outcome after stroke.

1.6.2 Depression

Depression affects approximately one third of stroke patients, although the frequency varies based on type of population, diagnosis criteria and length of follow-up (Hackett et al., 2005b). Prevalence is typically lower in community studies compared to outpatient studies (Robinson, 2003). Screening tools and diagnostic criteria vary among studies, obscuring the
exact severity of post-stroke depression and the frequency of minor and major depression; some studies report higher frequencies of minor depression (Paolucci et al., 2005; Kauhanen et al., 1999), while others have found greater frequencies of major depression (Pohjasvaara et al., 1998; Spalletta, Guida, De Angelis, & Caltagirone, 2002). Both forms of depression are more frequent in stroke patients than sex- and age-matched controls at approximately 1.7 years post-stroke (Lindén, Blomstrand, & Skoog, 2007).

The length of follow-up is a critical factor in evaluating post-stroke depression and associated with the dynamic course of post-stroke depression. The incidence of depression, especially major depression, appears to decrease over time (Bour et al., 2010); however depressive symptoms may persist for up to 18 months (Berg, Palomäki, Lehtihalmes, Lönnqvist, & Kaste, 2003). The prevalence of depression appears to remain stable, between 28 to 33% over 5 years post-stroke (Ayerbe, Ayis, Rudd, Heuschmann, & Wolfe, 2011), with the lowest prevalence at 1 year and highest at 3 months. Depression may resolve in some patients, persist in others, surface in few, and reoccur in certain cases (Bour et al. 2010, Ayerbe et al., 2011; Burvill et al., 1995; Wade, Legh-Smith, & Hewer, 1987). Astrom et al. (1993) delineated the progression of depression and found that depression appears to increase between the acute phase and up to 3 months, decrease between 3 and 12 months, and then increase again up to 3 years. Depression at 3 months and at 3 years was almost equivalent (31% vs. 29%), despite slight fluctuations at other time points (Astrom et al., 1993). A similar observation was made by Ayerbe et al. (2011)–depression prevalence at 3 months was similar to prevalence at 3 years (33% vs. 32%).

The mechanism, etiology and risk factors of post-stroke depression are currently being studied. A post-stroke depression epidemiology review by Whyte & Mulsant (2002) suggests that both biological and psychosocial mechanisms could potentially independently or concurrently cause depression after stroke. They propose biological mechanisms such as disruption of neural circuits and neurochemicals and psychosocial mechanisms such as overwhelmed coping skills may be at play. Salter et al. (2013) propose similar mechanisms, suggesting that neurological (i.e. neurotransmitter imbalance), reactive (i.e. response to physical losses) and coincidental (i.e. similar risk factor profiles) may explain the emergence of depression after stroke. Accordingly, certain factors that predispose a patient to post-stroke depression have been identified. Neurological impairment (biological risk factor), female sex (biological risk factor) and previous history of depression (psychosocial risk factor) appear to be
risk factors for depressive symptoms (Herrmann et al., 1998). Stroke location has been studied extensively as a risk factor for depression, however given the methodological differences in post-stroke depression literature, research on the relationship between stoke location and post-stroke depression is inconclusive (Bhogal, Teasell, Foley, & Speechley, 2004).

Despite evidence to support the high prevalence of post-stroke depression and numerous studies confirming possible mechanisms of the condition, depression appears to remain under-assessed and under-treated in stroke populations (Herrmann et al., 2011; Swartz et al., 2016b). The current Canadian Stroke Best Practice Recommendation Guidelines state that all patients with stroke should be screened for depressive symptoms (2015). Only 4.8% and 6.7% of stroke patients were diagnosed and treated, respectively, for depression between 2003 and 2008 at 13 designated stroke centres in Ontario. Although these guidelines were first published in 2006, compliance still remains low (Swartz et al., 2016b). Lack of screening, diagnosis and treatment of post-stroke depression may impede recovery and contribute to functional deterioration in the long-term.

Depression has been associated with deficits on multiple levels of functioning after stroke. During hospitalization and after rehabilitation treatment, severe activity limitations are significantly more common in depressed patients compared to non-depressed, however the correlation between depression at hospitalization and activity limitations at 6 weeks is weak (Zikic et al., 2014). Sinyor et al. (1986) found similar results–depressed patients had greater activity limitations compared to non-depressed patients, but correlational analyses failed to show an association between the two. Nonetheless, depressive symptoms correlate with activity limitations at 3 months (Astrom et al. 1993; Herrmann et al., 1998) and 1 year post-stroke (Herrmann et al., 1998). The lack of correlation between depression and activity limitations in the acute phase (Astrom et al., 1993) or at 1 month (Andersen, Vestergaard, Ingemann-Nielsen, & Lauritzen, 1995) may imply that depression influences activity limitations in the long-term but not immediately after a stroke. Alternatively, it is also possible that correlational analyses are underestimating “the degree of meaning association due to the inappropriate inclusion of low scores that do not show a linear relationship with either the construct of depression or functional impairment” (Sinyor et al., 1986, p. 1105). Given that significant association have been reported at 3 months and beyond, this suggestion may only apply to the acute phase, when depression may not have fully developed and a greater proportion of scores are low.
The association between depression and activity limitations persists in the long-term. Depression within 2 weeks of stroke is correlated with activity limitations even 2 years later (Parikh et al., 1990) and 2 month depression impairs functional and cognitive recovery at 14 months (Morris, Raphael, & Robinson, 1992). Numerous other studies have also confirmed an association between short-term (i.e. 3 month) depression and long-term (i.e. one year) activity limitations (Kotila, Numminen, Waltimo, & Kaste, 1999; Pohjasvaara et al., 2001). Patients with depression are even more likely to show functional deterioration over time (Morris et al., 1992). Absence of close personal relationships, basic and instrumental activity limitations, and cognitive impairment are all more prevalent in depressed patients at 3 to 5 years post-stroke (Sharpe et al., 1994). However, majority of these studies did not explore the impact of short-term depression on long-term activity limitations after controlling for traditional predictors such as age and stroke severity. Two prognostic studies employed multivariable analyses, using short-term depression to predict long-term activity limitations—one assessed depression extremely early (e.g. 7-10 days; Willey et al., 2010), and the other had a follow-up period of only 1 year (Donnellan, Hickey, Hevey, & O'Neill, 2010). Both found conflicting results, neither explored the influence of cognition and neither assessed participation as an outcome. Post-stroke depression is believed to peak at 3 months (Astrom et al., 1993), is associated with cognition and is believed to influence post-stroke participation. These observations, along with traditional predictors, must be considered together to understand whether short-term depression independently predicts long-term function.

Participation restrictions are commonly associated with post-stroke depression, both as a cause and a result (Astrom et al., 1993); depressed patients have fewer social contacts than non-depressed stroke patients after stroke and even 3 years later (Astrom et al. 1993) and are unable to resume premorbid social activities at 6 months (Feibel & Springer, 1982). Even patients who have achieved peak activity levels are often unable to reintegrate into society (Labi et al., 1980). Given that age, activity limitations and neurological deficits are unable to explain these participation restrictions, Labi et al., (1980) propose that psychosocial factors may be key determinants. Increased depressive symptomology has been related to increased odds of social isolation (Hinojosa, Haun, Hinojosa, & Rittman, 2011), however multivariable prognostic models accounting for traditional predictors as well as long-term participation studies are limited.
Body function, specifically cognition and mobility, also appears to be negatively affected by depression. Activity, cognitive problems, fatigue and depression at 1 year predict mobility decline between 1 and 3 years post-stroke (Van De Port, Kwakkel, Van Wijk, & Lindeman, 2006) and depressive symptoms are associated with the development of mild cognitive impairment (Barnes, Alexopoulos, Lopez, Williamson, & Yaffe, 2006). Therefore, body function, activity and participation are all vulnerable to the negative effects of post-stroke depression.

Depression may be explained by “the biological effects of stroke and concerns about the residual neurological impairments, financial problems, anxiety and uncertainty about future” (Kapelle et al., 1994, p. 1364). Identifying the role of depression in predicting function could facilitate the development of treatments that address these underlying concerns.

1.6.3 Obstructive Sleep Apnea

Sleep apnea is very common after stroke, affecting 50% to 70% of patients (Hermann & Bassetti, 2009). Approximately 60% of patients show symptoms of sleep apnea at 3 months post-stroke (Parra et al., 2000). Obstructive sleep apnea is the most common sleep-related breathing disturbance after stroke. The severity of sleep apnea is evaluated using the apnea-hypopnea index (AHI; Davis, Billings, Longstreth, & Khot, 2013). A diagnosis of OSA entails either (1) AHI ≥ 5 events per hour with associated symptoms, or (2) AHI ≥ 15 (Flemons et al., 1999, American Academy of Sleep Medicine; Park, Ramar, & Olson, 2011). A polysomnogram (PSG) is considered the accepted standard for diagnosis of obstructive sleep apnea, but it is expensive and not feasible in an acute stroke setting (Park et al., 2011). Questionnaires are unable to accurately determine OSA risk (Srijithesh et al. 2011), rendering detection of post-stroke sleep apnea difficult. However, research on questionnaires is limited and combining a quick, robust questionnaire combined with OSA-associated risk factors such as body mass index (BMI), age and gender may allow risk stratification for OSA (Swartz et al., 2016b; see 3.4.2).

OSA increases the likelihood of having a stroke (Bradley & Floras, 2009; Yaggi et al., 2005) and is also a consequence of stroke (Arzt, Young, Finn, Skatrud, & Bradley, 2005). It is associated with numerous conditions that are risk factors for stroke; sleep-disordered breathing is a risk factor for hypertension (Peppard, Young, Palta, & Skatrud, 2000; Nieto et al., 2000) and OSA is prevalent in atrial fibrillation patients (Gami et al., 2004), both of which are also risk
factors for stroke. Yaggi and Mohsenin (2004) propose that hypoxaemia, hypercapnia, changes in intrathoracic pressure and sleep disruptions as a result of sleep apnea-related airway occlusion may trigger “autonomic, haemodynamic, coagulopathic and vascular injury processes that serve as plausible mechanisms by which sleep apnea may cause stroke” (p. 339). Thus, common risk factors, associated conditions and pathophysiological processes may explain the increased prevalence of sleep apnea after stroke.

Treatment of sleep apnea using nasal continuous positive airway pressure (CPAP) is highly effective. Improved daytime function has been observed in patients with mild and moderate to severe sleep apnea (Ballester et al., 1999; Engleman & Joffe, 1999; Young, Peppard, & Gottlieb, 2002). However, compliance is low (Bassetti, Milanova, & Gugger, 2006) and low detection combined with low treatment (Swartz et al., 2016b) may mean that patients with post-stroke sleep apnea are at risk of poor long-term functioning (see 1.6.3).

Severe sleep-disordered breathing (SDB) is associated with activity limitations at 3 months (Yan-fang & Yu-ping, 2008; Good, Henkle, Gelber, Welsh, & Verhulst, 1996), 6 months (Turkington, Allgar, Bamford, Wanklyn, & Elliott, 2004) and 12 months (Good et al., 1996) post-stroke. At discharge from stroke rehabilitation unit, a 10 unit increase in obstructive AHI decreases FIM score (i.e. activity) by 2.3, after accounting for stroke severity and cognition (Kaneko, Hajek, Zivanovic, Raboud, & Bradley, 2003). Other studies, however, have reported no association between sleep-disordered breathing and outcome. Bassetti et al. (2006) found that at approximately 5 years post-stroke, patients with an acute AHI ≥ 30 did not have significantly worse activity outcome than those with an AHI < 10. Parra et al. (2004) reported no correlation between sleep-related breathing disorders and activity limitations in patients admitted to the stroke unit and sleep apnea during the first night is not associated with activity limitations at 6 months (Iranzo, Santamaria, Berenguer, Sanchez, & Chamorro, 2002). Overestimation of SDB severity in the acute phase could be a possible explanation for the lack of association between SDB and long-term functioning reported by some studies, since most studies with sleep recordings > 1 month post-stroke show an association (Bassetti et al., 2006). Persistent (i.e. beyond the acute phase) and untreated sleep apnea may be responsible for poor long-term functioning.
Few studies have also demonstrated a link between sleep disturbances and cognition (i.e. body function). Executive functions (Saunamaki & Jehkonen, 2007) and attention (Redline et al., 1997) appear to be most affected. White matter disease is also strongly associated with SBD in acute stroke (Harbison, Gibson, Birchall, Zammit-Maempel, & Ford, 2003). Kerner and Roose (2016) propose that OSA may trigger the development or exacerbation of depressive symptoms and cognitive deficits by initiating or amplifying the pathological processes of small vessel disease (e.g. white matter hyperintensities) and blood brain barrier dysfunction. However, the long-term impact of persistent post-stroke apnea on cognition is unknown.

To the best of our knowledge, there are currently no studies exploring the impact of obstructive sleep apnea on participation restrictions, and few exploring the body function impairments (e.g. cognition) due to post-stroke sleep apnea. Further research on the impact of sleep apnea on multiple functional domains, especially in the long-term, is warranted, given that it can be easily modified with the use of CPAP.

1.6.4 Cognitive Impairment

Vascular cognitive impairment (VCI), which encompasses vascular cognitive impairment-not dementia (VCIND), vascular dementia (VaD) and mixed VaD and AD (Roman et al., 2004), is common after stroke. At 3 months, 39% to 61% of stroke patients experience some cognitive impairment (Patel, Coshall, Rudd, & Wolfe, 2003; Poojasvaara et al., 1997) and patients with mild VCI (e.g. VCIND) may be at risk of progressing to severe forms of VCI (e.g. VaD; Black, 2011). Like sleep apnea, dementia is both a risk factor as well as a consequence of stroke: 10% of patients have dementia prior to first stroke, 10% develop dementia after their stroke and 30% have dementia after recurrent stroke (Pendlebury & Rothwell, 2009). New onset dementia occurs even years after stroke, with a cumulative incidence of 48% after 25 years (Leys, Hénon, Mackowiak-Cordoliani, & Pasquier, 2005). Stroke also doubles the relative risk of developing dementia for up to 25 years (Leys et al., 2005). Thus, VCI, even in severe forms, is not only common, but also persistent after a stroke.

Exposure to vascular risk factors (Hennerici, 2009) and the stroke itself (Pendlebury & Rothwell, 2009) could both trigger the development of dementia. Vascular factors, such as hypertension (Launer, Masaki, Petrovitch, Foley, & Havlik, 1995) and diabetes (Censori et al., 1996), are associated with cognitive decline. Similarly, stroke-related factors such as silent
infarcts, stroke recurrence, and multiple lesions and stroke severity have also been linked to post-stroke cognition (Leys et al., 2005; Pendlebury & Rothwell, 2009). Given that multiple strokes increase the absolute rate of dementia, stroke-related factors may add to vascular risk factors to precipitate cognitive impairment (Pendlebury & Rothwell, 2009). Similarly, interactions between post-stroke neuroinflammation and amyloid beta could potentially explain cognitive decline in stroke patients (Thiel, Cechetto, Heiss, Hachinski, & Whitehead, 2014). The exact underlying pathology of post-stroke cognitive impairment is currently unclear and remains an area of active research (Gorelick et al., 2011).

Identifying and treating those with post-stroke cognitive impairment is crucial (Eskes et al., 2015; Canadian Stroke Best Practice Recommendations). Management of vascular factors, efficient acute stroke care and other stroke prevention strategies may all play a significant role in tackling cognitive impairment. However, aggressive management is only possible if patients at-risk are promptly identified. Unfortunately, detecting cognitive impairment in stroke patients is challenging, primarily due to the lack of quick cognitive screens that can be implemented in high-volume urgent stroke clinics (Swartz et al., 2016b; see 3.4.2). A potential solution is to reduce screening time by specifically assessing cognitive domains that are susceptible to decline after stroke (Swartz et al., 2016b). Although stroke can affect perception, language and memory, it has the greatest impact on attention and executive function and results in slowed information processing (Cumming, Marshall, & Lazar, 2013); memory and orientation deficits become more apparent in severe forms of VCI (i.e. vascular dementia; Stephens et al., 2004). Specifically evaluating vulnerable cognitive domains may allow detection of cognitive impairment in stroke clinics and facilitate risk stratification.

Cognitive impairment is also a covert post-stroke comorbidity and may not be identified based purely on behavioural changes. Thus, the current lack of appropriate tools combined with the latent nature of this condition may lead to low detection and treatment (Swartz et al., 2016b), and subsequently, result poor long-term functioning or progression to severe VCI.

Like depression, cognitive impairment has been associated with dysfunction on multiple levels. Cognition impairment at admission to rehabilitation unit is associated with limited functional gains, in terms of activity, at discharge (Heruti et al., 2002), with higher-order cognitive impairments (e.g. judgement, abstract thinking) being especially important in
increasing length of stay and functional status (Galski, Bruno, Zorowitz, & Walker, 1993). After accounting for age and activity limitations, cognitive impairment is associated with dependent living (i.e. nursing home or at home care) following hospital discharge (Tatemichi et al., 1994). Cognitive impairment at 3 months has also been found to be associated with basic as well as instrumental ADL limitations at 3 and 4 years, after controlling for age and indicators of stroke severity but not post-stroke activity limitations (Patel, Coshall, Rudd, & Wolfe, 2002). On the contrary, Mok et al., (2004) found that in patients with stroke associated with small vessel disease (SSVD), cognitive impairment was only associated with instrumental ADLs but not basic ADLs at 3 months, after controlling for age, stroke severity and other factors. Zinn et al. (2004) reported similar results—cognitive impairment restricted instrumental ADL recovery but not basic ADL recovery. Nonetheless, stroke patients with executive dysfunction at 3 months perform poorly on basic and instrument ADL measures and are more depressed than those with no executive dysfunction (Pohjasvaara et al., 2002), and sustained attention capacity at 2 months correlates with basic activity limitations at 2 years (Robertson, Ridgeway, Greenfield, & Parr, 1997).

Cognition and depression appear to be related after stroke, but the mechanism of this relationship and how it affects functioning is unclear. Attention and executive function are both impaired in non-stroke depressed patients (Mialet, Pope, & Yurgelun-Todd, 1996; Degl’Innocenti et al., 1998) and both these cognitive functions are especially impaired in stroke patients (Cummings et al., 2013). Cognitive impairments are also more frequent in depressed stroke patients at 12 months, with memory, nonverbal problem solving and attention and psychomotor speed being most affected (Kauhanen et al., 1999). Long-term decline in depression and cognition are both correlated with dependent living at 15 months post-stroke (Pohjasvaara et al., 2002). Melkas et al. (2010) found that stroke patients with concurrent depression and executive dysfunction (Depressive-executive dysfunction syndrome or DES) had poor survival up to 12 years compared to those with no depression or executive dysfunction. Executive functions and depression are both associated with rehabilitation participation, with executive functions being a significant predictor even after accounting for baseline disability (Skidmore et al., 2010). Similarly, Saxena, Ng, Koh, Yong and Fong (2007) established that limitations in ADLs at 6 months are predicted by cognitive impairments, after controlling for stroke severity, but not by depression. However, depression appears to affect rate of functional
recovery (Saxena et al., 2007). The authors argue that while improving depressive symptoms may facilitate faster recovery, the eventual level of activity is limited by cognitive impairment and stroke severity.

Data on the impact of cognitive impairment on participation after stroke is limited. Viscogliosi et al. (2011) observed that the presence of cognitive deficits appears to impair participation, but may not necessarily impede improvements in participation restrictions over 6 months. After accounting age, depression and stroke severity, information processing speed and visuoperceptual/construction are associated with participation restrictions and visual memory with activity limitations at 5 years (Barker-Collo et al., 2012). However, the ability of short-term cognitive impairment to predict long-term functioning in terms of participation restrictions has not been examined.

1.6.5 Social Factors

Social factors such as support and socioeconomic status may also be crucial factors that indirectly affect functional outcome. Larger social networks are associated with fewer ADL limitations 6 weeks after hospital discharge, after controlling for sociodemographic factors and health-related factors such as stroke severity and post-stroke complications (Colantonio, Kasl, Ostfeld, & Berkman, 1993). Social support is also associated with faster ADL recovery (Glass, Matchar, Belyea, & Feussner, 1993). A meta-ethnography exploring stroke and social support found that stroke survivors perceived disability, fatigue, lost activities, internal barriers and stigma as causes of reduced participation. Factors that facilitated social participation included support from family, nature of pre-stroke friendships and attitude of stroke survivor (Northcott, Moss, Harrison, & Hilari, 2015). A systematic review of qualitative studies demonstrated a significant association between low functional social support and depression post-stroke but most studies found no significant association between functional social support and concurrent ADL (Northcott et al., 2015). Living alone is associated with depression immediately after stroke and Astrom et al. (1993) argue that “under the stressful condition of an acute stroke, being without the social support of a family seems to promote the development of depression” (p. 981). Education also appears to play a role; at 3 months, those with a college or university degree are more likelihood to have a good ADL outcome compared to those with no completed education (Grube et al., 2012). Nunnari, Bramanti and Marino (2014) even suggest that education may
serve as ‘cognitive reserve’ and provide resilience to cognitive deficits after stroke. Social support and education may influence long-term functioning through their association with depression and cognition.
### Summary of Literature

<table>
<thead>
<tr>
<th>Factor</th>
<th>Outcome</th>
<th>Time Points</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Body Function</td>
<td>2-Month</td>
<td>Meyer et al., 2015</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6-Month</td>
<td></td>
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<td></td>
<td></td>
<td>5-Year</td>
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<tr>
<td></td>
<td>Activity</td>
<td>2-Month</td>
<td>Meyer et al., 2015</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3-Month</td>
<td>Knoflach et al., 2012</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6-Month</td>
<td>Meyer et al., 2015</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1-Year</td>
<td>Kotila et al., 1964</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5-Year</td>
<td>Meyer et al., 2015</td>
</tr>
<tr>
<td>Participation</td>
<td></td>
<td>2-Year</td>
<td>Sturm et al., 2004</td>
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<tr>
<td>Stroke Severity</td>
<td>Body Function</td>
<td>2-Month</td>
<td>Meyer et al., 2015</td>
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<td></td>
<td></td>
<td>6-Month</td>
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<tr>
<td></td>
<td></td>
<td>5-Year</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Activity</td>
<td>2-Month</td>
<td>Meyer et al., 2015</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3-Month</td>
<td>Weimar et al., 2002</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6-Month</td>
<td>Kwakkel et al., 2010</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5-Year</td>
<td>Meyer et al., 2015</td>
</tr>
<tr>
<td></td>
<td>Participation</td>
<td>2-Year</td>
<td>D’Alisa et al., 2005</td>
</tr>
<tr>
<td>Baseline Activity</td>
<td>Activity</td>
<td>3-Month</td>
<td>Weimar et al., 2002</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4-Year</td>
<td>Kissela et al., 2009</td>
</tr>
<tr>
<td></td>
<td>Participation</td>
<td>2-Year</td>
<td>D’Alisa et al., 2005</td>
</tr>
<tr>
<td>Depressive Symptoms</td>
<td>Activity</td>
<td>3-Month</td>
<td>Herrmann et al., 1998</td>
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<td></td>
<td></td>
<td>1-Year</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>2-Year</td>
<td>Parikh et al., 1990</td>
</tr>
<tr>
<td></td>
<td>Participation</td>
<td>6-Month</td>
<td>Feibel &amp; Springer, 1982</td>
</tr>
<tr>
<td>Obstructive Sleep Apnea Symptoms</td>
<td>Activity</td>
<td>3-Month</td>
<td>Yan-fang &amp; Yu-ping, 2008</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6-Month</td>
<td>Turkington et al., 2004</td>
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<td></td>
<td>12-Month</td>
<td>Good et al., 1996</td>
</tr>
<tr>
<td>Cognitive Impairment</td>
<td>Activity</td>
<td>3-Month</td>
<td>Mok et al., (2004)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6-Month</td>
<td>Saxena et al. (2007)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 Years</td>
<td>Robertson et al., 1997</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3-4 Year</td>
<td>Patel et al., 2002</td>
</tr>
<tr>
<td></td>
<td>Participation</td>
<td>5-Year</td>
<td>Barker-Collo et al., 2012</td>
</tr>
</tbody>
</table>

**Table 1.1 Previously Reported Associations between Predictors and Outcome**

Summary of previously established associations and correlations between age, stroke severity, depressive symptoms, OSA symptoms, cognitive impairment and the three primary levels of human functioning and the time points at which these associations have been observed.
Literature To Date

In spite of WHO guidelines that define function as extending beyond physical disability, our understanding of post-stroke function is still limited to ADLs. Few studies have explored restriction in participation, such as inability to reintegrate into society, as an outcome. Post-stroke prevalence and predictors of participation and to some extent, of body function and activity, remain unknown. Similarly, studies on long-term outcome after stroke are scarce. Short-term outcomes, especially up to 90 days, have been studied extensively, with numerous studies elucidating the impairments and limitations that occur during the period. However, long-term outcomes and its predictors have been overlooked.

Although functional status may remain stable for some time after a stroke, it appears to decline in the long-term. This decline may be a consequence of post-stroke comorbidities, which are often not included in prognostic models of functional outcome. Stroke severity and age are established predictors of post-stroke activity limitations but these non-modifiable factors are unable to explain all of the variability in outcomes and whether they significantly predict functioning in complex domains such as social reintegration, especially in the long-term, is unknown. Depression, cognitive impairment and sleep apnea are common post-stroke conditions that have all been associated with poor functional outcome in multiple domains of functioning. However, the independent impact of these concomitant conditions on body function, activities and participation years after a stroke has yet to be explored.

The following gaps in the literature remain: (1) The full range of functional difficulties caused by a stroke is not well understood, (2) long-term functioning after a stroke is currently not well-studied, and (3) Few studies have explored the impact of post-stroke depression, cognitive impairment and sleep apnea on multiple domains of functioning and the predictive value of these variables in a comprehensive prognostic model.
Chapter 2
Research Aims and Hypotheses

2.1 Aims

This current study aimed to determine post-stroke predictors of all the 3 levels of functioning 2 years after a stroke, and to specifically evaluate the impact of depressive symptoms, OSA and cognitive impairment, while accounting for established predictors, on long-term body function, activity and participation.

2.2 Predictors of Functional Outcome

2.2.1 Hypothesis 1: Traditional Predictors of Functional Outcome

We hypothesized that established predictors, namely age and short-term activity limitations, will be predictive of the activity, body function and participation levels of functioning. Specifically, greater age and activity limitations would be associated with greater dysfunction on all levels of functioning.

2.2.2 Hypothesis 2: Depression, Obstructive Sleep Apnea and Cognitive Impairment (DOC) Conditions as Predictors of Functional Outcome

Based on current evidence, we hypothesized that baseline depressive symptoms, OSA and cognitive impairment would increase the predicative power of traditional models of outcome which include age and stroke severity/baseline activity.

2.2.2.1 Predictions

Based on prior associations (Table 1.1), we anticipated that (1) greater baseline depressive symptoms will predict long-term activity limitations and participation restrictions but not body function impairments in terms of cognition, (2) greater baseline apnea symptoms will predict greater activity limitations and, (3) poor baseline cognition will predict long-term activity limitations, participation restrictions as well as long-term body function in terms of cognition.
2.3 Function Beyond Activity

2.3.1 Outcome in Physically Stable Patients

Given that previous studies suggest a greater prevalence of participation restrictions than activity limitations in the stroke survivors, we hypothesized that patients who achieved a good outcome in terms of activity (mRS score ≥ 2) will exhibit dysfunction on the participation and body function level.

2.4 A Priori Exploratory Analysis

2.4.1 Frequency of Depression, OSA & Cognitive Impairment Treatment

We anticipated a low treatment rate, given prior reports of under-assessment and under-treatment of these conditions after stroke.

2.4.2 Associations at Baseline and Follow-Up

We hypothesized a weak to moderate correlation between baseline depression and cognitive impairment as well as sleep apnea and cognitive impairment. Additionally, we predicted that follow-up outcomes will be weakly correlated, given the modest overlap between function at the activity, body function and participation levels.
Chapter 3

Methods

3.1 Ethics Approval

This study was approved by the Research Ethics Board of Sunnybrook Health Sciences Centre which operates in compliance with the Tri-Council Policy Statement 2nd edition and ICH GCP Guidelines.

3.2 Study Design

This was a longitudinal study that entailed a baseline and follow-up assessment. The baseline screen was conducted during the first outpatient clinic visit within 6 months of stroke and the follow-up functional outcome assessment was conducted via telephone at 2 years and 3 months (±6 months) after the clinic visit. Functional recovery stabilizes by 1.5 years, even in severe stroke patients, and is typically maintained between 1.5 and 3 years (Katz et al. 1966; Skilbeck et al., 1983; Teasell & Hussein, 2013), thus the current study only included patients who could be contacted between 1.75 years - 2.75 years from their first visit. The value of baseline patient characteristics and comorbidity risk (independent variables) in predicting long-term functioning (dependent variables) was evaluated using logistic and linear regression analyses and variables predicting poor outcome were identified.

3.3 Patient Population

3.3.1 Patient Selection: Exclusion & Inclusion Criteria

All patients were recruited from the Sunnybrook Stroke Prevention Clinic patient database. The database includes 1504 (See Figure 3.1) consecutive patients referred to the stroke prevention clinic with either stroke or TIA as the referral reason. This database excludes patients with severe aphasia, severe motor dysfunction and non-fluent English, who would be unable to complete a depression, cognition or OSA screen. The same exclusion criteria applied to the present study.

This study was also restricted to those patients who received a definite diagnosis of stroke by a neurologist (N=413). Neuroimaging (CT or MRI) and clinical evidence were both
Figure 3.1: Patient Selection Process

Sunnybrook Stroke Prevention Clinic Patient Database
1504

Patients with Stroke
413

Initial Visit within 6 Months of Stroke
293

Eligible Patients
270

Enrolled
162

Initial Visit beyond 6 Months Post-Stroke
120

Beyond Follow-up Window
23

64 Declined to Participate
44 Lost to Follow-Up
considered in determining diagnosis. Each patient’s medical records were reviewed to confirm a diagnosis of stroke. Both ischemic and hemorrhagic stroke patients were included, based on evidence from a recent long-term study indicating similar long-outcomes for both patient populations (Meyer et al., 2015).

Only patients who visited the clinic within 6 months of their stroke (N=293) were included in this study, allowing us to capture depression, cognitive impairment and OSA when they are most prevalent in the stroke population and limiting acute stroke influences such as medical instability. Twenty three patients could not be contacted within our predetermined follow-up window of 2 years and 3 months (± 6 months) and thus, were excluded from this study. A total of 270 patients were eligible to participate in our study.

3.3.2 Sample Size Calculation and Power Estimates

A sample size calculation for our primary outcome (see 3.5.2) was conducted prior to enrolment (See Figure 3.2). We conservatively estimated that we would lose 10% of patients to follow-up and 30% would decline to participate, leaving us with a projected enrollment of 162 patients. As suggested by Peduzzi, Concato, Kemper, Holford, and Feinstein (1996), the number of independent variables and the proportion of negative or positive cases were both taken into account when determining the ideal sample size for our logistic regression model. Considering previous literature (Mayo et al., 2002; Patel et al., 2006; Wilkinson et al., 1997) and population characteristics (i.e. stable post-stroke patients seen in a stroke prevention clinic), we initially anticipated that approximately 40% of patients will have poor outcome. We estimated that we should be able to include 6 variables into our model with sufficient power even if we only enrolled 150 patients.

3.4 Baseline Visit

Initial clinic visits occurred between April 2012 and April 2014. For all patients, baseline demographics, medical history (including stroke risk factors), stroke characteristics and functional assessment scores were abstracted from patient charts. All patients attending clinic were screened for depression, obstructive sleep apnea and cognitive impairment using an integrated screen (DOC screen; Appendix B; www.do screen.ca).
Figure 3.2: Sample Size Calculation

\[ N = 10 \frac{k}{p} \]

\[ k = \text{number of independent variables} \]

\[ p = \text{proportion of negative or positive cases} \]

Anticipated proportion negative cases: 40%
Maximum anticipated variables in model: 6

\[ N = 10 \frac{6}{0.4} \]

\[ N = 150 \]
3.4.1 Chart Abstraction

Patient demographics abstracted from charts included medical record number, gender, date of birth, years of education, height, weight and place of residence. Additionally, systolic and diastolic blood pressure, stroke date, stroke type as well as presence of hypertension, diabetes, cardiac disease and smoker status were also abstracted when available. Functional assessments were done during the clinic using the modified Rankin Scale (mRS), which was also used as a proxy for stroke severity in our prognostic models; these scores were also abstracted. All independent variables were defined as noted in Table 3.1.

3.4.1.1 Modified Rankin Scale

The modified Rankin scale mRS is a 6-point measure of global functioning which assesses the extent of activity limitations, specifically ADLs, after a stroke (Bonita & Beaglehole, 1988; Rankin, 1957). MRS scores range from 0 (no symptoms) to 6 (death) with a score of 5 representing severe disability (i.e. patient requires constant nursing care and attention). This scale accounts for level of functioning prior to stroke and is the most versatile of all outcome measures. Although it is primarily a measure of basic ADLs and focuses on mobility, it could be utilized to gauge instrumental ADLs (Weisscher, Vermeulen, Roos, & De Haan, 2008) and may be able to capture some participation restrictions. MRS is a valid tool (Banks & Marotta, 2007; however its reliability is often challenged due to its subjective nature (Wolfe, Taub, Woodrow, & Burney, 1991; Quinn et al., 2009). Using a structured interview may improve inter-rater reliability (Wilson et al., 2002; Banks & Marotta, 2007). Bruno et al. (2010) developed a simplified mRS questionnaire with good inter-rater reliability (78% agreement), similar to that of a structured interview, that can be administered in person and over the telephone with excellent reliability (82% agreement).

3.4.2 Depression, OSA & Cognition Screening

Risk of depression, OSA and cognitive impairment was evaluated for all patients using an integrated screen (DOC screen; docscreener.ca) which includes the Patient Health Questionnaire-2 for depression (Hajek, Rutman, & Scher, 1989), the STOP questionnaire for OSA, (Chung et al., 2008, 2012) and 10 items from the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005).
Table 3.1: Definition of Independent Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Education</td>
<td>Years of formal education (total of highest grade, undergraduate years and graduate years)</td>
</tr>
<tr>
<td>Initial/Baseline Stroke Severity</td>
<td>Patient's level of activity limitations, measured by mRS, within 6 months of stroke</td>
</tr>
<tr>
<td></td>
<td>0= No Symptoms</td>
</tr>
<tr>
<td></td>
<td>1= No Significant Disability</td>
</tr>
<tr>
<td></td>
<td>2= Slight Disability</td>
</tr>
<tr>
<td></td>
<td>3= Moderate Disability</td>
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<tr>
<td></td>
<td>4= Moderately Severe Disability</td>
</tr>
<tr>
<td></td>
<td>5= Severe Disability</td>
</tr>
<tr>
<td></td>
<td>6= Death</td>
</tr>
<tr>
<td>Age</td>
<td>Patient age at first clinic visit after stroke</td>
</tr>
<tr>
<td>Depression Risk (Baseline Depressive Symptoms)</td>
<td>DOC Mood Score</td>
</tr>
<tr>
<td></td>
<td>Patient's PHQ-2 score, with 0 indicating no symptoms and 6 indicating the following symptoms of depression nearly every day:</td>
</tr>
<tr>
<td></td>
<td>1) Loss of interest or pleasure in doing things (rated 0-3)</td>
</tr>
<tr>
<td></td>
<td>2) Feeling down, depressed or hopeless (rated 0-3)</td>
</tr>
<tr>
<td>Obstructive Sleep Apnea Risk (Baseline Apnea Symptoms)</td>
<td>DOC Apnea Score</td>
</tr>
<tr>
<td></td>
<td>Patient's STOP questionnaire score, calculated out of 4, based on presence or absence of the following apnea symptoms:</td>
</tr>
<tr>
<td></td>
<td>S= Snoring</td>
</tr>
<tr>
<td></td>
<td>T= Tiredness</td>
</tr>
<tr>
<td></td>
<td>O= Observed breathing cessation during sleep</td>
</tr>
<tr>
<td></td>
<td>P= Blood pressure treatment</td>
</tr>
<tr>
<td>Cognitive Impairment Risk (Baseline Cognition)</td>
<td>DOC Cog Score</td>
</tr>
<tr>
<td></td>
<td>Patient's total score, out of 10 (higher score indicating better cognition), on the following MoCA components:</td>
</tr>
<tr>
<td></td>
<td>Executive (Clock drawing; 3 points)</td>
</tr>
<tr>
<td></td>
<td>Abstraction (2 points)</td>
</tr>
<tr>
<td></td>
<td>Memory (5 points)</td>
</tr>
</tbody>
</table>
3.4.2.1 DOC Screen

The DOC screen is an integrated, evidence-based tool that allows quick identification and stratification of stroke patients at risk of depression, OSA and cognitive impairment in high-volume stroke clinics (Swartz et al., 2016b; docscren.ca). The three components of the screen are labeled DOCMood, DOCApnea and DOCCog respectively.

**DOC Mood (PHQ-2)**

The PHQ-2 is 2 item scale that assesses depression severity (Kroenke, Spitzer, & Williams, 2003). It evaluates the frequency of depressive symptoms on a range from 0 (i.e. not at all) to 3 (i.e. nearly every day). A total score of 6 is possible. Raw scores on the DOCMood can be stratified as follows: high risk (score of 4), intermediate risk (1-3) and low risk (0).

**DOC Apnea (STOP Questionnaire)**

The STOP questionnaire is screen for OSA (Chung e al., 2008). It includes 4 items which evaluate the presence of snoring, tiredness, observation of breathing cessation during sleep and high blood pressure. Each item is scored as yes or no. A total score of 4 is possible. DOC Apnea scores can be categorized as low (score of 0), intermediate (1-3) and high (4).

**DOC Cog (MoCA Components)**

DOC Cog consists of the memory, executive function (i.e. clock drawing) and abstraction components of the MoCA (Nasreddine et al., 2005). The memory component involves recall of 5 words and is scored out of 5. Clock drawing involves accurately drawing the contour, numbers and hands of a clock and is scored out of 3. The abstraction component entails recognition of similarities between two objects and is scored out of 2. A total score of 10 is possible, with higher score indicating less impairment. DOC Cog scores can be categorized as low (score of 10), intermediate (6-9) and high (0-5) risk.

The DOC screen is feasible in high-volume stroke clinics–89% of patients can be screened in ≤ 6 minutes. DOC Cog is able to predict impairment on a full battery cognitive assessment (i.e. ≥ 2 SD or < 5 scaled score on two or more subtests) with 83% sensitivity and 59% specificity, which is comparable to the ability of MoCA to predict cognitive impairment.
DOC Mood is able to predict impairment on the Structured Clinical Interview for DSM-IV (i.e. meeting criteria for minor or major depression) with 76.7% sensitivity and 87.3% specificity. DOC Apnea is able to predict impairment on a polysomnogram (i.e. AHI $\geq 15$) with 59.1% sensitivity and 66% specificity. Stratification of DOC scores into high, intermediate and low risk further improves the sensitivity and specificity of the screen and accounting for age, sex, education and BMI enhances risk assessment.

After accounting for age, sex and education, DOC Mood and DOC Cog can classify patients at high risk with 92% and 100% sensitivity respectively, and those with low risk with 99% and 95% specificity respectively. DOC Apnea can classify those with high risk with 90% sensitivity and 96% specificity after accounting for BMI, age and sex. Therefore, the DOC screen is a valid tool to identify patients at risk of high, intermediate or low risk of the DOC conditions.
3.5 Follow-Up Assessment

Follow-up telephone assessments were conducted between February 2015 and February 2016. All eligible stroke patients (N=270) were notified by mail of the study and then contacted by telephone for follow-up assessments between 1.75 years and 2.75 years from their visit. Based on the WHO International Classification of Functioning, Disability and Health Framework (ICF:WHO, 2002), we selected at least one outcome measure to evaluate each level of functioning. The follow-up outcome assessment also included questions regarding current self-perceived health, medical events and personal life events since the stroke as well as current treatments for depression, OSA and cognitive impairment. Our primary outcome was global functioning as assessed by the modified Rankin Scale.

3.5.1 Initial Contact

All eligible stroke patients were initially contacted via mail 2 to 4 weeks before they were contacted by telephone. An information letter (Appendix C) outlining the purpose, details, risks and benefits of the study was mailed to each patient. The letter also notified patients that they will be contacted within the next few weeks, that the telephone interview will require 15 to 20 minutes of their time and that they can choose to contact us if they would like to have their name removed for our contact list. A statement regarding privacy and confidentiality was included. Patients were informed that their participation was voluntary, and that there are no benefits to participating in the study. Informed consent was also obtained over the phone before the telephone interview was conducted. If a patient was unable to complete the assessment autonomously and a caregiver was available and willing to participate, a proxy assessment was conducted for the primary outcome. In order to maintain consistency, a verbal telephone script was also devised for the interview (see Appendix D).

3.5.2 Outcome Measures

We selected at least one outcome measure to evaluate each level of functioning. Outcomes had to have robust psychometric validity, be brief enough to administer as part of a larger battery and be amenable to telephone administration. Based on the Evidence-Based Review of Stroke Rehabilitation, 45 scales were evaluated for inclusion in the assessment (See Figure 3.3). Twenty five measures could not be conducted over a telephone and were eliminated
Based on the Evidence-Based Review of Stroke Rehabilitation, 45 scales were evaluated for inclusion in the assessment. Outcomes measures had to have robust psychometric validity, be brief enough to administer as part of a larger battery and be amenable to telephone administration. Based on these criteria, 4 measures which were included in the follow-up assessment.
because they required observational assessment. Another 6 were eliminated because they
assessed more than one domain of functioning, making it difficult to study each domain
individually. Six were eliminated due to overlap with constructs already assessed by the DOC
screen at follow-up. Finally, 4 measures took longer than 20 minutes and thus, were eliminated
to avoid patient burden. This process yielded 4 outcome measures which were all included in the
follow-up outcome assessment (See Appendix E; See Figure 3.4): Body function (impairment)
was assessed using the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005), while
activity (limitations) was assessed using the modified Rankin Scale (mRS; Rankin, 1957) and
Frenchay Activities Index (FAI; Wade et al., 1985) and participation (restrictions) were
evaluated using the Reintegration to Normal Living Index (RNLI; Wood-Dauphinee, Opzoomer,
Williams, Marchand, & Spitzer, 1988). All outcomes, except the FAI, were dichotomized as
poor or good based on suggested cut-off scores. No cut-offs have been recommended for the
FAI. Dependent variables (outcomes) were defined as noted in Table 3.2.

3.5.2.1 Primary Outcome- Modified Rankin Scale

See 3.4.1 for description. The mRS is most commonly used outcome in stroke literature
(McArthur et al., 2013). This scale was chosen as the primary outcome as it assesses global
functioning, accounts for pre-stroke level of functioning and allows inclusion of deceased
patients. There is currently little consensus on the ideal cut-off for mRS scores, however 0-1 and
0-2 are typically defined as good outcome (Weisscher et al., 2008). We chose to define poor
outcome as a score $\geq 2$ for three reasons: (1) it is estimated to be more powerful than cut-offs at
higher scores (Banks & Marotta, 2007), (2) it clinically signifies a change in ability to perform
activities due to stroke, and (3) to avoid ceiling effects and detect subtle changes in our mild and
moderate stroke population. Given that this is a long-term study, we anticipated attrition and
survivorship bias and we expected that our data may be skewed. Accordingly, mRS scores were
dichotomized, as opposed to analyzed continuously, to detect differences in outcome if they
exist.

3.5.2.2 Secondary Outcomes

3.5.2.2.1 Montreal Cognitive Assessment

The MoCA is a commonly used, quick and comprehensive cognitive screening tool. Since the
follow-up was conducted by telephone, we used the Blind MoCA, which excluded visual
Figure 3.4: Outcome Measures Selected & Corresponding Level of Functioning

<table>
<thead>
<tr>
<th>Level of Functioning</th>
<th>Outcome Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activity</td>
<td>Modified Rankin Scale (mRS; Global Functioning/Basic ADLs)</td>
</tr>
<tr>
<td>Activity</td>
<td>Frenchay Activities Index (Instrumental ADLs)</td>
</tr>
<tr>
<td>Body Function</td>
<td>Montreal Cognitive Assessment (Cognition)</td>
</tr>
<tr>
<td>Participation</td>
<td>Reintegration to Normal Living Index (Social Reintegration)</td>
</tr>
</tbody>
</table>
Table 3.2: Definition of Dependent Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Definition</th>
</tr>
</thead>
</table>
| Activity Limitations (Basic ADLs)| Patient’s follow-up mRS at 2-3 years post-stroke  
MRS score ≥ 2: poor outcome; presence of disability; inability to return to pre-stroke level of function; limitation in basic ADL function; impaired global function |
| Activity Limitations (Instrumental ADLs) | Patient’s FAI score at 2-3 years post-stroke on total scale from 0 to 45, with greater score indicating higher level of involvement in instrumental activities. |
| Body Function (Cognition)       | Patient’s MoCA score (memory, attention, language, abstraction, orientation) at 2-3 years post-stroke  
MoCA score < 26: poor outcome; cognitive impairment; impairment in body function |
| Participation (Reintegration)    | Patient’s RNLI score at 2-3 years post-stroke  
RNLI score > 0: poor outcome; difficulties in social reintegration; restrictions in participation |
elements, but is still a feasible and valid test of cognition after stroke (Pendlebury et al., 2013). This version includes memory, attention, language, abstraction and orientation tasks and excludes the visuospatial/executive and naming tasks. A total score out of 22 is computed and then converted back to 30, with higher scores indicating better cognition function. Although numerous different cutoff scores have been recommended for a stroke population, we chose to use the original cut-off of 26 or greater to signify normal function (i.e. favorable outcome). This cut-off captures mild cognitive impairment with 90% sensitivity and 87% specificity (Nasreddine et al., 2005).

3.5.2.2.2 Frenchay Activities Index

The Frenchay Activities Index (FAI; Wade et al., 1985) evaluates instrumental activities of daily living. Unlike basic ADLs, these are tasks that are not essential self-care tasks but activities that are often necessary in day-to-day life, such as driving and housework. The FAI assesses frequency of involvement in 3 types of activities over the past 3 or 6 months: domestic, leisure/work and outdoor activity. Level or frequency of each activity is scored on a scale from 0-3 and total score out of 45 is computed based on 15 activities. Higher scores on the FAI indicate a high level of activity in instrumental tasks. There are currently no established cut-off scores to determine poor outcome on this index; FAI scores were analyzed as a continuous variable. Although the reliability and validity of this scale has not been extensively studied, preliminary data suggests that the FAI is valid and reliable tool in a population of stroke patients (Schuling, de Haan, Limburg, & Groenier, 1993; Piercy, Carter, Mant, & Wade, 2000).

3.5.2.2.3 Reintegration to Normal Living Index

The Reintegration to Normal Living Index (RNLI; Wood-Dauphinee et al., 1988) assesses how well patients are able to assimilate back into their environment and serves as an indicator of socialization. There are numerous scoring systems for the RNLI, including the visual analog scale (VAS) for in-person assessment and the agree/disagree response format for the postal version. We chose to use the 3-point scoring system that has been validated for telephone use (Korner-Bitensky, Wood-Dauphinee, Siemiatycki, Shapiro, & Becker, 1994). The RNLI includes 11 declarative statements that are each scored on a scale from 0 to 2, yielding a total score out of 22. The patient reports the extent to which each statement describes their situation. Higher scores indicate poor reintegration and higher restrictions in a social context. Although
cut-off scores are not well established, a classification system has been suggested; Korner-Bitensky et al. (1994) propose transforming the score out of 22 to a score out of 100 and the applying the following classification: no disability (score of 0), mild to moderate disability (score of 1 to 50), and severe disability (score greater than 50). We chose to define poor outcome based on this definition, with a score greater than 0 indicating some restrictions in being able to reintegrate into society. Preliminary data suggests that the RNLI is valid and reliable tool in a community-dwelling population (Miller, Clemson, & Lannin, 2011a), however the reliability and validity of the 3-point scoring system, especially in a stroke population, has not been determined.

3.5.2.2.4 STOP Questionnaire & PHQ-2

Sleep apnea and depression symptoms were evaluated at follow-up using the DOCApnea and DOCMood components of the DOC screen, similar to baseline assessment. See 3.4.2.

3.5.3 Supplementary Measures

In addition to outcome measures, the follow-up also included questions regarding current self-perceived health, medical events and personal life events since the stroke as well as treatments for depression, OSA and cognitive impairment. Patients were asked to rate their self-perceived current overall health on scale from 1 to 10. Similar to Pettersen et al. (2002), they were also asked to indicate whether they believe their or their family’s activity is limited by any health condition(s). Patients were also asked to report any major life events since their stroke and whether they experienced a recurrent stroke, TIA, sudden painless weakness, loss of vision or heart attack since their stroke 2 years ago. In addition to this, patients were asked whether they received any treatments for depression, sleep apnea or cognitive impairment after their stroke. Examples were provided (e.g. talking therapy or antidepressants for depression, continuous positive airway pressure or positional therapy for sleep apnea, and cholinesterase inhibitors for cognitive impairment). Finally, in order to determine baseline functioning, patients were asked whether they were able to drive before their stroke and whether they were employed before their stroke. The follow-up assessment was designed to be completed in 15 to 20 minutes and to involve minimal patient burden.

3.6 Statistical Analyses

All analyses were performed using IBM SPSS Statistics 22.
3.6.1 Descriptive Statistics

Descriptive statistics were run to characterize the study population at baseline and follow-up. Normality was tested using the Shapiro-Wilk test. Demographic characteristics of patients who were lost to follow-up and those who declined to participate were compared to those enrolled using a one-way ANOVA or Kruskal-Wallis test. Specifically, age, education, baseline mRS as well as baseline risk of depression, OSA and cognitive impairment were compared to rule out systematic differences.

3.6.2 Multicollinearity

Multicollinearity between independent variables was checked using Pearson’s correlation coefficients and tolerance statistics. A correlation coefficients of 0.6 or less and tolerance statistic greater than 0.4 were chosen as cut-offs to signify no multicollinearity. The following variables were checked: age, baseline mRS, education, DOCMood, DOCApnea and DOCCog.

3.6.3 Univariate Analyses

Univariate logistic regression analyses were first employed to determine the individual relationship between baseline data (independent variables) and follow-up outcomes (dependent variables). The relationship between the following independent variables and follow-up mRS was assessed: age, baseline mRS, DOCMood, DOCApnea and DOCCog. The relationship between the same independent variables and follow-up FAI scores was calculated. The relationship between follow-up MoCA scores and the following variables was assessed: age, baseline mRS, education, DOCCog. Finally, the association between RNLI scores and age, baseline mRS, DOCMood and DOCCog was evaluated. Raw DOC scores were used for all univariate and multivariate analyses. Alpha was set at 0.05.

3.6.4 Multivariate Analyses

Multivariate logistic and linear regression analyses were run to determine significant independent baseline predictors of outcomes. Variables were entered into the based on accepted theory, previous studies, and univariate analyses (Stoltzfus, 2011). Multivariable logistic regression models were fit to the primary outcome, dichotomized mRS score, using baseline characteristics such as age, stroke severity and risk of depression, OSA and cognitive impairment. Similar models were run for follow-up MoCA and RNLI, however different
variables were entered into the model based on previous literature. Age and stroke severity was included in all models. For MoCA, education and DOCCog were also entered as independent variables. For RNLI, DOCMood and DOCCog were entered. A linear regression model was run for FAI because scores could not be validly dichotomized; risk of all DOC conditions along with age and stroke severity were entered. Alpha was set at 0.05.

3.6.5 Sub-Analysis

In patients who had a good activity follow-up outcome on the mRS (score $\geq 2$), the frequency of cognitive impairment, participation restrictions, symptoms of depression and change in work-status was determined.

3.6.6 Exploratory Analyses

3.6.6.1 A Priori

Frequency of treatment for depression, OSA and cognitive impairment was determined. Pearson correlations were run to determine whether a correlation between treatment and outcomes existed. Associations within baseline variables and follow-up variables were explored.

3.6.6.2 Post-Hoc

Given the strong indication of a relationship between depression and poor social reintegration, we explored whether stratified baseline depression risk, using DOCMood scores, age, sex and education, combined with baseline mRS was able to predict follow-up RNLI scores using multivariate logistic regression analyses. Frequency of change in work and driving status was determined. Additionally, baseline and follow-up mRS scores for patients were compared using the Wilcoxon signed ranks test to explore whether a change in activity level had occurred in the long-term. The influence of sex differences, education, assessment time, stroke risk factors, stroke type and stroke recurrence on outcomes was explored. Lastly, the association between specific cognitive functions and outcomes was examined.
Chapter 4
Results

4.1 Descriptive Statistics

Of the 270 eligible patients, 43 (15.9%) were lost to follow-up, 65 (24.1%) declined and a total of 162 (60.0%) were enrolled (See Table 4.1). At baseline clinic visit, age of study participants ranged from 17 to 100 years (M= 61.0, SD=15.4), education ranged from 4 to 26 years (M=14.5, SD=4.0) and 90 (55.6%) were male. Most (92.4%) resided at home, 1.4% resided in a nursing home or long-term care, 2.1% were in an inpatient rehabilitation facility and 4.1 in a retirement home. At follow-up, 95.7% were at home, 0.7% at a nursing home, 0.7% at an inpatient rehabilitation facility, 2.1% at a retirement home and 0.7% at other residential facilities. Medical history (including baseline mRS, stroke type and stroke risk factors) was missing for 1 patient. For those with available data (n= 161), 90.7% had an ischemic stroke, 8.7% had an ICH and 0.6% had a SAH. Hypertension was present in 115 (71.4%) of patients, diabetes in 36 (22.4%) and cardiac disease (including atrial fibrillation) in 72 (44.7%). Smoker status could not be determined for 12 patients but for those with available data (n=150), 10% were current smokers. The average duration from stroke to initial visit was 83.0 days (SD=42.5) and ranged from 1 day to 178 days. The average time from initial visit to follow-up assessment was 812.2 days (SD=129.0)– approximately 2 years and 3 months– and ranged from 620 days (≈1 year and 8 months) to 1029 days (≈ 2 years and 10 months).

4.1.1 Lost to Follow-Up & Declined

The Kruskal-Wallis test, instead of a one-way ANOVA, was employed to compare those who were lost to follow-up (See Table 4.2), those who declined to participate and enrolled patients, given that age, baseline mRS, baseline DOCMood, DOCApnea and DOC Cog as well as education were all non-normally distributed in the lost to follow-up and declined groups (p < 0.05). For those in the enrolled group, all variables except education (p = 0.091) were non-normally distributed. There was no difference between the three groups in education (p=0.08), baseline mRS (p=0.12), baseline DOCMood (p=0.47), DOCApnea (p=0.41), and DOCCog (p=0.15). However, average age varied between the three groups (p=0.01), with the difference
<table>
<thead>
<tr>
<th>Table 4.1: Baseline &amp; Follow-Up Patient Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td><strong>Stroke Type</strong></td>
</tr>
<tr>
<td>Ischemic</td>
</tr>
<tr>
<td>ICH</td>
</tr>
<tr>
<td>SAH</td>
</tr>
<tr>
<td><strong>Risk Factors</strong></td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Diabetes</td>
</tr>
<tr>
<td>Cardiac Disease</td>
</tr>
<tr>
<td>Smoker Status</td>
</tr>
<tr>
<td><strong>Residence</strong></td>
</tr>
<tr>
<td>Home</td>
</tr>
<tr>
<td>Nursing Home/Long-Term Care</td>
</tr>
<tr>
<td>Inpatient Rehabilitation Facility</td>
</tr>
<tr>
<td>Retirement Home</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>Age, Mean (SD)</td>
</tr>
<tr>
<td>Education, Mean (SD)</td>
</tr>
<tr>
<td>Modified Rankin Score, Mean (SD)</td>
</tr>
<tr>
<td>Depression Risk (Adjusted)</td>
</tr>
<tr>
<td>Low</td>
</tr>
<tr>
<td>Intermediate</td>
</tr>
<tr>
<td>High</td>
</tr>
<tr>
<td>Obstructive Sleep Apnea Risk (Adjusted)</td>
</tr>
<tr>
<td>Low</td>
</tr>
<tr>
<td>Intermediate</td>
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<td>High</td>
</tr>
<tr>
<td>Cognitive Impairment Risk (Adjusted)</td>
</tr>
<tr>
<td>Low</td>
</tr>
<tr>
<td>Intermediate</td>
</tr>
<tr>
<td>High</td>
</tr>
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</table>
Table 4.2: Comparison of Lost to Follow-Up, Declined & Enrolled Patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>$\chi^2$ (Kruskal-Wallis Test Statistic)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>8.53</td>
<td>.014*</td>
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<tr>
<td><strong>Pairwise Comparisons</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lost to Follow-Up – Enrolled</td>
<td>$Mann$-$Whitney$ Test</td>
<td></td>
</tr>
<tr>
<td>Lost to Follow-Up – Declined</td>
<td>U= 25.0</td>
<td>.185</td>
</tr>
<tr>
<td>Enrolled – Declined</td>
<td>U= 44.7</td>
<td>.011*</td>
</tr>
<tr>
<td>Enrolled – Declined</td>
<td>U= -19.7</td>
<td>.257</td>
</tr>
<tr>
<td>Education</td>
<td>4.96</td>
<td>.084</td>
</tr>
<tr>
<td>Baseline mRS</td>
<td>4.30</td>
<td>.116</td>
</tr>
<tr>
<td>Baseline Depressive Symptoms</td>
<td>1.53</td>
<td>.467</td>
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<tr>
<td>Baseline Apnea Symptoms</td>
<td>1.76</td>
<td>.414</td>
</tr>
<tr>
<td>Baseline Cognition</td>
<td>3.78</td>
<td>.151</td>
</tr>
</tbody>
</table>
lying between those who were lost to follow-up and those who declined (p=0.01). There was no age difference between enrolled patients and lost to follow-up or declined patients.

4.1.2 Missing Data

Of the 162 patients, 20 had passed away (12%). Deceased patients were assigned a score of 6 on the mRS and a score of 0 on the RNLI, but they were excluded from all other analysis (i.e. MoCA, FAI, Follow-Up DOCMood and DOCApnea). Nine patients were unable to complete the assessment autonomously; consenting caregivers were asked to complete the mRS and other supplementary measures that could be objectively evaluated. Data were missing primarily due to patient unavailability to complete the entire interview (i.e. incomplete assessment), proxy assessment, and death. Missing data points were excluded from analyses for the MoCA, FAI, follow-up DOC Mood and follow-up DOC Apnea. Dichotomized RNLI outcome was abstract from mRS scores if a patient scored a 4 or higher on the mRS, indicating an inability to walk and poor outcome on the RNLI. MRS score was missing for one patient, however dichotomized outcome could be reliably determined based on RNLI score, change in work status and change in driving ability.

4.1.3 Multicollinearity

Age, baseline mRS, baseline DOC Mood, DOC Apnea, DOC Cog and education were all tested for multicollinearity. Using Pearson correlations, none of the variables were strongly correlated (r > 0.6; See Table 4.3). Collinearity statistics (i.e. tolerance and VIF) demonstrated the same results, with no tolerance statistics below 0.7 (See Table 4.4). No evidence of multicollinearity was observed.

4.1.4 Baseline & Follow-Up Activity Measures

At baseline, mRS scores (out of 6) ranged from 0 to 4 (M=1.5, SD=1.2; See Figure 4.1). Raw mRS scores were available for all but one patient at follow-up (n=161). Scores ranged from 0 to 6 (M=1.89, SD=1.87).
### Correlations

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>Initial mRS</th>
<th>Depression Risk</th>
<th>Apnea Risk</th>
<th>Cognition</th>
<th>Education</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>**</td>
<td>.169*</td>
<td>-.097</td>
<td>-.077</td>
<td>-.399**</td>
<td>-.151</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>1</td>
<td>.189*</td>
<td>.060</td>
<td>-.321**</td>
<td>-.090</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td>1</td>
<td>.176*</td>
<td>-.182*</td>
<td>-.065</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-.013</td>
<td>-.013</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>.313**</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>

* Correlation is significant at the 0.05 level (2-tailed).
** Correlation is significant at the 0.01 level (2-tailed).

**Table 4.3: Correlation between Independent Variables**

Age, baseline mRS, baseline DOC Mood, DOC Apnea, DOC Cog and education were all tested for multicollinearity. Using Pearson correlations, none of the variables were strongly correlated (r > 0.6).
<table>
<thead>
<tr>
<th>Comparison Variable</th>
<th>Tolerance</th>
<th>Variance Inflation Factor (VIF)</th>
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</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>mRS</td>
<td>.88</td>
<td>1.14</td>
</tr>
<tr>
<td>Depressive Symptoms</td>
<td>.92</td>
<td>1.09</td>
</tr>
<tr>
<td>Apnea Symptoms</td>
<td>.97</td>
<td>1.03</td>
</tr>
<tr>
<td>Cognition</td>
<td>.88</td>
<td>1.14</td>
</tr>
<tr>
<td>mRS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>.90</td>
<td>1.11</td>
</tr>
<tr>
<td>Depression Symptoms</td>
<td>.97</td>
<td>1.04</td>
</tr>
<tr>
<td>Apnea Symptoms</td>
<td>.78</td>
<td>1.28</td>
</tr>
<tr>
<td>Cognition</td>
<td>.80</td>
<td>1.25</td>
</tr>
<tr>
<td>Depressive Symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>.83</td>
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<tr>
<td>mRS</td>
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<td>Apnea Symptoms</td>
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<td>1.01</td>
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<tr>
<td>Cognition</td>
<td>.77</td>
<td>1.29</td>
</tr>
<tr>
<td>Apnea Symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>.80</td>
<td>1.25</td>
</tr>
<tr>
<td>mRS</td>
<td>.87</td>
<td>1.14</td>
</tr>
<tr>
<td>Depressive Symptoms</td>
<td>.90</td>
<td>1.11</td>
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<tr>
<td>Cognition</td>
<td>.74</td>
<td>1.35</td>
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<tr>
<td>Cognition</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>.95</td>
<td>1.06</td>
</tr>
<tr>
<td>mRS</td>
<td>.93</td>
<td>1.08</td>
</tr>
<tr>
<td>Depressive Symptoms</td>
<td>.92</td>
<td>1.09</td>
</tr>
<tr>
<td>Apnea Symptoms</td>
<td>.96</td>
<td>1.04</td>
</tr>
</tbody>
</table>

**Table 4.4: Multicollinearity between Independent Variables**

Collinearity statistics (i.e. tolerance and VIF) demonstrated no tolerance statistics below 0.7. No evidence of multicollinearity was observed.
Figure 4.1: Baseline and Follow-Up Modified Rankin Score Distribution
4.1.5 Baseline & Follow-Up DOC Risk

Raw DOCMood scores (out of 6) ranged from 0 to 6 ($M=1.1$, $SD=1.7$), DOCApnea scores (out of 4) from 0 to 4 ($M=1.7$, $SD=1.0$) and DOCCog (out of 10) from 0 to 10 ($M=7.4$, $SD=2.3$). When raw depression scores were combined with age, sex and education, 58.6% were at low risk of depression, 28.4% were at intermediate risk and 13% were at high risk of depression (See Figure 4.2). Raw apnea scores combined with age, sex and BMI yielded the following risk stratification: 14.2% at low risk, 76.5% at intermediate risk, 9.3% at high risk (Figure 4.3). When cognition scores were combined with age, sex and education, 24.1% were at low risk, 49.4% were at intermediate risk, and 26.5% were at high risk (Figure 4.4).

Follow-up DOC Mood (PHQ-2) scores (n=128) ranged from 0 to 6 ($M=0.8$, $SD=1.4$) and follow-up DOC Apnea (STOP Questionnaire) scores (n=114) ranged from 0 to 4 ($M=1.6$, $SD=0.9$). When raw DOC scores were combined with age, sex and education for DOCMood, 86 (67.2%) were at low depression risk, 32 (25.0%) at intermediate risk and 10 (7.8%) at high risk. DOCApnea scores combined with age, sex and BMI showed that 15 (13.2%) were at low risk, 88 (77.2%) at intermediate risk, and 11 (9.6%) at high risk.
Figure 4.2: Baseline and Follow-Up Depression Risk

DOC Mood scores combined with age, sex and education allow risk stratification into high, intermediate and low risk of depression.
Figure 4.3: Baseline and Follow-Up Obstructive Sleep Apnea Risk

DOC-Apnea scores combined with age, sex and BMI allow risk stratification into high, intermediate and low risk of obstructive sleep apnea.
Figure 4.4: Baseline and Follow-Up Cognitive Impairment Risk

DOC Cog scores combined with age, sex and education allow risk stratification into high, intermediate and low risk of cognitive impairment.
### 4.2 Primary Outcome (Modified Rankin Scale) Results

When dichotomized, 59.3% of patients had a favorable (0-1) and 40.7% had an unfavorable (2-6) outcome on the modified Rankin Scale. Univariate logistic regression analyses (See Table 4.5) showed that poor activity outcome was significantly predicted by greater age (OR = 0.95, 95% CI 0.93-0.98, \( p < .001 \)), higher baseline mRS (OR = 0.38, 95% CI 0.27-0.54, \( p < .001 \)) and lower DOC Cog scores (OR = 1.28, 95% CI 1.11-1.49, \( p = 0.001 \)) but not DOC Mood (OR = 0.89, 95% CI 0.74-1.07, \( p = .225 \)) or DOC Apnea (OR = 0.82, 95% CI 0.60-1.11, \( p = .193 \)). Age explained 14.2% (Nagelkerke \( R^2 \)) of the variance in mRS outcome, baseline mRS explained 28.3% and DOC Cog explained 9.6%.

Multivariate logistic regression analyses (See Table 4.5) were run to explore the influence of all variables–age, baseline mRS, DOC Mood, DOC Apnea and DOC Cog–on follow-up mRS. This model was statistically significant, \( \chi^2(5)=54.58, p < 0.001 \), explained 38.8% (Nagelkerke \( R^2 \)) of the variance in long-term outcomes and correctly classified outcome in 78.3% of patients. Age and baseline mRS were the only significant independent predictors of mRS outcome. A one point increase in age resulted in a 5% decrease in the likelihood of a good outcome and increasing baseline mRS was also associated with decreased odds (OR = 0.40) of good outcome at follow-up. Sensitivity and specificity were 86.3% and 66.7%, respectively (AUC: 810; See figure 4.5). A model including only age and baseline mRS explained 36.7% (Nagelkerke \( R^2 \)) of the variance in long-term outcomes (\( \chi^2(2)=51.10, p < 0.001 \)) and had similar sensitivity (84.2%) and specificity (66.7%; AUC: .806; See figure 4.6).

### 4.3 Secondary Outcomes Results

#### 4.3.1 Frenchay Activities Index (Instrumental Activity)

Scores on the FAI (out of 45) were available for 118 patients, ranging from 6 to 45 (M=27.1, SD=7.5). Linear univariate regression analyses were employed to determine the individual effect of age, baseline mRS, DOC Mood, DOC Apnea and DOC Cog on FAI score (see Table 4.6). The following variables significantly negatively affected outcome: greater age (\( \beta = -.13, 95\% \ CI [-0.22,-0.04], p = .006 \)), greater baseline mRS (\( \beta = -3.05, 95\% \ CI [-4.26,-1.84], p < .001 \)), greater DOC Mood (\( \beta = -1.09, 95\% \ CI [-1.95,-0.22], p = .014 \)) and lower DOC Cog (\( \beta = 1.45, 95\% \ CI [1.11,2.14], p = .001 \)).
Table 4.5: Univariate & Multivariate Analyses: Baseline Variables and Follow-Up Basic Activity (mRs)

Univariate logistic regression analyses showed that poor activity outcome was significantly predicted by greater age, higher baseline mRS and lower DOC Cog scores but not DOC Mood or DOC Apnea. Age and baseline mRS were independent significant predictors using multivariate analysis.

<table>
<thead>
<tr>
<th></th>
<th>Univariate OR (95% CI)</th>
<th>p value</th>
<th>Multivariate OR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.952 (0.929-0.976)</td>
<td>.000*</td>
<td>0.950 (0.921-0.980)</td>
<td>.001*</td>
</tr>
<tr>
<td>Baseline mRS</td>
<td>0.383 (0.270-0.544)</td>
<td>.000*</td>
<td>0.400 (0.272-0.586)</td>
<td>.000*</td>
</tr>
<tr>
<td>Depressive Symptoms</td>
<td>0.890 (0.738-1.074)</td>
<td>.225</td>
<td>0.933 (0.721-1.208)</td>
<td>.600</td>
</tr>
<tr>
<td>Apnea Symptoms</td>
<td>0.817 (0.604-1.107)</td>
<td>.193</td>
<td>0.733 (0.498-1.079)</td>
<td>.115</td>
</tr>
<tr>
<td>Cognition</td>
<td>1.282 (1.106-1.486)</td>
<td>.001*</td>
<td>1.029 (0.852-1.243)</td>
<td>.765</td>
</tr>
</tbody>
</table>
Figure 4.5: Activity/Global Functioning (mRS) Regression Model ROC Curve Including All Independent Variables

Age, baseline mRS, depressive symptoms, apnea symptoms and cognitive impairment together predicted outcome with 86.3% and 66.7% sensitivity and specificity, respectively (AUC: 810).
A model including only age and baseline mRS explained 36.7% (Nagelkerke $R^2$) of the variance in long-term outcomes ($\chi^2(2)=51.10$, $p < 0.001$) and had 84.2% sensitivity and 66.7%; specificity (AUC: .806) to predict mRS outcome.
<table>
<thead>
<tr>
<th></th>
<th>Univariate β (95% CI)</th>
<th>p value</th>
<th>$R^2$</th>
<th>Multivariate β (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-.125 (-0.215, -0.036)</td>
<td>.006*</td>
<td>0.063</td>
<td>-1.16 (-0.200, -0.032)</td>
<td>.007*</td>
</tr>
<tr>
<td>Baseline mRS</td>
<td>-3.050 (-4.259, -1.841)</td>
<td>.000*</td>
<td>0.177</td>
<td>-2.431 (-3.613, -1.249)</td>
<td>.000*</td>
</tr>
<tr>
<td>Depressive Symptoms</td>
<td>-1.087 (-1.954, -0.220)</td>
<td>.014*</td>
<td>0.225</td>
<td>-0.679 (-1.522, 0.163)</td>
<td>.113</td>
</tr>
<tr>
<td>Cognition</td>
<td>1.447 (0.790, 2.105)</td>
<td>.000*</td>
<td>0.141</td>
<td>0.897 (0.252, 1.542)</td>
<td>.007*</td>
</tr>
<tr>
<td>Apnea Symptoms</td>
<td>-0.476 (-1.803, 0.852)</td>
<td>.479</td>
<td>0.004</td>
<td>-0.348 (-1.498, 0.802)</td>
<td>.550</td>
</tr>
</tbody>
</table>

Table 4.6: Univariate & Multivariate Analyses: Baseline Variables and Follow-Up Instrumental Activity (FAI)

Greater age, baseline mRS and DOC Mood as well as lower DOC Cog all predicted greater instrumental activity limitations using univariate analysis. Depressive symptoms were not a significant predictor using multivariate analysis.
Age explained 6.3% (R2) of the variance in outcomes, baseline mRS explained 17.7%, DOC Mood explained 5% and DOC Cog explained 14.1%.

When all variables were included in a multiple regression model together (see Table 4.6), the model was significant, $F(5,117)=10.609$, $p<0.001$, $R^2=0.32$. The only independent predictors of FAI score were age ($\beta = -0.12$, 95% CI [-0.20, -0.03], $p = .007$), baseline mRS ($\beta = -2.43$, 95% CI [-3.61, -1.25], $p < .001$), and DOC Cog ($\beta = .90$, 95% CI [0.25, 1.54], $p = .007$).

### 4.3.2 Montreal Cognitive Assessment (Body Function/Cognition)

A total of 108 patients completed the MoCA at follow-up. Scores ranged from 11 to 30 ($M=23.3$, $SD=5.0$) and 58.3% were cognitively impaired (MoCA < 26). Poor MoCA outcome was significantly predicted by greater age (OR = 0.96, 95% CI 0.94-0.99, $p = .008$), fewer years of education (OR = 1.19, 95% CI 1.06-1.33, $p = .003$) and low DOC Cog scores (OR = 1.63, 95% CI 1.21-2.20, $p = 0.001$) but not baseline mRS (OR = 0.75, 95% CI 0.52-1.10, $p = .145$) using univariate analyses (see Table 4.7). Age explained 9.1% (Nagelkerke $R^2$) of the variance in MoCA outcome, education explained 12.8% and DOC Cog explained 16.9%.

The multivariate model including age, baseline mRS, DOC Cog and education was statistically significant, $\chi^2(4)=24.40$, $p < 0.001$, explained 27.2% (Nagelkerke $R^2$) of the variance in long-term cognition and correctly classified outcome in 71.3% of patients. In the multivariate model, the only independent predictors of follow-up MoCA outcome were baseline DOC Cog ($p = .037$) and education ($p = .016$). A one point increase in DOC Cog and education resulted in a 41.2% and 15.7% increase in the likelihood of a good outcome, respectively. Sensitivity was 60.0% and specificity was 79.4% (AUC: .763; See Figure 4.7).
### Table 4.7: Univariate & Multivariate Analyses: Baseline Variables and Follow-Up Body Function (MoCA)

Poor MoCA outcome was significantly predicted by greater age, fewer years of education and low DOC Cog scores but not baseline mRS using univariate analyses. Baseline cognition and education were the only significant independent predictors.

<table>
<thead>
<tr>
<th></th>
<th>Univariate OR (95% CI)</th>
<th>p value</th>
<th>Multivariate OR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.963 (0.936-0.990)</td>
<td>.008*</td>
<td>0.973 (0.943-1.003)</td>
<td>.081</td>
</tr>
<tr>
<td>Baseline mRS</td>
<td>0.754 (0.515-1.103)</td>
<td>.145</td>
<td>0.855 (0.557-1.313)</td>
<td>.475</td>
</tr>
<tr>
<td>Baseline Cognition</td>
<td>1.628 (1.206-2.198)</td>
<td>.001*</td>
<td>1.412 (1.020-1.953)</td>
<td>.037*</td>
</tr>
<tr>
<td>Education</td>
<td>1.187 (1.062-1.326)</td>
<td>.003*</td>
<td>1.157 (1.028-1.302)</td>
<td>.016*</td>
</tr>
</tbody>
</table>
Figure 4.7: Body Function/Cognition (MoCA) Regression Model ROC Curve Including All Independent Variables

Age, education and DOC Cog scores and baseline mRS predicted outcome with 60.0% sensitivity was and 79.4% specificity (AUC: .763).
Reintegration to Normal Living Index (Participation)

Hundred and twenty four completed the RNLI and scores (out of 100) ranged from 0 to 73 ($M=11.7$, $SD=15.4$). Dichotomized outcome could be determined for 146 patients; 67.8% were impaired (RNLI score > 0, dead, or mRS $\geq 4$). Univariate analyses (see Table 4.8) revealed that poor RNLI outcome was significantly predicted by greater baseline mRS (OR = 0.48, 95% CI 0.33-0.69, $p < .001$) and lower DOC Cog scores (OR = 1.26, 95% CI 1.03-1.53, $p = 0.023$) but not by age (OR = 0.99, 95% CI 0.96-1.01, $p = .223$) or DOC Mood (OR = 0.79, 95% CI 0.62-1.02, $p = .07$). Seventeen percent (Nagelkerke $R^2$) of the variance in RNLI outcomes was explained by baseline mRS and 5.6% by DOC Cog scores.

Including age, baseline mRS, DOC Mood and DOC Cog into a multivariate logistic regression model (see Table 4.8) revealed that this model was statistically significant, $\chi^2(4)=23.11$, $p < 0.001$, explained 20.6% (Nagelkerke $R^2$) of the variance in long-term outcomes and correctly classified outcome in 74% of patients. However, baseline mRS was the only significant predictor in this model (OR = 0.53, 95% CI 0.36-0.77). Sensitivity and specificity were 43.5% and 88%, respectively. A model including only baseline mRS had slightly better sensitivity (45.7%) but lower specificity (82.0%). The model including all variables was more accurate (AUC: .735; see Figure 4.8) than the model including only mRS (AUC: .708; see Figure 4.9).
<table>
<thead>
<tr>
<th></th>
<th>Univariate OR (95% CI)</th>
<th>p value</th>
<th>Multivariate OR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.986 (0.964-1.009)</td>
<td>.223</td>
<td>0.987 (0.960-1.016)</td>
<td>.372</td>
</tr>
<tr>
<td>Baseline mRS</td>
<td>0.476 (0.330-0.686)</td>
<td>.000*</td>
<td>0.528 (0.361-0.773)</td>
<td>.001*</td>
</tr>
<tr>
<td>Depressive Symptoms</td>
<td>0.794 (0.619-1.019)</td>
<td>.070</td>
<td>0.786 (0.580-1.065)</td>
<td>.121</td>
</tr>
<tr>
<td>Cognition</td>
<td>1.255 (1.032-1.525)</td>
<td>.023*</td>
<td>1.068 (0.843-1.353)</td>
<td>.585</td>
</tr>
</tbody>
</table>

**Table 4.8: Univariate & Multivariate Analyses: Baseline Variables and Follow-Up Participation (RNLI)**

Poor RNLI outcome was significantly predicted by greater baseline mRS and lower DOC Cog scores but not by age or DOC Mood. Baseline mRS was the only significant predictor using multivariate analysis.
Figure 4.8: Participation/Reintegration (RNLI) Regression Model ROC Curve Including All Independent Variables

Sensitivity and specificity to predict RNLI outcome were 43.5% and 88%, respectively, for a model including age, baseline mRS, depressive symptoms and cognition.
A model including only baseline mRS to predict RNLI had slightly better sensitivity (45.7%) but lower specificity (82.0%) than one that included all independent variables (See figure 4.8 above).
# Summary of Results

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Variables Entered</th>
<th>Significant Factors (Univariate)</th>
<th>Significant Factors (Multivariate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modified Rankin (Basic Activity)</td>
<td>Age, Baseline mRS, Depressive Symptoms, Apnea Symptoms, Cognition</td>
<td>Age, Baseline mRS</td>
<td>Age, Baseline mRS</td>
</tr>
<tr>
<td>Frenchay Activities (Instrumental Activity)</td>
<td>Age, Baseline mRS, Depressive Symptoms, Apnea Symptoms, Cognition</td>
<td>Age, Baseline mRS, Depressive Symptoms, Cognition</td>
<td>Age, Baseline mRS, Cognition</td>
</tr>
<tr>
<td>Montreal Cognitive Assessment (Body Function)</td>
<td>Age, Baseline mRS, Cognition, Education</td>
<td>Age, Cognition, Education</td>
<td>Cognition, Education</td>
</tr>
<tr>
<td>Reintegration To Normal Living Index (Participation)</td>
<td>Age, Baseline mRS, Depressive Symptoms, Cognition</td>
<td>Baseline mRS, Cognition</td>
<td>Baseline mRS</td>
</tr>
</tbody>
</table>

Table 4.9: Summary of Regression Analyses

Variables were entered into regression models based on previously reported associations. Cognition was a significant predictor of all three levels of functioning, and remained a significant predictor of instrumental activities and cognition at approximately 2 years post-stroke after accounting for established predictors. Established predictors, age and baseline mRS, were both only significant predictors of the activity level of function.
4.4 Exploratory and Sub-Analyses Results

4.4.1 Sub-Analysis

*Outcome in Physically Stable Patients*

Of those with a favorable mRS outcome (0-1), 70 and 91 patients completed the MoCA and RNLI, respectively. Forty three (54.4%) were cognitively impaired (MoCA <26), 47 (51.6%) had some restrictions in reintegration to society. Thirty percent were both cognitively impaired and had restrictions in reintegration, 32% endorsed symptoms of depression (on PHQ-2) and 19% reported a change in work status.

4.4.2 A Priori Exploratory Analyses

*Depression, OSA and Cognitive Impairment Treatment*

Patient reported treatment records were available for: mood medications (n = 134), other mood treatments (n = 136 patients), CPAP (n = 140) and memory medications (n = 134). At follow-up, 12 (9%) were taking mood medications and 13 (9.6%) were receiving or had received other treatments (i.e. therapy) after their stroke. Many patients on mood medications also received other mood treatments (50%). Of those at intermediate or high risk of depression (n=67), 16.6% were on mood medications and 14.8% received other treatments. Seventy five percent and 72.7% of patients on mood medications were at intermediate or high risk of depression at baseline and follow-up, respectively. Both baseline and follow-up depression risk was available for 11 patients who were on mood medications; 4 (36.4%) exhibited risk reduction, 4 (36.4%) showed no change, and 3 (27.3%) exhibited an increase in depression risk at follow-up.

Twenty six (18.6%) reported owning a CPAP machine and 18 (12.9%) reported using it (69.2% compliance). Of those at intermediate or high risk of apnea (n=139), 21.0% owned a CPAP machine and 14.3% were using it and of those using their CPAP, 94.4% were at intermediate or high baseline risk and 88.2% were at high or intermediate risk at follow-up. Both baseline and follow-up apnea risk was available for 17 patients using CPAP; 3 (17.6%) exhibited a decrease in risk, 10 (58.8%) displayed no change, and 4 (23.5%) exhibited increased risk of sleep apnea.
Only 2 (1.5%) patients received any treatment for cognitive impairment. A weak but significant correlation was observed between follow-up mRS and mood treatment with medications, \( r(133)=.20, p = .02 \). Presence of treatment was also positively associated with DOC Mood at follow-up \( (r(122)=.28, p = .002) \) as well as RNLI \( (r(120)=.21, p = .02) \) but not baseline DOC Mood \( (r(134)=.10, p = .25) \). Use of CPAP was associated with baseline DOC Apnea \( (r(140)=.18, p = .03) \) but not follow-up DOC Apnea \( (r(113)=.18, p = .06) \).

**Baseline Associations**

At baseline, mRS was significantly but weakly correlated with DOC Mood \( (r(161)=.19, p = .02) \) and DOC Cog \( (r(161)= -.32, p < .001) \) but not DOC Apnea \( (r(161)=.06, p = .448) \). DOC Mood was associated with DOC Apnea \( (r(162)= .18, p = .025) \) as well as DOC Cog \( (r(162)=-.18, p = .021) \). None of these associations were strong enough to indicate multicollinearity (see 4.1.3).

**Follow-Up Associations**

At follow-up, mRS was associated all follow-up outcome measures: MoCA \( (r(108)=-.26, p = .007) \), RNLI \( (r(123)=.42, p < .001) \), FAI \( (r(117)=-.52, p < .001) \), DOC Mood \( (r(128)=.25, p = .004) \) and DOC Apnea \( (r(113)=.31, p = .001) \). Follow-up DOC Mood was positively correlated with DOC Apnea at follow-up \( (r(111)=-.23, p = .015) \), MoCA \( (r(106)=-.21, p = .029) \) as well as RNLI \( (r(121)=-.35, p < .001) \). DOC Apnea at follow-up was also associated with RNLI \( (r(108)=.26, p = .007) \), and MoCA was associated with FAI \( (r(104)=.35, p < .001) \). RNLI and FAI were moderately associated \( (r(118)=-.53, p < .001) \).

Comparing those with poor and good outcome on the mRS, there was no difference in DOC Mood scores \( (U = 1346, p = .079) \) and MoCA scores \( (U = 916, p = .110) \). However, there was a difference in DOC Apnea scores \( (U = 868, p = .004) \) and self-perceived health \( (U = 583, p < .001) \). Those who were cognitively impaired \( (\text{MoCA} < 26) \), were more likely to exhibit depressive symptoms \( (U = 1076, p = .027) \) but self-perceived health was not affected \( (U = 998, p = .662) \). Patients who were unable to reintegrate into society, were more likely to be depressed \( (U = 1219, p = .001) \), exhibited poorer cognition \( (U = 973, p = .037) \), experience symptoms of apnea \( (U = 1013, p = .006) \) and lower self-perceived health \( (U = 570, p < .001) \).
4.4.3 Post-Hoc Exploratory Analyses

**Stratified DOC Risk & Reintegration to Normal Living**

The effect of risk-adjusted (i.e. accounting for age, sex and education) DOC Mood and DOC Cog on RNLI was evaluated using univariate as well as multivariate regression analyses. Employing univariate analyses, RNLI was significantly predicted by adjusted DOC Mood (OR = 0.48, 95% CI 0.27-0.84, \( p = .011 \)) as well as adjusted DOC Cog (OR = 0.60, 95% CI 0.36-1.01, \( p = .05 \)). When both, adjusted DOC Mood and DOC Cog, were combined with baseline mRS, this multivariate model was statistically significant, \( \chi^2(3)=26.20, p < 0.001 \), explained 23.1% (Nagelkerke R2) of the variance in long-term RNLI outcome and correctly classified outcome in 73.3% of patients. However, baseline mRS and adjusted DOC Mood were the only independent significant predictors of outcome, with a point increase in baseline mRS or DOC Mood risk increasing the odds of a poor outcome by a factor of 2.0 (OR = 0.51, CI 95% 0.35-0.75, \( p < .001 \)), and 2.1 (OR = 0.48, 95% CI 0.25-0.91, \( p = .024 \)), respectively.

**Change in Work Status & Driving**

Work status prior to stroke was available for 139 patients, after stroke for 120 patients, and change in work status was available for 120 patients. Eighty (57.6%) were employed prior to their stroke, 42 (35.0%) were employed after their stroke and 30 (25.0%) experienced a negative change in work status. Ability to drive prior to stroke was available for 139 patients, after stroke for 124 patients and change in status for 124 patients. Hundred and fifteen (82.7%) were able to drive prior to stroke and 96 (77.4%) were able to drive or commute independently after stroke. Seventeen (13.7%) experienced a negative change in driving ability.

**Long-term Change in Activity Function**

MRS scores at baseline and follow-up were compared using the Wilcoxon Signed Ranks Test, given that mRS scores were non-normally distributed. When death (mRS score of 6) at follow-up was included, a statistically significant change was observed between baseline and follow-up (\( Z = -2.40, p = 0.016 \)), with greater limitations at follow-up. Without death (mRS scores between 0 – 5), no statistically significant change occurred between activity level at baseline and follow-up (\( Z = -.92, p = .356 \)). Mean scores at baseline and follow-up (not including death) were 1.51 and 1.30, respectively.
Sex Differences & Influence of Education on Outcomes

Sex was associated with baseline mRS ($r(161) = .20, p = .01$), with females having worse outcomes, but no associations were evident between sex and follow-up mRS, follow-up DOC Mood, DOC Apnea, MoCA, RNLI or FAI.

Education was associated with baseline DOC Cog ($r(162) = .31, p < 0.001$) and follow-up MoCA ($r(108) = .45, p < .001$), but did not affect any other outcomes.

Assessment Time & Outcomes

Time from stroke onset to DOC screen was not associated with baseline or follow-up mRS, DOC Mood, DOC Apnea or DOC Cog and did not appear to affect any of the outcomes. Time from initial clinic visit to follow-up assessment was not associated with any outcome measures.

Effect of Stroke Risk Factors & Type on Outcomes

Presence of hypertension was associated with baseline DOC Apnea ($r(161) = .30, p < .001$) as well as follow-up DOC Apnea ($r(113) = .35, p < .001$). Cardiac disease was associated with DOC Apnea ($r(161) = .25, p = .001$) and DOC Cog ($r(161) = -.23, p = .003$) at baseline as well as mRS at follow-up ($r(160) = .19, p = .02$). Diabetes and smoker status were not associated with any follow-up outcome measures.

Stroke type did not affect baseline or follow-up mRS, DOC Mood, DOC Apnea or DOC Cog and was not correlated with any of the outcomes.

Stroke Recurrence

Data on stroke recurrence, including experiencing symptoms of stroke, were available for 138 patients; TIA occurrence data was available for 137 patients and myocardial infarction incidence records were available for 139. Only 2 patients (1.4%) reported recurrent stroke since initial visit, 2 patients (1.4%) reported experiencing sudden painless weakness (with or without stroke diagnosis) and 5 (3.6%) reported sudden loss of vision (with or without stroke diagnosis). New TIA was reported by 3 patients (2.2%) and 1 (0.7%) reported a myocardial infarction at 2 year follow-up.
Specific Cognitive Functions & Outcomes

Executive, memory and abstraction functions at baseline were all associated with follow-up mRS and MoCA (all $ps < 0.05$), however only executive function ($r(118) = .35, p < .001$) and memory ($r = .30, p = .001$) were correlated with FAI, and abstraction was not ($r = .12, p = .193$).

At follow-up, language, abstraction and orientation were not associated with any outcome measures. Attention was associated with follow-up mRS ($r(110) = -.20, p = .033$) as well as FAI ($r(107) = .28, p = .004$). Memory at follow-up was associated with follow-up mRS ($r(112) = -.30, p = .001$), RNLI ($r(110) = -.21, p = .027$), FAI ($r(109) = .31, p = .001$) as well as follow-up DOC Mood ($r(111) = .23, p = .016$).
Chapter 5
Discussion

Stroke is a challenging disease, impacting multiple levels of human functioning and causing disability in complex ways. Survivors often face debilitating neurological and functional deficits and complications, despite remarkable acute and rehabilitation interventions. The burden of stroke results not only from impairments in body function but also from limitations in daily activities and restrictions in social roles and situations (ICF: WHO, 2002). Identifying those at risk of one or more these poor outcomes provides an opportunity for early intervention and optimized recovery. This study provides insight into the importance of recognizing post-stroke comorbidities that may indicate a possibility of poor outcome and of appreciating the multifaceted nature of functioning after stroke.

In this study, we aimed to specifically appraise the impact of depressive symptoms, OSA and cognitive impairment, while accounting for established predictors, on long-term body function, activity and participation. Based on previous findings, we hypothesized that established predictors, age and baseline activity, would predict long-term functioning on all three levels and that depressive symptoms, OSA and cognitive impairment would increase the predictive power of prognostic models that only include age and stroke severity. We also hypothesized that patients with a good mRS outcome (i.e. physically stable) would experience dysfunction in other domains such as participation.

5.1 Predictions of Functional Outcome

5.1.1 Predictors of Activity Limitations

At approximately 2 years post-stroke, 41% of patients were experiencing basic activity limitations, signifying an inability to return to pre-stroke level of activity (i.e. mRS ≥ 2). This is higher than Patel et al., (2006), who found that 26% of patients had a poor activity outcome at 1 and 3 years. However, activity was assessed in that study using the Barthel Index—which evaluates specific ADLs as opposed to global basic ADL functioning—making comparison difficult.
As expected, it was found that age and baseline activity were both associated with long-term activity limitations, as assessed by the modified Rankin scale. Baseline activity explained a large proportion of the variability in outcomes (28.3%), consistent with previous literature suggesting that baseline activity is an important predictor of long-term outcome. Post-stroke cognition was also associated with activity limitations but depression and apnea were not. When all factors were included in the model, age and baseline activity were the only independent significant predictors of activity limitations in the long-term. Our model including only age and baseline activity had 84.2% sensitivity and 66.7% specificity, similar to short-term prognostic models (Weimar et al., 2002, 2004), indicating the importance of these factors even in the long-term.

The association of short-term cognitive impairment with long-term activity limitations is in keeping with previous studies showing such correlations at 3 months (Zinn et al., 2004), at 6 months (Zinn et al., 2004) and 3 and 4 years (Patel et al., 2002). Our study adds to current literature by illustrating that cognition is an important factor in determining long-term basic activity outcome but not over and above the influence of age and baseline activity. Yet, cognition played a greater role in instrumental activities.

Our linear univariate regression analyses revealed that cognition explained 14.1% of the variance in outcomes whereas age only explained 6.3%. The association between cognition and IADLs held even after all the factors were included in a multivariate model. In mild cognitive impairment and Alzheimer’s disease patients, executive dysfunction is the key determinant of impairment in instrumental activities of daily living (Marshall et al., 2011). Instrumental activities such as driving and cooking require higher order cognition and the ability to plan, focus and pay attention. Given that executive dysfunction is one of the most impacted cognitive functions in stroke patients (Cummings et al., 2013), it is possible that executive dysfunction is also responsible for the impairment in IADLs in stroke patients. Our exploratory analyses suggest that the impact of cognition on IADLs is driven primarily by executive function and memory, and not abstraction. Executive function at baseline showed the strongest correlation with FAI scores \( r = 0.35 \) compared to other cognitive functions. On the contrary, basic activities at follow-up were associated with all cognitive functions at baseline; overall cognitive abilities—which may affect ability to participate and benefit from rehabilitation, adherence to
treatment or therapy regimes, as well as ability to recognize self-care needs—appear to be important for global basic ADL functioning.

The lack of association between depressive symptoms at baseline and follow-up basic activity level was unexpected. It is possible that no relationship was observed because we evaluated depressive symptoms only and no formal diagnosis of depression was made. However, given that depressive symptoms at follow-up were correlated with follow-up activity limitations in basic ADLs, we suspect that persistent, long-term depression, as opposed to short-term post-stroke depression, may be responsible for activity limitations. Depression may resolve, persist, develop or reoccur at any point after a stroke. Patients who continue to experience symptoms of depression in the long-term may be at risk of poor activity outcome in terms of basic ADLs. Conversely, IADLs were vulnerable to the effects of baseline depression. Executive dysfunction, which also is common in depressed patients (Degl’Innocenti, Agren, & Bäckman, 1998), may be responsible for this association. When age, baseline activity, baseline cognition, depressive symptoms and OSA were included in a multivariate model, depressive symptoms were no longer a significant predictor of IADLs, suggesting that the relationship between depression and IADLs may be mediated by cognition to some degree. Surprisingly, depressive symptoms at follow-up were not significantly correlated with IADLs. Thus, long-term or persistent depression in stroke patients appears only to be associated with limitations in basic ADLs and not instrumental IADLs. One explanation for this finding could be that although both, mRS and FAI, assess participation restrictions to a small extent, the mRS might be able to capture participation restrictions to greater degree than the activity-specific FAI. The correlation between follow-up depressive symptoms and mRS may be a result of prevailing participation restrictions captured by the mRS. Further research is needed to confirm the relationship between long-term depression and basic and instrumental ADLs.

Only 16.6% of patients with high or intermediate risk of depression were treated with medications and only 14.8% were treated with other treatments (i.e. therapy). Presence of treatment was not associated with baseline depression risk, also indicating that those at greater risk of depression were not more likely to be treated. Although our sample of patients treated for depression was extremely small (n=12), exploratory analyses hint that mood medication appears to reduce the risk of depression in some patients (36%). Yet, taking medications for mood was correlated with increased activity limitations and higher risk of depression at follow-up. This
associated may be driven by the fact that patients who were taking mood medications at follow-up had likely received a definite diagnosis of depression and thus, were more likely to be limited in activities (Robinson & Spalletta, 2010) and more likely to be experiencing depressive symptoms. However, this also suggests that mood medications may not facilitate improvements in ADLs or even depressive symptoms. A previous meta-analysis exploring the effect of antidepressants in post-stroke depression found inconsistent evidence on the effect of medication on basic activity limitations (Chen et al., 2006) and one systematic review argues that although antidepressants may improve mood, their modest effect may not be clinically significant and whether antidepressants produce a remission of diagnosable depression is unclear (Hackett, Anderson, & House, 2005a). New and unique treatments combined with pharmacological interventions may be warranted to specifically target activity limitations and depression in the stroke population.

Few studies have explored the impact of post-stroke sleep apnea on long-term activity limitation. In this study, baseline sleep apnea did not affect activity outcome in univariate or multivariate analyses. However, sleep apnea at follow-up was correlated with mRS at follow-up. Like depression, it is possible that persistent or long-term sleep apnea has a greater impact on activity limitations. At follow-up, patients with a good activity outcome had significantly lower risk of sleep apnea compared to those with poor outcome. CPAP use was associated with baseline apnea risk, suggesting that patients at risk were receiving appropriate treatment. In fact, 21.0% of those at intermediate or high risk reported owning a CPAP machine. Although compliance was only 69%, it is possible that the lack of association between baseline symptoms of sleep apnea and follow-up outcome was due to CPAP use. However, our study showed no correlation between CPAP use and follow-up activity limitations. Further research on the impact of CPAP use on outcomes is warranted.

5.1.2 Predictors of Body Function Impairments

At approximately 2 years post-stroke, 58% of patients were cognitively impaired (MoCA < 26). We hypothesized that age and baseline activity would predict body function, in terms of cognition, in the long-term. Using univariate analyses, age was associated with long-term cognition, however baseline activity was not. Instead, baseline cognition and education predicted long-term outcome. In fact, short-term cognition, assessed through DOC Cog, explained more of
the variance in long-term outcomes (17%) compared to a traditional predictor of outcome, age (9%). Multivariate analysis revealed that education and baseline cognition were the only independent predictors of long-term cognition. Age and baseline activity are established predictors of post-stroke function outcome and yet, they are unable to explain majority of the variance in long-term cognitive outcome. These findings elucidate the importance of post-stroke cognitive assessments and demonstrate the need for interventions. At follow-up, patients who were cognitively impaired exhibited more depressive symptoms than those who were not and cognition was also related to basic and instrumental activities. Long-term impairments in body function may negatively affect multiple other outcomes and consequently, need to be targeted early.

5.1.3 Predictors of Participation Restrictions

At follow-up, 68% of patients were experiencing participation restrictions. We predicted that age and baseline activity will predict functioning in terms of participation and that cognition and depression would improve prediction of outcome. It was found that baseline activity as well as cognition were associated with reintegration to normal living; however, age and depressive symptoms showed no relationship with participation using univariate analyses. Multivariate analyses revealed that the only significant predictor of outcome was baseline activity. When we compared the area under the curve of a model including only baseline activity, with one including age, baseline activity, depressive symptoms as well as cognition, the model including all variables was slightly more accurate. Given that we used baseline modified Rankin scores as a measure of baseline activity, it is possible that participation restrictions captured by the mRS at baseline are responsible for the association between baseline mRS and follow-up RNLI.

Few studies have previously explored the relationship between post-stroke cognition and long-term participation. This study demonstrated the important role cognition plays in one’s ability to reintegrate into society after stroke. Young stroke survivors are often unable to return to work, despite a full physical recovery. Cognition, which is a better predictor of participation outcome than age, may be responsible for dysfunction in this complex domain of functioning.

In view of the strong association between depression and participation restrictions observed in previous studies, our findings were unexpected. Depressed stroke patients have fewer social contacts than non-depressed patients at 3 years post-stroke (Astrom et al., 1993) and
are at higher risk of social isolation (Hinojosa et al., 2011). Yet, our study showed no association between depressive symptoms and ability to reintegrate to normal living 2 years after stroke. In order to further explore this finding, we examined whether using stratified risk of depression, as opposed to raw DOC Mood scores, would clarify the relationship between depression and participation. We explored the relationship of risk-adjusted (i.e. accounting for age, sex and education) and stratified DOC Mood and DOC Cog risk with participation restrictions. Using univariate analyses, we found that adjusted DOC Mood risk and DOC Cog risk were associated with RNLI scores. When both DOC Mood and DOC Cog risk were combined with baseline activity in a multivariate regression model, baseline activity and DOC Mood were both significant predictors of outcome. We propose two explanations for these results (1) Using stratified depression risk, which separated patients into homogenous groups at low, intermediate and high risk, facilitated a clear link between depressive symptoms and reintegration (Swartz et al., 2016a) or (2) Accounting for age, sex and education increased the precision of depression risk, allowing a more accurate association. Our exploratory analysis also confirmed the role of cognition in participation, given that we observed the same relationship between cognition and participation using both raw scores and stratified risk; employing univariate analysis, cognition was a significant predictor in both cases.

We also observed a correlation between depressive and apnea symptoms at follow-up, and participation, indicating that persistent, long-term symptoms may be hindering social reintegration. Patients who were unable to re-assimilate had more depressive symptoms, exhibited poorer cognition, and experienced more symptoms of apnea than those who were. On the contrary, patients with activity limitations did not have more depressive symptoms or greater cognitive impairment than those who did not have activity limitations. Thus, participation may be able to encapsulate dysfunction in more domains than activity and may be a better indicator of functioning.

5.1.4 Comparison of Established & Exploratory Predictors

Age and baseline activity are established and traditional predictors of outcome after stroke. However, once a stroke is complete and recovery has stabilized, these factors are relatively non-modifiable. These factors also do not explain all of the variability in long-term outcomes. Our analysis showed that age and baseline mRS only explained 37% of the variance in
activity outcome, age only explained 9% of the variance in body function and baseline mRS only explained 17% of the variance in participation. A large proportion of the variance is not explained by these factors. In fact, both these variables are only strong predictors of long-term activity limitations, but not body function impairments and participation restrictions.

We explored the impact of depressive symptoms, cognitive impairment and sleep apnea—all potentially modifiable factors—on different levels of functioning. Unlike age and baseline activity, cognition is a predictor of outcome on every level of functioning. Cognition after stroke affects long-term body function, activity as well as participation. Canadian Stroke Best Practice Recommendations suggest routine cognitive testing, but implementing this recommendation has been challenging (Swartz et al., 2016b). In view of the widespread and debilitating impact of post-stroke cognitive impairment on every level of human functioning, routine post-stroke cognitive screening and early target interventions are urgently warranted.

Numerous other modifiable and non-modifiable predictors have also previously been studied. We explored the impact of previously suggested factors such as sex, stroke risk factors, stroke type, and education on outcome. We found no correlation between sex and any of our outcome measures. Similarly, stroke type did not appear to influence outcome. This finding is consistent with a previous long-term study illustrating that both ischemic and hemorrhagic stroke patients have similar long-term outcome (Meyer et al., 2015). Education was associated with baseline as well as follow-up cognition, was included in our prognostic model of cognition and was a significant independent predictor of outcome. While diabetes and smoker status were not associated with any of the outcome measures, we did find that presence of hypertension and cardiac disease was associated with baseline as well as follow-up function. Baseline and follow-up risk of sleep apnea was correlated with the presence of hypertension. We did not include hypertension in our prognostic models; however, hypertension may be a modifiable predictor of long-term risk of sleep apnea, which is correlated with activity limitations and participation restrictions in the long-term. Aggressive management of hypertension and direct treatment of sleep apnea with CPAP may lower risk of sleep apnea in the long-term and consequently, improve long-term activity and participation. Presence of cardiac disease was correlated with activity at follow-up. Although the correlation was weak (r = 0.19), cardiac disease may be contributing to activity limitations, possibly also due to its association with post-stroke apnea and cognitive impairment.
5.1.5 Mechanisms of Depression & Cognitive Impairment Post-Stroke

Post-stroke depression and cognitive impairment could result in poor long-term functioning for a number of reasons, which can be understood through the biopsychosocial model of disease. We found that depressive symptoms predicted long-term limitations in instrumental activities and restrictions in participation. Possible explanations for this association include: (1) executive dysfunction triggered by stroke, (2) lack of motivation, (3) personality-related factors (i.e. poor coping skills) and (4) lack of social support. In this study, depressive symptoms after stroke were weakly correlated with increased risk of cognitive impairment at baseline, suggesting some overlap between the conditions. Instrumental activities as well as social reintegration require higher-order cognitive abilities, such as executive function. It is possible that cognition, specifically executive function, mediates the relationship between depression and functional deficits. Lack of motivation, with is common symptom of depression, could also be a potential explanation. Depressed stroke patients may not be motivated to participate in rehabilitation, return to work or socialize and personality style could be an important determinant of motivation as well as level of functioning. Post-stroke depression could potentially be a marker for poor coping skills (Whyte & Mulsant, 2002) and thus, depressed patients may be less likely to handle complex daily tasks and social situations or relationships. Finally, social support may play a critical role in the development of activity limitations and participation restrictions. Patients who have a strong support system may be less likely to remain depressed and less likely to experience the negative functional outcomes associated with depression. Caregivers, family and friends could potentially facilitate reintegration to society and help patients relearn instrumental activities such as managing money or cooking.

Similar mechanism could be driving the relationship between cognition and functional outcomes. In this study, cognition was associated with all levels of functioning. The mechanism of post-stroke cognitive impairment is currently unclear. Large cortical infarcts, white matter lesions as well as small infarcts, which all result in brain atrophy, are potential mechanisms of post-stroke cognitive impairment (O’Brien et al., 2003) and given that there are currently no standard treatments for this condition, short-term cognitive impairment (i.e. impairment in body function) may simply continue to persevere in the long-term. In terms of long-term activity, cognition impairment could be operating through multiple mechanisms such as: (1) reduced ability to take care of oneself and (2) inability to plan and organize (i.e. employ executive
functions). Cognitive impairments, such as memory and attention deficits or executive dysfunction, could reduce one’s ability to perform self-care tasks. Executive functions may be specifically important in one’s ability to perform instrumental tasks such as managing finances. Thus, cognitive impairments may be diminishing behaviors that allow ADL function. Finally, the ability to pay attention, communicate and regulate behaviors are crucial components of social interactions and impairments in these cognitive abilities may restrict participation. Individuals with cognitive impairments may not be able to maintain meaningful relationships or respond to appropriately to social situations, which may result in social isolation and even depressive states.

5.2 Multidimensionality of Function

Reviews of stroke trials have consistently demonstrated the lack of participation and quality of life outcome measures (Roberts & Counsell, 1998; Duncan et al., 2000). Yet, participation may be the outcome most important to a patient (Quinn et al., 2009). Our study demonstrates that of those with a favorable activity outcome, 54% were cognitively impaired (MoCA <26), 52% had some restrictions in reintegration to society, 30% were both cognitively impaired and had restrictions in reintegration, 32% endorsed symptoms of depression (on PHQ-2) and 19% reported a change in work status. While these patients had recovered in terms of physical disability, returned to their pre-stroke activity level and were able to perform ADLs independently, they were still experiencing dysfunction on multiple different levels. Most stroke trials and outcome studies define functional outcome in terms of activity limitations and may not be capturing other deficits. When we compared patients with a good and poor outcome on the mRS, there was no difference in depressive symptoms or cognitive impairments between the two groups. However, when we compared patients with a good and poor outcome on the RNLI, we found that those who were unable to reintegration had more depressive symptoms, poorer cognition and more symptoms of apnea. The RNLI may be able to capture dysfunction on multiple levels. In fact, in our study as well as previous studies (e.g. Mayo et al., 2002), more patients were impaired in participation (68%) compared to activity (41%), illustrating the pervasiveness of restrictions in participation.

The lack of emphasis on participation may simply be because established and robust instruments to measure dysfunction in this domain are currently not available (Quinn et al.,
and participation by its very nature is difficult to measure. Still, it is the most impacted domain of functioning post-stroke and robust scales to measure this domain are necessary.

5.3 Long-Term Outcomes

Long-term outcome studies are uncommon in stroke literature; most studies evaluate outcome at 3 months (Duncan et al., 2000; Quinn et al., 2009). Yet, understanding long-term outcomes may be more meaningful, given that stroke patients may be more concerned about their prognosis beyond 3 months. Although it was previously believed that short-term activity limitations are maintained in the long-term, recent studies have demonstrated that patients appear to decline in terms of ADL function at 5 years (Meyer et al., 2015) and long-term decline may be due to comorbid diseases and recurrent stroke (Pettersen et al., 2002). Only a small proportion of our sample experienced recurrent stroke (1.4%), however comorbid conditions were common even in the long-term; intermediate or high risk of depression was present in 33% of patients at follow-up, of apnea in 87% of patients and cognitive impairment was present in 58%.

Meyer et al. (2015) demonstrated that at 5 years, patients had declined to 2-month level of functioning. In their study, ADL function was not evaluated between 6 months and 5 years and the point at which recovery plateaus or begins to decline was not determined. Our study used a short interval, allowing us to examine whether declined in ADL function begins as early as 2 years after stroke. We found no significant difference in mRS scores (excluding death at follow-up) at baseline (within 6 months) compared to follow-up (approximately 2 years later), indicating that functional decline naturally does not commence at 2 years post-stroke. Although, our study assessed baseline function at varying time points within 6 months of stroke and thus, studies using specific, fixed time point are needed to confirm our findings. We did demonstrated, however, that patients with comorbid conditions were more susceptible to poor outcomes.
5.4 Strengths & Limitations

Strengths of this study include our relatively large sample size, assessment of multiple domains of function as well as the duration of follow-up. We enrolled a total of 162 patients at approximately 2 years post-stroke, with a relatively small proportion of patients lost to follow-up. Function was assessed in multiple domains, allowing a thorough understanding of functional deficits after stroke. Finally, long-term studies are limited in stroke literature. This study was conducted at 2 years and 3 months (± 6 months) post-stroke and thus, provides insight into the impact of stroke and common comorbidities on outcome years later.

One of the limitations of our study is that we evaluated risk of depression, cognitive impairment and sleep apnea and no definite diagnosis was established. It is possible, especially in OSA patients, that patients with a definite diagnosis are more likely to experience functional impairments than those who are simply exhibiting symptoms of the condition. While this is a valid drawback of our study, the DOC screen is a valid tool to screen for risk of depression, cognitive impairment and OSA and is able to reliably predict scores on gold standard assessments which are typically used to diagnose these conditions. More importantly, in high-volume stroke clinics, where risk of these conditions should be evaluated, it is not possible to complete gold standard testing. Instead, appropriate referrals may need to be made based on determined risk and treatment interventions can then be employed. While more detailed baseline assessments may have greater predictive power, the purpose of this study was to explore whether quick routine assessments that can feasibly be acquired in clinic are valid predictors of long-term function. We demonstrated that even the risk of depression and cognitive impairment based on a quick screen can reliably be used to identify vulnerable individuals who are at risk of poor long-term functional outcomes.

Another limitation of our study is attrition and survivor bias. Our secondary outcome measures could only be tested on patients who were alive at approximately 2 years after their stroke. It is possible that patients who passed away were experiencing greater activity limitation, body function impairments or participation restrictions than patients who were alive. Similarly, we lost some patients to follow-up and it is possible that these patients were experiencing more functional deficits than the patients we enrolled. In order to rule out these concerns to some extent, we did compare age, baseline activity, education and baseline risk of depression, apnea
and cognitive impairment between the patients we enrolled, those who were lost of follow-up and those who declined to participate. We did not find any differences in these variables between the enrolled and declined or lost patients. Nonetheless, it is difficult to completely eliminate these biases. Patients who survive the first few months after a stroke and those who are alive up to 2 years later are typically patients who had mild or moderate strokes, as evidenced by the average modified Rankin scores at baseline ($M = 1.5$) and follow-up ($M = 1.9$) in our study. Accordingly, the findings of this study may only apply to patients with mild or moderate strokes.

There was also a large variability in the time interval between stroke onset and baseline screening in our study. We included all patients who visited the stroke prevention clinic within 6 months of their stroke and thus, patients were seen anywhere from 1 day to 178 days post-stroke ($M = 83$ days). The first few months after a stroke are highly unstable and dynamic; it is possible that patients were at different stages of recovery when they were screened, which could potentially increase or decrease the predictive value of baseline factors. However, we explored whether time from stroke onset to DOC screen as well as time from DOC screen to follow-up influenced any of our outcome measures and we did not find any associations.

Our study was based primarily on patient reported outcomes. Except for the MoCA, all assessments were subjectively based on the patient’s perspective. It is possible, especially for depression, that patients reported feeling well, despite experiencing depressive symptoms due to concerns such as stigma. Nonetheless, all the tools that we utilized are valid assessment tools that are commonly used to evaluate their respective constructs, limiting the likelihood of biased responses.

Finally, we did not include variables such as acute interventions, rehabilitation or treatments for depression, apnea and cognition into our prognostic model. There is currently limited evidence to suggest that rehabilitation interventions influence long-term outcomes, few patients typically receive tPA and very few of our patients were being treated for the DOC conditions. The impact of these variables on long-term functional outcome is likely not as significant as the variables we included in our model; however, further research on the influence of these interventions is needed.
Chapter 6
Conclusion

A stroke can impact an individual in numerous complex ways. Survivors often face debilitating neurological impairments, physical disability and handicaps. Identifying those at risk of one or more these poor outcomes may facilitate early intervention and optimized recovery. The results of this study illustrate the prevalence of functional limitations after stroke across the range of functions from body impairment to social/role participation, establish the impact of post-stroke comorbidities on long-term functional outcome and elucidate the importance of post-stroke depression and cognitive assessments in affecting future functional status.

As our population ages and the number of stroke victims increases, identifying and treating those who are at risk of a poor outcome will become essential. This study examined post-stroke functioning in accordance with the definition of functioning established by the WHO across the full spectrum of function. Social isolation and inability to participate in social situations and roles in the years following a stroke may lead to further difficulties in mental and physical health in future years and result in a cyclic pattern of maladaptive behaviors that promote illness. Social isolation in the long-term may indicate an inability to cope with the aftereffects of stroke and thus, identifying individuals who would be at risk of restrictions in participation may allow targeted intervention and facilitate a smoother recovery.

The current design also extends post-stroke functional assessment beyond the 90-day or 1-year time horizon. Functional recovery plateaus by 1.5 years in most patients (Katz et al., 1966) and while intervening/recurrent events can happen at any time point, they may be increasingly frequent and important beyond 3 years (Dhamoon et al., 2009). Long-term assessments can attest to a stable patient’s eventual functioning once recovery has plateaued. The period immediately following a stroke is highly unstable and functioning may change dramatically during this time. Post-stroke depressive symptoms and cognitive impairment are important in the maintenance of function recovery and how patients cope over time.

The impact of a stroke goes far beyond physical disability. Simple physical, environmental or social interventions could improve body impairments, disability in activities and social/role participation for people living with stroke, even many years later. The results of
this study demonstrate the need for post-stroke depression, sleep apnea and cognitive assessment, establish the impact of these comorbidities on stroke recovery, pave the way for targeted interventions and could ultimately, change practice.
Chapter 7
Future Directions

7.1 Unexplained Variance

Majority of the variance in outcomes on all levels of functioning cannot be explained by traditional factors and the factors we explored. It is possible that significant predictors of outcome, especially in terms of participation, are yet to be recognized. The biopsychosocial model should be employed as a guideline to understand patient outcomes. In our prognostic models, we have explored the influence of biological (e.g. age, baseline activity, cognition) and psychological (e.g. depression) factors but not social factors. Future research should examine the impact of factors such as social support and major stressful life events (e.g. divorce or death of a loved one) on outcome. These factors may be especially important in understanding participation—the outcome with the largest unexplained variance—after stroke. Accordingly, this study also illustrates that different outcomes (i.e. different levels of functioning) may be predicted by different factors. Age and baseline activity are important in terms of activity but both these factors are not significant predictors on other levels. This elucidates the importance of evaluating each level of functioning independently. In fact, Weimar et al. (2002) demonstrated that different prognostic factors predict functional independence and mortality and Kissela et al. (2009) believe that morbidity and mortality may confound each other and thus, should not be combined in one model. This has two implications for further research: (1) prognostic factors and their value may vary based on the outcome being measured and thus, separating activity, body function, participation or death as different end-points is necessary and (2) the impact of depression symptoms, obstructive sleep apnea and cognitive impairment on mortality, which was combined with morbidity in this study, is warranted.

7.2 Neuroimaging Markers

While imaging markers may not be readily available in all clinical settings, they may be strong predictors of functional outcome. One previous study (Kissela et al., 2009) has elucidated the importance of periventricular white matter disease (PVWMD) in clinical prediction of functional outcome, concluding that severe PVWMD may be a better predictor of activity outcome than traditional predictors at 3 months. Kissela et al. (2009) propose the possibility that
“recovery is limited for those patients with severe PVWMD because of structural damage to the white matter tracts, limiting the physiological process of neuroplasticity” (p. 534) and that poor outcome due to traditional risk factors may be mediated by increased PVWMD. Given the association between white matter disease and cognitive decline and the importance of cognition in predicting outcome, the prognostic value of this neuroimaging marker is worth exploring. Including visual quantification of white matter lesion burden in a predictive model may also allow prediction of long-term vascular cognitive impairment and early identification of vulnerable patients. Similarly, lesions in certain locations such as the left uncinate fasciculus and right parietal lobe have been associated with worse activity outcome at 90-day (Yassi et al., 2015), when compared to other locations. The impact of lesion location—especially in view of its specific effect of cognition—on long-term outcomes may also be worth exploring.

7.3 Development & Enhancement of Assessment Tools

Participation is the most patient-centered and least assessed outcome after stroke, partly because of the lack of valid, reliable and appropriate tools to measure it. In this study, we used the most frequently used index, the Reintegration to Normal Living Index; however, even this measure has not been extensively studied in the stroke population. While the developers suggest a score classification system (Korner-Bitensky et al., 1994), there are no “generally accepted standards for interpretation” (Salter et al., 2013, p. 93). Thus, there is a need to validate currently available tools and to develop new tools that are able to capture this complex domain of functioning. Such measures will facilitate the integration of participation outcomes into stroke literature, emphasize and highlight dysfunction on this level and illustrate the need for focused interventions.

7.4 Additional Components of Functioning

The ICF Core Set for Stroke includes numerous functions that could be influenced by stroke. In this study, we evaluated cognition on the level of body function, basic and instrumental ADLs on the level of activity and social reintegration on the level of participation. On the level of body function, we did not explore sensory functions or personality functions and on the level of activity and participation, we did not explore reading or writing ability or economic self-sufficiency. These functions may also be impacted and future research should explore these outcomes in stroke patients.
7.5 Depression, Obstructive Sleep Apnea and Cognitive Impairment Treatments

One of the most important implications of this study is the need to assess, identify and treat patients who are at risk of depression, obstructive sleep apnea and cognitive impairment. This study illustrates that stroke patients are at risk of poor outcomes due to these conditions, demonstrates that a quick screen can be implemented in stroke clinics to identify high risk patients and will hopefully facilitate the development of novel interventions to alter the trajectory of this vulnerable population and help them achieve optimal recovery.

Further research is required to evaluate the efficacy of antidepressants in stroke patients. Antidepressants have been found to improve depressive symptoms in stroke patients (Chen et al., 2006; Hackett et al., 2005a). However, the effect of medication on activity limitations is inconsistent (Chen et al., 2006) and whether antidepressants lead to remission of diagnosed depression is unclear (Hackett et al., 2005a). Future research is warranted to confirm previous findings and to determine which patients are more likely to benefit from antidepressants. Similarly, high intensity exercise protocols have been found to reduce depressive symptoms in stroke patients (Eng & Reime, 2014) and further research is warranted to examine the effect of exercise interventions on functional outcomes. Cognitive behavioral therapy, repetitive transcranial magnetic stimulation (rTMS) and electroconvulsive therapy are other treatment options that require further evaluation in the stroke population.

The influence of continued CPAP use on functional outcome is currently unknown. Long-term use of CPAP may have the potential to improve outcomes in terms of activity, body function as well as participation, which all seem to be associated with sleep apnea in the long-term. Randomized controlled trials are warranted.

Although cognitive impairment may be more challenging to treat than sleep apnea and depression, numerous treatment options do exist. Cholinesterase inhibitors, especially donepezil, appear to improve cognition in vascular dementia patients (Roman et al., 2010; Black et al., 2003; Wilkinson et al., 2003) and the American Heart Association/American Stroke Association recommendations propose donepezil as an effective drug treatment to enhance cognition in VCI patients (Gorelick et al., 2011), with a NNT = 10 (Demaerschalk & Wingerchuk, 2007). Like depression, exercise interventions and rTMS are possible treatment options in VCI patients and
some stroke prevention therapies may be beneficial as well. Antihypertensive treatments may prevent or delay cognitive decline (Duron & Hanon, 2010), aspirin therapy may improve cognitive outcomes in multi-infarct dementia patients (Meyer, Rogers, McClintic, Mortel, & Lotfi, 1989) and dual antiplatelet therapy as well as lipid-lowering drugs may protect against cognitive impairment (Douiri, McKevitt, Emmett, Rudd, & Wolfe, 2013). Future research should explore these treatment options and examine whether they improve outcome in terms of activity and participation as well.

7.6 Clinical Impact

We have the potential to change practice now by reinforcing the importance of post-stroke assessment and treatments for depression, sleep apnea and cognitive impairment and by further facilitating research on targeted interventions. Canadian Best Practice Guidelines recommend routine screening as well as ongoing monitoring, support and education of depression, sleep apnea and cognitive impairment. An annual review of psychosocial needs is suggested and yet, these conditions are under-assessed, under-diagnosed and under-treated in the stroke population. This discrepancy in clinical practice may be due to our lack of understanding of the impact of these conditions on recovery. The dearth of research exploring the long-term consequences of post-stroke depression, sleep apnea and cognitive impairment reveals a significant gap in our understanding of long-term post-stroke functional outcomes. Thus, identifying the particular impact of these conditions could facilitate the implementation of these best practice guidelines. Further research to confirm our findings is necessary.
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Appendices
## BODY FUNCTIONS

= physiological functions of body systems (including psychological functions)

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
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| b110 | Consciousness functions  
General mental functions of the state of awareness and alertness, including the clarity and continuity of the wakeful state.  
Inclusions: functions of the state, continuity and quality of consciousness; loss of consciousness, coma, vegetative states, fugues, trance states, possession states, drug-induced altered consciousness, delirium, stupor  
Exclusions: orientation functions (b114); energy and drive functions (b130); sleep functions (b134) |
| b114 | Orientation functions  
General mental functions of knowing and ascertaining one's relation to self, to others, to time and to one's surroundings.  
Inclusions: functions of orientation to time, place and person; orientation to self and others; disorientation to time, place and person  
Exclusions: consciousness functions (b110); attention functions (b140); memory functions (b144) |
| b117 | Intellectual functions  
General mental functions, required to understand and constructively integrate the various mental functions, including all cognitive functions and their development over the life span.  
Inclusions: functions of intellectual growth; intellectual retardation, mental retardation, dementia  
Exclusions: memory functions (b144); thought functions (b168); higher-level cognitive functions (b164) |
| b126 | Temperament and personality functions  
General mental functions of constitutional disposition of the individual to react in a particular way to situations, including the set of mental characteristics that makes the individual distinct from others.  
Inclusions: functions of extraversion, introversion, agreeableness, conscientiousness, psychic and emotional stability, and openness to experience; optimism; novelty seeking; confidence; trustworthiness  
Exclusions: intellectual functions (b144); energy and drive functions (b130); psychomotor functions (b147); emotional functions (b152) |
| b130 | Energy and drive functions  
General mental functions of physiological and psychological mechanisms that cause the individual to move towards satisfying specific needs and general goals in a persistent manner.  
Inclusions: functions of energy level, motivation, appetite, craving (including craving for substances that can be abused), and impulse control  
Exclusions: consciousness functions (b110); temperament and personality functions (b126); sleep functions (b134); psychomotor functions (b147); emotional functions (b152) |
| b134 | Sleep functions  
General mental functions of periodic, reversible and selective physical and mental disengagement from one's immediate environment accompanied by characteristic physiological changes.  
Inclusions: functions of amount of sleeping, and onset, maintenance and quality of sleep; functions involving the sleep cycle, such as in insomnia, hypersomnia and narcolepsy  
Exclusions: consciousness functions (b110); energy and drive functions (b130); attention functions (b140); psychomotor functions (b147) |
| b140 | Attention functions  
Specific mental functions of focusing on an external stimulus or internal experience for the required period of time.  
Inclusions: functions of sustaining attention, shifting attention, dividing attention, sharing attention; concentration; distractibility  
Exclusions: consciousness functions (b110); energy and drive functions (b130); sleep functions (b134); memory functions (b144); psychomotor functions (b147); perceptual functions (b156) |
| b144 | Memory functions  
Specific mental functions of registering and storing information and retrieving it as needed.  
Inclusions: functions of short-term and long-term memory, immediate, recent and remote memory; memory span; retrieval of memory; remembering; functions used in recalling and learning, such as in nominal, selective and dissociative amnesia  
Exclusions: consciousness functions (b110); orientation functions (b114); intellectual functions (b117); attention functions (b140); perceptual functions (b156); thought functions (b160); higher-level cognitive functions (b164); mental functions of language (b167); calculation functions (b172) |
| b152 | Emotional functions  
Specific mental functions related to the feeling and affective components of the processes of the mind.  
Inclusions: functions of appropriateness of emotion, regulation and range of emotion; affect; sadness, happiness, love, fear, anger, hate, tension, anxiety, joy, sorrow; liability of emotion; flattening of affect  
Exclusions: temperament and personality functions (b126); energy and drive functions (b130) |
| b156 | Perceptual functions  
Specific mental functions of recognizing and interpreting sensory stimuli.  
Inclusions: functions of auditory, visual, olfactory, gustatory, tactile and visuospatial perception, such as a hallucination or illusion  
Exclusions: consciousness functions (b110); orientation functions (b114); attention functions (b140); memory functions (b144); mental functions of language (b167); seeing and related functions (b210-b229); hearing and vestibular functions (b230-b249); additional sensory functions (b250-b279) |
<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>b164</td>
<td>Higher-level cognitive functions</td>
</tr>
<tr>
<td></td>
<td>Specific mental functions especially dependent on the frontal lobes of the brain, including complex goal-directed behaviours such as decision-making, abstract thinking, planning and carrying out plans, mental flexibility, and deciding which behaviours are appropriate under what circumstances; often called executive functions.</td>
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<tr>
<td></td>
<td>Inclusions: functions of abstraction and organization of ideas; time management, insight and judgement; concept formation, categorization and cognitive flexibility</td>
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<td></td>
<td>Exclusions: memory functions (b144); thought functions (b160); mental functions of language (b167); calculation functions (b172)</td>
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<tr>
<td>b167</td>
<td>Mental functions of language</td>
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<td></td>
<td>Specific mental functions of recognizing and using signs, symbols and other components of a language.</td>
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<tr>
<td></td>
<td>Inclusions: functions of reception and decryption of spoken, written or other forms of language such as sign language; functions of expression of spoken, written or other forms of language; integrative language functions, spoken and written, such as involved in receptive, expressive, Broca’s, Wernicke’s and conduction aphasia</td>
</tr>
<tr>
<td></td>
<td>Exclusions: attention functions (b140); memory functions (b144); perceptual functions (b156); thought functions (b160); higher-level cognitive functions (b164); calculation functions (b172); mental functions of complex movements (b176)</td>
</tr>
<tr>
<td></td>
<td>Chapter 2 Sensory Functions and Pain; Chapter 3 Voice and Speech Functions</td>
</tr>
<tr>
<td>b172</td>
<td>Calculation functions</td>
</tr>
<tr>
<td></td>
<td>Specific mental functions of determination, approximation and manipulation of mathematical symbols and processes.</td>
</tr>
<tr>
<td></td>
<td>Inclusions: functions of addition, subtraction, and other simple mathematical calculations; functions of complex mathematical operations</td>
</tr>
<tr>
<td></td>
<td>Exclusions: attention functions (b140); memory functions (b144); thought functions (b160); higher-level cognitive functions (b164); mental functions of language (b167)</td>
</tr>
<tr>
<td>b176</td>
<td>Mental functions of sequencing complex movements</td>
</tr>
<tr>
<td></td>
<td>Specific mental functions of sequencing and coordinating complex, purposeful movements.</td>
</tr>
<tr>
<td></td>
<td>Inclusions: impairments such as in ideation, ideomotor, dressing, oculomotor and speech apraxia</td>
</tr>
<tr>
<td></td>
<td>Exclusions: psychomotor functions (b147); higher-level cognitive functions (b164); Chapter 7 Neurornusculoskeletal and Movement-Related Functions</td>
</tr>
<tr>
<td>b180</td>
<td>Experience of self and time functions</td>
</tr>
<tr>
<td></td>
<td>Specific mental functions related to the awareness of one’s identity, one’s body, one’s position in the reality of one’s environment and of time.</td>
</tr>
<tr>
<td></td>
<td>Inclusions: functions of experience of self, body image and time</td>
</tr>
<tr>
<td>b210</td>
<td>Seeing functions</td>
</tr>
<tr>
<td></td>
<td>Sensory functions relating to sensing the presence of light and sensing the form, size, shape and colour of the visual stimuli.</td>
</tr>
<tr>
<td></td>
<td>Inclusions: visual acuity functions; visual field functions; quality of vision; functions of sensing light and colour, visual acuity of distant and near vision, monocular and binocular vision; visual picture quality; impairments such as myopia, hypermetropia, astigmatism, hemianopia, colour-blindness, tunnel vision, central and peripheral scotoma, diplopia, night blindness and impaired adaptability to light</td>
</tr>
<tr>
<td></td>
<td>Exclusion: perceptual functions (b156)</td>
</tr>
<tr>
<td>b215</td>
<td>Functions of structures adjoining the eye</td>
</tr>
<tr>
<td></td>
<td>Functions of structures in and around the eye that facilitate seeing functions.</td>
</tr>
<tr>
<td></td>
<td>Inclusions: functions of internal muscles of the eye, eyelid, external muscles of the eye, including voluntary and tracking movements and fixation of the eye, lachrymal glands, accommodation, pupillary reflex; impairments such as in nystagmus, xerophthalmia and ptosis</td>
</tr>
<tr>
<td></td>
<td>Exclusions: seeing functions (b210); Chapter 7 Neurornusculoskeletal and Movement-related Functions</td>
</tr>
<tr>
<td>b260</td>
<td>Proprioceptive function</td>
</tr>
<tr>
<td></td>
<td>Sensory functions of sensing the relative position of body parts.</td>
</tr>
<tr>
<td></td>
<td>Inclusions: functions of statesthesisa and kinaesthesia</td>
</tr>
<tr>
<td></td>
<td>Exclusions: vestibular functions (b235); sensations related to muscles and movement functions (b780)</td>
</tr>
<tr>
<td>b265</td>
<td>Touch function</td>
</tr>
<tr>
<td></td>
<td>Sensory functions of sensing surfaces and their texture or quality.</td>
</tr>
<tr>
<td></td>
<td>Inclusions: functions of touching, feeling of touch; impairments such as numbness, anaesthesia, tingling, paraesthesia and hyperaesthesia</td>
</tr>
<tr>
<td></td>
<td>Exclusions: sensory functions related to temperature and other stimuli (b270)</td>
</tr>
<tr>
<td>b270</td>
<td>Sensory functions related to temperature and other stimuli</td>
</tr>
<tr>
<td></td>
<td>Sensory functions of sensing temperature, vibration, pressure and noxious stimulus.</td>
</tr>
<tr>
<td></td>
<td>Inclusions: functions of being sensitive to temperature, vibration, shaking or oscillation, superficial pressure, deep pressure, burning sensation or a noxious stimulus</td>
</tr>
<tr>
<td></td>
<td>Exclusions: touch functions (b265); sensation of pain (b280)</td>
</tr>
<tr>
<td>b280</td>
<td>Sensation of pain</td>
</tr>
<tr>
<td></td>
<td>Sensation of unpleasant feeling indicating potential or actual damage to some body structure.</td>
</tr>
<tr>
<td></td>
<td>Inclusions: sensations of generalized or localized pain in one or more body part; pain in a dermatome, stabbing pain, burning pain, dull pain, aching pain; impairments such as myalgia, analgesia and hyperalgesia</td>
</tr>
<tr>
<td>b310</td>
<td>Voice functions</td>
</tr>
<tr>
<td></td>
<td>Functions of the production of various sounds by the passage of air through the larynx.</td>
</tr>
<tr>
<td></td>
<td>Inclusions: functions of production and quality of voice; functions of phonation, pitch, loudness and other qualities of voice; impairments such as aphony, dysphonia, hoarseness, hypernasality and hyponasality</td>
</tr>
<tr>
<td></td>
<td>Exclusions: mental functions of language (b167); articulation functions (b320)</td>
</tr>
</tbody>
</table>
Articulation functions
Functions of the production of speech sounds.
Inclusions: functions of enunciation, articulation of phonemes; spastic, ataxic, flaccid dysarthria; anarthria
Exclusions: mental functions of language (b167); voice functions (b310)

Fluency and rhythm of speech functions
Functions of the production of flow and tempo of speech.
Inclusions: functions of fluency, rhythm, speed and melody of speech; prosody and intonation; impairments such as stuttering, stammering, stuttering, bradyphalia and tachypnoea
Exclusions: mental functions of language (b167); voice functions (b310); articulation functions (b320)

Heart functions
Functions of pumping the blood in adequate or required amounts and pressure throughout the body.
Inclusions: functions of heart rate, rhythm and output; contraction force of ventricular muscles; functions of heart valves; pumping the blood through the pulmonary circuit; dynamics of circulation to the heart; impairments such as tachycardia, bradycardia and irregular heart beat and as in heart failure, cardiomyopathy, myocarditis and coronary insufficiency
Exclusions: blood vessel functions (b415); blood pressure functions (b420); exercise tolerance functions (b455)

Blood vessel functions
Functions of transporting blood throughout the body.
Inclusions: functions of arteries, capillaries and veins; vasomotor function; functions of pulmonary arteries, capillaries and veins; functions of valves of veins; impairments such as in blockage or constriction of arteries; atherosclerosis, arteriosclerosis, thromboembolism and varicose veins
Exclusions: heart functions (b410); blood pressure functions (b420); haematological system functions (b430); exercise tolerance functions (b455)

Blood pressure functions
Functions of maintaining the pressure of blood within the arteries.
Inclusions: functions of maintenance of blood pressure; increased and decreased blood pressure; impairments such as in hypotension, hypertension and postural hypotension
Exclusions: heart functions (b410); blood vessel functions (b415); exercise tolerance functions (b455)

Exercise tolerance functions
Functions related to respiratory and cardiovascular capacity as required for enduring physical exertion.
Inclusions: functions of physical endurance, aerobic capacity, stamina and fatigability
Exclusions: functions of the cardiovascular system (b410-b429); haematological system functions (b430); respiration functions (b440); respiratory muscle functions (b445); additional respiratory functions (b450)

Ingestion functions
Functions related to taking in and manipulating solids or liquids through the mouth into the body.
Inclusions: functions of sucking, chewing and biting, manipulating food in the mouth, salivation, swallowing, burping, regurgitation, spitting and vomiting; impairments such as dysphagia, aspiration of food, aerophagia, excessive salivation, drooling and insufficient salivation
Exclusion: sensations associated with the digestive system (b535)

Defecation functions
Functions of elimination of wastes and undigested food as faeces and related functions.
Inclusions: functions of elimination, faecal consistency, frequency of defecation; faecal continence, flatulence; impairments such as constipation, diarrhoea, watery stool and anal sphincter incompetence or incontinence
Exclusions: digestive functions (b515); assimilation functions (b520); sensations associated with the digestive system (b535)

Urination functions
Functions of discharge of urine from the urinary bladder.
Inclusions: functions of urination, frequency of urination, urinary continence; impairments such as in stress, urge, reflex, overflow, continuous incontinence, dribbling, automatic bladder, polyuria, urinary retention and urinary urgency
Exclusions: urinary excretory functions (b610); sensations associated with urinary functions (b630)

Sexual functions
Mental and physical functions related to the sexual act, including the arousal, preparatory, orgasmic and resolution stages.
Inclusions: functions of the sexual arousal, preparatory, orgasmic and resolution phase; functions related to sexual interest, performance, penile erection, clitoral erection, vaginal lubrication, ejaculation, orgasm; impairments such as in impotence, frigidity, vaginismus, premature ejaculation, priapism and delayed ejaculation
Exclusions: procreation functions (b660); sensations associated with genital and reproductive functions (b670)

Mobility of joint functions
Functions of the range and ease of movement of a joint.
Inclusions: functions of mobility of single or several joints, vertebral, shoulder, elbow, wrist, hip, knee, ankle, small joints of hands and feet; mobility of joints generalized; impairments such as in hypermobility of joints, frozen joints, frozen shoulder, arthritis
Exclusions: stability of joint functions (b715); control of voluntary movement functions (b760)

Stability of joint functions
Functions of the maintenance of structural integrity of the joints.
Inclusions: functions of the stability of a single joint, several joints, and joints generalized; impairments such as in unstable shoulder joint, dislocation of a joint, dislocation of shoulder and hip
Exclusion: mobility of joint functions (b710)
<table>
<thead>
<tr>
<th>Code</th>
<th>Function Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>b730</td>
<td><strong>Muscle power functions</strong>&lt;br&gt;Functions related to the force generated by the contraction of a muscle or muscle groups. Inclusions: functions associated with the power of specific muscles and muscle groups, muscles of one limb, one side of the body, the lower half of the body, all limbs, the trunk and the body as a whole; impairments such as weakness of small muscles in feet and hands, muscle paresis, muscle paralysis, monoplegia, hemiplegia, paraplegia, quadriplegia and akinetic mutism&lt;br&gt;Exclusions: functions of structures adjoining the eye (b215); muscle tone functions (b735); muscle endurance functions (b740)</td>
</tr>
<tr>
<td>b735</td>
<td><strong>Muscle tone functions</strong>&lt;br&gt;Functions related to the tension present in the resting muscles and the resistance offered when trying to move the muscles passively. Inclusions: functions associated with the tension of isolated muscles and muscle groups, muscles of one limb, one side of the body and the lower half of the body, muscles of all limbs, muscles of the trunk, and all muscles of the body; impairments such as hypotonia, hypertonia and muscle spasticity&lt;br&gt;Exclusions: muscle power functions (b730); muscle endurance functions (b740)</td>
</tr>
<tr>
<td>b740</td>
<td><strong>Muscle endurance functions</strong>&lt;br&gt;Functions related to sustaining muscle contraction for the required period of time. Inclusions: functions associated with sustaining muscle contraction for isolated muscles and muscle groups, and all muscles of the body; impairments such as in myasthenia gravis&lt;br&gt;Exclusions: exercise tolerance functions (b455); muscle power functions (b730); muscle tone functions (b735)</td>
</tr>
<tr>
<td>b750</td>
<td><strong>Motor reflex functions</strong>&lt;br&gt;Functions of involuntary contraction of muscles automatically induced by specific stimuli. Inclusions: functions of stretch motor reflex, automatic local joint reflex, reflexes generated by noxious stimuli and other exteroceptive stimuli; withdrawal reflex, biceps reflex, radius reflex, quadriceps reflex, patellar reflex, ankle reflex</td>
</tr>
<tr>
<td>b755</td>
<td><strong>Involuntary movement reaction functions</strong>&lt;br&gt;Functions of involuntary contractions of large muscles or the whole body induced by body position, balance and threatening stimuli.&lt;br&gt;Inclusions: functions of postural reactions, righting reactions, body adjustment reactions, balance reactions, supporting reactions, defensive reactions&lt;br&gt;Exclusion: motor reflex functions (b750)</td>
</tr>
<tr>
<td>b760</td>
<td><strong>Control of voluntary movement functions</strong>&lt;br&gt;Functions associated with control over and coordination of voluntary movements.&lt;br&gt;Inclusions: functions of control of simple voluntary movements and of complex voluntary movements, coordination of voluntary movements, supportive functions of arm or leg, right left motor coordination, eye hand coordination, eye foot coordination; impairments such as control and coordination problems, e.g. dysdiadochokinesia&lt;br&gt;Exclusions: muscle power functions (b730); involuntary movement functions (b765); gait pattern functions (b770)</td>
</tr>
<tr>
<td>b770</td>
<td><strong>Gait pattern functions</strong>&lt;br&gt;Functions of movement patterns associated with walking, running or other whole body movements.&lt;br&gt;Inclusions: walking patterns and running patterns; impairments such as spastic gait, hemiplegic gait, paraplegic gait, asymmetric gait, limping and stiff gait pattern&lt;br&gt;Exclusions: muscle power functions (b730); muscle tone functions (b735); control of voluntary movement functions (b760); involuntary movement functions (b765)</td>
</tr>
</tbody>
</table>
BODY STRUCTURES
= anatomical parts of the body such as organs, limbs and their components

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>s110</td>
<td>Structure of brain</td>
</tr>
<tr>
<td>s410</td>
<td>Structure of cardiovascular system</td>
</tr>
<tr>
<td>s720</td>
<td>Structure of shoulder region</td>
</tr>
<tr>
<td>s730</td>
<td>Structure of upper extremity</td>
</tr>
<tr>
<td>s750</td>
<td>Structure of lower extremity</td>
</tr>
</tbody>
</table>
# ACTIVITIES AND PARTICIPATION

= execution of a task or action by an individual and involvement in a life situation

<table>
<thead>
<tr>
<th>Code</th>
<th>Activity Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>d115</td>
<td>Listening</td>
</tr>
<tr>
<td></td>
<td>Using the sense of hearing intentionally to experience auditory stimuli, such as listening to a radio, music or a lecture.</td>
</tr>
<tr>
<td>d155</td>
<td>Acquiring skills</td>
</tr>
<tr>
<td></td>
<td>Developing basic and complex competencies in integrated sets of actions or tasks so as to initiate and follow through with the acquisition of a skill, such as manipulating tools or playing games like chess.</td>
</tr>
<tr>
<td></td>
<td>Inclusion: acquiring basic and complex skills</td>
</tr>
<tr>
<td>d160</td>
<td>Focusing attention</td>
</tr>
<tr>
<td></td>
<td>Intentionally focusing on specific stimuli, such as by filtering out distracting noises.</td>
</tr>
<tr>
<td>d166</td>
<td>Reading</td>
</tr>
<tr>
<td></td>
<td>Performing activities involved in the comprehension and interpretation of written language (e.g. books, instructions or newspapers in text or Braille), for the purpose of obtaining general knowledge or specific information.</td>
</tr>
<tr>
<td></td>
<td>Exclusion: learning to read (d140)</td>
</tr>
<tr>
<td>d170</td>
<td>Writing</td>
</tr>
<tr>
<td></td>
<td>Using or producing symbols or language to convey information, such as producing a written record of events or ideas or drafting a letter.</td>
</tr>
<tr>
<td></td>
<td>Exclusion: learning to write (d145)</td>
</tr>
<tr>
<td>d172</td>
<td>Calculating</td>
</tr>
<tr>
<td></td>
<td>Performing computations by applying mathematical principles to solve problems that are described in words and producing or displaying the results, such as computing the sum of three numbers or finding the result of dividing one number by another.</td>
</tr>
<tr>
<td></td>
<td>Exclusion: learning to calculate (d150)</td>
</tr>
<tr>
<td>d175</td>
<td>Solving problems</td>
</tr>
<tr>
<td></td>
<td>Finding solutions to questions or situations by identifying and analysing issues, developing options and solutions, evaluating potential effects of solutions, and executing a chosen solution, such as in resolving a dispute between two people.</td>
</tr>
<tr>
<td></td>
<td>Inclusions: solving simple and complex problems</td>
</tr>
<tr>
<td></td>
<td>Exclusions: thinking (d163); making decisions (d177)</td>
</tr>
<tr>
<td>d210</td>
<td>Undertaking a single task</td>
</tr>
<tr>
<td></td>
<td>Carrying out simple or complex and coordinated actions related to the mental and physical components of a single task, such as initiating a task, organizing time, space and materials for a task, pacing task performance, and carrying out, completing, and sustaining a task.</td>
</tr>
<tr>
<td></td>
<td>Inclusions: undertaking a simple or complex task; undertaking a single task independently or in a group</td>
</tr>
<tr>
<td></td>
<td>Exclusions: acquiring skills (d155); solving problems (d175); making decisions (d177); undertaking multiple tasks (d220)</td>
</tr>
<tr>
<td>d220</td>
<td>Undertaking multiple tasks</td>
</tr>
<tr>
<td></td>
<td>Carrying out simple or complex and coordinated actions as components of multiple, integrated and complex tasks in sequence or simultaneously.</td>
</tr>
<tr>
<td></td>
<td>Inclusions: undertaking multiple tasks; completing multiple tasks; undertaking multiple tasks independently and in a group</td>
</tr>
<tr>
<td></td>
<td>Exclusions: acquiring skills (d155); solving problems (d175); making decisions (d177); undertaking a single task (d210)</td>
</tr>
<tr>
<td>d230</td>
<td>Carrying out daily routine</td>
</tr>
<tr>
<td></td>
<td>Carrying out simple or complex and coordinated actions in order to plan, manage and complete the requirements of day-to-day procedures or duties, such as budgeting time and making plans for separate activities throughout the day.</td>
</tr>
<tr>
<td></td>
<td>Inclusions: managing and completing the daily routine; managing one's own activity level</td>
</tr>
<tr>
<td></td>
<td>Exclusion: undertaking multiple tasks (d220)</td>
</tr>
<tr>
<td>d240</td>
<td>Handling stress and other psychological demands</td>
</tr>
<tr>
<td></td>
<td>Carrying out simple or complex and coordinated actions to manage and control the psychological demands required to carry out tasks demanding significant responsibilities and involving stress, distraction, or crises, such as driving a vehicle during heavy traffic or taking care of many children.</td>
</tr>
<tr>
<td></td>
<td>Inclusions: handling responsibilities; handling stress and crisis</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
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<tr>
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<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>d310</td>
<td>Communicating with - receiving - spoken messages</td>
</tr>
<tr>
<td></td>
<td>Comprehending literal and implied meanings of messages in spoken language,</td>
</tr>
<tr>
<td></td>
<td>such as understanding that a statement asserts a fact or is an idiomatic</td>
</tr>
<tr>
<td></td>
<td>expression.</td>
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<tr>
<td>d315</td>
<td>Communicating with - receiving - nonverbal messages</td>
</tr>
<tr>
<td></td>
<td>Comprehending the literal and implied meanings of messages conveyed by</td>
</tr>
<tr>
<td></td>
<td>gestures, symbols and drawings, such as realizing that a child is tired</td>
</tr>
<tr>
<td></td>
<td>when she rubs her eyes or that a warning bell means that there is a fire.</td>
</tr>
<tr>
<td></td>
<td>Inclusions: communicating with - receiving - body gestures, general signs</td>
</tr>
<tr>
<td></td>
<td>and symbols, drawings and photographs</td>
</tr>
<tr>
<td>d325</td>
<td>Communicating with - receiving - written messages</td>
</tr>
<tr>
<td></td>
<td>Comprehending the literal and implied meanings of messages that are</td>
</tr>
<tr>
<td></td>
<td>conveyed through written language (including Braille), such as following</td>
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<tr>
<td></td>
<td>political events in the daily newspaper or understanding the intent of</td>
</tr>
<tr>
<td></td>
<td>religious scripture.</td>
</tr>
<tr>
<td>d330</td>
<td>Speaking</td>
</tr>
<tr>
<td></td>
<td>Producing words, phrases and longer passages in spoken messages with literal</td>
</tr>
<tr>
<td></td>
<td>and implied meaning, such as expressing a fact or telling a story in oral</td>
</tr>
<tr>
<td></td>
<td>language.</td>
</tr>
<tr>
<td>d335</td>
<td>Producing nonverbal messages</td>
</tr>
<tr>
<td></td>
<td>Using gestures, symbols and drawings to convey messages, such as shaking</td>
</tr>
<tr>
<td></td>
<td>one's head to indicate disagreement or drawing a picture or diagram to</td>
</tr>
<tr>
<td></td>
<td>convey a fact or complex idea.</td>
</tr>
<tr>
<td></td>
<td>Inclusion: producing body gestures, signs, symbols, drawings and photographs</td>
</tr>
<tr>
<td>d345</td>
<td>Writing messages</td>
</tr>
<tr>
<td></td>
<td>Producing the literal and implied meanings of messages that are</td>
</tr>
<tr>
<td></td>
<td>conveyed through written language, such as writing a letter to a friend.</td>
</tr>
<tr>
<td>d350</td>
<td>Conversation</td>
</tr>
<tr>
<td></td>
<td>Starting, sustaining and ending an interchange of thoughts and ideas,</td>
</tr>
<tr>
<td></td>
<td>carried out by means of spoken, written, sign or other forms of language,</td>
</tr>
<tr>
<td></td>
<td>with one or more people one knows or who are strangers, in formal or casual</td>
</tr>
<tr>
<td></td>
<td>settings.</td>
</tr>
<tr>
<td></td>
<td>Inclusions: starting, sustaining and ending a conversation; conversing with</td>
</tr>
<tr>
<td></td>
<td>one or many people</td>
</tr>
<tr>
<td>d360</td>
<td>Using communication devices and techniques</td>
</tr>
<tr>
<td></td>
<td>Using devices, techniques and other means for the purposes of communicating</td>
</tr>
<tr>
<td></td>
<td>such as calling a friend on the telephone.</td>
</tr>
<tr>
<td></td>
<td>Inclusions: using telecommunication devices, using writing machines and</td>
</tr>
<tr>
<td></td>
<td>communication techniques</td>
</tr>
<tr>
<td>d410</td>
<td>Changing basic body position</td>
</tr>
<tr>
<td></td>
<td>Getting into and out of a body position and moving from one location to</td>
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<tr>
<td></td>
<td>another, such as getting up out of a chair to lie down on a bed, and getting</td>
</tr>
<tr>
<td></td>
<td>into and out of positions of kneeling or squatting.</td>
</tr>
<tr>
<td></td>
<td>Inclusion: changing body position from lying down, from squatting or</td>
</tr>
<tr>
<td></td>
<td>kneeling, from sitting or standing, bending and shifting the body's centre</td>
</tr>
<tr>
<td></td>
<td>of gravity.</td>
</tr>
<tr>
<td></td>
<td>Exclusion: transferring oneself (d420)</td>
</tr>
<tr>
<td>d415</td>
<td>Maintaining a body position</td>
</tr>
<tr>
<td></td>
<td>Staying in the same body position as required, such as remaining seated or</td>
</tr>
<tr>
<td></td>
<td>remaining standing for work or school.</td>
</tr>
<tr>
<td></td>
<td>Inclusions: maintaining a lying, squatting, kneeling, sitting and standing</td>
</tr>
<tr>
<td></td>
<td>position</td>
</tr>
<tr>
<td>d420</td>
<td>Transferring oneself</td>
</tr>
<tr>
<td></td>
<td>Moving from one surface to another, such as sliding along a bench or</td>
</tr>
<tr>
<td></td>
<td>moving from a bed to a chair, without changing body position.</td>
</tr>
<tr>
<td></td>
<td>Inclusion: transferring oneself while sitting or lying</td>
</tr>
<tr>
<td></td>
<td>Exclusion: changing basic body position (d410)</td>
</tr>
<tr>
<td>d430</td>
<td>Lifting and carrying objects</td>
</tr>
<tr>
<td></td>
<td>Raising up an object or taking something from one place to another, such</td>
</tr>
<tr>
<td></td>
<td>as when lifting a cup or carrying a child from one room to another.</td>
</tr>
<tr>
<td></td>
<td>Inclusions: lifting, carrying in the hands or arms, or on shoulders, hip,</td>
</tr>
<tr>
<td></td>
<td>back or head; putting down</td>
</tr>
<tr>
<td>d440</td>
<td>Fine hand use</td>
</tr>
<tr>
<td></td>
<td>Performing the coordinated actions of handling objects, picking up,</td>
</tr>
<tr>
<td></td>
<td>manipulating and releasing them using one's hand, fingers and thumb, such</td>
</tr>
<tr>
<td></td>
<td>as required to lift coins off a table or turn a dial or knob.</td>
</tr>
<tr>
<td></td>
<td>Inclusions: picking up, grasping, manipulating and releasing</td>
</tr>
<tr>
<td></td>
<td>Exclusion: lifting and carrying objects (d430)</td>
</tr>
<tr>
<td>Code</td>
<td>Task Description</td>
</tr>
<tr>
<td>-------</td>
<td>------------------------------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| d445  | Hand and arm use                                                                                      | Performing the coordinated actions required to move objects or to manipulate them by using hands and arms, such as when turning door handles or throwing or catching an object.  
Exclusions: fine hand use (d440). |
| d450  | Walking                                                                                               | Moving along a surface on foot, step by step, so that one foot is always on the ground, such as when strolling, sauntering, walking forwards, backwards, or sideways.  
Inclusions: walking short or long distances; walking on different surfaces; walking around obstacles.  
Exclusions: transferring oneself (d420); moving around (d455). |
| d455  | Moving around                                                                                        | Moving the whole body from one place to another by means other than walking, such as climbing over a rock or running down a street, skipping, scampering, jumping, somersaulting or running around obstacles.  
Inclusions: crawling, climbing, running, jogging, jumping, and swimming.  
Exclusions: transferring oneself (d420); walking (d450). |
| d460  | Moving around in different locations                                                                | Walking and moving around in various places and situations, such as walking between rooms in a house, within a building, or down the street of a town.  
Inclusions: moving around within the home, crawling or climbing within the home; walking or moving within buildings other than the home, and outside the home and other buildings.  
Exclusions: transferring oneself (d420); walking (d450). |
| d465  | Moving around using equipment                                                                           | Moving the whole body from place to place, on any surface or space, by using specific devices designed to facilitate moving or create other ways of moving around, such as with skates, skis, or scuba equipment, or moving down the street in a wheelchair or a walker.  
Exclusions: transferring oneself (d420); walking (d450); moving around (d455); using transportation (d470); driving (d475). |
| d470  | Using transportation                                                                                   | Using transportation to move around as a passenger, such as being driven in a car or on a bus, rickshaw, jinney, animal-powered vehicle, or private or public taxi, bus, train, tram, subway, boat or aircraft.  
Inclusions: using human-powered transportation; using private motorized or public transportation.  
Exclusions: moving around using equipment (d465); driving (d475). |
| d475  | Driving                                                                                               | Being in control of and moving a vehicle or the animal that draws it, travelling under one’s own direction or having at one’s disposal any form of transportation, such as a car, bicycle, boat or animal-powered vehicle.  
Inclusions: driving human-powered transportation; motorized vehicles; animal-powered vehicles.  
Exclusions: moving around using equipment (d465); using transportation (d470). |
| d510  | Washing oneself                                                                                        | Washing and drying one’s whole body, or body parts, using water and appropriate cleaning and drying materials or methods, such as bathing, showering, washing hands and feet, face and hair, and drying with a towel.  
Inclusions: washing body parts, the whole body; and drying oneself.  
Exclusions: washing oneself (d510); toileting (d530). |
| d520  | Caring for body parts                                                                                  | Looking after those parts of the body, such as skin, face, teeth, scalp, nails and genitals, that requires more than washing and drying.  
Inclusions: caring for skin, teeth, hair, finger and toe nails.  
Exclusions: washing oneself (d510); toileting (d530). |
| d530  | Toileting                                                                                             | Planning and carrying out the elimination of human waste (menstruation, urination and defecation), and cleaning oneself afterwards.  
Inclusions: regulating urination, defecation and menstrual care.  
Exclusions: washing oneself (d510); caring for body parts (d520). |
| d540  | Dressing                                                                                              | Carrying out the coordinated actions and tasks of putting on and taking off clothes and footwear in sequence and in keeping with climatic and social conditions, such as by putting on, adjusting and removing shirts, skirts, blouses, pants, undergarments, saris, kimono, tights, hats, gloves, coats, shoes, boots, sandals and slippers.  
Inclusions: putting on or taking off clothes and footwear and choosing appropriate clothing. |
<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>d550</td>
<td><strong>Eating</strong>&lt;br&gt;Carrying out the coordinated tasks and actions of eating food that has been served, bringing it to the mouth and consuming it in culturally acceptable ways, cutting or breaking food into pieces, opening bottles and cans, using eating implements, having meals, feasting or dining.&lt;br&gt;Exclusion: drinking (d560)</td>
</tr>
<tr>
<td>d570</td>
<td><strong>Looking after one’s health</strong>&lt;br&gt;Ensuring physical comfort, health and physical and mental well-being, such as by maintaining a balanced diet, and an appropriate level of physical activity, keeping warm or cool, avoiding harms to health, following safe sex practices, including using condoms, getting immunizations and regular physical examinations.&lt;br&gt;Inclusions: ensuring one’s physical comfort; managing diet and fitness; maintaining one’s health</td>
</tr>
<tr>
<td>d620</td>
<td>Acquisition of goods and services&lt;br&gt;Selecting, procuring and transporting all goods and services required for daily living, such as selecting, procuring, transporting and storing food, drink, clothing, cleaning materials, fuel, household items, utensils, cooking ware, domestic appliances and tools; procuring utilities and other household services.&lt;br&gt;Inclusions: shopping and gathering daily necessities&lt;br&gt;Exclusion: acquiring a place to live (d610)</td>
</tr>
<tr>
<td>d630</td>
<td>Preparing meals&lt;br&gt;Planning, organizing, cooking and serving simple and complex meals for oneself and others, such as by making a menu, selecting edible food and drink, getting together ingredients for preparing meals, cooking with heat and preparing cold foods and drinks, and serving the food.&lt;br&gt;Inclusions: preparing simple and complex meals&lt;br&gt;Exclusions: eating (d550); drinking (d560); acquisition of goods and services (d620); doing housework (d640); caring for household objects (d650); caring for others (d660)</td>
</tr>
<tr>
<td>d640</td>
<td>Doing housework&lt;br&gt;Managing a household by cleaning the house, washing clothes, using household appliances, storing food and disposing of garbage, such as by sweeping, mopping, washing counters, walls and other surfaces; collecting and disposing of household garbage; tidying rooms, closets and drawers; collecting, washing, drying, folding and ironing clothes; cleaning footwear; using brooms, brushes and vacuum cleaners; using washing machines, driers and irons.&lt;br&gt;Inclusions: washing and drying clothes and garments; cleaning cooking area and utensils; cleaning living area; using household appliances, storing daily necessities and disposing of garbage&lt;br&gt;Exclusions: acquiring a place to live (d610); acquisition of goods and services (d620); preparing meals (d630); caring for household objects (d650); caring for others (d660)</td>
</tr>
<tr>
<td>d710</td>
<td>Basic interpersonal interactions&lt;br&gt;Interacting with people in a contextually and socially appropriate manner, such as by showing consideration and esteem when appropriate, or responding to the feelings of others.&lt;br&gt;Inclusions: showing respect, warmth, appreciation, and tolerance in relationships; responding to criticism and social cues in relationships; and using appropriate physical contact in relationships</td>
</tr>
<tr>
<td>d750</td>
<td>Informal social relationships&lt;br&gt;Entering into relationships with others, such as casual relationships with people living in the same community or residence, or with co-workers, students, playmates or people with similar backgrounds or professions.&lt;br&gt;Inclusions: informal relationships with friends, neighbours, acquaintances, co-inhabitants and peers</td>
</tr>
<tr>
<td>d760</td>
<td>Family relationships&lt;br&gt;Creating and maintaining kinship relationships, such as with members of the nuclear family, extended family, foster and adopted family and step-relationships, more distant relationships such as second cousins, or legal guardians.&lt;br&gt;Inclusions: parent-child and child-parent relationships, sibling and extended family relationships</td>
</tr>
<tr>
<td>d770</td>
<td>Intimate relationships&lt;br&gt;Creating and maintaining close or romantic relationships between individuals, such as husband and wife, lovers or sexual partners.&lt;br&gt;Inclusions: romantic, spousal and sexual relationships</td>
</tr>
<tr>
<td>d845</td>
<td>Acquiring, keeping and terminating a job&lt;br&gt;Seeking, finding and choosing employment, being hired and accepting employment, maintaining and advancing through a job, trade, occupation or profession, and leaving a job in an appropriate manner.&lt;br&gt;Inclusions: seeking employment; preparing a resume or curriculum vitae; contacting employers and preparing interviews; maintaining a job; monitoring one’s own work performance; giving notice; and terminating a job</td>
</tr>
<tr>
<td>Code</td>
<td>Category</td>
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</tr>
<tr>
<td>d850</td>
<td>Remunerative employment</td>
</tr>
<tr>
<td>d855</td>
<td>Non-remunerative employment</td>
</tr>
<tr>
<td>d860</td>
<td>Basic economic transactions</td>
</tr>
<tr>
<td>d870</td>
<td>Economic self-sufficiency</td>
</tr>
<tr>
<td>d910</td>
<td>Community life</td>
</tr>
<tr>
<td>d920</td>
<td>Recreation and leisure</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>------</td>
<td>-------------</td>
</tr>
</tbody>
</table>
| e110 | Products or substances for personal consumption  
|      | Any natural or human-made object or substance gathered, processed or manufactured for ingestion.  
|      | Inclusions: food and drugs |
| e115 | Products and technology for personal use in daily living  
|      | Equipment, products and technologies used by people in daily activities, including those adapted or specially designed, located in, on or near the person using them.  
|      | Inclusions: general and assistive products and technology for personal use |
| e120 | Products and technology for personal indoor and outdoor mobility and transportation  
|      | Equipment, products and technologies used by people in activities of moving inside and outside buildings, including those adapted or specially designed, located in, on or near the person using them.  
|      | Inclusions: general and assistive products and technology for personal indoor and outdoor mobility and transportation |
| e125 | Products and technology for communication  
|      | Equipment, products and technologies used by people in activities of sending and receiving information, including those adapted or specially designed, located in, on or near the person using them.  
|      | Inclusions: general and assistive products and technology for communication |
| e135 | Products and technology for employment  
|      | Equipment, products and technology used for employment to facilitate work activities.  
|      | Inclusion: general and assistive products and technology for employment |
| e150 | Design, construction and building products and technology of buildings for public use  
|      | Products and technology that constitute an individual’s indoor and outdoor human-made environment that is planned, designed and constructed for public use, including those adapted or specially designed.  
|      | Inclusions: design, construction and building products and technology of entrances and exits, facilities and routing |
| e155 | Design, construction and building products and technology of buildings for private use  
|      | Products and technology that constitute an individual’s indoor and outdoor human-made environment that is planned, designed and constructed for private use, including those adapted or specially designed.  
|      | Inclusions: design, construction and building products and technology of entrances and exits, facilities and routing |
| e165 | Assets  
|      | Products or objects of economic exchange such as money, goods, property and other valuables that an individual owns or of which he or she has rights of use.  
|      | Inclusions: tangible and intangible products and goods, financial assets |
| e210 | Physical geography  
|      | Features of land forms and bodies of water.  
|      | Inclusions: features of geography included within orography (relief, quality and expanse of land and land forms, including altitude) and hydrography (bodies of water such as lakes, rivers, sea) |
| e310 | Immediate family  
|      | Individuals related by birth, marriage or other relationship recognized by the culture as immediate family, such as spouses, partners, parents, siblings, children, foster parents, adoptive parents and grandparents.  
|      | Exclusions: extended family (e315); personal care providers and personal assistants (e340) |
| e315 | Extended family  
|      | Individuals related through family or marriage or other relationships recognized by the culture as extended family, such as aunts, uncles, nephews and nieces.  
|      | Exclusion: immediate family (e310) |
| e320 | Friends  
|      | Individuals who are close and ongoing participants in relationships characterized by trust and mutual support. |
| e325 | Acquaintances, peers, colleagues, neighbours and community members  
|      | Individuals who are familiar to each other as acquaintances, peers, colleagues, neighbours, and community members, in situations of work, school, recreation, or other aspects of life, and who share demographic features such as age, gender, religious creed or ethnicity or pursue common interests.  
|      | Exclusions: associations and organizational services (e5550) |
| e340 | Personal care providers and personal assistants  
|      | Individuals who provide services as required to support individuals in their daily activities and maintenance of performance at work, education or other life situation, provided either through public or private funds, or else on a voluntary basis, such as providers of support for home-making and maintenance, personal assistants, transport assistants, paid help, nannies and others who function as primary caregivers.  
|      | Exclusions: immediate family (e310); extended family (e315); friends (e320); general social support services (e5750); health professionals (e355) |
| e355 | Health professionals  
|      | All service providers working within the context of the health system, such as doctors, nurses, physiotherapists, occupational therapists, speech therapists, audiologists, orthotist-prosthetists, medical social workers.  
|      | Exclusion: other professionals (e360) |
| e360 | Other professionals  
|      | All service providers working outside the health system, including lawyers, social workers, teachers, architects and designers.  
<p>|      | Exclusion: health professionals (e355) |</p>
<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>e410</td>
<td>Individual attitudes of immediate family members</td>
</tr>
<tr>
<td></td>
<td>General or specific opinions and beliefs of immediate family members about the person or about other matters (e.g. social, political and economic issues), that influence individual behaviour and actions.</td>
</tr>
<tr>
<td>e420</td>
<td>Individual attitude of friends</td>
</tr>
<tr>
<td></td>
<td>General or specific opinions and beliefs of friends about the person or about other matters (e.g. social, political and economic issues), that influence individual behaviour and actions.</td>
</tr>
<tr>
<td>e425</td>
<td>Individual attitudes of acquaintances, peers, colleagues, neighbours and community members</td>
</tr>
<tr>
<td></td>
<td>General or specific opinions and beliefs of acquaintances, peers, colleagues, neighbours and community members about the person or about other matters (e.g. social, political and economic issues), that influence individual behaviour and actions.</td>
</tr>
<tr>
<td>e440</td>
<td>Individual attitudes of personal care providers and personal assistants</td>
</tr>
<tr>
<td></td>
<td>General or specific opinions and beliefs of personal care providers and personal assistants about the person or about other matters (e.g. social, political and economic issues), that influence individual behaviour and actions.</td>
</tr>
<tr>
<td>e450</td>
<td>Individual attitudes of health professionals</td>
</tr>
<tr>
<td></td>
<td>General or specific opinions and beliefs of health professionals about the person or about other matters (e.g. social, political and economic issues), that influence individual behaviour and actions.</td>
</tr>
<tr>
<td>e455</td>
<td>Individual attitude of health-related professionals</td>
</tr>
<tr>
<td></td>
<td>General or specific opinions and beliefs of health-related professionals about the person or about other matters (e.g. social, political and economic issues), that influence individual behaviour and actions.</td>
</tr>
<tr>
<td>e460</td>
<td>Societal attitudes</td>
</tr>
<tr>
<td></td>
<td>General or specific opinions and beliefs generally held by people of a culture, society, subcultural or other social group about other individuals or about other social, political and economic issues, that influence group or individual behaviour and actions.</td>
</tr>
<tr>
<td>e515</td>
<td>Architecture and construction services, systems and policies</td>
</tr>
<tr>
<td></td>
<td>Services, systems and policies for the design and construction of buildings, public and private. Exclusion: open space planning services, systems and policies (e520)</td>
</tr>
<tr>
<td>e525</td>
<td>Housing services, systems and policies</td>
</tr>
<tr>
<td></td>
<td>Services, systems and policies for the provision of shelters, dwellings or lodging for people.</td>
</tr>
<tr>
<td>e535</td>
<td>Communication services, systems and policies</td>
</tr>
<tr>
<td></td>
<td>Services, systems and policies for the transmission and exchange of information.</td>
</tr>
<tr>
<td>e540</td>
<td>Transportation services, systems and policies</td>
</tr>
<tr>
<td></td>
<td>Services, systems and policies for enabling people or goods to move or be moved from one location to another.</td>
</tr>
<tr>
<td>e550</td>
<td>Legal services, systems and policies</td>
</tr>
<tr>
<td></td>
<td>Services, systems and policies concerning the legislation and other law of a country.</td>
</tr>
<tr>
<td>e555</td>
<td>Associations and organizational services, systems and policies</td>
</tr>
<tr>
<td></td>
<td>Services, systems and policies relating to groups of people who have joined together in the pursuit of common, noncommercial interests, often with an associated membership structure.</td>
</tr>
<tr>
<td>e570</td>
<td>Social security services, systems and policies</td>
</tr>
<tr>
<td></td>
<td>Services, systems and policies aimed at providing income support to people who, because of age, poverty, unemployment, health condition or disability, require public assistance that is funded either by general tax revenues or contributory schemes. Exclusion: economic services, systems and policies (e565)</td>
</tr>
<tr>
<td>e575</td>
<td>General social support services, systems and policies</td>
</tr>
<tr>
<td></td>
<td>Services, systems and policies aimed at providing support to those requiring assistance in areas such as shopping, housework, transport, self-care and care of others, in order to function more fully in society. Exclusions: personal care providers and personal assistants (e340); social security services, systems and policies (e570); health services, systems and policies (e580)</td>
</tr>
<tr>
<td>e580</td>
<td>Health services, systems and policies</td>
</tr>
<tr>
<td></td>
<td>Services, systems and policies for preventing and treating health problems, providing medical rehabilitation and promoting a healthy lifestyle. Exclusion: general social support services, systems and policies (e575)</td>
</tr>
<tr>
<td>e590</td>
<td>Labour and employment services, systems and policies</td>
</tr>
<tr>
<td></td>
<td>Services, systems and policies related to finding suitable work for persons who are unemployed or looking for different work, or to support individuals already employed who are seeking promotion. Exclusion: economic services, systems and policies (e565)</td>
</tr>
</tbody>
</table>
Date: ____________________
Patient of: ____________________

Sex:
☐ M
☐ F

Modified Rankin Scale: _________
0 – No symptoms
1 – No significant disability despite symptoms; able to carry out all usual duties and activities
2 – Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3 – Moderate disability; requiring some help, but able to walk without assistance (with or without cane or walker)
4 – Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5 – Severe disability; bedridden, incontinent and requiring constant nursing care and attention

Clinical Frailty Scale: _______
1 – Very fit - Robust, active, energetic, well-motivated and fit
2 – Well - Without active disease, but less fit than those in 1
3 – Well, with treated comorbid disease - Disease symptoms well controlled
4 – Apparently vulnerable - Not dependent, but common complaints about being ‘slowed up’ or having disease symptoms
5 – Mildly frail - Limited dependence for IADLs
6 – Moderately frail - Help required for both IADLs/ADLs
7 – Severely frail - Completely dependent on others for ADLs, or terminally ill

Unable to complete due to:
☐ Language
☐ Aphasic/Dysphasic
☐ Unable to translate
☐ Motor
☐ Vision
☐ Too ill
☐ Other: ________

Resides at:
☐ Home
☐ Nursing Home/ LTC/CCC
☐ Inpatient rehab facility
☐ Retirement Home
☐ Other Residential Facility
☐ No Fixed Address
☐ UTD

Language:
☐ English 1st language
☐ ESL, fluent
☐ ESL, not fluent

Completed by:
☐ RN
☐ MD
☐ RA

Education: highest grade (1-13) _____ # of undergraduate years _____ # of graduate years _____

Systolic BP: _________

Diastolic BP: _________

Height: ________

Weight: ________

Waist/Hip Circumference: ______ / ________

Please see reverse side!
Version Date Mar 24 2014
DOC SCREEN VER 2 PART 2

Time to complete: _____ min _____ s

Memory (Registration)
Read list of words, subject must repeat them. Do 2 trials. Do a recall after 5 minutes.

<table>
<thead>
<tr>
<th></th>
<th>1st trial</th>
<th>2nd trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRAIN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EGG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HAT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHAIR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BLUE</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DOC Mood1 “Over the last 2 weeks, how often have you been bothered by any of the following problems?”

<table>
<thead>
<tr>
<th></th>
<th>Not at all (0)</th>
<th>Several days (1)</th>
<th>More than half the days (2)</th>
<th>Nearly every day (3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Little interest or pleasure doing things</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feeling down, depressed or hopeless</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Score (D): /6

DOC Apnea2
Do you snore loudly (louder than talking, heard through a door, or bother other people)?
Do you often feel tired, fatigued or sleepy during the daytime?
Has anyone observed you stop breathing during your sleep?
Do you have, or are you being treated for high blood pressure?

Score (O): /4

Draw a Clock (Ten Past Nine)

Abstraction “What is the similarity between: (e.g. banana – orange = fruit)”
An eye and an ear? [ ] A trumpet and a piano? [ ]

Score (C): /2

Memory (Delayed Recall)
What were those 5 words?

<table>
<thead>
<tr>
<th>WITHOUT CUE</th>
<th>TRAIN</th>
<th>EGG</th>
<th>HAT</th>
<th>CHAIR</th>
<th>BLUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category cue</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple choice cue</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Score (C): /5


TOTAL DOC SCORE = D + O + (10 – C) = /20

Dear

We are contacting you on behalf of Dr. ______, who you saw in the Sunnybrook Stroke Clinic. You may remember that a research assistant asked you some questions about your memory, your mood and how well you sleep. We hope that you are recovering well since your last visit, and we would like to talk to you again, if possible, to ask some similar questions so that we can hear how you are healing, and what activities you still find challenging.

This interview will take about 15 minutes and your participation is completely voluntary. You will be contacted by telephone within the next couple of weeks. It is important that you understand that you do not have to participate when we call, and that we can stop the questions at any time during the call. It is your choice, and your future care will not be affected by your decision.

Everything we discuss on the phone will be confidential and your privacy will be respected at all times. There are no benefits to participating in this study. However, your answers will help us understand more about long term outcomes after stroke as well as help us understand how to improve the lives of those who experience a stroke. If you do not wish to be contacted, please call (416) 480 6100 (ext. 85426) to have your name removed from the list.

If you have questions about this study, you can call (416) 480 6100 (ext. 85426) or call the study principal investigator, Dr. Richard Swartz at (416) 480 4866 at any time. If you have questions about the rights of research participants you may contact the Chair of the Sunnybrook Research Ethics Board at (416) 480 6100 (ext. 88144).

We look forward to getting in touch with you.

Sincerely,

Sunnybrook Stroke Research Unit
Appendix D

**Telephone Follow-Up Script**

→ Hello, I am calling from Sunnybrook Health Sciences, May I please speak to __________?

**If not available:**
→ When would be the best time to contact __________?
**Call back on:**
   Date: ____________________________
   Time: ____________________________

**If available:**
→ My name is __________
I am calling from Sunnybrook Health Sciences Centre. I work with Dr. __________.
You may recall that you answered some questions while you were at Sunnybrook, about your memory, your mood and how well you sleep. We are calling patients to follow up and see how they are doing now. The questions/interview should take us about 15 mins. Is it okay if I ask you some questions? Can we do this right now?

   **If not interested:**
   → We understand. Thank you for your time.

   **If not available:**
   → When would be the best time to contact you?
   **Call back on:**
   Date: ____________________________
   Time: ____________________________

   **If yes/at time of interview:**
   → Our study looks at how well you are able to carry out day-to-day activities. We hope to learn more about long-term outcomes after stroke and understand how to improve the lives of those who experience a stroke. We will be asking questions to learn how you are doing and what activities you still find challenging. You do not have to participate, and you can stop the questions at any time during the call. It is your choice, and your future care will not be affected by your decision. Your answers will remain confidential. Do you have any questions or would you like more information about this study?

   *Do you understand what we are looking for? Would you like more information about the study?*

   **Ask probe questions to assess patient’s understanding of the study and their involvement, probes will differ depending on individual.**

   **If patient understands:**
   → Do you agree to take part in this research study?

      **If no:**
      → We understand. Thank you for your time.

      **If yes:**
      → Okay. We will first start with a few questions regarding your medical history over the past 2-3 years.
DOC Follow-Up Form

Patient’s Name: ________________________________

Study ID #: ________________________________

Date: ________________________________

Resides at: ________________________________

- Home
- Nursing Home/ LTC/CCC
- Inpatient rehab facility
- Retirement Home
- Other Residential Facility
- No Fixed Address
- UTD

Tx for Comorbidities

☐ Y ☐ N Are you on medications for problems with your mood?
  If yes, when started? ________________________________
  If yes, which one? ________________________________

☐ Y ☐ N Are you receiving any other treatments for problems with your mood?
  If yes, when started? ________________________________

☐ Y ☐ N Do you own a CPAP machine?

☐ Y ☐ N Are you using a CPAP machine?

☐ Y ☐ N Are you taking any medications to help your memory?
  If yes, when started? ________________________________
  If yes, which one? ________________________________

Events Reporting

Any health condition(s) that limit(s) your/your family’s activity?

Any major life events over past 2 years?

Notes

Completed by: ________________________________
Compared to before your stroke, how would you rate your current overall health?

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
</table>

**Poor**

<table>
<thead>
<tr>
<th>Question</th>
<th>Y</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Were you able to drive before your stroke?</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Were you employed before your stroke?</td>
<td>Y</td>
<td>N</td>
</tr>
</tbody>
</table>

Over the past 2 years, have you had any of the following:

<table>
<thead>
<tr>
<th>Question</th>
<th>Y</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>New stroke?</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>New TIA?</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Sudden painless weakness?</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Loss of vision?</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Heart attack?</td>
<td>Y</td>
<td>N</td>
</tr>
</tbody>
</table>

Notes
Could you live alone without any help from another person? This means being able to bathe, use the toilet, shop, prepare or get meals, and manage finances.

- **Yes**
  - Can you do everything that you were doing right before your stroke, even if slower and not as much?
    - **Yes**
      - Are you completely back to the way you were right before your stroke?
        - **Yes**
          - 0
        - **No**
          - 1
    - **No**
      - 2

- **No**
  - Can you walk from one room to another without help from another person?
    - **Yes**
      - Can you sit up in bed without any help?
        - **Yes**
          - 4
        - **No**
          - 5
    - **No**
      - 3
### MODIFIED RANKIN SCALE (MRS)

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No symptoms at all</td>
</tr>
<tr>
<td>1</td>
<td>No significant disability despite symptoms; able to carry out all usual duties and activities</td>
</tr>
<tr>
<td>2</td>
<td>Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance</td>
</tr>
<tr>
<td>3</td>
<td>Moderate disability; requiring some help, but able to walk without assistance</td>
</tr>
<tr>
<td>4</td>
<td>Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance</td>
</tr>
<tr>
<td>5</td>
<td>Severe disability; bedridden, incontinent and requiring constant nursing care and attention</td>
</tr>
<tr>
<td>6</td>
<td>Dead</td>
</tr>
</tbody>
</table>

**TOTAL (0–6): ____**

### References

Rankin J. “Cerebral vascular accidents in patients over the age of 60.” *Scott Med J* 1957;2:200-15


*Provided by the Internet Stroke Center — www.strokecenter.org*
## THE BARTHEL INDEX

**Activity** | **Score**
--- | ---
FEEDING | 
0 = unable
5 = needs help cutting, spreading butter, etc., or requires modified diet
10 = independent | [ ]

BATHING | 
0 = dependent
5 = independent (or in shower) | [ ]

GROOMING | 
0 = needs to help with personal care
5 = independent face/hair/teeth/shaving (implements provided) | [ ]

DRESSING | 
0 = dependent
5 = needs help but can do about half unaided
10 = independent (including buttons, zips, laces, etc.) | [ ]

BOWELS | 
0 = incontinent (or needs to be given enemas)
5 = occasional accident
10 = continent | [ ]

BLADDER | 
0 = incontinent, or catheterized and unable to manage alone
5 = occasional accident
10 = continent | [ ]

TOILET USE | 
0 = dependent
5 = needs some help, but can do something alone
10 = independent (on and off, dressing, wiping) | [ ]

TRANSFERS (BED TO CHAIR AND BACK) | 
0 = unable, no sitting balance
5 = major help (one or two people, physical), can sit
10 = minor help (verbal or physical)
15 = independent | [ ]

MOBILITY (ON LEVEL SURFACES) | 
0 = immobile or < 50 yards
5 = wheelchair independent, including corners, > 50 yards
10 = walks with help of one person (verbal or physical) > 50 yards
15 = independent (but may use any aid; for example, stick) > 50 yards | [ ]

STAIRS | 
0 = unable
5 = needs help (verbal, physical, carrying aid)
10 = independent | [ ]

**TOTAL (0–100):** [ ]

---

**THE**

**Patient Name:** __________________________

**BARTHEL**

**Rater Name:** __________________________

**INDEX**

**Date:** __________________________

**Activity**

**Score**

---

---

---
The Barthel ADL Index: Guidelines

1. The index should be used as a record of what a patient does, not as a record of what a patient could do.
2. The main aim is to establish degree of independence from any help, physical or verbal, however minor and for whatever reason.
3. The need for supervision renders the patient not independent.
4. A patient's performance should be established using the best available evidence. Asking the patient, friends/relatives and nurses are the usual sources, but direct observation and common sense are also important. However direct testing is not needed.
5. Usually the patient's performance over the preceding 24-48 hours is important, but occasionally longer periods will be relevant.
6. Middle categories imply that the patient supplies over 50 per cent of the effort.
7. Use of aids to be independent is allowed.

References


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**DOC Screen & Modified MoCA**

<table>
<thead>
<tr>
<th>DOC Mood&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Not at all (0)</th>
<th>Several days (1)</th>
<th>More than half the days (2)</th>
<th>Nearly every day (3)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>“Over the last 2 weeks, how often have you been bothered by any of the following problems?”</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Little interest or pleasure doing things</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feeling down, depressed or hopeless</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DOC Apnea<sup>2</sup>**

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you snore loudly (louder than talking, heard through a door, or bother other people)?</td>
<td></td>
</tr>
<tr>
<td>Do you often feel tired, fatigued or sleepy during the daytime?</td>
<td></td>
</tr>
<tr>
<td>Has anyone observed you stop breathing during your sleep?</td>
<td></td>
</tr>
<tr>
<td>Do you have, or are you being treated for high blood pressure?</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>D (DOC-Mood) :</th>
<th>/6</th>
</tr>
</thead>
<tbody>
<tr>
<td>O (DOC-Apnea) :</td>
<td>/4</td>
</tr>
</tbody>
</table>

---

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

<table>
<thead>
<tr>
<th></th>
<th>FACE</th>
<th>VELVET</th>
<th>CHURCH</th>
<th>DAISY</th>
<th>RED</th>
<th>POINTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st trial</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2nd trial</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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 point if ≥ 2 errors


__/ 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

<table>
<thead>
<tr>
<th></th>
<th>FACE</th>
<th>VELVET</th>
<th>CHURCH</th>
<th>DAISY</th>
<th>RED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optional Category cue</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple choice cue</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Points for UNCUED recall only

__/ 5

### ORIENTATION

- [ ] Date
- [ ] Month
- [ ] Year
- [ ] Day
- [ ] Place
- [ ] City

__/ 6

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Administered by: ____________________________
**Modified Reintegration to Normal Living Index (mRNL Index)**

For each of the following statements, please indicate how well each statement describes you and/or your situation by placing a mark in a box. Please mark only one box per question.

<table>
<thead>
<tr>
<th></th>
<th>Does not describe me or my situation</th>
<th>Partially describes me or my situation</th>
<th>Fully describes me or my situation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>I move around my house as I need to.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>I move around my community as I need to.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>I am able to make longer trips as I need to.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>I am comfortable with how my self-care needs are met (dressing, feeding toileting bathing).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>I spend most of my days occupied in work activity that is necessary or important to me (such as paid or voluntary work, housework, or studying etc.).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>I am able to participate in recreational activities as I want to (hobbies, crafts, sports, reading, television, games, computers etc.).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>I socialise with friends, family and/or business acquaintances as I want to or is necessary.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td>I have a role in my family which meets my needs and those of my family members. (Family means people with whom you live and/or relatives with whom you don’t live but see on a regular basis.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9.</td>
<td>In general, I am comfortable with my personal relationships.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10.</td>
<td>In general, I am comfortable with myself when I am in the company of others.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11.</td>
<td>I feel that I can deal with life events as they happen.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


# The Frenchay Activities Index

Name: _____________________________ Date: ___________________

**In the last 3 months how often have you undertaken:**

<table>
<thead>
<tr>
<th></th>
<th>Activity</th>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Preparing main meals</td>
<td>0</td>
<td>= Never</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>= Less than once a week</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>= 1-2 times per week</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td>= Most days</td>
</tr>
<tr>
<td>2</td>
<td>Washing up after meals</td>
<td>0</td>
<td>= Never</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>= Less than once a week</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>= 1-2 times per week</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td>= Most days</td>
</tr>
<tr>
<td>3</td>
<td>Washing clothes</td>
<td>0</td>
<td>= Never</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>= 1-2 times in 3 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>= 3-12 times in 6 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td>= At least weekly</td>
</tr>
<tr>
<td>4</td>
<td>Light housework</td>
<td>1</td>
<td>= 1-2 times in 3 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>= 3-12 times in 6 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td>= At least weekly</td>
</tr>
<tr>
<td>5</td>
<td>Heavy housework</td>
<td>0</td>
<td>= Never</td>
</tr>
<tr>
<td>6</td>
<td>Local Shopping</td>
<td>1</td>
<td>= 1-2 times in 3 months</td>
</tr>
<tr>
<td>7</td>
<td>Social occasions</td>
<td>2</td>
<td>= 3-12 times in 6 months</td>
</tr>
<tr>
<td>8</td>
<td>Walking outside for &gt; 15 minutes</td>
<td>3</td>
<td>= At least weekly</td>
</tr>
<tr>
<td>9</td>
<td>Actively pursuing hobby</td>
<td>1</td>
<td>= 1-2 times in 3 months</td>
</tr>
<tr>
<td>10</td>
<td>Driving car-going on bus</td>
<td>2</td>
<td>= 3-12 times in 6 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td>= At least weekly</td>
</tr>
</tbody>
</table>

**In the last 6 months how often have you undertaken:**

<table>
<thead>
<tr>
<th></th>
<th>Activity</th>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>Travel outing/car ride</td>
<td>0</td>
<td>= Never</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>= 1-2 times in 6 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>= 3-12 times in 6 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td>= At least weekly</td>
</tr>
<tr>
<td>12</td>
<td>Gardening</td>
<td>0</td>
<td>= Never</td>
</tr>
<tr>
<td>13</td>
<td>Household maintenance</td>
<td>1</td>
<td>= Light</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>= Moderate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td>= Heavy/All necessary</td>
</tr>
<tr>
<td>14</td>
<td>Reading books</td>
<td>0</td>
<td>= None</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>= 1 in 6 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>= Less than 1 in 2 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td>= More than 1 every 2 weeks</td>
</tr>
<tr>
<td>15</td>
<td>Gainful work</td>
<td>0</td>
<td>= None</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>= Up to 10 hours/week</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>= 10-30 hours/week</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td>= Over 30 hours/week</td>
</tr>
</tbody>
</table>

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