MOTOR OUTCOMES AND THEIR IMPACT ON ACTIVITIES OF DAILY LIVING, FOLLOWING PAEDIATRIC ARTERIAL STROKE

ANNA NICOLE COOPER

ORCID no. 0000-0002-5184-5009

October 2017

Department of Paediatrics

The University of Melbourne

Murdoch Childrens Research Institute

Submitted in the fulfilment of the requirements for the degree of

Doctor of Philosophy
ABSTRACT

Paediatric arterial ischaemic stroke (AIS) affects between 1.6-2.7 per 100,000 children per year. Motor impairments are the most commonly reported adverse consequence following paediatric arterial ischaemic stroke, yet the long-term impact of stroke remains poorly understood. As childhood is a time of rapid brain development and growth, stroke during this developmental stage has the potential to affect not only established skills, but also the development on new and emerging skills with resultant difficulties spanning a lifetime.

The aim of this study was to measure and describe motor and functional difficulties of children following AIS and to explore factors associated with outcomes including lesion characteristics (size, location and laterality), early neurological impairment and age at stroke onset. This thesis addresses these aims through three studies with supplementary data presented in a fourth results chapter.

Study one explored motor and functional outcomes across the first year following AIS. Early predictors of 12-month outcomes were also explored, as was the relationship between fine motor and gross motor function and adaptive behaviour. A larger lesion size was associated with poorer gross motor outcome. Trajectories of recovery differed depending on age at stroke onset and poorer fine and gross motor outcomes were associated with poorer adaptive behaviour skills.

Study two evaluated the relationship between neurological outcome at 1 month following diagnosis of paediatric AIS and motor and adaptive behaviour outcomes at 12 months. Presence of impairment on the paediatric stroke outcome measure (PSOM) at 1 month was associated with poorer 12-month fine motor (FM) skills, gross motor (GM) skills and adaptive behaviour. One month PSOM impairment score was more predictive than age group or lesion size of 12-month motor and adaptive behaviour outcome.

Study three investigated motor impairment and functional motor outcomes 4-6 years after AIS as well as factors associated with these outcomes. At 4-6 years post stroke,
motor function, quality of life, fatigue, adaptive behaviour, activities of daily living and speed of handwriting were significantly poorer than age expectations. The pre-school group had the highest percentage of fine and gross motor impairment. Poorer fine motor skills were associated with subcortical only strokes and large lesion size. Poorer gross motor outcomes were correlated with pre-school age, bilateral lesions and PSOM impairment at 1 month.

The findings from these studies highlight the fact that children are at elevated risk for motor and functional impairments following AIS, with the pre-school age group most vulnerable. Early predictors of poor outcomes were identified, including age at stroke onset, lesion size and early neurological impairment, which helps to facilitate targeted early intervention and long-term rehabilitation. These results support the need for long term surveillance following paediatric stroke with children demonstrating changes in function beyond the first year following diagnosis. These findings indicate the need for functional measures to be used in routine follow up screening.
DECLARATION

This is to certify that:

1. The thesis comprises only of my original work towards the PhD except where indicated in the preface;
2. Due acknowledgement has been made in the text to all other material used;
3. The thesis is fewer than 100,000 words in length, exclusive of tables, figures, bibliography and appendices.

Anna Nicole Cooper
Phase one of this thesis was based on a prospective, longitudinal study conducted by my three supervisors (AG, PM, VA), with the acute data presented in AG’s PhD thesis which explored the health and development of children in the first year following arterial ischaemic stroke. Subsequently, I analysed the post-acute longitudinal data and led the manuscripts for these studies.

Phase two of this thesis explored outcomes of a subgroup of participants from phase one. For this phase, I worked with another PhD student. Together we designed and conceptualised the study, obtained ethics approval, recruited the patients, administered all the relevant assessments, analysed the data as well as primarily wrote the resultant manuscripts. I was responsible for the motor outcomes component of the study, while MG led the explorations of psychosocial outcomes.

Author contributions:

This statement provides an explanation of the contribution of all parties involved in the multi-author papers included in this part of the dissertation.

**Paper one:**

Anna Cooper: Data analysis, manuscript preparation, manuscript submission, reply to reviewer’s comments and manuscript revisions.

Vicki Anderson: Study conception and design, manuscript review, editing, and manuscript revisions.

Stephen Hearps: Statistical advice and analysis, manuscript review, editing, and manuscript revisions.
Mardee Greenham: Study conception and design, data collection, manuscript review, editing, and manuscript revisions.

Michael Ditchfield: Data collection, manuscript review, editing, and manuscript revisions

Lee Coleman: Data collection, manuscript review, editing, and manuscript revisions

Rod Hunt: Manuscript review, editing and manuscript revisions.

Mark Mackay: Manuscript review, editing and manuscript revisions.

Paul Monagle: Study conception and design, manuscript review, editing and manuscript revisions.

Anne Gordon: Study conception and design, data collection, manuscript review, editing, and manuscript revisions.

**Paper two:**

Anna Cooper: Data analysis, manuscript preparation, replies to reviewer’s comments and manuscript revisions.

Vicki Anderson: Study conception and design, manuscript review, editing and manuscript revisions.

Stephen Hearps: Statistical advice and analysis, manuscript review, editing and manuscript revisions.

Mardee Greenham: Study conception and design, data collection, manuscript review, editing and manuscript revisions.
Michael Ditchfield: Data collection, manuscript review, editing, and manuscript revisions.

Lee Coleman: Data collection, manuscript review, editing, and manuscript revisions.

Rod Hunt: Manuscript review, editing and manuscript revisions.

Mark Mackay: Manuscript review, editing and manuscript revisions.

Paul Monagle: Study conception and design, manuscript review, editing and manuscript revisions.

Anne Gordon: Study conception and design, data collection, manuscript submission, editing and manuscript revisions.

Paper three:

Anna Cooper: Study conception and design, data collection, data analysis, manuscript preparation, manuscript submission, reply to reviewer’s comments and manuscript revisions.

Vicki Anderson: Study conception and design, manuscript review, editing and manuscript revisions.

Stephen Hearps: Statistical advice and analysis, manuscript review, editing and manuscript revisions.

Mardee Greenham: Study conception and design, data collection, manuscript review, editing and manuscript revisions.

Michael Ditchfield: Data collection, manuscript review, editing, and manuscript revisions.
Lee Coleman: Data collection, manuscript review, editing, and manuscript revisions.

Rod Hunt: Manuscript review, editing and manuscript revisions.

Mark Mackay: Manuscript review, editing, and manuscript revisions.

Paul Monagle: Study conception and design, manuscript review, editing and manuscript revisions.

Anne Gordon: Study conception and design, data collection, manuscript review, editing and manuscript revisions.
PUBLICATIONS

First Author:


Co-author:


Book chapter:


Conference presentation with published abstract:


Media:

Publication in Melbourne University’s Pursuit: *Child stroke survivors have time on their side.* [https://pursuit.unimelb.edu.au/articles/child-stroke-survivors-have-time-on-their-side](https://pursuit.unimelb.edu.au/articles/child-stroke-survivors-have-time-on-their-side)

ACKNOWLEDGEMENTS

This study would not have been possible without the support and contribution of many people. Firstly, my heartfelt thanks to my supervisors Professor Paul Monagle, Professor Vicki Anderson and Dr Anne Gordon for believing in me and for offering me to join your team with this PhD opportunity. Thank you Paul for always helping me to put this research into perspective and making sure I’ve always focused of what’s important in life. Vicki and Anne, I have learnt so much from you, you have been very generous in sharing your time and your wealth of experience in child brain injury. Thank you Anne for your original vision and the incredible amount of work that went into initiating and developing the Stroke Recovery Study, without which this PhD would never have been possible.

To members of my advisory committee, Professor Katrina Williams and Dr Melinda Randall for your direction and feedback and clinical advice along the way. To the co-authors on the papers included in this thesis, thankyou for your contributions towards this work.

Thankyou to Mardee Greenham, my co-PhD candidate, not only for your help with recruitment and data collection but for always being someone I can talk to and always knowing which direction to point me in. Thankyou also to Stephen Hearps for advice and assistance with statistical analysis and for you patience with all of my questions.

Thankyou to my family, who sparked my initial interest in research, particularly to my Mum and my mother-in-law for looking after our boys while I’ve been studying. To my Husband Chris and our two boys Tommy and Billy, your love and support has kept me going, you have been my inspiration, my motivation and my drive to make a difference through research.

I would like to acknowledge the funding support from the Murdoch Children’s Research Institute for making this study possible. Finally, thankyou to all of the children and their families for giving up your time to participate in this study. I am incredibly grateful for you to share your stroke experiences without which this research would not exist.
LIST OF TABLES

Table 6.1 Summary of measures carried out at each time point ..................................................34

Paper one: Trajectories of Motor Recovery in the First Year after Pediatric Arterial Ischemic Stroke.
Table 1: Patient and Lesion Characteristics .............................................................................43
Table 2: Total Motor and Adaptive Behaviour Scores ................................................................46
Table 3: Multivariate Regression Models Predicting FM and GM z Scores at 12 months .................................................................46
Table 4: Relationships Between VABS2 (Adaptive Behavior) Scores and Motor z Scores ........................................................................46

Paper two: The Pediatric Stroke Outcome Measure: a predictor of outcome following arterial ischemic stroke
Table 1. Patient and Lesion Characteristics .............................................................................56
Table 2: Hierarchical regression predicting impairment in FM, GM and VABS at 12 months, reporting model improvement due to PSOM impairment beyond age group and lesion size .............................................................................60

Paper three: Motor function and adaptive abilities 5 years following paediatric arterial ischemic stroke.
Table i. Sample demographics and clinical characteristics .........................................................72
Table ii Motor function and functional performance: comparison to published normative data (whole sample) .................................................................................74
Table iii. Motor and functional abilities according to age at stroke onset ................................75

Supplementary results:
Table 9.1 Summary of children with unilateral motor impairments ..........................................81
Table 9.2 Summary of children with bilateral motor impairments ............................................82
Table 9.3 Changes in sensorimotor outcomes on the PSOM between 12 months and 4 years ........................................................................................................83
LIST OF FIGURES

Figure 2.1 ICF-CY framework .................................................................7
Figure 6.1 Recruitment flow chart ..........................................................27

Paper one: Trajectories of Motor Recovery in the First Year after Pediatric Arterial Ischemic Stroke.
Figure 1: Percentage of children with sensorimotor impairments ..................................................43
Figure 2a: Percentage of children with unilateral or bilateral FM impairments (z scores ≤-1) ..................................................44
Figure 2b: Percentage of children with unilateral or bilateral GM impairments (z scores ≤-1) ..................................................44
Figure 3a: FM outcomes across the first year after stroke: linear growth model of standardized FM scores between the 3 age groups ..................................................45
Figure 3b: GM outcomes across the first year after stroke: linear growth model of standardized GM scores between the 3 age groups ..................................................45

Paper two: The Pediatric Stroke Outcome Measure: a predictor of outcome following arterial ischemic stroke
Figure 1. Percentage of children with a sensorimotor motor impairment on the PSOM ........58
Figure 2: Relationship between age of onset and PSOM total scores (predicted means and 95% confidence intervals)* ..................................................59
Figure 3. Relationship between PSOM impairment at 1 month and % of impairments at 12 months ..................................................................................61
Figure 4. Figure 4: ROC curves (with AUC) examining the discriminant ability of 1-month PSOM to distinguish 12-month impairment (FMZ, GMZ and VABS total) .............62

Paper three: Motor function and adaptive abilities 4 years following paediatric arterial ischemic stroke.
No figures
# LIST OF ABBREVIATIONS AND ACRONYMS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABI</td>
<td>Acquired brain injury</td>
</tr>
<tr>
<td>AIS</td>
<td>Arterial ischaemic stroke</td>
</tr>
<tr>
<td>ANOVA</td>
<td>Analysis of variance</td>
</tr>
<tr>
<td>BOT2</td>
<td>Bruininks Oseretsky Test of Motor Proficiency, 2nd Edition</td>
</tr>
<tr>
<td>BSID-111</td>
<td>Bayley Scales of Infant and Toddler Development, 3rd edition</td>
</tr>
<tr>
<td>CNS</td>
<td>Central nervous system</td>
</tr>
<tr>
<td>CP</td>
<td>Cerebral Palsy</td>
</tr>
<tr>
<td>FM</td>
<td>Fine motor</td>
</tr>
<tr>
<td>GM</td>
<td>Gross motor</td>
</tr>
<tr>
<td>GMFCS</td>
<td>Gross motor function classification system</td>
</tr>
<tr>
<td>ICF-CY</td>
<td>International classification of functioning, disability and health for children and youth</td>
</tr>
<tr>
<td>MACS</td>
<td>Manual ability classification system</td>
</tr>
<tr>
<td>MCA</td>
<td>Middle cerebral artery</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td>MRA</td>
<td>Magnetic resonance angiography</td>
</tr>
<tr>
<td>PCA</td>
<td>Posterior cerebral artery</td>
</tr>
<tr>
<td>PedsQL</td>
<td>Pediatric quality of life inventory</td>
</tr>
<tr>
<td>PedsQL-MFS</td>
<td>Pediatric quality of life – Multidimensional Fatigue Scale</td>
</tr>
<tr>
<td>PEM-CY</td>
<td>Participation and Environment Measure for Children and Youth</td>
</tr>
<tr>
<td>PSOM</td>
<td>Pediatric Stroke Outcome Measure</td>
</tr>
<tr>
<td>QoL</td>
<td>Quality of life</td>
</tr>
<tr>
<td>RCHM</td>
<td>Royal Children’s Hospital, Melbourne</td>
</tr>
<tr>
<td>TBI</td>
<td>Traumatic brain injury</td>
</tr>
<tr>
<td>UL</td>
<td>Upper limb</td>
</tr>
<tr>
<td>VABS-11</td>
<td>Vineland Adaptive Behavior Scale, Second Edition</td>
</tr>
</tbody>
</table>
# CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABSTRACT</td>
<td>ii</td>
</tr>
<tr>
<td>DECLARATION</td>
<td>iv</td>
</tr>
<tr>
<td>PREFACE</td>
<td>v</td>
</tr>
<tr>
<td>CO-AUTHOR CONTRIBUTIONS</td>
<td></td>
</tr>
<tr>
<td>PUBLICATIONS</td>
<td>ix</td>
</tr>
<tr>
<td>ACKNOWLEDGEMENTS</td>
<td>xi</td>
</tr>
<tr>
<td>LIST OF TABLES</td>
<td>xii</td>
</tr>
<tr>
<td>LIST OF FIGURES</td>
<td>xiv</td>
</tr>
<tr>
<td>LIST OF ABBREVIATION AND ACRONYMS</td>
<td>xv</td>
</tr>
</tbody>
</table>

## CHAPTER 1: OVERVIEW
1.1 BACKGROUND TO THE STUDY ..........................................................1
1.2 AIM OF THE STUDY .............................................................................2
1.3 OVERVIEW OF THESIS ........................................................................2

## CHAPTER 2: INTRODUCTION
2.1 STROKE IN CHILDREN ..........................................................................4
2.2 STROKE IN ADULTS ...............................................................................5
2.3 CURRENT STROKE GUIDELINES ............................................................6
2.4 INTERNATIONAL CLASSIFICATION OF FUNCTIONING DISABILITY AND HEALTH FOR CHILDREN AND YOUTH (ICF-CY) ..................................................7

## CHAPTER 3: BODY STRUCTURE AND FUNCTION
3.1 TYPICAL MOTOR DEVELOPMENT IN CHILDREN ........................................9
3.2 PRINCIPLES OF BRAIN PLASTICITY .....................................................10
3.3 MOTOR OUTCOMES FOLLOWING ARTERIAL ISCHAEMIC STROKE ...............11
3.4 MOTOR OUTCOMES IN CHILDREN WITH CEREBRAL PALSY .....................12
3.5 MEASURING MOTOR FUNCTION IN CHILDREN WITH ARTERIAL ISCHAEMIC STROKE ..................................................................................20
3.6 INTERVENTIONS AND REHABILITATION .............................................13
3.7 FACTORS ASSOCIATED WITH OUTCOME .............................................13

## CHAPTER 4: ACTIVITY AND PARTICIPATION
4.1 PARTICIPATION ..................................................................................18
4.2 ACTIVITIES OF DAILY LIVING ..........................................................18
4.3 ADAPTIVE BEHAVIOUR ........................................................................19
APPENDICES

APPENDIX 1. FEATURED ARTICLE IN THE UNIVERSITY OF MELBOURNE'S PURSUIT

...
1. OVERVIEW

1.1 Background to the study

Over the last 10 years, paediatric stroke has been increasingly recognised as an important cause of disability and research in the field is emerging rapidly. The impact of stroke in children can last a lifetime with language, cognitive, behavioural, social, economic and motor implications, but with motor impairment being the most frequently reported adverse consequence (1-9).

The focus of existing research has been on diagnosis, acute management and more recently, recovery in the first 12 months post-stroke (10, 11). A child’s recovery may be more protracted and continue beyond this first year, however, there are no prospective longitudinal studies reporting motor outcomes over time (12, 13). There is also a lack of valid and reliable tools to measure motor outcomes in this population, with most research describing motor outcomes as a subsection of overall neurological outcome (6, 7, 9). To the author’s knowledge, no studies have explored the relationship between motor outcomes and long-term independence in daily life activities, participation or quality of life (QoL) following paediatric stroke.

Anecdotally, when a child sustains a brain injury or insult, one of the first questions families ask is ‘will my child fully recover?’ Currently, the understanding of long term motor and functional outcomes following arterial ischaemic stroke (AIS) is limited and therefore the information about physical recovery is speculative. This uncertainty can be challenging for children and their families, not knowing what to expect or how the stroke will affect their child’s long term ability to participate in their everyday lives.

For paediatric therapists, the impact of impaired motor function on a child’s ability to participate and to function independently in their everyday activities is of particular interest. Impaired motor function affects many areas of the child’s life and also impacts their family’s lives (14, 15). Such consequences have been shown to negatively impact physical independence, mobility, financial stability, social
integration, participation and QoL of children with cerebral palsy (CP) (16, 17). Evidence suggests that early intervention is critical to maximise long term motor outcomes, therefore, early identification of children at risk of developing motor or functional impairments is important to help facilitate timely intervention, to optimise long-term outcomes (1, 18).

1.2 Aim of the study

This study aimed to measure and describe motor outcomes following a diagnosis of paediatric arterial ischaemic stroke (AIS) and to describe the relationship between motor outcomes and activity and participation including, adaptive behaviour, fatigue, independence with activities of daily living and QoL. Further, the study aimed to explore acute factors that contribute to motor recovery at 12 months and the 5 year motor outcomes. A comprehensive understanding of longer-term motor outcomes, early predictors and recovery trajectories over time would assist in early identification of children needing rehabilitation or who are at risk of emerging motor or functional impairments.

1.2 Overview of the thesis

The Stoke Recovery Study is a multidisciplinary, prospective, longitudinal study, established in 2007 to explore the health and development of children following AIS. This thesis will discuss and report outcomes in two phases. Phase One of this study recruited children from December 2007 to November 2013 and examined motor and functional outcomes at multiple time points in the first 12 months following diagnosis of AIS. The design of this process and the original data collection was performed by supervisor, AG, as part of her PhD thesis. The analysis of the data was performed as part of this thesis.

Phase two of the study, designed and implemented by the author of this thesis, recruited a sub-group of children from the original cohort between January 2014 and
August 2015, at 4 years post stroke onset. These data focused on a more detailed analysis specifically exploring motor and functional outcomes at one time point. This study was completed alongside another project (by another PhD student) investigating social and behavioural outcomes of the same cohort of children. This provided us with a global perspective of the physical, functional, cognitive and social challenges that these children experience 4 years following stroke onset. To minimise participant burden, AC and MG collaborated and collected demographic data at one time point only. These data were used by both PhD students. In addition, parent completed measures were collected and shared by both students.

The results from these two phases are presented as published and submitted papers in this thesis. Phase one resulted in two published papers titled ‘Trajectories of motor recovery in the first year after arterial ischemic stroke’ and ‘The Pediatric Stroke Outcome Measure: a predictor of outcome following arterial ischemic stroke’. Results from the second phase of the thesis are presented in a submitted paper titled ‘Motor function and daily living skills five years following paediatric arterial ischemic stroke’. Supplementary results, where sample numbers were too small for formal analysis are presented in chapter 9.
2. INTRODUCTION

2.1 Stroke in children

The two main types of stroke in childhood are haemorrhagic stroke (HS) and arterial ischaemic stroke (AIS). HS occurs when there is a rupture to one or more of the blood vessels of the brain. HS occurs in 1.5-2.9 per 100,000 children per year and the most common presenting symptoms include headaches, vomiting, seizures or focal neurological deficits(19). AIS occurs when there is a disruption to the blood supply to one or multiple areas of the brain causing focal cerebral infarction and consequent damage or disruption to the neural pathways that control the functioning of the body (2). The date of onset of an AIS can usually be relatively accurately specified using magnetic resonance imaging (MRI), which will also identify the lesion location, often with defined margins. This differentiates AIS from more diffuse brain injuries, such as haemorrhages and traumatic brain injury (TBI), and means that AIS provides a unique opportunity to explore the lesion characteristics and their relationship with stroke outcomes. This thesis will focus specifically on AIS.

AIS occurs with an estimated incidence of 1.6 -2.7 per 100 000 children per year (19-21). Thirty three per cent of children have recurrent strokes (22). Although estimates vary, AIS occurs more frequently in neonates (≤28 days of life) with an incidence of 1 in 4000 live births (23). Approximately fifty per cent of all paediatric strokes occur in the first year of life (19). The incidence of childhood AIS (onset at 29 days-18 years) drops dramatically and is estimated between 2-8 per 100,000 children, per year (21, 22, 24). The prevalence of stroke in children has slowly increased over time, likely to be reflecting more sensitive neuroimaging techniques and improvements in acute diagnosis and management (22, 25). Acute presentation differs with age; hemiplegia is the most common acute clinical sign of childhood AIS, present in 72% to 90% of cases (2-4, 21, 26, 27). Other common acute neurological signs in the childhood onset group include aphasia, other speech and language difficulties and headaches. In contrast, neonates typically present with seizures or behavioural disturbances (2, 28, 29). For AIS that occurs in utero, there are commonly no clinical signs at birth and,
consequently, stroke is not detected until later in infancy when motor signs such as hemiplegia emerge, typically at about 3-4 months of age, when voluntary hand use starts to develop (25). With increasing awareness, education, and recent improved radiological techniques, it is anticipated that the incidence of childhood and neonatal stroke will continue to increase.

Perinatal arterial ischemic stroke is the most common cause of hemiplegic CP in term neonates and hemiplegic CP is the most common form of CP in children born at term (30). Extensive research has been carried out in the area of hemiplegic CP exploring trajectory of recovery, early intervention and outcomes (1, 18, 31-33). It is important to also acknowledge that although there is some overlap between children with CP and arterial ischaemic stroke they need to be considered as two different groups with varying aetiology, presentation and trajectory of recovery and outcomes.

2.2 Stroke in adults

There are a number of factors that differentiate paediatric from adult stroke. Instead of lifestyle risk factors such as hypertension, smoking and arteriosclerosis (34), the most common risk factors in children include, infection (24%), cardiac conditions (31%), and arteriopathy (53%). Other, less common risk factors include genetic conditions and blood disorders (3, 4, 27, 35). In contrast to adults, stroke aetiology in children is more likely to be idiopathic, with estimates ranging from 49-80% (36-38). In addition, multifactorial infarcts with the presence of comorbidities add to the complexities of early diagnosis and planning intervention.

Outcomes and recovery following stroke in adults are relatively well understood and extensive research exists in this field. The motor systems are the most commonly affected neurologic domains following adult stroke and include hemiparesis, spasticity and fine motor impairments (39). Following adult stroke, the most rapid motor recovery occurs during the first three months post-diagnosis, with less improvement thereafter with a plateau of recovery at about six months (39-45). Early intervention, within this window of improvement, is critical for optimising outcomes and minimising impairments. In contrast, brain injury research suggests that the trajectory of motor recovery in children may be more protracted and may vary by age.
at diagnosis (12).

Stroke in adults occurs at a time in life when the mature brain is more robust and the focus of rehabilitation following adult stroke is on regaining lost or impaired skills. In contrast, a child may experience a stroke at a time in his/her life when motor skills may not be fully established and the focus of intervention is therefore on both regaining lost or impaired skills and acquiring new skills. Differences in aetiology, maturity and plasticity of the brain and existing understanding about early recovery suggest that outcomes and trajectories of recoveries of adults and children are likely to differ.

2.3 Current stroke guidelines

In recent years, guidance for acute medical management of AIS has emerged specifically for children (46). A working party from the UK developed ‘Stroke in Childhood Clinical Guidelines for Diagnosis, Management and Rehabilitation’ in November 2004 (47) however, given the limited available research at the time, these rehabilitation guidelines are based mainly on data from allied populations such as acquired brain injuries (ABI) and cerebral palsy (CP).

Other medical guidelines have focused on facilitating early identification and diagnosis of paediatric stroke and optimising acute management (46, 48). These guidelines recommend ‘age-appropriate rehabilitation and therapy’ however offer little guidance as to why, how or when this should happen. The updated Canadian stroke guidelines include a new rehabilitation section focusing on paediatric rehabilitation, recognising the importance of targeting the specific needs of children and recommending that children have their own specialized stroke care team (49).

The most comprehensive paediatric stroke guidelines have recently been published by the UK working party which recommend a holistic model of care encompassing medical, nursing, allied health and rehabilitation management from the acute period through to ongoing management and longer term rehabilitation (50). The development of these longer-term guidelines and models of care has been impeded until recently,
by a lack of research detailing long-term outcomes in this population. However, in the absence of research specifically in paediatric stroke population, expert consensus level agreement was reached. Long-term outcome research supports the development of evidence based, rehabilitation guidelines.

2.4 International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY).

This study has used the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY) as a framework for exploring health outcomes in children. The ICF-CY is a theoretical framework that illustrates the interaction between the key domains of health in children including body structure and function, activity and participation (51).

Figure 2.1 ICF-CY framework

ICF-CY is an adaptation of the original international classification of functioning, disability and health (ICF) that was published in 2007 to include developmental considerations specifically for children. The classification provides a tool for a common and universal language and terminology for measurement of limitations as
well as the importance of personal factors and within an environmental context from infancy to adolescence. This framework has been used to guide the methodology of this study to ensure a holistic assessment addressing all of the key domains of health of this population. Motor functions are commonly impaired following paediatric stroke and using the ICF-CY, allows the description and analysis of motor functions as well as a child’s daily activities and their participation within the home, educational and community environments.
3. **BODY STRUCTURE AND FUNCTION**

3.1 Typical motor development in children

Motor development begins in utero and continues into adulthood. The corticospinal tract (CST) runs through the internal capsule and is the primary neural pathway responsible for many of the complex, skilled movements performed with the upper limb (52). The CST development begins within the first 6 weeks following conception reaching the lower cervical spinal cord by 24 weeks post conception. By 40 weeks, the myelination of the nerve fibres begins and the CST fibres project to each side of the spinal cord (53). In the first two years of life, there is a gradual progression for the CST fibres to cross over to the ipsilateral side, with the most marked changes within the first year of life (1, 54). The connections of these pathways are influenced by genetic predispositions, environmental factors, and the neuroplastic responses of the brain to experiences throughout childhood (55).

A child is born with a very limited repertoire of motor skills. In addition to the rapid development of the central nervous system (CNS), developmental changes occur throughout childhood, particularly within the first year of life (1). Through exploration and interaction with their environment, these motor skills typically develop most rapidly over the first few years of a child’s life but continue to be refined into adolescence and adulthood.

Movement and mobility is essential to allow a child to access and explore their environment. Impaired motor function has the ability to impact upon all areas of a child and their family’s lives and has been shown be negatively associated with physical independence, mobility, financial stability, social integration, participation and QoL of children with cerebral palsy (16, 17). While there are many aspects of motor function that underpin a child’s motor abilities, the importance of using standardised, valid and reliable measures has directed the focus of this research to detailing gross and fine motor function.
3.2 Principles of brain plasticity

Plasticity refers to the dynamic nature of the CNS and its ability to adapt, regenerate and reorganise in response to experiences and environments to which it is exposed (12, 53). With regards to healthy child development and growth, this adaptive process is thought to occur in a set sequence throughout a lifespan. The way in which brain plasticity responds to its environment and the activities to which it is exposed is critical in a child’s ability to learn, retain information and develop. Over the first few years of a child’s life, he/she experiences periods of rapid dendritic growth as well as selective elimination or ‘pruning’ of these networks to increase efficiency and to develop the most functional branches (12, 45). Dendritic pruning also helps to explain the ‘use it or lose it’ phenomenon and suggests that neural pathways to areas of the brain that are not used through lack of motor abilities shrink and at times, disappear.

When brain injury or insult occurs during childhood, it has the potential to not only disrupt previously learnt skills but also the development of emerging or new skills (12). The nature and severity of impact of any given insult to specific brain areas will depend on the level of maturity of that section of the brain at the time as well as the complexity of involved brain systems. The age for optimal motor recovery from brain injury remains unclear. Theoretically, neonates have the most potential for plasticity because their brains are rapidly reorganising and myelinating during the first two years of life. In contrast, older children may have less plasticity but functional outcome may be improved by the possession of a wider set of learnt skills and behaviours at the time of injury, creating greater potential for true rehabilitation. We don’t yet know the exact relationship between timing of brain insult and functional impairment, although we do understand that it is not linear, but rather reflects growth spurts occurring within the brain (12).
3.3 Motor outcomes following arterial ischaemic stroke

Clinical experience suggests a broad spectrum for the type and severity of motor difficulties and the clinical course following paediatric AIS. Long-term motor impairments and disabling consequences remains unclear. In most cases of paediatric AIS, motor dysfunction is unilateral and hemiplegia is the most frequently reported motor impairment. Estimates of the prevalence of chronic hemiplegia following childhood AIS vary from 25-56% (3, 26). Following neonatal AIS the prevalence of chronic hemiplegia is lower, and estimates range between 20% and 28% (4, 26, 56, 57). Severity of motor outcomes vary in the literature, however, most children who develop a hemiplegia following paediatric AIS, generally ambulate independently and their upper limbs are more severely affected than their lower limbs (3, 4, 58, 59).

The literature describes motor outcomes following paediatric AIS in board terms, reporting ‘good’ or ‘poor’ outcome, usually determined by the presence or absence of a hemiplegia, often as part of overall neurological dysfunction (60). These neurological assessments measure motor impairment in basic terms describing it as either the presence or absence of a hemiplegia, abnormal tone or spasticity (7, 34, 61-64). To date, there are no detailed descriptions of fine or gross motor function following paediatric stroke. Current understanding of motor outcomes vary due to a wide variation and a lack of sensitivity of the outcome measures used (60). The stroke outcome literature is predominantly retrospective and cross-sectional in nature. Samples are usually heterogeneous with child age at the time of the stroke and the length of time until follow up varying significantly (3).

Mercuri et al. (4) was the only study identified that used a standardised assessment (the Movement Assessment Battery for Children (Movement ABC) to measure overall motor function, however this was limited to neonatal stroke. They concluded that following neonatal AIS, motor impairments become more apparent at school age when more specific assessments can be carried out. They also reported that of the children without hemiplegia, minor neuromotor impairments emerged by early school age (4).
Motor function is complex and outcomes can be impacted by variables beyond a child’s physical abilities including cognition (motor planning, sequencing, attention), sensation and vision. From clinical experience, children have a variety of motor disorder classifications following stroke that have not yet been described in the literature including motor planning difficulties, ataxia, spasticity and dystonia.

3.4 Motor outcomes of children with cerebral palsy

The literature exploring motor outcomes of children following AIS is limited, however, when we look at the outcomes for similar populations, for example, children with hemiplegic CP, the literature is more extensive. CP is defined as ‘an umbrella term covering a group of non-progressive, but often changing, motor impairment syndromes secondary to lesions or anomalies of the brain arising in the early stages of its development’ (65). Perinatal stroke is the most common cause of hemiplegic CP in term neonates so the motor outcomes of these children, particularly in the neonatal population who develop unilateral motor impairment, are likely to be similar (1).

The Gross Motor Classification System (GMFCS) is a universally used tool to classify children and young people with cerebral palsy’s gross motor functional abilities (37). Children with hemiplegic cerebral palsy who ambulate independently (i.e. GMFCS levels 1 and 2) often have coexisting upper limb motor difficulties including impaired bimanual coordination and impaired manipulation (66-68). Early abnormal hand and wrist posturing is also common (69), particularly with postures such as thumb adduction and/or flexion with reduced wrist extension (18).

Two non-linear models have been generated to describe the progression of gross motor abilities in children with CP. The first model suggests a rapid progression of GM function in the first few years of life with a plateau occurring after the age of 5 (70). The second model shows a similar progression in the early years with a peak at about 7 years followed by a decline in motor skills. The decline was only noticed in the children with more severe forms of CP (GMFCS levels 3-5) (32).
There have also been non-linear growth curves published describing the development of hand function in children. Nordstrand et al reported that children with unilateral spastic cerebral palsy have a rapid development of hand function at a young age, which plateaus between 30 months and 8 years (31). Another study suggests that the developmental curve may differ depending on the body-site distribution of CP and the severity of impairments. They reported that hand function in this clinical population develops differently from overall upper-extremity skills with declines in function in upper-extremity skills being more common and pronounced among older children (33).

### 3.5 Measuring motor function in children with arterial ischaemic stroke

A range of outcome measures are used to measure motor function in children with neurodisability, with varying degrees of sensitivity. Gordon has summarised the literature evaluating outcomes following paediatric stroke using the ICF-CY as a framework (71). Sixty-seven different standardised measures were used to measure paediatric stroke outcomes, across 28 studies, and, even though hemiparesis was the most common motor deficit, task-based hand use was not evaluated in any of the papers reviewed (71). In their systematic review of outcome measures used in paediatric stroke studies Engelmann et al identified 38 different assessments, with 79% used in two or fewer studies (60), highlighting the lack of consistency in evaluating paediatric stroke outcomes.

No standardised motor assessments are valid for all age groups, which makes it challenging to measure change in motor function over time as often a number of different assessments need to be utilised, depending on the age of the child. The Paediatric Stroke Outcome Measure (PSOM) (72), developed specifically for use in child stroke, is the only assessment validated to assess neurological function in the paediatric stroke population in both review papers (60). Other assessments used were either non-standardised, or standardised assessments not validated for paediatric stroke. This makes the current literature difficult to compare and interpret.

When measuring motor outcomes in children, assessments may be conducted through
direct child testing, primarily focusing on a child’s ‘capacity’ (what a child can do) as well as through parent or carer rated assessments that aim to measure a child’s actual ‘performance’ (what a child does do). In recent years, assessments have emerged that allow clinicians to assess a child’s ‘performance’ through direct child testing, for example, the Assisting Hand Assessment (AHA) (73). As what a child does do doesn’t always align with what they can do, it is important to encompass both performance and capacity measures when exploring outcomes in children.

The nature of motor impairments varies significantly following paediatric AIS which adds to the challenges of assessing this population. Further, changing handedness (depending on age at stroke onset and premorbid hand dominance), the emergence of impairments in a developing brain and the need for diverse measures to cover age bands and variety of motor presentation (ataxia, hemiplegia, dystonia, spasticity), add to the complexity of measuring motor function in this group of children.

Reliable and valid standardised, age-appropriate assessments are essential in clinical practice to assist with early detection of motor and functional impairments to facilitate early intervention and rehabilitation.

3.6 Intervention and rehabilitation

Two papers were identified that explored motor interventions following paediatric AIS (1, 24). Both papers suggest, that early, intensive intervention is essential to minimise impairments and to optimise functional outcomes and that therapy should be delivered from a multidisciplinary team of allied health professionals (1, 24).

Several reviews have explored the efficacy of interventions for similar populations such as hemiplegic CP, and identified a wide variety of interventions, which provided varying degrees of evidence to support their use (18, 38, 50, 74-76). In their review, Novak et al (77) reported that 40% of interventions for this population had no reported evidence for their use, while another 20% were ineffective, unnecessary or even harmful. In a later review, Abbaskhanian et al highlighted the current
methodological quality issues, namely small sample sizes, a lack of randomised control trials and variety of outcome measures used. This paper did, however, recommend that functional ability and social participation should be the primary outcome measures used when evaluating the efficacy of rehabilitation for children with CP (74).

3.7 Factors associated with outcome

3.7.1 Age at stroke onset

In the paediatric stroke literature there are two distinct populations, neonatal stroke (stroke occurring in the first 28 days of life) and childhood stroke (from 29 days to 18 years old). Infants with ‘presumed perinatal’ strokes are not identified at birth, instead, they are most commonly diagnosed with the development of a hemiplegia at about 4-6 months, which is typically when a child develops voluntary control over their movements and motor impairments become more readily observable.

The aetiology, the maturity of the CNS, and acute presentation of the neonatal and the childhood onset groups differ, which suggests they may have different trajectories of recovery and outcomes. Postnatal brain development is incredibly rapid in the first few months of life and it is therefore likely that small differences in age at stroke onset may result in large difference in longer-term outcome (5). As previously stated, traditionally it has been believed that younger children have more ‘plastic’, less functionally defined brains, particularly for skills that are more localised within the brain, and thus better functional outcomes. However, this is not necessarily the case because the young brain is undergoing very rapid developmental changes, it may be more vulnerable to insult or injury than the mature brain (78). However, neither of these views fully explains the wide range of outcomes seen following early brain insult and the literature regarding outcomes and recovery across different neurobehavioural domains is inconsistent.

There are mixed views on the impact of age at diagnosis and cognitive outcome for children following AIS. Following early focal brain injury, cognitive deficits have
been found to emerge later in development with pre-schoolers who show no cognitive deficits, falling below the mean on working memory and processing speed during their school years (79, 80). This is supported by research into similar populations (such as TBI) suggesting that with increasing cognitive demands (such as starting school) where children are expected to process more complex information, cognitive impairments tend to emerge (13). Earlier studies have suggested that the most vulnerable age is during the first year of life (81), however, subsequent studies reported that stroke that occurs between the age of 1 month and 5 years result in the poorest cognitive outcomes as judged by IQ scores (82). In contrast, paediatric acquired brain injury (ABI) literature suggests that with regards to cognitive function recovery, the pre-school aged children (>30 days-5 years old) may have a different trajectory of recovery to neonates and school aged children (> 5 years old) (12) and that the pre-school aged children may have better cognitive outcomes. Other studies exploring cognitive outcomes following childhood stroke also suggest a protective period with poorest outcomes occurring when stroke occurs before age one or after age 6 (83, 84). The influence of age at injury on motor outcomes has not yet been described. The relationship between age at injury and outcomes does not appear to be linear; rather it’s likely to be determined by what’s happening in the brain at the time. There are critical periods around age 2 and 5, and again around age 8, where there is rapid synaptogenesis, and these ‘windows of opportunity’ may also lead to vulnerability of plasticity, depending on their nature or even the specific skill of interest.

3.72 Lesion characteristics:

Magnetic Resonance Imaging (MRI) with diffusion weighted imaging and magnetic resonance angiography (MRA) are the most frequently used diagnostic tools for AIS in children (19, 48, 49). Unlike many other forms ABI, where damage to the brain is diffuse, AIS usually affects specific and well-defined areas of the brain. Targeted imaging techniques provide a unique opportunity for exploring the relationships between discrete lesion location and outcomes.

The territory of the middle cerebral artery (MCA) is the most commonly affected
territory in both neonatal and childhood populations (26, 85, 86). The MCA supplies blood to a number of brain structures involved in both fine and gross motor skills, including the motor cortex, the genu of the corpus callosum, the anterior limb and the posterior limb of the internal capsule and the basal ganglia. When the blood supply to these structures of the brain is disrupted, motor dysfunction commonly occurs.

The relationship between lesion location and motor outcomes in children following paediatric AIS is not well understood (26, 56, 61, 87-90). In neonatal stroke, AIS more commonly occurs in the left hemisphere. Children with bilateral infarcts have been reported to have a lower chance of walking independently than children with unilateral infarcts (58). Main-branch MCA infarction has been associated with development of spasticity in neonates (91). Poorer motor outcomes have been found in children with involvement of cortical tissue as opposed to subcortical tissue damage (92, 93). Basal ganglia infarcts alone have been associated with better motor outcome and a lower incidence of developing a hemiplegia in the neonatal populations (4, 56).

Several studies have explored the relationship between lesion location and the development of a hemiplegia. Mercuri et al. (4) followed up 22 neonates at school age and found that neonatal AIS with involvement of the cerebral cortex, internal capsule and basal ganglia on MRI were predictive of a hemiplegia. They also found that, even though children who had a lesion involving the internal capsule and either the basal ganglia or the hemispheric lesions did not develop a hemiplegia, they exhibited other motor difficulties. This study was supported by results from Boardman et al. (26), who also concluded that concomitant involvement of these three areas in neonates was a predictor of hemiparesis. In childhood AIS, however, hemiparesis was identified in children when only one or two of these structures were involved (4, 26).

Several studies have concluded that infarct volume is an important predictor of motor outcome with poorer outcomes found in children who have more than 10% intracranial volume infarction (92) as well as children with greater than one third of the cerebral hemisphere affected (94). Kirton et al., however, studied a group of 14 neonates and concluded that there was a much stronger correlation between volume of the descending corticospinal tract (DCST) affected (which refers to caudally directed
motor fibre tracts definable at levels of the posterior limb of the internal capsule (PLIC), cerebral peduncle, basis pontis, and medullary pyramid) than total infarct volume with motor outcome (89). This was supported by Husson at al., who concluded that the absence of the corticospinal tract involvement results in normal motor development 94% of the time and 66% of the children in their study who did have CST involvement developed a hemiplegia (56). More recently, Dinomais et al supported findings that large lesions were associated with poorer motor outcomes, however, found that some small lesions were also associated with poor motor outcomes which reinforced that lesions in the CST were strongly related to poorer motor outcomes. These studies however, have primarily focused on neonatal populations. More specific evidence has emerged in the last year suggesting that isolated perforator strokes may have better motor outcomes (95) although many of the children in this study were premature and most of them had additional brain injuries.

Paediatric stroke is often associated with comorbid medical conditions, such as sickle cell anaemia and cardiac conditions. Large variations in lesion volumes, location and comorbidities experienced by the paediatric stroke population places added complexities on studying outcomes as various factors may interact and influence outcomes and trajectory of recovery.

3.73 Early presentation:

Neuromotor impairment is a commonly reported clinical sign at diagnosis and has also been identified as a long-term sequelae (1, 57). Acute presentations are markedly different between neonates and older children. Following childhood stroke, hemiplegia is the most common acute clinical sign (2-4, 21, 26). In contrast, neonates present predominantly with seizures or behavioural difficulties such as hypotonia, poor feeding or lethargy (2, 24, 28, 29).

In neonatal stroke, signs of hemiplegia are generally not present in the first month of life (96), but tend to emerge at about 3-4 months of age, which is when voluntary hand use typically develops. Therefore, there is often a delay between diagnosis of neonatal stroke and the emergence of a hemiplegia (61).
A relationship between early qualities of a child’s general movements with the later emergency of hemiplegia is discussed in a number of papers (1, 96-98). ‘Fidgety’ general movements are defined as small, circular movements of moderate speed, in all directions and involving the whole body. The absence of ‘fidgety’ movements, or movements of abnormal quality, between 9 and 13 weeks has been associated with the development of hemiplegia (97).

The emergence of more complex hand and finger movements in infants is related to the maturation and function of the cortical spinal tract (97). Asymmetries in wrist and digit movements at 3 months old and a reduction in the frequencies of wrist and digit movements at 5 months old have both been correlated with an increased chance of developing a hemiplegia in later childhood (97).
4. ACTIVITY AND PARTICIPATION

During the acute phase of AIS, intrinsic factors (body structure and function components) are the target of medical, allied health professionals, children and their families. Over time, as children become stable and begin the recovery phase, focus shifts to maximising independence and participation in daily activities and transitioning back into their homes, their communities and their educational environments. Various factors may impact a child’s activity and participation including social, cognitive, family, cultural, economic and physical factors. A study by Forsyth et al. reported that intrinsic factors (body structures and functions) were as significant in influencing a disabled child’s participation as environmental factors (supports, attitudes and services) (99).

4.1 Participation

Motor impairments have the potential to impact a child’s activity limitations and restrictions in participation within their home, educational and community environments (15, 100). Participation in daily activities is a key focus for occupational therapists and is well recognised as an important indicator of health and wellbeing (101, 102). Extensive research has explored the relationship between motor dysfunction (including hemiplegic CP, global developmental delay (GDD) and neuromuscular conditions) and children’s participation in their home, education and community lives (103-105). Motor impairments in strength, coordination, spasticity and contractures have been associated with reduced participation in adults with hemiplegic CP (103) and poorer gross motor function has been associated with reduced functional outcome in children with CP.

4.2 Activities of daily living

Coordinated use of use of both hands is important for children’s functional activities (ie. using cutlery, putting on a t-shirt or tying shoelaces.) As upper limbs are more
severely affected than lower limbs following paediatric stroke, and one side of the body more commonly affected more than the other, the coordinated use of hands and arms in functional activities becomes difficult (3, 4, 58, 59). Children are more likely to complete bimanual tasks inefficiently using only one hand, or avoid them altogether (106) with functional implications in all areas of a child’s life. Children, unlike adults, will usually have a primary caregiver who will be able to assist with any task they find difficult at home. This may mask some difficulties, as these children do not present as relying on community supports, services or environmental modifications.

4.3 Adaptive behaviour

Adaptive behaviour is a collective term used to describe a child’s practical and social skills that underpins independent function in daily life and participation in all areas of their lives. Adaptive behaviour difficulties are commonly reported after paediatric AIS with outcomes varying widely, possibly due to a wide range of time since stroke as well as a wide variety of outcome measures used frequently, non-standardised questionnaires (3, 7, 9, 14, 15, 34, 59, 86, 107, 108). Poorer adaptive behaviour has been associated with limitations in gross motor function in children with CP, (101) however, this relationship is yet to be described in the paediatric stroke literature.

4.4 Fatigue

Fatigue is commonly reported following adult stroke and has an impact upon activities of daily living (109). Anecdotally, fatigue is one of the most frequently reported areas of concern for parents and their children following stroke. Although this relationship has not yet been explored following paediatric stroke, in other ABI populations and CP, fatigue is reported to be a persisting symptom and has been associated with poorer QoL and poorer school functioning (110-112).
4.5 Gaps in current knowledge base

The literature to date presents a very reductionist view on motor function and description of motor function beyond that detected in neurological examinations is limited. Several studies report on children either having a hemiplegia or not, or being independently mobile or not, however, literature that measures motor function in detail using standardised, valid and reliable measures is scarce (7, 34, 59, 61, 62, 64).

Research to date tends to describe small, cross-sectional samples with time since stroke varying significantly within studies. The paediatric AIS literature has been focused on short-term outcomes, predominantly the first year following diagnosis, and although it is anticipated that children may change over time with increasing social and physical demands, long-term motor and functional outcomes remain unknown. Further, studies tend to be focused on either neonatal or childhood stroke outcomes which limits the ability to compare and contrast differences in outcomes between age groups.

Finally, there are few studies exploring predictive factors of outcome, mainly limited to lesion characteristics and the relationship with developing a hemiplegia. A thorough and detailed understanding of early predictors of long term outcome would assist greatly in facilitating early intervention, targeting scarce resources, and providing children and their families with an understanding of the prognosis of their condition.

4.6 Summary

Paediatric stroke is increasingly recognised as a cause of childhood disability, morbidity and mortality. Extensive research has been conducted detailing the pattern of recovery and disability resulting from adult stroke, however, in children this research and understanding is lacking (41, 42, 44, 113-115). Children are vulnerable to a vast array of adverse outcomes following AIS including cognitive, social, emotional, language and behavioural difficulties, however, motor impairment is the most common presenting symptom and most frequently reported adverse consequence in both neonatal and childhood populations (3, 6, 86).
When AIS presents in childhood, it occurs during a time of rapid brain development and growth. This has the potential to affect already developed motor skills as well as disrupting the development of emerging and new motor skills with residual deficits spanning a lifetime. Motor dysfunction has a major impact on activity and participation in children. Functional impairments and activity limitations may emerge over time with increasing social and developmental demands. These outcomes have yet to be explored in the child stroke literature.
5. **RATIONALE**

5.1 **Relevance and importance of this study**

Motor impairments are the most common presenting symptom following childhood stroke and most frequently reported adverse consequence in both neonatal and childhood populations, however, they are poorly understood (3, 6, 86). An evaluation of motor function need to use the ICF-CY as a holistic framework for overall health and well-being, to ensure a comprehensive assessment of motor function and the implications to a child’s daily life.

A clear and detailed understanding of the pattern of motor function recovery and factors associated with long term motor function outcomes will assist with targeting scarce resources to support long term follow-up for both medical and allied health professionals. This will facilitate identification of critical times for rehabilitation input to maximise recovery, independence and support children to participate in all areas of their childhood, as teenagers and as they transition into their adult lives.

Research into the long-term motor outcomes for this population is scarce and a detailed study that explores fine motor (FM), gross motor (GM) function, at the level of activity limitations and environmental barriers, and the impact on participation, using valid and reliable measures is warranted.

5.2 **Research aims**

**Aim 1:**
The aim of this study was to describe early and long-term motor outcomes of children post stroke onset, and the impact of these motor outcomes on everyday function using standardised, valid and reliable measures.
Hypotheses:

1. Body structure and function:

- Children will have co-existing gross motor (GM) and fine motor (FM) impairments post-stroke
- Hemiplegia will be the most commonly presenting motor impairment

2. Activities and participation:

- Children will participate less frequently than their age matched peers at home, school and community environments compared to age norms
- Children with gross and fine motor impairments at 5 years will participate less frequently than their age matched peers at home, school and community environments

Aim 2:
To measure and describe the various factors (lesion characteristics, child/family, environmental) associated with different levels of motor outcomes.

Hypotheses:

1. Body structure and function (lesion characteristics, age at stroke,)

- Neonates will have better motor outcomes than pre-school aged and school aged at 12 months and 4 years
- Neonates with subcortical infarctions only, will have better motor outcomes than children with combined cortical and subcortical infarctions.
- Neurological impairment at 1 month would be associated with poorer motor and adaptive behaviour outcomes at 12 months and 4 years

2. Environment (family function, access to therapeutic intervention/services)

- Children with gross or fine motor impairments at 4 years are more likely to be in receipt of intervention from occupational therapists or physiotherapists at the time of assessment compared to children without motor impairments at 4 years.
**Aim 3:** To measure and describe the relationship between motor function and activity/participation at both 12 months and 4 years post stroke

**Hypotheses:**
- Motor impairments at 4 years will be associated with difficulties with activities of daily living, fatigue, participation and QoL.

The analysis and findings at 12-months post AIS diagnosis are presented in chapter 7.1 in the first published paper titled ‘Trajectories of motor recovery in the First Year after Arterial Ischaemic Stroke.’ The early predictors of 12 months outcomes are presented in chapter 7.2, in the second published paper titled ‘The Pediatric Stroke Outcome Measure: a predictor of outcome following arterial ischemic stroke’. The 5-year motor and functional outcomes as well as early predictors of 5-year outcomes are presented in chapter 8 titled ‘Motor function and daily living skills four years following paediatric arterial ischemic stroke.’
6. METHODOLOGY

This study represents several substudies from the Stroke Recovery Study, a prospective, longitudinal study, which aims to assess outcomes associated with paediatric AIS from acute presentation to 4-6 years post-stroke (108).

6.1 Design

This prospective, longitudinal cohort study was conducted between 2007 and 2016, which included two cross sectional studies. The original study, explored the health and development outcomes of a group of 64 children in the first 12 months following AIS (Stroke Recovery Study)(108). A subgroup of 33 children was recruited at 4-6 years post stroke. There were four assessment time point which included: acute, 1 month, 6 months, 12 months and 4 years.

6.2 Participants

Participants aged between term newborn and 18 years with acute AIS, were consecutively recruited to the study from a single tertiary level children's hospital, The Royal Children’s Hospital (RCH), Melbourne, between December 2007 and November 2013 (108). Eligibility criteria for the original study were: i) parent or guardian with sufficient English to complete the protocol ii) capacity to complete assessments iii) evidence of acute parenchymal infarct corresponding to one or more arterial territories confirmed by brain magnetic resonance imaging (MRI). Children with previously diagnosed stroke, coexisting diffuse brain injury due to a traumatic or hypoxic ischaemic event, and pre-term infants (ie born prior to 36 weeks gestation) were excluded. To maintain consistency with time since stroke onset as well as to minimise differences in CNS development, presumed perinatal strokes were also excluded.
Acute study (0-12 months post-stroke): One hundred and seven children met eligibility criteria to participate in the original study: 33 were not approached (12 died acutely; 6 resided interstate; 15 were missed/ not referred in time), and 7 declined participation (1 due to employment; 3 were too busy/stressed; 3 no reason was provided). Sixty-seven children (62.6%) were recruited between December 2007 and November 2013. Two participants were unable to be contacted for follow-up appointments and one child died (of non-stroke related issues) prior to their 12-month assessment.

Five year post-stroke study: A subgroup of children from the original sample was recruited for the second phase of the study, when they had reached 4-6 years post stroke between January 2014 and August 2015. From the original sample, all children were invited to participate if they had turned 5 years of age within the time frame of the study. Forty-one children were eligible to take part (27 children were < 5 years). Three families declined to participate with no reason given and four families were unable to be contacted. One participant was excluded due to unexplained developmental regression, unrelated to the stroke; therefore, 33 children were included in this study, 13 neonates (≤ 30 days at diagnosis), 14 preschool-aged (>30 days-5 years) and 6 school-aged (≥ 5 years old).
6.3 Measures

Outcome measures were selected based on their relevance to the age range of children under study and the quality of their psychometric properties. In a systematic review of upper-limb activity measures for children with congenital hemiplegia, 38 measures were identified and reviewed for their validity, reliability, evaluative validity and clinical utility. The authors concluded that the Melbourne Assessment was the best measure for unilateral upper limb capacity and the Assisting Hand Assessment was the best tool to measure bimanual upper limb activity (116).

A non-standardised questionnaire was devised to include demographic information. Questionnaires were completed by the child’s primary caregiver (the parent who carried out the majority of the care at home). Children over the age of 6 also completed a child and adolescent questionnaire, which consisted of the same questions. Questionnaires completed by the children were read to them by the
examiners (AC or MG). The questionnaires included questions about the child’s intervention and services that they had received, their motor, communication and cognitive abilities, fatigue, emotional/psychological/behavioural and their participation.

Outcome measures and classification tools administered in the protocol and are summarised in table 6.1. Both parent and child measures are included.

6.3.1 Body structure and function

6.3.1.1 MRI scan
All children underwent an brain imaging at acute presentation either at the RCH or their local hospital. Any subsequent magnetic resonance imaging (MRI) was undertaken on a 1.5 or 3 Tesla scanner at the RCH using a standard MRI protocol developed for children with AIS.

6.3.1.2 MRI lesion coding
Infarct number and laterality, lesion location, and vascular territory affected were rated by a neuroradiologist (MD, LC) and occupational therapist (AG) based on visual inspection of imaging obtained at the time of diagnosis and clinical data regarding presentation using a standardised coding system (as described in Gordon et al (108)). Where diagnostic scans were undertaken outside RCH, MRI or CT data were obtained from the referring hospital. Lesion size was dichotomised into small/medium or large according to degree of vascular territory impacted. Lesion location was categorised as cortical, subcortical, both, or infratentorial. Subcortical classification included grey matter/nuclei, subcortical white matter, or both.

6.3.1.3 The Pediatric Stroke Classification (117)
The Pediatric Stroke Classification was applied to classify AIS subtype. Lesion size was dichotomised into either small/medium or large. The small/medium category included the infarcts of the perforator and branch and the large category included entire territory infarcts (108).
6.3.1.4 The Bruininks-Oseretsky Test of Motor Proficiency, Second Edition (BOT-2) (118)

The BOT-2 is a standardised, norm-referenced, comprehensive motor assessment for children aged 4-21 years. The BOT-2 assesses both fine and gross motor function across four domains: fine manual control, manual coordination, body coordination and speed and agility and has established test-retest reliability, inter-rater reliability and internal consistency (119). Standard scores were generated across the four subdomains (M=50, SD=10), as well as overall motor composite score (M=50, SD=10). The subdomains of fine manual control and manual coordination were combined and averaged to generate a FM score, and body coordination and strength and agility were combined and averaged for a GM score. These were then converted into z-scores for both FM and GM function. Mean standard scores were then transformed into Z-scores (mean = 0, SD = 1) using SPSS computer package. Z-scores were then categorized as either a good (Z score of >-1) or poor (z-score ≤-1) outcomes.

6.3.1.5 Bayley Scales of Infant and Toddler Development (BSID-III) (120).

The BSID-III is a standardised, norm-referenced, comprehensive assessment of development for babies and young children aged 1-42 months and was used to measure both FM and GM function. Subdomains of the assessment include: Cognition, language (expressive and receptive) and motor (fine and gross motor). Scaled scores were generated for the FM and GM subscales of the motor function domain (M=10, SD=3).

6.3.1.6 Pediatric stroke outcomes measure (PSOM) (2)

The PSOM is a detailed neurological assessment for children that measures impairments across the domains of left sensorimotor, right sensorimotor, language production, language comprehension and cognitive/behavioural. Subscale scores range from 0, which indicates ‘no deficit’ to 2, which indicates ‘severe deficit’ or ‘missing function’. Overall score is the total of all subdomains and ranges from 0-10. Both total scores and the subscale scores for the sensorimotor subdomain were used in the analysis. The PSOM was used to determine the presence of a hemiplegia following clinical examination, as indicated by a score of 0.5 or above on the sensorimotor domain. Where it was not possible for a clinician experienced in the
PSOM to examine the child, the Recovery and Recurrence Questionnaire (RRQ) was administered. The RRQ is a parent-administered tool demonstrated to correlate strongly with the clinician administered PSOM (121). In presenting the findings, when we reference the PSOM, we are referring to either the PSOM or RRQ.

Both total impairment score and sensorimotor subdomain scores of the PSOM were used in the analysis. Sub-domain scores were collapsed into good (0) or poor (0.5 or above) outcomes. Total scores were collapsed into good (a total score of 0.5 or below) or poor (a total score of 1 or above) outcomes. This approach is consistent with the approach used by Gordon et al in previous papers (2, 72, 108).

6.3.2 Activity and Participation

6.3.2.1 Vineland Adaptive Behavior Scales: second edition (Vineland-II) (122)
The Vineland -II is a parent rated questionnaire measuring a child’s activity and participation across four domains: communication, daily living, motor and social skills, as well as total adaptive behaviour. Scores are calculated as standard scores (M = 100, SD = 15), with lower scores reflecting poorer functioning (122). The motor subscale is only administered to children < 6 years. The VABS-2 was completed for all children and both the total scores and the individual subscale scores were used in the analysis.

6.3.2.2 Pediatric Quality of Life Inventory (Peds-QL) (36)
The Pediatric Quality of Life Inventory (Peds-QL) is a standardised, parent-rated measurement tool for children aged 2-18 that assesses health-related QoL across four domains of physical functioning, emotional functioning, social functioning and school functioning. Total scores were used in the analysis (M=87.61, SD=12.33)

6.3.2.3 Pediatric Quality of Life Inventory: Multidimensional Fatigue Scale (PedsQL-MFS)
The PedsQL-MFS is a parent rated assessment that rates a child’s fatigue symptoms across three domains (general, sleep/rest and cognitive). There are 18 items rated using a Likert scale from 1-100. Higher scores indicate fewer fatigue symptoms. Total
fatigue scores were used in the analysis. Data were compared to published data of healthy children (n=259) (M=88.2, SD=11.1) (123).

6.3.2.4 Participant and environment measure for children and youth (PEM-CY) (102)
The PEM-CY is a parent-rated assessment that measures participation across three domains (home, school, and the community). PEM-CY is validated to children aged 5-17 years and rates a child’s level of engagement in an activity on a scale of 1 (minimally involved) - 5 (extremely involved). Scores are averaged across each activity, with higher scores representing greater involvement within each setting. The Average Involvement score for home (M=3.9, SD=0.54), school (M=4.21, SD=0.7) and community (M=4.2, SD=0.56) were used in analysis. Participant data are compared to comparative data of children without a disability (n = 245–294).

6.3.2.5. The Assisting Hand Assessment (AHA) (124)
The AHA measures how well a child (18m-12y) uses their assisting hand (i.e. the hemiplegic hand) in bimanual play at an activity level (73, 124). The AHA is a criterion-referenced test that assesses what a child ‘does do’ rather than what they ‘can do’. A semi-structured play session is carried out using specific toys from the AHA test kit and is video recorded. The recordings are scored and 22 individual items are each given a score out of 4 deriving a raw score of between 22-88 with higher scores indicating higher abilities. The AHA raw scores were converted into logit-based AHA units (0-100) to allow comparison over time (125). The AHA was completed on any child with a hemiplegia, as determined by the PSOM.

6.3.2.6 The Mini Assisting Hand Assessment (Mini-AHA)
The Mini-AHA is an adapted version of the AHA that measures how well a younger child (aged 8-18 months) uses their assisting hand (i.e. the hemiplegic hand) in bimanual play at an activity level (126). Scores are reported as raw scores and mini-AHA units. The mini-AHA was completed on any child between 8 and 18 months old with a hemiplegia, as determined by the PSOM.

6.3.2.7 The Detailed Assessment of Speed of Handwriting (DASH): (37)
Handwriting is a specialised motor skill that requires both fine motor and gross motor abilities. The DASH is a standardised assessment of a child’s speed and legibility of handwriting for children aged 9 – 16 years 11 months with established validity and reliability. There are four tasks included in the assessment (copy best, alphabet writing, copy fast and free writing) as well as one optional task (graphic speed). The authors report good inter-rater reliability, reliability across the domains with ICCs ranging from 0.853 (graphic speed) to 0.999 (free writing). They report a standard error (SE) of measurement of 5.0, which the authors report that the assessments are ‘fairly accurate’ with their measurement of the true score of the child. The DASH was completed with any child in the specified age bracket.

6.3.3 Classification tools

6.3.3.1 Gross Motor Functional Classification System (GMFCS) (37)
The GMFCS is a tool that classifies children and young people’s gross motor functional abilities. GMFCS is a 5-point scale that categorizes children from GMFCS level one (where a child is independent with their mobility) to GMFCS level 5 (where a child is wheelchair-bound and completely dependent with their mobility). The system distinguishes between children that may need a mobility device to assist as well as the environments within which they mobilise (indoors/outdoors/schools etc.).

6.3.3.2 Manual Ability Classification System (MACS) (75)
The MACS is a tool that classifies how children use their hands and upper limbs to manipulate objects in daily activities. MACS is also a 5 point scale that categorises children from level 1 (handles objects easily and successfully) to level 5 (does not handle objects and has severely limited ability to perform even simple actions.) A flow chart is provided to assist clinicians with the categorizing process so that each child is rated appropriately.

The Gross Motor Classification System (GMFCS) and the Manual Ability System (MACS) are two well-recognised tools that were used to describe our sample. They are descriptive tools rather than assessments and are used to describe a child’s current functions.
Table 6.1 Summary of measures carried out at each time point

<table>
<thead>
<tr>
<th>Measure</th>
<th>Age range</th>
<th>Admin time (mins)</th>
<th>Mode of testing</th>
<th>Time post stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body Structure and Function</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brain pathology</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>✓</td>
</tr>
<tr>
<td>MRI scan and stroke classification</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bruininks-Oseretsky Test of Motor Proficiency (BOT-2)</td>
<td>4-20y</td>
<td>30-45</td>
<td>Child assessment</td>
<td>✓    ✓    ✓    ✓</td>
</tr>
<tr>
<td>Bayley Scales of Infant and Toddler development (BSID-111)</td>
<td>1m-3.5y</td>
<td></td>
<td>Child assessment</td>
<td>✓    ✓    ✓    ✓</td>
</tr>
<tr>
<td>Pediatric Stroke Outcome Measure (PSOM)</td>
<td>4-18y</td>
<td>15</td>
<td>Child assessment</td>
<td>✓    ✓    ✓    ✓</td>
</tr>
<tr>
<td><strong>Activity and participation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vineland adaptive Behavior scales, second edition (Vineland-11)</td>
<td>4-20y</td>
<td>30-45</td>
<td>Parent questionnaire</td>
<td>✓    ✓    ✓    ✓</td>
</tr>
<tr>
<td>Pediatric QoL Inventory (PEDS-QL)</td>
<td>4-18y</td>
<td>5-10</td>
<td>Parent questionnaire</td>
<td>✓    ✓    ✓    ✓</td>
</tr>
<tr>
<td>Pediatric QoL Inventory: Fatigue Module (PEDS-QL)</td>
<td>4-18y</td>
<td>5-10</td>
<td>Parent questionnaire</td>
<td>✓    ✓    ✓    ✓</td>
</tr>
<tr>
<td>Participation and Environment Measure</td>
<td>4-20y</td>
<td>25</td>
<td>Parent questionnaire</td>
<td>✓    ✓    ✓    ✓</td>
</tr>
<tr>
<td>for Children and Youth (PEM-CY)</td>
<td>questionnaire</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---------------------------------</td>
<td>---------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>The Assisting Hand Assessment (AHA)</td>
<td>4-18y 10-15</td>
<td>Child assessment ✓ ✓ ✓ ✓ ✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>The Mini Assisting Hand Assessment (mini-AHA)</td>
<td>8-18m 10-15</td>
<td>Child assessment ✓ ✓ ✓ ✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detailed Assessment of Speed of Handwriting (DASH)</td>
<td>9-16y11m 30</td>
<td>Child assessment ✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detailed Assessment of Speed of Handwriting (DASH 17)</td>
<td>17y-25y 30</td>
<td>Child assessment ✓</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Classification tools**

| Gross Motor Function Classification System (GMFCS) | 2-18y N/A | Researcher rated ✓ ✓ ✓ ✓ ✓ ✓ |
| Manual Ability Classification System (MACS) | 4-18y N/A | Researcher rated ✓ ✓ ✓ ✓ ✓ ✓ |
6.4 Procedure

*Ethics:*

Phase one and two were both approved by the Human Research Ethics Committee of The RCH. Information letters were sent at the commencement of both phases of the study. Families were then contacted via telephone to discuss the study and for the families to ask any questions or concerns. Written consent was obtained from each child’s parent or guardian. Written consent was also obtained from children over the age of 12. All data collected were de-identified and treated as confidential and used only in this project unless otherwise specified. All information is stored securely in the Child Neuropsychology department at the Murdoch Childrens Research Institute.

The following people have access to information collected as part of this research project:

- The research team involved with this project
- The Royal Children’s Hospital Human Research Ethics Committee

Any video recordings of participants are stored on an external hard drive in a locked cabinet, which will only be accessible to the research team.

We did not expect there to be any risks for the participants of this study. It may, however, be inconvenient for children and their families to participate with taking time off work or school. To minimise the inconvenience we offered families to have assessment at their own homes. Participants were able to withdraw from this study at any time.

We didn’t expect there to be direct benefit from taking part, however, after the assessment we sent a written summary of the results, which detailed the participants strengths and any possible areas of weakness. If the assessment suggested that a participant might benefit from referral to e.g. therapy or for educational input, then with consent a referral for these services would be made. If they were already receiving therapy services, they may like to share the reports with their therapists or school.
Phase two was run jointly with a study exploring social outcomes of the cohort. The assessments were carried out at either the Murdoch Children’s Research Institute (MCRI), or the child’s home, depending on the preference of the family. Where possible, both researchers completed the assessments in the same day, however, younger children and children with known attention or concentration difficulties sometimes had their assessments completed over two sittings.

Where children were residing interstate, families were offered either flights or accommodation to Melbourne, or for the therapists to travel to their hometowns to complete the assessments. Where children were residing rurally (over 2hrs from Melbourne), families were offered accommodation for a night close to the hospital.

Parent-completed assessments and questionnaires were mailed a week prior to their assessments. Families also completed a demographics questionnaire at the commencement of the child assessment. Standardised, direct child assessments took between 1-2 ½ hours to complete depending on the capabilities of the child and which assessments were administered.
6.5 Statistical analysis

Data were entered into an excel database and analysed in IBM Statistical Package for Social Sciences (SPSS) version 23. Children were stratified into three groups according to age at onset. 1. Neonates (≥ 20 weeks gestation <30 days), preschool (≥ 30 days <5 years) and school aged (≥ 5 years ≤18 years). Significance levels were set at <0.05. Demographic data were reported descriptively, as means ±SD for normally distributed variables and median ±SE for others, proportions and percentages.

Descriptive analyses were reported for patient demographic and lesion characteristics between stratified age groups: neonatal (≤ 30 days at diagnosis), preschool (>30 days-5 years) and school-aged (≥ 5 years old). Means and standard deviations were reported for continuous variables, and compared between groups with analysis of variance (ANOVA). Frequencies and proportions were reported for categorical variables, and compared using Fisher’s exact tests (due to low cell counts).

First paper: Trajectories of Motor Recovery in the First Year After Pediatric Arterial Ischaemic Stroke.

Motor z-scores were entered into analysis, with functional impairment indicated as a z-score of ≤ -1. Linear growth curve models were undertaken to explore change in FM and GM outcomes (obtained from the BOT-2 and the BSID-III) over the 1, 6 and 12-month time points for the whole population, and stratified by age group. This method of analysis utilises all available information, without the requirement of participant data at all time points (with data missing at random) (127). Participant ID was entered as a random variable; time (in months) entered as a random slope, and an unstructured covariance matrix was applied. Model estimates were plotted for each outcome, including 95% confidence intervals.

Multiple regressions explored the prediction of FM and GM z-scores at 12 months from dichotomised demographic and lesion characteristics. For age dummy variables a linear joint test was conducted to determine the overall effect of age categories. Unstandardised beta coefficients and significances were reported, as were model
effect sizes ($R^2$) and p-values. Finally, Pearson correlations were calculated to explore a relationship between total adaptive behaviour scores and both FM and GM z-scores. A strong correlation was indicated by a correlation coefficient of above 0.7, moderate in the range of 0.5–0.7, and low correlation was less than 0.5 (128).

Second paper: The Pediatric Stroke Outcome Measure: a predictor of outcome following arterial ischemic stroke

Between-group trajectories of mean PSOM over time were explored using a generalised estimating equation (GEE) model. This approach to modelling allowed for the inclusion of all available data without listwise loss. Within-person variation was accounted for by entering participant study number as a random effect, and an unstructured variance-covariance matrix was specified. Due to non-normality of model residuals, PSOM was log-transformed in all analyses.

Multiple logistic regressions were employed to explore the relationships between 1-month total PSOM impairment (binary: impaired vs. not impaired) and age group with 12 month FMZ, GMZ, and VABS total. Hierarchical logistic regression explored the prediction of PSOM scores at 1 month with 12-month motor and adaptive behaviour outcomes above and beyond lesion size and age group.

Fisher’s exact tests were conducted between motor and functional outcome impairment (FMZ, GMZ and VABS) and a 6-level combined PSOM/age group variable (due to perfect prediction, a logistic regression approach including an interaction between the two predictors was not possible). Finally, Receiver Operator Characteristic (ROC) curves assessed the ability of 1-month PSOM impairment to discriminate impairment on 12 month FMZ, GMZ, and VABS total. Area under the curve (AUC) values assessed the discriminant validity, with AUC>0.7 indicating acceptable discrimination (65)

Third paper: Motor function and adaptive abilities 5 years following paediatric arterial ischemic stroke.
There were four children younger than 5 years and 1 child over 17 years so the PEM-CYs for these children were excluded from the analyses. One child had an incomplete data set, as the parents did not return the parent questionnaire (Peds-QL, the PedsQL-MFS, VABS and PEM-CY).

One-sample t-tests were conducted to compare measures of body structure and function (BOT-2), activity and participation (PEM-CY: home, school, and community; DASH: copy best, alphabet writing, copy fast, free writing, and graphic speed), quality of life (PedsQL, PedsQL Multidimensional Fatigue Scale), and adaptive function (VABS-II: total adaptive behaviour and activities of daily living) with population norms or comparative data. Analyses were performed for the sample as a whole, then again within age groups. Values were adjusted for multiple comparisons by using false discovery rate adjustment. This adjustment was selected as it is less conservative than traditional family-wise error rate controlling methods, not unduly penalizing the smaller sample size and exploration of like outcomes.

Spearman correlations ($r$) were conducted to explore a relationship between fine motor and gross motor z-scores with adaptive behaviour total scores (VABS-II), activities of daily living subdomain score (VABS-II), quality of life total scores (PedsQL), fatigue total scores (PedsQL Multidimensional Fatigue Scale), and participation at home, school, and in the community (PEM-CY). A strong correlation was indicated by a correlation coefficient above 0.7, moderate in the range 0.5 to 0.7, and a low correlation if less than 0.5. (128).

Finally, multiple regression models with bootstrapped confidence intervals (CI; 1000 replications)$^{33}$ explored the prediction of fine motor and gross motor z-scores at 5 years from dichotomized demographic, 1-month PSOM impairment, and lesion characteristics. To explore effect of age at diagnosis across age groups, age dummy variables were generated. Likelihood ratio tests determined model improvement with each predictor. Non-significant improvement resulted in predictor exclusion, and the most parsimonious models were presented. Unstandardized $\beta$ coefficients and significances were reported, and model assumptions verified.
7. TWELVE MONTH OUTCOMES

7.1 Trajectories of motor recovery in the First Year after Arterial Ischaemic Stroke
Trajectories of Motor Recovery in the First Year After Pediatric Arterial Ischemic Stroke

Anna K Cooper, MD,a,b Vicki Anderson, PhD,c,d Stephen Horoup, PhDc,e,f,g Marjorie Brownham, MLSc,f,g Michael Hitchfield, PhDh,i Leo Coleman, MSc,i Rod W Hunt, PhDj,k,l Mark T MacKay, PhDl,m,n Paul McAlane, MDk,l,m,n Anne L Gordon, PhDo

BACKGROUND: Neuromotor impairments are common after pediatric stroke, but little is known about functional motor outcomes. We evaluated motor function and how it changed over the first 12 months after diagnosis. We also examined differences in outcome according to age at diagnosis and whether fine motor (FM) or gross motor (GM) function was associated with adaptive behavior.

METHODS: This prospective, longitudinal study recruited children (N = 64) from The Royal Children’s Hospital, Melbourne who were diagnosed with acute arterial ischemic stroke (AIS) between December 2007 and November 2013. Motor assessments were completed at 3 time points after the diagnosis of AIS (1, 6, and 12 months). Children were grouped as follows: neonates (n = 24), preschool-aged (n = 19), and school-aged (n = 11).

RESULTS: A larger lesion size was associated with poorer GM outcomes at 12 months (P < .016). Neonatal AIS was associated with better FM and GM function initially but with a reduction in z scores over time. For the preschool- and school-aged groups, FM remained relatively stable over time. For GM outcomes, the preschool- and the school-aged age groups displayed similar profiles, with gradual recovery over time. Overall, poor FM and GM outcomes at 12 months were associated with poorer adaptive behavior scores.

CONCLUSIONS: Motor outcomes and the trajectory of recovery post-AIS differed according to a child’s age at stroke onset. These findings indicate that an individualized approach to surveillance and intervention may be needed that is informed by part age at diagnosis.
Long-term neurodevelopmental disability occurs in 50% of childhood strokes and 50% to 60% of symptomatic neonatal strokes. Arterial ischemic stroke (AIS) occurs more frequently in neonates (≤28 days old), with an incidence of 1 in 4000 live births, when compared with 2 to 8 per 100,000 in childhood (29 days–19 years old). Acute presentation differs between the 2 groups; hemiplegia is the most common acute clinical sign of childhood AIS and is present in 72% to 90% of cases with estimates of the prevalence of chronic hemiplegia varying from 25% to 56%. In contrast, neonates typically present with seizures and have lower rates of chronic hemiplegia (ranging from 20% to 28%).

After an adult stroke, rapid motor recovery occurs in the first few months postdiagnosis with less improvement thereafter. In contrast, brain injury researchers suggest that the trajectory of motor recovery in children may be more protracted.

Lesion characteristics may play an important role in motor outcomes after a pediatric stroke. Studies revealing poorer outcomes in children who have more than 10% intracranial volume infarction. Authors of other studies (primarily of neonates) have noted poorer outcomes for cortical (as opposed to subcortical) infarct location and for cortical lesions with corticospinal tract involvement.

Clinical experience suggests a wide variation in the nature and severity of functional motor difficulties. Researchers have conducted several cross-sectional studies that describe motor function outcomes in children after AIS, but these assessments are mainly descriptive and usually confined to identifying a presence or absence of motor impairments. To date, most studies in which the researchers measure motor function in children have been limited to clinical judgments using qualitative tools. More specific characterization of gross motor (GM) and fine motor (FM) function after pediatric AIS and how they change over time is lacking in the literature, which limits the ability to develop targeted rehabilitation strategies to optimize motor outcomes.

We aimed to examine changes in motor function in the first year after acute presentation of AIS across 3 age groups (neonates, preschool-aged, and school-aged children) by using robust, age-appropriate measurement tools. We also investigated the relationship between GM and FM function at 12 months post-AIS with adaptive behavior.

**METHODS**

**Design**

This is a single site, prospective, longitudinal observational cohort study. Participants were assessed at 3 time points: 1, 6, and 12 months after an acute diagnosis of AIS. The first time point was selected based on clinical experience of the earliest likely time point at which all children would be likely to undertake the study protocol. The subsequent time points were selected to capture changes over time. Ethics approval was obtained through the Human Research Ethics Committee of The Royal Children’s Hospital, Melbourne.

**Participants**

Participants aged between term newborn and 18 years with acute AIS were consecutively recruited from a single tertiary-level children’s hospital between December 2007 and November 2013, as detailed in a previous article. Children were included if their brain MRIs confirmed an acute parenchymal ischemic infarction on diffusion-weighted imaging that corresponded to 1 or more arterial territories. Children with previously diagnosed AIS, coexisting diffuse brain injury caused by a traumatic or hypoxic-ischemic event, and preterm infants (born <36 weeks’ gestation) were excluded.

One hundred and seven children met the eligibility criteria for the study. Thirty-three were not approached (of which 12 died acutely, 6 resided interstate, and 15 were missed and/or not referred in time), and 7 declined participation (1 because of employment, 3 were too busy and/or stressed, and 3 gave no reason). Sixty-seven children were recruited between December 2007 and November 2013. Two participants were unable to be contacted for follow-up appointments, and 1 child died (of non-stroke-related issues) before the 12-month assessment. A total of 66 children completed the assessments for the current study.

**Measures**

**Clinical Characteristics**

Infract laterality, lesion location, and the vascular territory affected were rated by 2 neuroradiologists (M.D. and L.C.) on the basis of visual inspection of images obtained at the time of diagnosis (as described in Gordon et al). Lesion size was dichotomized as “small or medium” or “large” according to the degree of vascular territory impacted. Lesion location was categorized as cortical, subcortical, both, or infratentorial. All clinical assessments were conducted by experienced pediatric clinicians (A.L.G. and M.G.). The presence of a hemiplegia was determined after a clinical examination, which is indicated by a score of ≥0.5 on the sensorimotor domain of the Pediatric Stroke Outcome Measure (POSOM).

**Primary Motor Outcomes**

GM and FM capacity were assessed by using standardized motor assessments at all time points either in an outpatient clinic or at

5 year stroke motor outcomes
home, according to child or parent preferences.

For infants and children aged <12 months, the motor domain of the Bayley Scales of Infant and Toddler Development, Third Edition (BSID-III) were administered. The BSID-III provides comprehensive assessment of infant and toddler development. Sealed scores were generated for the FM and GM subscales of the motor function domain (mean = 10, SD = 3).

For children aged >12 months, the Bruininks-Oseretsky Test of Motor Proficiency, Second Edition (BOT-2) was conducted. The BOT-2 is a standardized, norm-referenced, comprehensive motor assessment for children aged 4 to 21 years. It assesses motor function across 4 domains: fine manual control, manual coordination, body coordination, and speed and agility. Standard scores were generated across the 4 subdomains (mean = 50, SD = 10), and an overall motor composite score was also generated (mean = 50, SD = 10). Thirty-eight children were assessed with the BSID-III at all time points, 28 children were assessed with the BOT-2 at all time points, and 3 children were assessed with both the BSID-III and the BOT-2.

Scores from subdomains of fine manual control and manual coordination were combined and averaged to generate an FM score, and body coordination and strength and agility were combined and averaged for a GM score. These were entered into z scores for both FM and GM function.

**Descriptive and Predictors**

The PSOM is a detailed neurologic assessment that measures impairments across 5 domains: left sensorimotor, right sensorimotor, language production, language comprehension, cognition, and behavior. When it was not possible to examine a child, the Recovery and Recurrence Questionnaire was administered, which is a parent-administered version of the PSOM that has been demonstrated to correlate strongly with the clinician-administered PSOM.

The Vineland Adaptive Behavior Scales, Second Edition (VABS2) is a parent-rated questionnaire that measures a child’s activity and participation across 4 domains: communication, daily living, motor skills, and socialization. These were employed in analyses (mean = 100, SD = 15). The motor subscale is only administered to children <6 years old, so scores for this subgroup were not entered into analyses.

**Statistical Analyses**

Descriptive analyses were reported for patient demographic and lesion characteristics between stratified age groups: neonatal (<30 days old at diagnosis), preschool-aged (30 days–5 years old), and school-aged (≥5 years old). Means and SDs were reported for continuous variables and compared between groups with an analysis of variance. Frequencies and proportions were reported for categorical variables and compared using Fisher’s exact tests (because of low cell counts).

Motor z scores were entered into analysis, with functional impairment indicated as a z score of ≤−1. Linear growth curve models were undertaken to explore changes in FM and GM outcomes over the time points of 1, 6, and 12 months for the whole population and were stratified by age group. This method of analysis utilizes all available information without the requirement of participant data at all time points (with data missing at random). Participant identification was entered as a random variable, time (in months) was entered as a random slope, and an unstructured covariance matrix was applied. Model estimates were plotted for each outcome, including 95% confidence intervals.

Multiple regression models explored the prediction of FM and GM z scores at 12 months by using dichotomized demographic and lesion characteristics. For age dummy variables, a linear joint test was conducted to determine the overall effect of age categories. Unstandardized b coefficients and significance were reported in addition to model effect sizes (R²) and P values.

Finally, Pearson correlations were calculated to explore the relationship between total adaptive behavior scores and both FM and GM z scores. A strong correlation was indicated by a correlation coefficient of >0.7, moderate was between 0.5 and 0.7, and low was <0.5.

**RESULTS**

**Sample Characteristics**

Sample demographics and lesion characteristics are presented in Table 1. There was a higher proportion of neonates (40%) than older children, more neonates had combined cortical and subcortical involvement (P = .001), and nearly double the number of neonates had left-sided lesions when compared with other age groups; however, this was not statistically significant (P = .26).

**Motor Outcomes Across the First Year After AIS Onset**

At 12 months after AIS onset, 19 (30%) children exhibited hemiplegia, with similar percentages of children in each age group (33% neonates, 21% preschool-aged, and 33% school-aged). Six (9%) children had a bilateral motor impairment (no neonates, 19% preschool-aged, and 14% school-aged) (see Fig. 1). For FM outcomes, the neonatal and school-aged groups demonstrated a gradual emergence of impairments over time, whereas the preschool-aged group
tended to improve. For GM outcomes, impairments again emerged over time in the neonatal group and for both the preschool-aged group and the school-aged group. GM impairments were greatest at 1 month and then steadily improved (see Fig 2). At 12 months, FM impairments tended to be more common in children with bilateral (36.4%) or infratentorial (35.5%) lesions than those with unilateral lesions (22%). At the same time, GM impairments tended to be more frequent in children with unilateral (52%) or bilateral (63%) lesions than in those with infratentorial lesions (25%). Nevertheless, injury location was not a significant predictor of motor outcomes at 12 months in our regression analysis.

Linear growth curve models plotted FM and GM z scores over time. For FM scores, significant main effects of age at AIS onset were identified (\( P < .001 \)), and time post-AIS was detected (\( P < .001 \)). A significant interaction between age group and time was found (\( P < .001 \)), which supported the differences in recovery trajectories across age groups. Overall, a younger age at AIS onset was associated with better FM function initially with reduced scores over time. For the preschool- and school-aged groups, z scores remained relatively stable over time, as illustrated in Fig 3A.

The GM z score model also found a significant main effect of age at AIS onset and time (both \( P < .001 \)) and a significant interaction effect (\( P = .001 \)). The neonates performed best overall at 1 month, but they showed a trend toward poorer scores over time. The preschool- and school-aged groups displayed similar profiles initially, all SD below the mean with gradual recovery over time (Fig 3B). FM and GM z scores at each time point, as well as VABS2 standard scores at 12 months, are summarized in Table 2.

### Table 1: Patient and Lesion Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total</th>
<th>Neonates</th>
<th>Preschool-aged</th>
<th>School-aged</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of cohort</td>
<td>64</td>
<td>27 (42.4)</td>
<td>19 (30.1)</td>
<td>16 (53.6)</td>
</tr>
<tr>
<td>Age at diagnosis, mo. (SD)</td>
<td>45 (27.0)</td>
<td>63.3 (2.06)</td>
<td>36.9 (1.10)</td>
<td>35.76 (4.12)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>16 (1.66-19.88)</td>
<td>3.50 (4.3)</td>
<td>1.26 (2.3)</td>
<td>0.83 (1.05)</td>
</tr>
<tr>
<td>Injury location</td>
<td>Unilateral (44%)</td>
<td>10 (50.0)</td>
<td>11 (55.0)</td>
<td>9 (40.0)</td>
</tr>
<tr>
<td>Lesion characteristics, n (%)</td>
<td>Left</td>
<td>45 (47.4)</td>
<td>23 (46.8)</td>
<td>11 (57.9)</td>
</tr>
<tr>
<td>Bilateral</td>
<td>Bilateral (63%)</td>
<td>24 (48.0)</td>
<td>4 (40.9)</td>
<td>2 (40.0)</td>
</tr>
<tr>
<td>Cerebral only</td>
<td>1 (1.7)</td>
<td>1 (1.1)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Subcortical only</td>
<td>10 (20.0)</td>
<td>2 (15.0)</td>
<td>7 (35.0)</td>
<td>5 (33.3)</td>
</tr>
<tr>
<td>Both</td>
<td>50 (60.0)</td>
<td>24 (48.0)</td>
<td>7 (35.0)</td>
<td>6 (33.3)</td>
</tr>
<tr>
<td>Neither</td>
<td>8 (10.0)</td>
<td>5 (6.0)</td>
<td>3 (15.0)</td>
<td>2 (12.5)</td>
</tr>
<tr>
<td>Lesion size, cm²</td>
<td>Small</td>
<td>32 (51.9)</td>
<td>26 (42.5)</td>
<td>17 (22.7)</td>
</tr>
<tr>
<td>Lesion location</td>
<td>Medium to large (46%)</td>
<td>12 (18.3)</td>
<td>7 (11.5)</td>
<td>2 (10.7)</td>
</tr>
<tr>
<td>Vascular territory, n (%)</td>
<td>Medulla</td>
<td>3 (4.7)</td>
<td>3 (5.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Midbrain</td>
<td>3 (4.7)</td>
<td>3 (5.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Frontal lobe</td>
<td>5 (7.9)</td>
<td>3 (5.0)</td>
<td>0 (0.0)</td>
<td>2 (4.0)</td>
</tr>
<tr>
<td>Temporal lobe</td>
<td>5 (7.9)</td>
<td>3 (5.0)</td>
<td>0 (0.0)</td>
<td>2 (4.0)</td>
</tr>
<tr>
<td>Ventral anterior</td>
<td>4 (5.9)</td>
<td>4 (6.7)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Multiple</td>
<td>15 (23.4)</td>
<td>7 (46.7)</td>
<td>6 (35.0)</td>
<td>2 (13.3)</td>
</tr>
</tbody>
</table>

* Infratentorial lesion, WIA, middle cerebral artery, PCA, posterior cerebral artery.

### Figure 1: Percentage of children with severe motor impairments.
Factors Associated With 12-Month Outcomes

Multiple-regression analyses explored the combination of demographic and clinical characteristics with 12-month FM and GM Z scores (Table 3). A large lesion size was associated with poorer GM outcomes but not FM outcomes. When exploring the effect of age at injury, the school-aged group exhibited poorer FM outcomes ($\beta = -91, P = .02$) when compared with neonates; however, the linear age category joint test was not significant. There were no significant relationships between sex, lesion laterality, or lesion location and 12-month GM and FM outcomes.

The Relationship Between Motor Scores and Adaptive Behavior, Activity, and Participation

Finally, a low-strength correlation was found between GM scores and total adaptive behavior scores ($r = 0.27, P < .001$), and a moderate relationship was found between FM scores and total adaptive behavior scores ($r = 0.51, P = .04$), with poorer adaptive behavior scores being associated with poorer GM and FM scores.

Examination of the relationship between children’s direct motor outcomes (BOT-2 and BSID-III) and parental ratings (VABS-2) identified significant correlations between the VABS-2 communication and both FM ($r = 0.30, P = .019$) and GM ($r = 0.43, P = .001$) Z scores. Daily living scores were also associated with FM ($r = 0.34, P = .008$) and GM ($r = 0.42, P = .001$) Z scores, but there were no significant relationships between socialization and motor outcomes (Table 4).

DISCUSSION

Motor impairments are the most commonly reported long-term sequela of pediatric AIS. In this prospective longitudinal study, we investigated age-related trajectories of motor recovery over time. At 1 month, poor FM and GM outcomes were associated with younger age at AIS onset. Over time, impairments emerged in the neonatal group for FM and GM function. This finding is consistent with previous research in which motor impairments have been reported to emerge in the neonatal population at 4 to 5 months of age, when infants typically develop voluntary hand use. In contrast, the preschool- and school-aged groups met criteria for “impairment,” with gradual recovery over time. Both groups had similar overall recovery trajectories, but the preschool-aged group performed better in both GM and GM domains at all time points, which suggests that these groups demonstrate a similar magnitude of recovery. The finding that the preschool-aged group had better motor outcomes is consistent with findings reported by researchers who have explored cognitive outcomes after pediatric AIS onset, and this
finding also suggests a protective period, meaning the poorest outcomes occur when AIS onset is before age 1 or after age 6.\textsuperscript{41,42}

Twelve months after AIS onset, the percentage of children with GM impairments was higher than those with FM impairments across all age groups. The neonatal group had 3 times as many GM impairments (50%) when compared with FM outcomes (15%). The development of hand functioning in children is refined over many years with skills such as regulation of grip force and in-hand manipulation that develop well beyond the first year of life. Thus, a neonate’s FM impairments may become more evident in the subsequent years that these skills typically develop.\textsuperscript{41}

Despite significant age-related differences in the trajectories of motor recovery, none of the 3 groups were significantly impaired in FM or GM function at 12 months after AIS onset. This could be because sensorimotor skills are considered by some investigators to be “lower-order” skills that have possibly less complex neural networks, and as a consequence, they could be less vulnerable to early brain injury than more complex, higher-order skills (such as attention or social cognition), which may rely on more diffuse neural networks.\textsuperscript{45} It is also important to acknowledge the involvement of cognitive skills in motor function testing, which adds complexity to assessing outcomes in children.

The age for optimal motor recovery from brain injury remains unclear. Motor plasticity is likely to be greatest in early childhood, when the young brain is rapidly reorganizing and myelinating. In contrast, older children may have less plasticity, but functional outcome may be improved by the possession of a wider set of learned skills and behaviors at the time of injury, which creates a greater potential for true rehabilitation. This study suggests that preschool-aged children may have the best motor outcomes and recovery trajectory, and therefore, they may be the age group in which there is an optimal balance between greater brain plasticity and lower vulnerability.\textsuperscript{44}

There were no significant relationships found between motor outcomes and lesion laterality or location (using dichotomized variables); however, as has been reported by others, larger lesions tended to be associated with poorer outcomes, particularly in GM function. A significant relationship was identified between communication

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure3}
\caption{A: FM outcomes across the first year after a stroke: linear growth model of standardized FM scores between the 3 age groups. B: GM outcomes across the first year after a stroke: linear growth model of standardized GM scores between age groups. CI: confidence interval.}
\end{figure}
skills and activities of daily living with GM and FM outcomes at 12 months, which suggests that AIS in children has broad-reaching implications in daily life.

This is the first published study to use a prospective longitudinal design to measure trajectories of motor recovery over 12 months after AIS onset in children. The focus on individual outcomes (specifically the proportion of children with persisting functional limitations) was a strength of the current study and contrasts it to previous literature that is limited to interpretation of group mean data, which can be misleading because it can mask underlying differences. Most participants’ scores fell within 1 SD of the mean (suggesting normal function), but analyses of FM and GM impairment rates revealed a high percentage of children who continued to have both FM and GM impairments.

A challenge of measuring motor function in this population is that the PDSM is the only standardized neurologic impairment outcome measure that is validated to the pediatric stroke population. The PDSM is, however, a neurologic screening tool, which may miss the finer details of motor function. It is also difficult to measure change over time in a pediatric population because standardized assessments are designed for specific age ranges. Different assessments are therefore needed at different ages, which adds complexity to this analysis. A strength of this study is that we used sensitive and comprehensive measures of motor function and so were able to link these assessments to adaptive function. Of note, handedness was not reported in our sample because approximately three-quarters of participants were younger than 4 years old at the time of AIS onset. Less than two-thirds of eligible children were...
enrolled in the study. Because of government regulations, we were unable to assess whether there were differences between participants and nonparticipants, which may influence interpretations of the findings.

Sample size was large for the field, but age at AIS onset subgroups were small, which limited the breadth of possible analyses. In addition, overrepresentation of bilateral and infratentorial AIS in the consecutively recruited sample may have impacted our results.

Westmacott et al.15 recently described the emergence of cognitive impairments after a unilateral stroke beyond the first year. Given that the trajectory of recovery from pediatric strokes in other domains is unclear and that recovery may continue beyond the first year, a long-term observational study is warranted.

CONCLUSIONS

FM and GM outcomes after pediatric AIS are variable. Factors that influence the recovery trajectory and long-term motor outcomes include age at AIS onset and lesion size. Neonates have a different recovery trajectory from older-onset age groups and appear to grow into their motor impairments over time. At 12 months after AIS onset, children with FM and GM difficulties also have difficulties with functional activities, which is evidenced by lower adaptive behavior scores. These findings support the need for long-term neurodevelopmental surveillance in the pediatric AIS population so that as developmental needs change or impairments emerge, needs can be addressed to optimize outcomes.

ABBREVIATIONS

AIS: arterial ischemic stroke
BOT-2: Bruininks-Oseretsky Test of Motor Proficiency, Second Edition
BSID-III: Bayley Scales of Infant and Toddler Development, Third Edition
FM: fine motor
GM: gross motor
PSQI: Pediatric Stroke Outcome Measure
VABS2: The Vineland Adaptive Behavior Scales, Second Edition

REFERENCES

Trajectories of Motor Recovery in the First Year After Pediatric Arterial Ischemic Stroke
Anna N. Cooper, Vicki Anderson, Stephen Hearps, Mardee Greenham, Michael Ditchfield, Lee Coleman, Rod W. Hunt, Mark T. Mackay, Paul Monagle and Anne L. Gordon

Pediatrics; originally published online July 14, 2017;
DOI: 10.1542/peds.2016-3870

Updated Information & Services
including high resolution figures, can be found at:
/content/early/2017/07/12/peds.2016-3870.full.html

References
This article cites 42 articles, 9 of which can be accessed free at:
/content/early/2017/07/12/peds.2016-3870.full.html#ref-list-1

Subspecialty Collections
This article, along with others on similar topics, appears in the following collection(s):
Neurology
/content/collection/neurology_sub
Neurologic Disorders
/content/collection/neurologic_disorders_sub
Cardiology
/content/collection/cardiology_sub
Cardiovascular Disorders
/content/collection/cardiovascular_disorders_sub

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
/site/misc/Permissions.xhtml

Reprints
Information about ordering reprints can be found online:
/site/misc/reprints.xhtml

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 11310 Westville Drive, Elk Grove Village, Illinois, 60007. Copyright © 2017 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.
7.2 The Pediatric Stroke Outcome Measure: a predictor of outcome following arterial ischemic stroke

The Pediatric Stroke Outcome Measure
A predictor of outcome following arterial ischemic stroke

Anna N. Cooper, BSc, Vicki Anderson, PhD, Stephen Huskens, PSQIP Research, Murdoch Childrens Hospital, Melbourne, Australia; Anne L. Gordon, PhD, University of Melbourne, Melbourne, Australia; Rod W. Hunt, PhD, Mark T. Mackay, PhD, Paul Monagle, MD, and Anne L. Gordon, PhD
Neurology® 2018;90(5):e372. doi:10.1212/WNL.0000000000004306

Abstract
Objective
To evaluate the relationship between neurologic outcome at 1 month following diagnosis of pediatric arterial ischemic stroke (AIS) and motor and adaptive behavior outcomes at 12 months.

Methods
This prospective longitudinal observational cohort study recruited children from a single tertiary children’s hospital diagnosed with first AIS between December 2007 and November 2013. Neurologic impairment was evaluated at 4 time points using the Pediatric Stroke Outcome Measure (PSOM) or Recovery and Recurrence Questionnaire following diagnosis of AIS (acute, 1, 6, and 12 months). Motor function and adaptive behavior were assessed at 12 months using standardized measures. Children were grouped for analysis, according to age at diagnosis (neonates vs preschool vs school-aged). The relationship between neurologic impairment and 12-month functional outcomes were examined.

Results
Sixty-four children were recruited (27 neonates, 19 preschool-aged, and 18 school-aged). Presence of impairment on the PSOM at 1 month was associated with lower 12-month fine motor z scores (p = 0.004), gross motor z scores (p = 0.001), and adaptive behavior standard scores (p = 0.004). One-month PSOM impairment score was more predictive than age group or lesion size of 12-month motor and adaptive behavior outcome.

Conclusions
The PSOM has value as a predictive tool when used at 1 month after first AIS diagnosed acutely in relation to motor and adaptive behavior, with variation according to age group.
Glossary

AIS = arterial ischemic stroke; AUC = area under the curve; BOT-2 = Bruininks Oseretsky Test of Motor Proficiency 2; BSID-III = Bayley Scales of Infant and Toddler Development III; CI = confidence interval; FM = fine motor; FMI = fine motor Z-score; GEE = generalized estimating equations; GM = gross motor; GMZ = gross motor Z-score; IQ = interquartile range; PSOM = Pediatric Stroke Outcome Measure; ROC = receiver operator characteristic; RQ = Recovery Questionnaire; VABS = Vineland Adaptive Behavior Scales.

After pediatric stroke, neurologic sequelae are commonly reported. Little is known about the relationships between acute neurologic impairment and functional motor outcomes, yet this may allow clinicians to better target early interventions and prognosticate. The incidence and acute presentation of arterial ischemic stroke (AIS) differs depending on the age at stroke onset. Neonates (<30 days) most frequently present with seizures or behavioral disturbances, and neurologic impairments are recognized later. In contrast, following childhood AIS (>30 days), acute hemiplegia is the most common presenting symptom. 1

The Pediatric Stroke Outcome Measure (PSOM) is a standardized neurologic outcome measure validated for pediatric stroke. 2 The PSOM is used widely in pediatric hospitals; however, the long-term predictive value is unknown. 3 Associations have been described between PSOM findings and cognitive, behavioral, adaptive behavior, social participation, and quality of life outcomes. 4 However, in these studies, the PSOM was administered at the same time point as the other outcome measures. The predictive value of the PSOM at 1 month after AIS has not previously been reported.

We aimed to explore the relationship between neurologic impairment (PSOM) at 1 month and motor and adaptive behavior outcomes at 12 months after AIS in children. We also measured neurologic outcome (PSOM) at 4 time points during the first year after AIS.

Methods

In a single-site, prospective, longitudinal observational cohort study, we assessed children at 4 time points—acute and 1, 6, and 12 months after AIS diagnosis. The acute assessment was completed at the earliest clinically possible time point. This study was one component of a larger longitudinal study exploring outcomes across multiple domains. 5

Standard protocol approvals, registrations, and patient consents

Prospective ethics approval was granted by the Human Research Ethics Committee of The Royal Children’s Hospital, Melbourne. Informed written consent was obtained from the parent/guardian for each participant and from the child as well if he or she was older than 12 years.

Participants

Participants aged between term newborn and 18 years with acute AIS were consecutively recruited to the study from a single tertiary level children’s hospital as previously detailed. 6 Children were included in the study if MRI confirmed acute parenchymal ischemic infarction on diffusion-weighted imaging, corresponding to one or more arterial territories. Acute arterial ischemic stroke was defined as the presence of an acute neurologic syndrome of any duration with features suggesting a vascular ischemic insult corresponding to the clinical signs and symptoms, confirmed by neuroimaging or pathology. 7,8 Excluded children had a previously diagnosed stroke, had coexisting diffuse brain injury due to a traumatic or hypoxic ischemic event, or were premature infants (i.e., born prior to 36 weeks’ gestation). A total of 107 children were eligible to participate. Thirty-three were not approached (12 died acutely, 6 resided interstate, and 15 were not referred in time), and 7 declined participation (1 due to employment, 5 due to study burden, and for 3 no reason was provided). Sixty-seven children were recruited between December 2007 and November 2013. Two participants were unable to be contacted for follow-up assessments, and 1 died (of non-stroke-related issues) prior to the 12-month assessment. A total of 64 children completed the assessments.

Measures

Infarct laterality, lesion location, and vascular territory affected were rated by 2 neuroradiologists (M.D., L.C.), using visual inspection of images obtained at the time of diagnosis (as described in Gordon et al. 9 and reported descriptively (table 1). Lesion size was classified according to degree of vascular territory affected upon visual assessment; for example, small when structures served by small perforating branches of arteries were affected (e.g., discrete area of injury to structures supplied by lenticulostriate arteries), medium a branch of a major cerebrovascular artery (e.g., temporal arteries), and large an entire vascular territory/multiple vascular territories. For analysis, these were dichotomized into small/medium or large. Lesion location was categorized as cortical, subcortical, both, or infratentorial. Clinical assessments were conducted by experienced pediatric clinicians (A.L.G., M.G.).

Neurologic function

Neurologic impairment was measured using the total PSOM score at each of the time points. The PSOM has established interrater reliability and construct validity and measures...
Table 1  Patient and lesion characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total</th>
<th>Neonates</th>
<th>Preschool</th>
<th>School-aged</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (% of cohort)</td>
<td>64</td>
<td>27 (42.4)</td>
<td>19 (29.7)</td>
<td>18 (28.1)</td>
</tr>
<tr>
<td>Age at diagnosis, mo, mean (SD) [range]</td>
<td>45 (57.8) [30.4-196.8]</td>
<td>6.13 (3.00) [0.33-3.0]</td>
<td>30.19 (18.13) [2.8-57.30]</td>
<td>125.76 (41.42) [66.23-195.5]</td>
</tr>
<tr>
<td>Sex, male, n (%)</td>
<td>36 (56.3)</td>
<td>18 (66.7)</td>
<td>8 (42.1)</td>
<td>10 (53.6)</td>
</tr>
<tr>
<td>Lesion characteristics, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unilateral</td>
<td>46 (71.8)</td>
<td>23 (85.2)</td>
<td>11 (57.9)</td>
<td>11 (61.1)</td>
</tr>
<tr>
<td>Left</td>
<td>25 (54.3)</td>
<td>15 (78.9)</td>
<td>5 (26.3)</td>
<td>4 (22.2)</td>
</tr>
<tr>
<td>Bilateral</td>
<td>11 (17.2)</td>
<td>4 (16.0)</td>
<td>5 (26.3)</td>
<td>2 (11.1)</td>
</tr>
<tr>
<td>Infrahtalinal only</td>
<td>8 (12.5)</td>
<td>0</td>
<td>3 (27.3)</td>
<td>5 (27.8)</td>
</tr>
<tr>
<td>Cortical only</td>
<td>1 (1.6)</td>
<td>1 (3.7)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Subcortical only</td>
<td>16 (25.3)</td>
<td>2 (7.4)</td>
<td>9 (47.4)</td>
<td>5 (27.8)</td>
</tr>
<tr>
<td>Both</td>
<td>35 (55.9)</td>
<td>24 (98.9)</td>
<td>7 (36.8)</td>
<td>8 (44.4)</td>
</tr>
<tr>
<td>Neither*</td>
<td>8 (12.5)</td>
<td>0 (0.0)</td>
<td>3 (15.8)</td>
<td>5 (27.8)</td>
</tr>
<tr>
<td>Lesion size</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small (small perforator and branch)</td>
<td>52 (81.3)</td>
<td>20 (74.1)</td>
<td>17 (89.5)</td>
<td>15 (83.3)</td>
</tr>
<tr>
<td>Large (major vessel, mean (SD))</td>
<td>12 (18.8)</td>
<td>7 (25.9)</td>
<td>2 (10.5)</td>
<td>3 (16.7)</td>
</tr>
<tr>
<td>Vascular territory, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCA Full</td>
<td>3 (4.7)</td>
<td>3 (11.1)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>MCA partial</td>
<td>33 (51.6)</td>
<td>14 (51.9)</td>
<td>19 (52.6)</td>
<td>9 (50.0)</td>
</tr>
<tr>
<td>PCA</td>
<td>5 (7.9)</td>
<td>5 (11.1)</td>
<td>0</td>
<td>2 (11.1)</td>
</tr>
<tr>
<td>Vertebrobasilar arteries</td>
<td>8 (12.5)</td>
<td>0</td>
<td>3 (15.8)</td>
<td>5 (27.8)</td>
</tr>
<tr>
<td>Multiple</td>
<td>15 (23.4)</td>
<td>7 (25.9)</td>
<td>0 (31.6)</td>
<td>2 (11.1)</td>
</tr>
<tr>
<td>Motor scores, mean (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GM (z scores)</td>
<td>0.08 (1.16)</td>
<td>-0.70 (1.32)</td>
<td>0.73 (1.26)</td>
<td>-0.94 (1.02)</td>
</tr>
<tr>
<td>FM (z scores)</td>
<td>0.49 (1.18)</td>
<td>0.33 (0.95)</td>
<td>0.34 (1.31)</td>
<td>-0.87 (1.03)</td>
</tr>
<tr>
<td>VABS (standard scores)</td>
<td>92.3 (14.0)</td>
<td>92.8 (15.5)</td>
<td>94.8 (7.8)</td>
<td>90.7 (17.3)</td>
</tr>
</tbody>
</table>

Abbreviations: GM = fine motor; GM = gross motor; MCA = middle cerebral artery; PCA = posterior cerebral artery; VABS = Vineland Adaptive Behavior Scales.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total</th>
<th>Neonates</th>
<th>Preschool</th>
<th>School-aged</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (% of cohort)</td>
<td>64</td>
<td>27 (42.4)</td>
<td>19 (29.7)</td>
<td>18 (28.1)</td>
</tr>
<tr>
<td>Age at diagnosis, mo, mean (SD) [range]</td>
<td>45 (57.8) [30.4-196.8]</td>
<td>6.13 (3.00) [0.33-3.0]</td>
<td>30.19 (18.13) [2.8-57.30]</td>
<td>125.76 (41.42) [66.23-195.5]</td>
</tr>
<tr>
<td>Sex, male, n (%)</td>
<td>36 (56.3)</td>
<td>18 (66.7)</td>
<td>8 (42.1)</td>
<td>10 (53.6)</td>
</tr>
<tr>
<td>Lesion characteristics, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unilateral</td>
<td>46 (71.8)</td>
<td>23 (85.2)</td>
<td>11 (57.9)</td>
<td>11 (61.1)</td>
</tr>
<tr>
<td>Left</td>
<td>25 (54.3)</td>
<td>15 (78.9)</td>
<td>5 (26.3)</td>
<td>4 (22.2)</td>
</tr>
<tr>
<td>Bilateral</td>
<td>11 (17.2)</td>
<td>4 (16.0)</td>
<td>5 (26.3)</td>
<td>2 (11.1)</td>
</tr>
<tr>
<td>Infrahtalinal only</td>
<td>8 (12.5)</td>
<td>0</td>
<td>3 (27.3)</td>
<td>5 (27.8)</td>
</tr>
<tr>
<td>Cortical only</td>
<td>1 (1.6)</td>
<td>1 (3.7)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Subcortical only</td>
<td>16 (25.3)</td>
<td>2 (7.4)</td>
<td>9 (47.4)</td>
<td>5 (27.8)</td>
</tr>
<tr>
<td>Both</td>
<td>35 (55.9)</td>
<td>24 (98.9)</td>
<td>7 (36.8)</td>
<td>8 (44.4)</td>
</tr>
<tr>
<td>Neither*</td>
<td>8 (12.5)</td>
<td>0 (0.0)</td>
<td>3 (15.8)</td>
<td>5 (27.8)</td>
</tr>
<tr>
<td>Lesion size</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small (small perforator and branch)</td>
<td>52 (81.3)</td>
<td>20 (74.1)</td>
<td>17 (89.5)</td>
<td>15 (83.3)</td>
</tr>
<tr>
<td>Large (major vessel, mean (SD))</td>
<td>12 (18.8)</td>
<td>7 (25.9)</td>
<td>2 (10.5)</td>
<td>3 (16.7)</td>
</tr>
<tr>
<td>Vascular territory, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCA Full</td>
<td>3 (4.7)</td>
<td>3 (11.1)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>MCA partial</td>
<td>33 (51.6)</td>
<td>14 (51.9)</td>
<td>19 (52.6)</td>
<td>9 (50.0)</td>
</tr>
<tr>
<td>PCA</td>
<td>5 (7.9)</td>
<td>5 (11.1)</td>
<td>0</td>
<td>2 (11.1)</td>
</tr>
<tr>
<td>Vertebrobasilar arteries</td>
<td>8 (12.5)</td>
<td>0</td>
<td>3 (15.8)</td>
<td>5 (27.8)</td>
</tr>
<tr>
<td>Multiple</td>
<td>15 (23.4)</td>
<td>7 (25.9)</td>
<td>0 (31.6)</td>
<td>2 (11.1)</td>
</tr>
<tr>
<td>Motor scores, mean (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GM (z scores)</td>
<td>0.08 (1.16)</td>
<td>-0.70 (1.32)</td>
<td>0.73 (1.26)</td>
<td>-0.94 (1.02)</td>
</tr>
<tr>
<td>FM (z scores)</td>
<td>0.49 (1.18)</td>
<td>0.33 (0.95)</td>
<td>0.34 (1.31)</td>
<td>-0.87 (1.03)</td>
</tr>
<tr>
<td>VABS (standard scores)</td>
<td>92.3 (14.0)</td>
<td>92.8 (15.5)</td>
<td>94.8 (7.8)</td>
<td>90.7 (17.3)</td>
</tr>
</tbody>
</table>

Impairments across the domains of left and right sensorimotor, expressive, and receptive language, behavior, and cognition. The sensorimotor and language subdomains are clinician-rated direct observations, while the cognitive and behavioral subdomains also take into account the parent's report. Total outcome scores were collapsed into good (a total score of 0.5 or below) or poor (a total score of 1 or above). For this study, the sensorimotor subscale was also collapsed into impaired (score of 0.5 or above) or not impaired (score of 0). Where it was not possible for a clinician experienced in the PSOM to examine the child, the Recovery and Recurrence Questionnaire (RRQ) was administered at each time point. The RRQ is a parent-administered tool demonstrated to correlate strongly with the clinician-administered PSOM. In presenting the findings, when we reference the PSOM, we are referring to either the PSOM or RRQ. At the acute time point, all children were assessed using the PSOM. At the subsequent time points, 22 children were assessed using the PSOM and 42 children were assessed using the RRQ.

Motor function

Gross motor (GM) and fine motor (FM) capacities were assessed using standardized motor assessments at 1, 6, and 12 months after diagnosis, either in an outpatient clinic or at home. For infants and children aged up to 42 months, the motor domains of the Bayley Scales of Infant and Toddler Development (BSID-III), third edition, were administered.
Scaled scores were generated for the FM and GM subsections (mean 10, SD 3). For children aged above 42 months, the Bruininks-Oseretsky Test of Motor Proficiency-2 (BOT-2) was administered.15,16 Using this measure, motor function is assessed across 4 domains generating standard scores (mean 50, SD 10) and an overall motor composite score (mean 50, SD 10). The subdomains of fine manual control and manual coordination were combined and averaged to generate a FM score, and body coordination and strength and agility were combined and averaged for a GM score. These scores were then converted into z-scores for both FM and GM function.

Adaptive behavior
The Vineland Adaptive Behavior Scales (VABS), second edition,17 is a parent-rated questionnaire that measures a child’s activity and participation across 4 domains: communication, daily living, and motor and social skills, as well as total adaptive behavior. Raw scores were converted to standard scores across each subdomain and to generate a total adaptive behavior composite score (mean 100, SD 15).17

Statistical analysis
Descriptive analyses were reported for patient demographic and lesion characteristics between stratified age groups: neonatal (<30 days at diagnosis); preschool (30 days to 4 years), and school-aged (≥5 years old). For continuous variables, means and SDs, and for categorical variables, frequencies and percentages were reported. For missing data at each time point, any summative measures were adjusted to reflect the true numbers contributing to that item.

Between-group trajectories of mean PSOM over time were explored using a generalized estimating equation (GEE) model. This approach to modeling allowed for the inclusion of all available data without list-wise loss. Within-person variation was accounted for by entering participant study number as a random effect, and an unstructured variance–covariance matrix was specified. Due to non-normality of model residuals, PSOM was log-transformed in all analyses.

Multiple logistic regressions were employed to explore the relationships between 1-month total PSOM impairment (binary: impaired vs not impaired) and age group with 12-month FM Z score (FMZ), GM Z score (GMZ), and VABS total. Hierarchical logistic regression explored the prediction of PSOM scores at 1 month with 12-month motor and adaptive behavior outcomes above and beyond lesion size and age group.

Fisher exact tests were conducted between motor and functional outcome impairment (FMZ, GMZ, and VABS) and a 6-level combined PSOM/age group variable (due to perfect prediction, a logistic regression approach including an interaction between the 2 predictors was not possible). Finally, receiver operator characteristic (ROC) curves assessed the ability of 1-month PSOM impairment to discriminate impairment on 12-month FMZ, GMZ, and VABS total. Area under the curve (AUC) values provided the discriminant validity, with AUC > 0.7 indicating acceptable discrimination.18

Results
Sample characteristics
Demographics and lesion characteristics are described in Table 1. Forty-two percent of patients were neonates at diagnosis, and more neonates had both cortical and subcortical involvement (p = 0.001) compared with older children. There was nearly double the number of neonates with left-sided lesions compared to older children at stroke onset groups. This finding approached significance (p = 0.085). Four (6%) children had a cardioembolic etiology, 3 (5%) children had moyamoya disease, 2 (3%) children had cervical arterial dissection, 7 (11%) children had sterno-occipital arteriopthy, and 32 (50%) had multiple possible etiologies at the time of diagnosis.

Neuromotor outcomes across the first year after stroke onset
The PSOM total scores in each age group at each time point (median and interquartile range [IQR]) were calculated. The median score was highest at the acute time point in both the preschool-aged (median 1.5, IQR 0.50–3.00) and the school-aged groups (median 2.00, IQR 1.00–3.00). These scores showed a trend in reduction over time and were lowest at the 12-month time point in both the preschool-aged (median 0.00, IQR 0.00–1.50) and school-aged groups (median 1.00, IQR 0.50–4.00). The neonates had a median of 0 at all time points.

Figure 1 shows the percentage of children with a sensorimotor impairment as rated on the PSOM at each time point according to age. Measurements were classified into either unilateral or bilateral sensorimotor impairments. At the acute time point, 3 (13%) neonates had a sensorimotor impairment detected by the PSOM, compared to 15 (94%) school-aged children. There was only one neonate with a bilateral impairment, which had resolved by 1 month after stroke onset. By 12 months after stroke onset, the number of neonates with clinically detectable unilateral sensorimotor impairment had more than doubled to 8 (31%) and the number of school-aged children with sensorimotor impairment had declined to 8 (57%).

Figure 2 illustrates change in mean PSOM scores over time according to age. The school-aged group had a mean and 95% confidence interval (CI) that fell above the red line (PSOM total score of 0.5, defining neurologic impairment) at every time point. In contrast, the neonatal group mean fell below the red line at all time points. A repeated GEE model was employed to explore the trajectories of log-transformed
PSOM between age groups. Means of predictions and 95% CIs are presented in figure 2. Model results indicate a significant main effect of age group ($p < 0.001$), as well as a significant interaction between age group and quadratic time term ($p = 0.006$). Figure 2 illustrates a consistent, low mean PSOM for the neonate group, whereas the preschool and school-aged groups show a decrease in scores from 0 to 6 months, leveling out between 6 and 12 months. The horizontal red line indicates the clinical cutoff for impairment, suggesting that on average the neonate group remains impaired, the preschool group becomes unimpaired around 6 months postinjury, and the school group is persistently impaired.

**PSOM as a predictor of 12-month motor and adaptive behavior outcomes**

Hierarchical regression analyses were conducted to examine age group, lesion site, and 1-month dichotomized PSOM impairment in the prediction of FM, GM, and adaptive behaviour scores at 12 months. When simultaneously testing PSOM and age, there were significant relationships between the 1-month PSOM scores and 12-month FM ($p = 0.004$), GM ($p = 0.004$), and VABS scores ($p = 0.004$) across all the groups. The relationship between age group and 12-month scores was only significant for the VABS ($p = 0.015$).
Further analysis investigating whether dichotomized PSOM predicts outcome beyond that predicted by age group and lesion size alone identified significant relationships between dichotomized PSOM and FM (p = 0.010), GM (p = 0.002), and adaptive ability (p = 0.007) (table 2).

Figure 3 illustrates the frequencies of children with GM, FM, and VABS impairments (identified by a z score >1 SD from mean) at 12 months in each age group according to dichotomized 1-month PSOM. A significant relationship was identified on all 3 measures (FMZ: p = 0.005, GMZ: p = 0.008, VABS: p < 0.001), suggesting that children with PSOM impairment at 1 month are more likely to have a higher rate of FM, GM, and adaptive behavior impairments.

Finally, ROC curves illustrate the discriminant validity of 1-month PSOM impairment predicting 12-month impairment on FMZ, GMZ, and VABS total. All AUC were statistically significantly different from chance (all p < 0.001). PSOM was in acceptable impairment discrimination for FMZ and VABS total models (AUC [95% CI]: 0.75 [0.62–0.88] and 0.73 [0.61–0.86], respectively), and just under the cutoff for GMZ (AUC [95% CI]: 0.69 [0.57–0.81]).

Discussion

This study employed a prospective longitudinal design to follow children for 12 months after their first pediatric AIS to plot trajectories of recovery across motor domains. Our findings have clinical relevance for counseling families and anticipating children’s support needs. They suggest that neurologic outcome following pediatric AIS varies and differs depending on age at stroke onset, and support the predictive value of 1-month PSOM outcomes for motor and adaptive outcomes at 12 months, particularly for older children (over 5 years old at stroke onset). Specifically, a neurologic impairment identified by the PSOM at 1 month was associated with lower FM and GM function and adaptive abilities at 12 months poststroke.

Despite the predictive value of the PSOM, many children with functional impairments at 12 months were not identified as

| Table 2 | Hierarchical regression predicting impairment in fine motor, gross motor, and Vineland Adaptive Behavior Scales (VABS) at 12 months, reporting model improvement due to Pediatric Stroke Outcome Measure (PSOM) impairment beyond age group and lesion size |

<table>
<thead>
<tr>
<th></th>
<th>FMZ</th>
<th></th>
<th>GMZ</th>
<th></th>
<th>VABS total</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>SE</td>
<td>Pseudo R²</td>
<td>p Value</td>
<td>OR</td>
<td>SE</td>
</tr>
<tr>
<td>N</td>
<td>69</td>
<td>63</td>
<td>61</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Block 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neonatal</td>
<td>Ref</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preschool</td>
<td>4.60</td>
<td>3.85</td>
<td>0.068</td>
<td>0.72</td>
<td>0.46</td>
<td>0.605</td>
</tr>
<tr>
<td>School</td>
<td>5.30</td>
<td>4.46</td>
<td>0.048</td>
<td>0.65</td>
<td>0.44</td>
<td>0.528</td>
</tr>
<tr>
<td>Lesion size (large)</td>
<td>5.93</td>
<td>4.67</td>
<td>0.024</td>
<td>4.80</td>
<td>3.54</td>
<td>0.034</td>
</tr>
<tr>
<td>Model</td>
<td>0.13</td>
<td>0.025</td>
<td>0.07</td>
<td>0.109</td>
<td>0.11</td>
<td>0.041</td>
</tr>
<tr>
<td>Block 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neonatal</td>
<td>Ref</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preschool</td>
<td>4.17</td>
<td>4.12</td>
<td>0.148</td>
<td>0.21</td>
<td>0.20</td>
<td>0.064</td>
</tr>
<tr>
<td>School</td>
<td>2.79</td>
<td>2.66</td>
<td>0.302</td>
<td>0.06</td>
<td>0.07</td>
<td>0.019</td>
</tr>
<tr>
<td>Lesion size (large)</td>
<td>4.84</td>
<td>4.17</td>
<td>0.067</td>
<td>5.49</td>
<td>5.70</td>
<td>0.161</td>
</tr>
<tr>
<td>PSOM impairment</td>
<td>6.60</td>
<td>4.83</td>
<td>0.010</td>
<td>24.40</td>
<td>25.75</td>
<td>0.002</td>
</tr>
<tr>
<td>Model</td>
<td>0.24</td>
<td>0.002</td>
<td>0.25</td>
<td>&lt;0.001</td>
<td>0.28</td>
<td>0.28</td>
</tr>
<tr>
<td>Likelihood ratio test</td>
<td>0.007</td>
<td></td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: FMZ = fine motor 2 scores; GMZ = gross motor 2 scores; OR = odds ratio.
* Likelihood ratio tests indicate model improvement by including PSOM impairment.
impairment using PSOM at 1 month. Figure 3 illustrates that a substantial proportion of the children who were classified as nonimpaired on the PSOM go on to develop FM, GM, or adaptive behavior impairments at 12 months. This is most evident in neonatal and preschool populations in relation to FM impairments. In contrast, there were no school-aged children with a nonimpaired PSOM score at 1 month who developed GM or adaptive behavior impairment at 12 months. This suggests that children over 5 years old, in the nonimpaired range on the PSOM (≤0.5) at 1 month post-stroke, are less likely to develop GM or adaptive behavior impairments at 12 months.

Accurate assessment of neurologic impairments following stroke is challenging in children. Motor outcome measures developed for children may also not be sufficiently sensitive to identify subtle impairments in the stroke population, where many children have unilateral motor impairment.9,10 Our clinical experience is that children can have a variety of motor disorders including ataxia or an evolving dystonia, which may be subtle on early post-diagnosis examination, but may nevertheless have substantial longer-term functional implications. Adult stroke outcome assessments do not consider differences in developmental stages, and often rely on self-reporting or independence in adult age-appropriate activities of daily living.

Although the relationship between 1-month PSOM impairment and FM outcomes at 12 months reached significance, it was not as strong as the relationship between 1-month PSOM and the GM outcomes. For GM outcomes, the sensitivity of the tools may vary. For example, FM test items on standardized tools such as the BSID-III and the BOT-2 primarily require unimanual ability and a child will often choose the less-affected upper limb to complete the task. It is also possible that the 12-month time point is too early to evaluate functional outcomes of neonatal stroke, a population known to have emerging deficits years beyond diagnosis.

Our findings suggest neurologic impairments tend to emerge in the neonatal population between 1 and 6 months after stroke onset as seen in Figure 3. This is consistent with previous studies reporting emergence of motor deficits at around 4–5 months of age, which is typically when a child starts to develop voluntary hand use.11 In contrast, the median PSOM total score in neonates does not vary over the course of the year, suggesting that the PSOM may not be the most appropriate neurologic assessment tool for infants. The measures used in this study evaluate different domains; the PSOM is primarily a measure of neurologic impairment reliant on a combination of clinical testing and child/parent report, while we have used motor capacity measures and parent report adaptive behavior tools to describe daily functional performance.

Age at onset is an important determinant of motor recovery in the first year following AES, with sensorimotor impairments emerging over time in the neonatal group, compared to
improved function in the older groups. Neurologic impair-
ment evaluation alone is however not sufficient to describe
motor function, and it is important to also use functional
measures as described in this study. An example of this is
the discrepancy in PSOM and GM outcomes. At 12 months, only
15.4% of neonates were impaired on the PSOM, whereas on
formal testing using the BSD-111, 50% of the neonates had
impaired GM skills.

Although the PSOM is the only standardized neurologic as-
sessment that has been validated for the pediatric stroke
population, it is a neurologic screening tool that may not
capture more subtle impairments that may have a relationship
with abilities in functional motor tasks and adaptive behavior.
Clinical experience suggests that changes in clinical pre-
sentation are likely to continue beyond this first year with
deficits potentially emerging and improving across all age
groups. Evaluation of the predictive nature of the PSOM at 1
month for motor and adaptive behavior outcomes, several
years after diagnosis and particularly for the neonatal and
infant group, is warranted.

The PSOM, when used at 1 month after AIS diagnosis, was
predictive of FM, GM, and adaptive behavior outcomes at 12
months. The PSOM was particularly predictive for GM and
adaptive behavior outcomes in children aged 5 years and older
diagnosis. In these children, further systematic evaluation of
functional abilities and impairments in the months and years
after AIS diagnosis may enable better understanding of re-
covery trajectories and better use of early interventions to
optimize outcomes.

Author contributions
Anna Cooper: analysis and interpretation of data, drafted
the initial manuscript, approved the final manuscript as
submitted. Vicki Anderson: study design and analysis, supported
identification of subjects for recruitment, critical revision
of manuscript for intellectual content, approved the final
manuscript as submitted. Stephen Hearps: analysis and intepretation
of data, critical revision of manuscript for intellectual content,
approved the final manuscript as submitted. Mardee Coenraad: undertook recruitment, acquisi-
tion of data, critical revision of manuscript for intellectual content,
approved the final manuscript as submitted. Rod Hunt: supported identification of subjects for recruitment and
contributed to study design, critical revision of manuscript for
intellectual content, approved the final manuscript as submitted.
Mark Mackay: supported identification of subjects for
recruitment and contributed to study design, critical revision
of manuscript for intellectual content, approved the final
manuscript as submitted. Paul Monagle: study design and
analysis, supported identification of subjects for recruitment,
contributed to the critical revisions of manuscript for
intellectual content, approved the final manuscript as submitted.

Anne Gordon: study concept and design, undertook rec-
ruitment, acquisition and interpretation of data, critical re-
vision of manuscript for intellectual content, approved the
final manuscript as submitted.

Study funding
This study was supported by the Victorian government op-
erational initiative scheme.

Disclosure
The authors report no disclosures relevant to the manuscript.
Go to Neurology.org/N for full disclosures.

References
1. Aoki GA, MacGregor BB, Curtis R, Maysick S. Neurologic outcome in survivors of
childhood arterial ischaemic stroke over two decades. J Child Neurol. 2009;
14:550–556.
infants with neonatal central infections: a clinical, electromyography, and mag-
6. Diener HC. Developmental plasticity in children: the role of biological risk de-
10. Stolzy G, Fallentine H, Wood J, McAvoy G. Toward the definition of central arte-
11. Lynch BE. Epileptology and identification of pediatric stroke. SIDS Final Report
13. Le WJ, Sheline EY. Development of the Pediatric Stroke Outcome Measures: a pro-
16. Duge T, Davis JS, Urech MJ, Miller T, Davis K. The assessment of Brunnstrom-
17. Spattam A, Binks J. Functional Adaptation of Children. 2nd ed. Maastricht:
Neurological Assessment, 2005.
19. Anderson JS, De Luca CA, Schumacher E, Rubert G, Fritz J, Vermeers Human Infan-
t Coharnation Group. Underestimation of developmental delay for the new Shirley II
Neurological Disorders and Stroke workshop on perinatal and childhood stroke.
The Pediatric Stroke Outcome Measure

A predictor of outcome following arterial ischemic stroke

Anna N. Cooper, BDT; Vicki Anderson, PhD; Stephen Heaps, PGCongDip; Narelle Bertram, MSc, NEL; Roy W. Harley, PhD; Mark T. Mackay, PhD; Paul Monagle, MSc, and Anne L. Gordon, PhD

Cite as: Neurology® 2016;96:e1365-e1372. doi:10.1212/WNL.0000000000004904

Study question

Can neurologic outcomes measured with the Pediatric Stroke Outcome Measure (PSOM), 1 month after a diagnosis of pediatric arterial ischemic stroke (AIS), predict motor and adaptive behavior outcomes 12 months after the diagnosis?

Summary answer

PSOM measurements of neurologic outcomes taken 1 month after an AIS diagnosis can predict motor and adaptive behavior outcomes 12 months after the diagnosis. The PSOM was most predictive for children over 5 years and was least predictive for neonates.

What is known and what this article adds

Little is known about the relationship between short-term neurologic impairment and long-term motor and adaptive behavior outcomes in children with AIS. However, this study shows that the PSOM can predict long-term motor and adaptive behavior outcomes based on short-term neurologic impairment.

Participants and setting

This study examined 64 children who had received a first diagnosis of AIS. This included 27 neonates (age ≤30 days), 19 preschool-aged children, and 18 school-aged children. The children were recruited through the Royal Children’s Hospital in Melbourne between December 2007 and November 2013.

Design, size, and duration

In this prospective observational cohort study, the children’s neurologic impairment levels 1 month after diagnosis were measured with the clinician-administered PSOM or, if no physician with PSOM experience was available, the parent-administered Recovery and Recurrence Questionnaire. At 12 months after diagnosis, the children underwent gross motor (GM) and fine motor (FM) assessments with age-appropriate tools and adaptive behavior assessments with the Vineland Adaptive Behavior Scales (VABS), 2nd edition.

Main results and the role of chance

The 1-month PSOM measurements revealed unilateral or bilateral sensorimotor impairments in 4 (15%) neonates, 11 (58%) preschool-aged children, and 16 (88%) school-aged children. Hierarchical regression analyses showed that 1-month PSOM scores were significantly related to 12-month GM (p = 0.001), FM (p = 0.004), and VABS (p = 0.004) scores in all age groups. Dichotomized PSOM outcomes (i.e., impaired or nonimpaired) at 1 month were significantly associated with GM (p = 0.008), FM (p = 0.005), and adaptive behavior (p < 0.001) impairments at 12 months.

Bias, confounding, and other reasons for caution

The PSOM may overlook subtle neurologic impairments, and motor and adaptive behavior deficits may appear later than the 12-month timepoint.

Generalizability to other populations

Clinical presentations in children with AIS vary with age. The PSOM appeared to have the strongest predictive power in school-aged children.

Study funding/potential competing interests

This study was funded by the Australian state of Victoria. The authors report no competing interests. Go to Neurology.org/ N for full disclosures.

A draft of the short-form article was written by M. Dulsfield, a writer with Edlounge, a division of Cactus Communications. The authors of the full-length article and the journal editors edited and approved the final version.
8. FIVE YEAR OUTCOMES

8.1 Motor function and daily living skills 5 years after paediatric arterial ischaemic stroke: a prospective longitudinal study.

ANNA N COOPER1,2 VICKI ANDERSON1,2,3 MARDEE GREENHAM1,2 STEPHEN HEARPS1,2 ROD W HUNT1,2,3 MARK T MACKAY1,2,3 MICHAEL DITCHFIELD4,5 LEE COLEMAN1,3,4 PAUL MONAGLE1,2,3 ANNE L GORDON6,7

1 Clinical Sciences, Murdoch Children’s Research Institute, Melbourne; 2 University of Melbourne, Melbourne; 3 The Royal Children’s Hospital, Melbourne; 4 Monash Medical Centre, Southern Health, Melbourne; 5 Monash University, Melbourne, Australia. 6 Evelina London Children’s Hospital, Guy’s and St Thomas’ NHS Foundation Trust, London; 7 Kings College London, UK.

Correspondence to Anna Cooper, Murdoch Children’s Research Institute, Flemington Road, Parkville, Victoria 3052, Australia. E-mail Anna.cooper@mcri.edu.au

PUBLICATION DATA
Accepted for publication 4th Month 2018.

ABBREVIATIONS
AIS Arterial ischaemic stroke
BOT-2 Bruininks-Oseretsky Test of Motor Proficiency 2
DASH Detailed Assessment of Speed of Handwriting
PedsQL Pediatric Quality of Life Inventory
PEM-CY Participation and Environment Measure for Children and Youth
PSOM Pediatric Stroke Outcome Measure
VABS-II Vineland Adaptive Behavior Scales, Second Edition

[Abstract]
AIM To describe 5-year motor and functional outcomes after paediatric arterial ischaemic stroke (AIS) and to explore factors associated with poorer long-term outcome.
METHOD Thirty-three children (21 males, 12 females) with AIS were recruited to a single-site, cross-sectional study, from a previously reported prospective longitudinal stroke outcome study. Children were stratified according to age at diagnosis: neonates (≤30d), preschool (>30d–5y), and school age (≥5y). Motor and functional outcomes were measured at 5 years after stroke. Neurological outcomes were evaluated using the Pediatric Stroke Outcome Measure (PSOM) at 1 month and more than 4 years after stroke.

RESULTS At 5 years after stroke, motor function, quality of life, fatigue, adaptive behaviour, activities of daily living, and handwriting speed were significantly poorer than age expectations. The preschool group had the highest percentage of fine and gross motor impairment. Poorer fine motor skills were associated with subcortical-only lesions and large lesion size. Poorer gross motor outcomes correlated with preschool age, bilateral lesions, and PSOM impairment at 1 month.

INTERPRETATION Children are at elevated risk for motor and functional impairments after AIS, with the preschool age group most vulnerable. Identifying early predictors of poorer outcomes facilitates targeted early intervention and long-term rehabilitation.

What this paper adds
- Following paediatric stroke, children are at elevated risk of motor and functional difficulties
- Stroke occurring between 30d-5y may result in poorer motor and functional outcomes.

[Main text]
Motor impairments after paediatric arterial ischaemic stroke (AIS) are frequently noted at diagnosis, and can persist into adulthood; yet, as current literature is limited, long-term motor outcomes remain poorly understood. The few studies exploring long-term motor outcomes after paediatric AIS have either focused primarily on neonates,1,2 or have used broad, non-standardized measures in samples where time since stroke onset has varied widely.3–5 Motor outcome is often described as the presence or absence of a hemiplegia.4,6,7 There remains limited understanding of the impact of neuromotor impairment on functional daily activities.

Motor skills play a fundamental role in a child’s ability to engage and participate in their lives, and motor impairments have broad-reaching implications for daily
functioning. The impacts of motor impairments on activity and participation have been described in children with neuromotor impairments,\textsuperscript{8–10} demonstrating that even mild motor deficits have the potential to limit a child’s ability to engage in social and recreational activities,\textsuperscript{11–13} and to learn through social interaction with peers.

Currently, the relationship between early predicting factors and motor outcomes remains unclear. We have previously reported that large lesion size, neurological impairment at 1 month, and school age (≥5y) at diagnosis are associated with poorer motor function at 12 months after diagnosis of AIS.\textsuperscript{14} Other studies, primarily in neonates, suggest poorer outcomes for cortical, as opposed to subcortical, infarct location,\textsuperscript{15} and for cortical lesions with descending corticospinal tract involvement.\textsuperscript{16–18}

This study aimed to measure and describe long-term motor and functional outcomes after AIS and factors associated with long-term outcome. We hypothesized that, at 5 years after stroke, (1) motor function would be poorer than normative expectations; (2) younger age at diagnosis, cortical only strokes, and poorer acute neuromotor impairment scores would be associated with poorer motor outcomes at 5 years; and (3) poorer motor function would be associated with poorer functional outcomes.

\textbf{METHOD}

\textbf{Participants}

This cohort represented a subgroup of children from a larger prospective longitudinal, observational study established in 2007.\textsuperscript{14,19} For the original study, 68 children aged between term newborn and 18 years with acute AIS were consecutively recruited from The Royal Children’s Hospital, Melbourne, Australia, between December 2007 and November 2013.\textsuperscript{19} Children were included if brain magnetic resonance imaging confirmed an acute parenchymal ischaemic infarction in diffusion-weighted imaging that corresponded to one or more arterial territories. Children with previously diagnosed AIS, coexisting diffuse brain injury caused by a traumatic or hypoxic ischaemic event, and infants born preterm (<36wks’ gestation) were excluded.

Forty-one children recruited to the original study were 4 to 6 years after stroke between January 2014 and August 2015, and thus eligible to participate (mean time since diagnosis 5y 2mo, range 3y 10mo–5y 10mo), referred to as ‘5 years’ throughout the paper. Three families declined to participate with no reason given and four families were unable to
be contacted. One participant was excluded owing to unexplained developmental regression, unrelated to the stroke. Therefore, 33 children were included in this study: 13 neonates (≤30d), 14 preschool age (>30d to <5y), and six school age (≥5y).

**Measures**

Measures were chosen to capture outcomes across the domains of the International Classification of Functioning, Disability and Health. Measures were chosen for their psychometric properties, on the basis of a previous study of the same cohort to allow comparison over time.

**Body Structure and function**

*Neurological function.* The Pediatric Stroke Outcome Measure (PSOM) measures neurological impairments across five domains: right and left sensorimotor, language comprehension, language production, and cognition/behaviour. Where it was not possible to conduct a clinical examination, the Recovery and Recurrence Questionnaire was administered. The Questionnaire is a parent-administered version of the PSOM that correlates strongly with the clinician-administered PSOM. PSOM was completed at the 1-month and 5-year time points with outcomes from the 1-month time point previously reported. At the 1-month time point, 22 children were assessed using the PSOM and 11 children were assessed using the Recovery and Recurrence Questionnaire. In presenting the findings, when we reference the PSOM, we are referring to either the PSOM or Recovery and Recurrence Questionnaire. At the 5-year time point all participants were assessed using the PSOM.

*Fine motor and gross motor function.* The Bruininks-Oseretsky Test of Motor Proficiency 2 (BOT-2) is a comprehensive, age-normed, standardized motor assessment for children aged 4 to 21 years. Motor function was assessed across four domains: fine manual control, manual coordination, body coordination, and speed and agility. Standard scores were generated for each subdomain, and an overall motor composite score was derived (mean=50, SD 10). A fine motor score was generated by combining and then averaging scores from the subdomains of fine manual control and manual coordination. Similarly, a gross motor score was calculated by combining and averaging
the subdomains of strength and agility and body coordination. Standard scores were converted into z-scores for both fine motor and gross motor functions.

**Activity and participation**

*Activity.* The Gross Motor Functional Classification System (GMFCS)\(^\text{25}\) classifies gross motor abilities on a scale of I to V, with I representing higher levels of independence. The Manual Ability Classification System\(^\text{26}\) measures and classifies use of upper limbs and hands to manipulate objects in daily activities on a scale of 1 to 5, with 1 representing better use of upper limbs.

*Participation.* The Participation and Environment Measure for Children and Youth (PEM-CY)\(^\text{27}\) is a parent-rated measure for children aged 5 to 17 years that measures participation activities in the home, school, and community. It measures how often a child participates, how involved they are, and whether there is anything that the parent would like to change in their participation. The average involvement scores for home (mean=3.9, SD 0.54), school (mean=4.21, SD 0.7), and community (mean=4.2, SD 0.56) were used in analysis, with higher scores representing higher levels of involvement.

*Quality of life.* The Pediatric Quality of Life Inventory (PedsQL) is a standardized, parent-rated measurement tool for children aged 2 to 18 years that assesses health-related quality of life across four domains of physical functioning, emotional functioning, social functioning, and school functioning. Total scores were used in analyses (mean=87.61, SD 12.33).\(^\text{28}\)

*Fatigue.* The PedsQL Multidimensional Fatigue Scale is an 18-item parent-rated assessment of child fatigue symptoms across three domains (general, sleep/rest, and cognitive). Higher scores indicate fewer fatigue symptoms. Total fatigue scores were used in analyses. Data were compared with published data of healthy children (n=259) (mean=88.2, SD 11.1).\(^\text{29}\)

*Adaptive behaviour.* Vineland Adaptive Behavior Scales, Second Edition (VABS-II)\(^\text{30}\) is a parent-rated questionnaire which measures a child’s activity and participation across four domains: communication, daily living, motor and social skills, as well as total
adaptive behaviour (mean=100, SD 15). Total adaptive behaviour and daily living scores were used in this analysis.

*Handwriting.* The Detailed Assessment of Speed of Handwriting (DASH)\textsuperscript{25} is a standardized assessment of a child’s speed and legibility of handwriting for children aged 9 years to 16 years 11 months with established validity and reliability. The DASH includes four tasks: copy best, alphabet writing, copy fast and free writing, and an optional task (graphic speed). Raw scores are converted into standard scores in each domain. These scores are combined and averaged to derive a total standard score and centile.

**Procedure**

Data captured in the first 12 months have been reported previously.\textsuperscript{19} Ethics approval for this study was obtained through Human Research Ethics Committee of The Royal Children’s Hospital, Melbourne. Families involved in the earlier study were recontacted by telephone and information documents were sent in the mail. Informed, written consent was obtained for participation in the study. Experienced paediatric clinicians (ANC or MG) administered all outcome measures at the 5-year time point, at either the family's home or hospital. Infarct location, lesion laterality, and vascular territory affected were rated by two neuroradiologists (MD, LC) on the basis of visual inspection of images obtained at the time of diagnosis (as described in Gordon et al.).\textsuperscript{19} Lesion size was dichotomized into small/medium or large according to degree of vascular territory impacted. Lesion location was categorized as cortical, subcortical, both, or infratentorial. Subcortical classification included grey matter/nuclei, subcortical white matter, or both.

**Statistical analysis**

There were four children younger than 5 years and one child over 17 years, so the PEM-CY for these children was excluded from analyses. One child had an incomplete data set (PedsQL, the PedsQL Multidimensional Fatigue Scale, VABS-II, and PEM-CY).

Data were entered into SPSS database (version 21; IBM SPSS Statistics, IBM Inc., Armonk, NY, USA) and stratified into three age groups depending on age at stroke onset: neonates (<30d), preschool (30 days to <5y), and school age (≥5y). Descriptive analyses were
reported for patient demographic and lesion characteristics between groups. Means and standard deviations were reported for continuous variables and frequencies, and proportions were reported for categorical variables. Total PSOM scores were dichotomized into good (total score ≤0.5) or poor (total score >0.5), consistent with previously published outcome studies. Children with ‘good’ PSOM outcomes seemed to have difficulties that were unlikely to interfere with activities of daily living, whereas children with ‘poor’ PSOM scores were more likely to experience more significant impairments, which were likely to affect their activities of daily living. The sensorimotor subscale was also dichotomized into impaired (score 0.5 or above) or not impaired (score 0) and used to determine the laterality of sensorimotor impairment (unilateral/bilateral).

One-sample t-tests were conducted to compare measures of body structure and function (BOT-2), activity and participation (PEM-CY: home, school, and community; DASH: copy best, alphabet writing, copy fast, free writing, and graphic speed), quality of life (PedsQL, PedsQL Multidimensional Fatigue Scale), and adaptive function (VABS-II: total adaptive behaviour and activities of daily living) with population norms or comparative data. Analyses were performed for the sample as a whole, then again within age groups. Values were adjusted for multiple comparisons by using false discovery rate adjustment. This adjustment was selected as it is less conservative than traditional family-wise error rate controlling methods, not unduly penalizing the smaller sample size and exploration of like outcomes.

Five-year gross motor and fine motor standard scores were dichotomized into ‘impaired’ (score >1 SD from mean) or ‘not impaired’ (≤1 SD from mean). Spearman correlations (r) were conducted to explore a relationship between fine motor and gross motor z-scores with adaptive behaviour total scores (VABS-II), activities of daily living subdomain score (VABS-II), quality of life total scores (PedsQL), fatigue total scores (PedsQL Multidimensional Fatigue Scale), and participation at home, school, and in the community (PEM-CY). A strong correlation was indicated by a correlation coefficient above 0.7, moderate in the range 0.5 to 0.7, and a low correlation if less than 0.5.

Finally, multiple regression models with bootstrapped confidence intervals (CI; 1000 replications) explored the prediction of fine motor and gross motor z-scores at 5 years from dichotomized demographic, 1-month PSOM impairment, and lesion characteristics. To explore effect of age at diagnosis across age groups, age dummy variables were generated. Likelihood ratio tests determined model improvement with
each predictor. Non-significant improvement resulted in predictor exclusion, and the most parsimonious models were presented. Unstandardized $\beta$ coefficients and significances were reported, and model assumptions verified.

RESULTS
Sample demographics and lesion characteristics are presented in Table I. Findings are presented for the cohort overall and according to age group at diagnosis. The school-aged group was proportionally smaller than the younger groups (18.2%) and there was a higher percentage of bilateral (71.4) and subcortical-only (66.7) strokes in the preschool age group.

Neurological examination identified four (12%) children with unilateral motor impairments and four (12%) children with bilateral motor impairments. Two children had visual impairments only, and two had auditory impairments only. Standardized motor assessments identified 15% (95% CI 0–35%) of neonates and 29% (95% CI 5–52%) of preschool children had gross motor impairments detected. Fifteen per cent (95% CI 0–35%) of neonates and 21% (95% CI 0–43%) of preschool children had fine motor impairments detected. No gross motor or fine motor impairments were detected in the school-aged group.

Outcomes compared with normative data: total sample
Mean scores for BOT-2 total scores and fine motor function were significantly poorer than population norms; however, mean gross motor function was within normal range. VABS-II total adaptive behaviour scores ($p<0.001$), daily living scores ($p<0.001$), PedsQL total ($p=0.001$), PedsQL fatigue ($p<0.001$), DASH ‘alphabet writing’ ($p=0.043$), and DASH ‘copy fast’ ($p=0.043$) were significantly lower than age-matched population norms. Participation scores for the PEM-CY fell within the expected range for home ($p=0.79$), school ($p=0.73$), and community ($p=0.86$) domains (Table II).

Outcomes compared with normative data: within age group
The preschool group differed from age norms for BOT-2 total motor ($p=0.048$) and fine motor scores ($p=0.044$), and for the PedsQL total ($p=0.001$), PedsQL fatigue ($p<0.001$), VABS-II daily living domain ($p=0.001$), and VABS-II total adaptive behaviour ($p=0.001$). The neonatal and school-aged groups fell within age expectations for all outcome measures across all domains (Table III).
Factors associated with 5-year outcomes

Bootstrapped multiple regression models predicted motor function z-scores. The most parsimonious models are presented; likelihood ratio tests with incremental predictor inclusion established model parsimony. Poorer fine motor outcomes were associated with 1-month PSOM impairment only (unstandardized regression coefficient \( \beta = -1.03 \), \( p = 0.001 \)). Better gross motor outcomes were associated with AIS in the school period (\( \beta = 1.25 \), \( p = 0.007 \)), and poorer gross motor outcomes with bilateral lesions (\( \beta = -0.85 \), \( p = 0.011 \)) and PSOM impairment at 1 month (\( \beta = -1.41 \), \( p < 0.001 \)). Lesion size also contributed to the most parsimonious model, but was not statistically significant (\( \beta = -0.53 \), \( p = 0.092 \)).

Relationship between motor outcomes and functional outcomes: total sample

Weak correlations (range: \( r = 0.37 \)–\( 0.48 \)) were found for fine motor scores and VABS-II total adaptive behaviour, the daily living domain, and on the PEM-CY, participation at school, as well as for gross motor scores and VABS-II daily living domain, fatigue, and PEM-CY participation in the community. Moderate correlations (range: \( r = 0.52 \)–\( 0.58 \)) were identified between gross motor scores and VABS-II total adaptive behaviour and PedsQL total score.

DISCUSSION

This study describes age-related motor outcomes at 5 years after paediatric stroke and explores the relationship between motor outcomes and functional abilities across different age groups. When exploring outcomes for the overall stroke cohort, fine motor function, adaptive behaviour, daily living skills, and overall quality of life were lower than population norms. Gross motor skills were within age expectations, as was participation in the home, school, and community. Bilateral lesions and PSOM impairment at 1 month were associated with poorer gross motor outcomes. PSOM impairment at 1 month was associated with poorer fine motor outcomes. Children in the school-aged group had better gross motor outcomes. Overall poorer motor abilities were associated with poorer daily living skills, poorer overall adaptive behaviour, reduced quality of life, increased fatigue, and reduced participation.
Examination of outcomes for specific age-at-onset groups demonstrated poorer outcomes for stroke diagnosed in the preschool period. Stroke diagnosis in the preschool period was linked to poorer fine motor abilities, poorer adaptive behaviour, particularly for daily living skills, higher levels of fatigue, and overall lower quality of life. This finding differs from those of our 12-month follow-up where the preschool group had the most favourable motor outcomes. These results are consistent with critical period models, which argue that recovery trajectories are not linear and may vary, depending on the age of the child as well as age at stroke onset. While the presence of higher rates of bilateral (71.4%) and subcortical-only (66.7%) strokes in the preschool group may contribute to poorer results, this is insufficient to explain these differences. These results suggest that 1-month neurological impairment (dichotomized variable), bilateral lesions, and age at stroke onset may be useful characteristics to identify children at higher risk of long-term motor impairments. Understanding early predictors for outcomes enables clinicians to provide children and their families with expectations about likely long-term outcomes, as well as intervention targets to help maximize motor and functional outcomes.

Gross motor impairments were associated with higher levels of fatigue, poorer adaptive behaviour, lower levels of community participation, and lower quality of life. Fine motor impairments were associated with poorer adaptive behaviour and lower levels of school participation. Interestingly, neither gross motor nor fine motor impairments were related to participation at home, suggesting that children may have more physical, environmental, or psychological support in the home environment, which results in fewer barriers to participation. These results highlight the broad-reaching implications of child stroke on daily life, and support the need for thorough, multidisciplinary assessment and treatment that looks beyond physical impairments to capture daily functional abilities.

In this study, we were able to measure motor outcomes across several different age-at-onset stroke groups using the same assessment tools, allowing reliable comparison across age groups. Interestingly, at the 5-year time point, only 12% of children had a unilateral motor impairment, which differs from previous research where estimates of chronic hemiplegia vary from 25% to 56%.3,34–37 Advances in medical imaging techniques being able to detect more mild strokes may account for this difference. Although gross motor outcomes were not significantly different from
age norms, it is possible that the motor assessments available for the stroke population may not be sufficiently sensitive to identify unilateral impairments or more subtle motor impairments such as dystonia and ataxia. The small sample size limited exploration of differences between age groups. In particular, the older age group was proportionally smaller, as these children were more difficult to re-recruit, limiting the breadth of analysis possible.

The study has several limitations. The small number of school-age children assessed limited the more detailed analysis that we could perform and tempered the positive conclusions drawn from this study. The lack of age-matched comparison individuals meant that we relied on normative and published comparison data.

Analysing data at a group level can mask impairments experienced by individual children, so we calculated rates of motor impairment in each age group. There were no gross motor or fine motor impairments identified in the school-aged group. There were, however, two school-aged children who had a unilateral sensorimotor impairment identified by the PSOM. The standardized motor assessments administered in our study may not have been sufficiently sensitive to identify unilateral motor difficulties. When assessing motor function of children after a stroke, a range of assessments may need to be used, specifically targeting the individual's motor presentation.

This study has important implications for future research. Given the trajectory of recovery is likely to change as social and developmental demands increase, a longer-term observational study is warranted. In addition, a larger sample size would allow greater depth of analysis and might allow identification of more subtle motor and functional changes.

In conclusion, our results suggest that paediatric AIS has a persistent impact on many areas of a child's life, including motor function, adaptive behaviour, participation, and quality of life. Outcomes may differ depending on the age at diagnosis, with preschool children being more vulnerable to poorer motor outcomes. Long-term clinical surveillance of motor and functional outcomes after paediatric AIS is critical using standardized, functional assessments, to understand the breadth of impact of brain injury and allow targeted early intervention and long-term rehabilitation strategies.
ACKNOWLEDGEMENTS

The authors have stated that they had no interests that might be perceived as posing a conflict or bias.

REFERENCES


### Table I: Sample demographics and clinical characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Neonates</th>
<th>Preschool</th>
<th>School age</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>33</td>
<td>13 (39.4)</td>
<td>14 (42.4)</td>
<td>6 (18.2)</td>
</tr>
<tr>
<td>Sex (male), n (%)</td>
<td>21 (63.6)</td>
<td>11 (84.6)</td>
<td>6 (28.6)</td>
<td>4 (57.1)</td>
</tr>
<tr>
<td>Mean age (range) at stroke onset, y:mo</td>
<td>2:9 (0:0–13:8)</td>
<td>0:0 (0:0–0:1)</td>
<td>2:5 (0:2–4:5)</td>
<td>8:6 (5:8–13:8)</td>
</tr>
<tr>
<td>Mean age (range) at assessment, y:mo</td>
<td>8:0 (4:0–20:6)</td>
<td>5:1 (4:0–6:6)</td>
<td>7:7 (5:10–9:6)</td>
<td>14:2 (11:5–20:5)</td>
</tr>
<tr>
<td>Lesion characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lesion size</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large (%)</td>
<td>8 (24.2)</td>
<td>4 (50.0)</td>
<td>3 (37.5)</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td>Small/medium (%)</td>
<td>25 (76.0)</td>
<td>9 (36.0)</td>
<td>11 (44.0)</td>
<td>5 (20.0)</td>
</tr>
<tr>
<td>Vascular territory, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle cerebral artery full</td>
<td>1 (3.0)</td>
<td>1 (100)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Middle cerebral artery partial</td>
<td>16 (48.5)</td>
<td>7 (43.8)</td>
<td>7 (43.8)</td>
<td>2 (12.5)</td>
</tr>
<tr>
<td>Posterior cerebral artery</td>
<td>5 (15.2)</td>
<td>3 (60.0)</td>
<td>0</td>
<td>2 (40.0)</td>
</tr>
<tr>
<td>Vertebro-basilar arteries</td>
<td>5 (15.2)</td>
<td>0</td>
<td>3 (60.0)</td>
<td>2 (40.0)</td>
</tr>
<tr>
<td>Multiple</td>
<td>6 (18.2)</td>
<td>2 (33.3)</td>
<td>4 (66.7)</td>
<td>0</td>
</tr>
<tr>
<td>Laterality</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>11 (33.3)</td>
<td>9 (81.8)</td>
<td>2 (18.2)</td>
<td>0</td>
</tr>
<tr>
<td>Right</td>
<td>10 (30.3)</td>
<td>3 (30.0)</td>
<td>4 (40.0)</td>
<td>3 (30.0)</td>
</tr>
<tr>
<td>Bilateral</td>
<td>7 (21.2)</td>
<td>1 (14.3)</td>
<td>5 (71.4)</td>
<td>1 (14.3)</td>
</tr>
<tr>
<td>Infratentorial only</td>
<td>5 (15.2)</td>
<td>0</td>
<td>3 (60.0)</td>
<td>2 (40.0)</td>
</tr>
<tr>
<td>Location</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortical only</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Subcortical only</td>
<td>9 (27.3)</td>
<td>1 (11.1)</td>
<td>6 (66.7)</td>
<td>2 (22.2)</td>
</tr>
<tr>
<td>Both cortical and subcortical</td>
<td>19 (57.6)</td>
<td>12 (63.2)</td>
<td>5 (26.3)</td>
<td>2 (10.5)</td>
</tr>
<tr>
<td>GMFCS levels I and II</td>
<td>31</td>
<td>13</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>GMFCS level III&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>MACS levels 1 and 2</td>
<td>29</td>
<td>11</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>MACS level 3&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

<sup>a</sup>No child scored in levels IV or V. GMFCS, Gross Motor Function Classification System; MACS, Manual Ability Classification System.
**Table II:** Motor and functional abilities: comparison with published normative data

(whole sample)

<table>
<thead>
<tr>
<th></th>
<th>Comparison value</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
<th>t</th>
<th>p[a]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Motor function</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BOT-2 total score</td>
<td>50</td>
<td>10</td>
<td>33</td>
<td>43.85</td>
<td>11.66</td>
<td>-3.03</td>
</tr>
<tr>
<td>BOT-2 fine motor</td>
<td>50</td>
<td>10</td>
<td>33</td>
<td>41.89</td>
<td>10.68</td>
<td>-4.36</td>
</tr>
<tr>
<td>BOT-2 gross motor</td>
<td>50</td>
<td>10</td>
<td>33</td>
<td>47.66</td>
<td>10.81</td>
<td>-1.27</td>
</tr>
<tr>
<td><strong>Fatigue</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEM-CY home</td>
<td>3.9</td>
<td>0.54</td>
<td>26</td>
<td>3.87</td>
<td>0.59</td>
<td>-0.26</td>
</tr>
<tr>
<td>PEM-CY school</td>
<td>4.21</td>
<td>0.7</td>
<td>26</td>
<td>4.26</td>
<td>0.75</td>
<td>0.35</td>
</tr>
<tr>
<td>PEM-CY community</td>
<td>4.2</td>
<td>0.56</td>
<td>26</td>
<td>4.23</td>
<td>0.77</td>
<td>0.18</td>
</tr>
<tr>
<td><strong>Handwriting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DASH copy best</td>
<td>10</td>
<td>3</td>
<td>8</td>
<td>7.50</td>
<td>4.27</td>
<td>-1.65</td>
</tr>
<tr>
<td>DASH alphabet writing</td>
<td>10</td>
<td>3</td>
<td>8</td>
<td>6.75</td>
<td>3.06</td>
<td>-3.01</td>
</tr>
<tr>
<td>DASH copy fast</td>
<td>10</td>
<td>3</td>
<td>7</td>
<td>5.86</td>
<td>3.63</td>
<td>-3.02</td>
</tr>
<tr>
<td>DASH free writing</td>
<td>10</td>
<td>3</td>
<td>5</td>
<td>5.20</td>
<td>3.49</td>
<td>-3.07</td>
</tr>
<tr>
<td>DASH graphic speed</td>
<td>10</td>
<td>3</td>
<td>7</td>
<td>9.14</td>
<td>3.24</td>
<td>-0.70</td>
</tr>
<tr>
<td><strong>Quality of life</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PedsQL total</td>
<td>87.61</td>
<td>12.33</td>
<td>32</td>
<td>73.97</td>
<td>18.04</td>
<td>-4.28</td>
</tr>
<tr>
<td>PedsQL fatigue</td>
<td>88.2</td>
<td>11.1</td>
<td>32</td>
<td>73.83</td>
<td>22.78</td>
<td>-4.99</td>
</tr>
<tr>
<td><strong>Adaptive function</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VABS activities of daily living</td>
<td>100</td>
<td>15</td>
<td>32</td>
<td>91.25</td>
<td>9.87</td>
<td>-5.01</td>
</tr>
<tr>
<td>VABS total – adaptive behaviour</td>
<td>100</td>
<td>15</td>
<td>32</td>
<td>89.59</td>
<td>11.53</td>
<td>-5.11</td>
</tr>
</tbody>
</table>

Bold type indicates statistically significant p values. *a*False discovery rate adjusted p value. BOT-2, Bruininks-Oseretsky Test of Motor Proficiency 2; PEM-CY, Participation and Environment Measure for Children and Youth; DASH, Detailed Assessment of Speed of Handwriting; PedsQL, Pediatric Quality of Life Inventory; VABS-11, Vineland Adaptive Behavior Scales.
Table III: Motor and functional abilities according to age at stroke onset

<table>
<thead>
<tr>
<th>Comparison value</th>
<th>Neonates (birth–30d)</th>
<th>Preschool (30d–5y)</th>
<th>School age (≥5y)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td><strong>Motor function</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BOT-2 total score</td>
<td>50</td>
<td>45.54</td>
<td>11.98</td>
</tr>
<tr>
<td>BOT-2 fine motor</td>
<td>50</td>
<td>41.88</td>
<td>9.82</td>
</tr>
<tr>
<td>BOT-2 gross motor</td>
<td>50</td>
<td>50.81</td>
<td>10.68</td>
</tr>
<tr>
<td><strong>Fatigue</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEM-CY home</td>
<td>3.90</td>
<td>0.54</td>
<td>8</td>
</tr>
<tr>
<td>PEM-CY school</td>
<td>4.21</td>
<td>0.70</td>
<td>8</td>
</tr>
<tr>
<td>PEM-CY community</td>
<td>4.20</td>
<td>0.56</td>
<td>8</td>
</tr>
<tr>
<td><strong>Quality of life</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PedsQL total</td>
<td>87.60</td>
<td>12.33</td>
<td>3</td>
</tr>
<tr>
<td>PedsQL fatigue</td>
<td>88.20</td>
<td>11.10</td>
<td>3</td>
</tr>
<tr>
<td><strong>Adaptive function</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VABS activities of daily living</td>
<td>100</td>
<td>93.31</td>
<td>9.86</td>
</tr>
<tr>
<td>VABS total, adaptive behaviour</td>
<td>100</td>
<td>91.23</td>
<td>9.85</td>
</tr>
</tbody>
</table>

Bold type indicates statistically significant p values. aWithin age-group false discovery rate adjusted p value. BOT-2, Bruininks-Oseretsky Test of Motor Proficiency 2; PEM-CY, Participation and Environment Measure for Children and Youth; PedsQL, Pediatric Quality of Life Inventory; VABS-11, Vineland Adaptive Behavior Scales.
9. SUPPLEMENTARY RESULTS

This section summarises the unilateral and bilateral motor impairments from the stroke group at 12 months and 5 years. These numbers were too small to analyse formally.

**Unilateral motor impairments: ‘hemiplegia’**

For this study, hemiplegia was defined as a score of ≥0.5 on the PSOM on either left or right sensorimotor subdomain. Children with only auditory, visual or sensory deficits were excluded. When a child’s PSOM score returned to 0, it was considered ‘resolved’. At the 12-month time point, children were assessed using either the RRQ or the PSOM. At the 5-year time point, all children were assessed using the PSOM.

Table 9.1. Summary of children with unilateral motor impairments

<table>
<thead>
<tr>
<th>SRID</th>
<th>Age group</th>
<th>12m PSOM/RRQ scores</th>
<th>4y PSOM scores</th>
<th>4y Hand pref</th>
<th>4y FM imp</th>
<th>4y GM imp</th>
<th>AHA SCORES 12m</th>
<th>AHA SCORES 4y</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>R</td>
<td>L</td>
<td>R</td>
<td>L</td>
<td></td>
<td></td>
<td>Sum</td>
</tr>
<tr>
<td>15</td>
<td>Pre-school</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>Right</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>27</td>
<td>School</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>Right</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>28</td>
<td>Neonate</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>Left</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>31</td>
<td>Neonate</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>Right</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>7</td>
<td>Neonate</td>
<td>0</td>
<td>0.5</td>
<td>0</td>
<td>0</td>
<td>Right</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>10</td>
<td>Pre-school</td>
<td>0.5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Right</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>19</td>
<td>Pre-school</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Left</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

*Pref=preference, m=months, y=years, imp=impairment*
Between 12 months and 4 years post stroke onset, as classified by the PSOM scores, 3 unilateral motor impairments resolved (scored 0 on the PSOM), 2 deteriorated (the PSOM score increased) and 2 remained unchanged. When these scores are compared to the AHA scores, it is evident that even when the PSOM scores don’t change, there is improvement in the AHA scores. This suggests that while their neuromotor deficits may remain unchanged, bimanual function may still improve.

**Bilateral motor impairment:**

Table 9.2 Summary of children with bilateral motor impairments

<table>
<thead>
<tr>
<th>SRID</th>
<th>Age group</th>
<th>12m PSOM/RRQ scores</th>
<th>4y PSOM scores</th>
<th>Hand preference at 4y</th>
<th>FM imp 4y</th>
<th>GM imp 4y</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>R</td>
<td>L</td>
<td>R</td>
<td>L</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Pre-school</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>Right</td>
</tr>
<tr>
<td>16</td>
<td>Pre-school</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>Right</td>
</tr>
<tr>
<td>14</td>
<td>Pre-school</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>Right</td>
</tr>
<tr>
<td>23</td>
<td>Pre-school</td>
<td>1</td>
<td>1</td>
<td>0.5</td>
<td>1</td>
<td>Right</td>
</tr>
<tr>
<td>9</td>
<td>School</td>
<td>1</td>
<td>0.5</td>
<td>0</td>
<td>0</td>
<td>Right</td>
</tr>
</tbody>
</table>

*Pref=preference, m=months, y=years, imp=impairment*

There were no neonates with bilateral motor impairments at either 12 months or 4 years. All children with bilateral involvements were pre-school at age of onset except one, which was school aged. The one school aged child completely resolved by 4 years, all other children still had bilateral motor involvement at 4 years post stroke onset. In the 5th and 6th columns, is whether or not a FM or GM impairment was identified by the BOT-2 at 4 years post stroke. This table shows us that a child can have a sensorimotor deficit on the PSOM and still have no FM impairments identified by the BOT-2. Four out of the 5 children with bilateral motor impairments improved the most on their dominant upper limb.
Table 9.3 Changes in sensorimotor outcomes on the PSOM between 12 months and 4 years

<table>
<thead>
<tr>
<th></th>
<th>12 months</th>
<th>4 years</th>
<th>Changes in PSOM scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>No impairments</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unilateral motor impairment on</td>
<td>7 (21%)</td>
<td>4 (12%)</td>
<td>• 2 children remained unchanged</td>
</tr>
<tr>
<td>PSOM</td>
<td></td>
<td></td>
<td>• 2 children deteriorated</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• 3 children completely resolved</td>
</tr>
<tr>
<td>Bilateral motor impairment on</td>
<td>5 (15%)</td>
<td>4 (12%)</td>
<td>• 1 child completely resolved</td>
</tr>
<tr>
<td>PSOM</td>
<td></td>
<td></td>
<td>• 1 child remained unchanged</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• 3 children improved on their dominant side only</td>
</tr>
<tr>
<td>Visual deficits</td>
<td>3 (9%)</td>
<td>2 (6%)</td>
<td>• 1 resolved</td>
</tr>
<tr>
<td>Auditory deficits</td>
<td>1 (3%)</td>
<td>2 (6%)</td>
<td>• 1 emerged</td>
</tr>
<tr>
<td>Sensory deficit (face)</td>
<td>0</td>
<td>1 (3%)</td>
<td>• 1 emerged</td>
</tr>
</tbody>
</table>
10. DISCUSSION

In recent years, research has emerged detailing the impact of stroke in children on cognitive, social, behavioural and motor domains, with impairments in children lasting a lifetime. Estimates of the prevalence of impairments vary, with motor impairments appearing to be the most widely recognised. The existing literature is limited by small sample sizes, cross sectional designs and the use of non-standardised outcomes measures. In addition to this, there is a lack of longer-term follow up studies and time since stroke varies significantly.

Using the ICF-CY as a theoretical framework, this thesis aimed to investigate motor and functional outcomes, from acute presentation to 4-6 years post-stroke, with outcomes at 4 time points across the first year following paediatric AIS. Factors associated with outcomes were explored and a detailed analysis was conducted of the widely used PSOM and its utility in predicting outcomes when used at 1m-post stroke onset. The second phase of this study is an extension of the original longitudinal cohort study exploring the motor and functional outcomes of a subgroup of the original cohort, at 5 years post AIS and the factors associated with outcome. In addition to this, the relationship between motor outcomes and activity and participation was explored. This is the first prospective longitudinal study that details motor and functional outcomes following paediatric AIS. This chapter will summarise the 5 key themes that have arisen from this research: 1) The frequency and extent of impairments 2) Predictors of outcome 3) Impact of motor outcomes on activity and participation 4) Methods of assessment 5) Allied health intervention. The clinical implications, limitations to this research, as well as directions for future research will then be discussed.

10.1 Frequency and extent of deficits

The first phase of the study explored outcomes at four time points across the first 12 months post stroke onset. Neonates were found to have emerging impairments in the first year, with very little detected in the first month. By 12m, 15% had FM impairments and 50% had GM impairments. This finding is consistent with previous research, where motor impairments have been reported to emerge in the neonatal population at around 4-5 months of age, when infants typically develop voluntary hand use (22). The pre-school aged group remained
relatively stable over the first year with 33% FM impairments and 39% GM impairments at 12 months. The school aged group remained relatively stable with regards the their FM impairments with the highest percentage of impairments at 12 months (40%). Their GM impairments improved over the course of the first year with 40% of school-aged children having GM impairment identified at 12 months.

At 4 years post stroke onset (range 4-6 years post stroke) the sample was compared to normative expectations. As a whole, the stroke had poorer overall motor skills, poorer FM and handwriting skills, poorer QOL, higher levels of fatigue difficulties with activities of daily and poorer adaptive behaviour. However, when exploring outcomes within age groups, the mean performances of the neonates and the school-aged groups were within age expectations across all assessments. In contrast, the preschool age group mean was significantly different in overall motor, fine motor, they had poorer QOL, higher levels of fatigue, difficulties with activities of daily living as well as poorer adaptive behaviour. All groups performed, on average, within age expectations for gross motor function and participation. This suggests that, despite physical and functional difficulties, there is minimal impact upon their overall participation at home, school or in the community.

Rates of impairments were also explored. Fifteen per cent of neonates displayed FM and GM impairments and the preschool age group had the highest percentage of FM (21%) and GM (29%) impairments. There were no GM or FM impairments identified in the school age group. These results differ from the 12-month time point where the pre-schooler had more favourable outcomes.

Sensorimotor impairments were explored at each time point. As expected, sensorimotor impairments tended to emerge in the neonates and improve in both the pre-school and school-aged groups across the first year post stroke. At 12 months, 8 (24%) children had unilateral sensorimotor impairments and 5 (15%) bilateral sensorimotor impairments. By 4-6 years post stroke, many of the sensorimotor impairments had improved or resolved. There were 4 (12%) children with unilateral sensorimotor impairments 4 (12%) with bilateral sensorimotor impairments.

All unilateral and bilateral motor impairments were identified at 12 months. This is important clinical information confirming that a bilateral or unilateral sensorimotor
impairment is unlikely to develop beyond the first year post stroke. Interestingly, for the children with bilateral motor impairments at 12 months, scores only improved on their pre-morbid dominant upper limb (UL). There are a number of factors that may contribute to this including, premorbid skill level, cognitive capacity, motivation to use each UL and ability to compensate using unimanual techniques. Although there were only four children with bilateral sensorimotor impairments, this has implications on rehabilitation as well as identifying areas for future research.

Similar to motor outcomes, sensorimotor outcomes improved beyond the first year. This is different from the understanding of recovery of adults post stroke, where most of the recovery takes place in the first 3-6 months with less recovery thereafter. A child’s recovery is much more protracted, beyond that first year and appears to differ depending on the age at stroke onset.

10.2 Potential contributors to outcome

Understanding early predictors of motor and functional outcomes can help us to better understand the impact of stroke, to target early interventions and rehabilitation and to help clinicians and families to understand what to expect following an ischaemic event. Several potential contributors of outcomes were explored at both the 12 months and 5 years post stroke: lesion characteristics, age at stroke onset and neurological impairment.

Lesion characteristics

Previous research has suggested that lesion characteristics play an important role in motor outcomes following paediatric stroke (4, 26, 56, 61, 87, 88), with poorer outcomes documented in children with more than 10% intracranial volume infarction (92). Other studies, primarily in neonates have noted poorer outcomes for cortical as opposed to subcortical infarct location (93), and for cortical lesions with corticospinal tract (CST) involvement (89, 90, 129). The literature to date, however, is varied and inconsistent.
At 12 months post stroke, this study showed that large lesion size was associated with poorer GM, but not FM, outcomes. There were no significant relationships between motor outcomes and lesion laterality or location (using dichotomised variables). In contrast to the 12-month data, by 5 years post stroke, bilateral lesions were associated with poorer GM outcomes, however, lesion location or size were not associated with FM outcomes.

Conclusions that can be drawn from these results are limited. Large lesion size was predictive of motor outcome at 12-months but not at the 5-year time point. Although the literature varies, it is possible that the larger the lesion is, the more likely it is going to affects the motor cortex and result in a motor impairment. Larger sample sizes would allow a more detailed analysis of the relationship between lesion location and motor outcomes.

**Age at stroke onset**

Until recently, it was believed that children might recover better than adults following stroke. This is not necessarily the case, however, the relationship between the age at stoke onset and outcome remains unclear. At 12 months post stroke, stroke sustained at school age was predictive of poorer FM function. Age was not associated with GM outcomes. The pre-school age group appeared to have the most favourable outcomes with gradual improvement over the first 12 months and the lowest percentage of GM outcomes at each time point. The neonatal group had the lowest percentage of FM outcomes, however it is possible that, at 12 months, the neonatal group may not have yet reached an age where these difficulties have become developmentally relevant. These preliminary results suggest that the pre-school aged children, with best outcomes, might be the age group where there is an optimal balance between greater brain plasticity and less vulnerability (130).

In contrast, by 5 years post stroke, the school-age at stroke onset was associated with more favourable GM outcomes but there was no age associated found with FM outcome. The pre-school age group also had the highest percentage of GM and FM impairments. These findings suggest that the trajectory of recovery is not linear and that it differs depending on the age of the child at stroke onset. Further, that recovery continues beyond the first year and therefore 12 months outcomes may not be a good indication of long-term motor and functional outcomes.
The age for optimal motor recovery from brain injury remains unclear. Motor plasticity is likely to be greatest in early childhood when the young brain is rapidly reorganising and myelinating. In contrast, older children may have less plasticity but functional outcome may be improved by the possession of a wider set of learnt skills and behaviours at the time of injury, creating greater potential for true rehabilitation.

**Neurological impairment**

Neurological impairment, assessed with the PSOM has previously been associated with cognitive ability, problem behaviours, adaptive behaviour, social participation, and QoL (131, 132). However, in these studies, the PSOM was administered at the same time point as the other outcome measures. The predictive value of the PSOM at one month post AIS, has not previously been reported.

Findings suggested that PSOM impairment score at 1m was predictive of 12 month FM, GM and adaptive behaviour, above and beyond lesion size and age at diagnosis. When exploring predictability between age groups, it appeared that PSOM at 1 month is most accurate for the school aged group and more so for GM and adaptive behaviour than FM. This suggests that the PSOM may not be sufficiently sensitive to accurately assess neurological impairments in younger children, particularly the neonatal age group as well as for FM function.

Five-year findings suggest that PSOM impairments at 1m is predictive of GM impairment and FM impairment.

**10.3 Activity and participation**

The impact of motor impairments on activity and participation, have been described in similar neurological conditions (103-105). Even mild motor impairment has the potential to limit a child’s ability to engage in social and recreational activities (133-135), limiting their capacity to learn through social interaction with peers.
Results from phase one of the thesis reported that FM and GM impairments at 12 months were associated with poorer adaptive behaviour, as well as difficulties with activities of daily living. At 5 years post stroke onset, FM impairments were associated with poorer adaptive behaviour, difficulties with activities of daily living and lower levels of participation at school. GM impairments were associated with poorer adaptive behaviour, difficulties with activities of daily living, poorer QoL, higher levels of fatigue and lower levels of participation within the community.

Despite many parents reporting that fatigue is one of the biggest challenges experienced after stroke, it has not yet been systematically examined in the literature. The mean scores for the stroke group differed significantly to normative expectations suggesting that fatigue is a persisting problem after stroke. This is an important consideration for both families and clinicians and suggests that long-term assessment and intervention following paediatric stroke needs to be cognizant of fatigue.

These results illustrate that motor skills play a fundamental role in a child’s ability to engage and participate in their lives, and motor impairments have broad reaching implications on daily functioning.

10.4 Methods of assessments

The motor assessments used in this thesis were chosen on the basis of their psychometric properties. They were the most appropriate assessments available at the time, however, given the varying nature of the motor outcomes of this group, it is difficult to measure such a diverse group of children with the same assessment, to allow comparisons between groups. The BOT-2 was chosen to assess FM and GM outcome across the cohort and the PSOM was chosen to measure neuromotor outcome. As previously mentioned, the PSOM is the only motor assessment that has been validated to the paediatric stroke population.

Clinical experience suggests that, following stroke, there is a vast array of subtle motor difficulties that may not be easily identified by standard motor assessments including dystonia, ataxia and subtle difficulties in asymmetries and hand function. For example, there
were 2 children that had a unilateral sensorimotor impairment identified by the PSOM at 5-years post stroke. Assessment scores on the BOT-2 for these children fell within age expectations despite having a clear unilateral sensorimotor impairment. This suggests that many of the tasks on the BOT-2 can be very efficiently completed with one functional side of the body completing the more refined skills and the other side of the body being the ‘assisting hand’. The older children, particularly those with high cognitive function were able to use effective compensatory strategies to complete the bimanual tasks well with one ‘less functioning’ upper limb (e.g., throwing, cutting, drawing).

It is possible that the assessments used may not be sufficiently sensitive to the motor difficulties of this population to adequately identify more subtle motor impairments in a population that unilateral motor impairments are frequently reported. The BSID, used in phase one of the study for the children under 4 years old, has been reported to underestimate developmental delays (136). In addition, as the activities of the BOT-2 are able to be completed with one more functional hand and one supporting hand, impairments in the less functional upper limb are not always captured. This has implications for clinicians when assessing functional outcomes following stroke and suggests that a range of assessment tools may be required depending on the nature of the motor presentation.

Results from this thesis also suggest that the PSOM may not be sufficiently sensitive to detect all neuromotor impairments in children under 5, particularly the neonatal population. The approach to assessing motor function in the newborn period is starting to change from traditional methods of testing reflexes and responses to a method that focuses instead on the quality of general movements. Given the very limited repertoire of movement patterns and abilities in the first few months of life, this approach may be a more accurate assessment in identifying impairments and predicting outcomes in neonatal populations. Neurological assessments such as the Prechtl's assessment of general movements (GMs) and the Hammersmith Infant Neurological Examination (HINE) have been reported to be able to reliably identify early signs of CP but are most effective when completed from 3 months (74, 137). The PSOM may therefore not be accurate to assess neurological function of neonates at the one-month time point, instead a 3 month time point may be able to more accurately reflect longer term motor difficulties. The development of a more comprehensive motor assessment tool for children with AIS >30 days old that includes assessment of dystonia, spasticity, bimanual function as well as assessing each limb individually is warranted.
There were several factors that may have impacted upon a child’s ability to complete the assessments to their full potential. Cognitive level undoubtedly impacts on the assessment of motor function. Cognitive impairments are commonly reported after paediatric stroke (5, 80, 137) and although estimates vary, it is likely that they're going to impact upon a child's ability to follow instructions, understand the requirements of an assessment task and to complete a motor assessment to their full potential.

Hyperactivity-inattention has also been reported at about 40% in a recent study of this same population exploring 12-month psychosocial problems after AIS. Comprehensive motor assessment requires the ability to attend to a task for the duration of the assessment ranging from 10 to 40 minutes. Difficulties with attention and concentration may also have impacted upon a child's ability to complete the assessment to their full potential resulting in underestimation of motor abilities.

Finally, a child’s hand dominance also impacted upon the ability to reliably assess motor function in this population. This was difficult to assess given that 40% of the cohort was in the neonatal age group and therefore didn’t have an established hand preference prior to diagnosis. Further, 42% were in the preschool age group, of which many did not have an established hand preference prior to diagnosis. Hand dominance may have had implications on whether a child chose to compensate by predominantly using their non-affected limb or if they were not as skilled in their non-affected limb and therefore chose to try and use their affected limb.

10.5 Allied health intervention received

Allied health (AH) intervention, specifically, occupational therapy, physiotherapy and speech therapy, is frequently provided following paediatric AIS. Several studies have highlighted the importance of early intervention to maximize functional outcomes after brain injury (1, 18, 36, 94). Therapists, therefore, rely on early predictors of outcomes to help to identify children at risk of adverse motor and functional outcomes. Intervention is aimed at maximising functional outcomes, minimizing impairments and guiding the development of
the CST towards a normal pattern of development, however, current interventions for physical disabilities following paediatric AIS have limited efficacy (5). There has been an emergence of evidence-based rehabilitation interventions to address motor impairments in children, particularly in children with hemiplegic CP (1, 16, 77, 138), however, little exists that focuses specifically on paediatric stroke.

There were 14 (42.4%) children who had received AH intervention in some capacity since 12 months after diagnosis (7 (50%) neonates, 5 (36%) pre-school aged and 2 (14.3%) school aged). These data correlated closely with the number of children that were identified on the PSOM as having either a unilateral or bilateral sensorimotor impairment, suggesting that the sensorimotor needs of these children as assessed by the PSOM are being addressed in some capacity. More detail is needed, however, regarding type, duration and intensity of allied health intervention for this relationship to be further understood.

10.6 Limitations

There are a number of limitations to this research. Firstly, although it is a long-term prospective longitudinal study for this population, the sample size is relatively small. This limited the analysis that could be done between age groups. This is a common issue in the stroke literature and highlights the need for and benefits of multi-centre studies. It did, however, allow a more comprehensive assessment protocol, which helped to develop a more detailed phenotype of this population.

At the 5-year follow-up, the older children were harder to recruit and therefore the age range of this group was relatively young. Given that the majority of the sample were pre-pubescent, it’s likely that the full extent of their motor and functional difficulties may not have emerged. As children get older, rely less on family supports and develop more independence it is possible that the full extent of their difficulties may become apparent.

Finally, the lack of standardised assessments that are validated to the paediatric stroke population has been discussed earlier in this chapter is a limitation. The existing standardised motor tools may lack the sensitivity to pick up more subtle motor impairments, particularly
those children with unilateral motor impairments, which means the full extent of the motor impairments may not have been captured.

### 10.7 Clinical implications

The findings from this thesis have developed our understanding of motor outcomes following paediatric AIS and the factors associated with different levels of outcome, which has implications for clinical practice. The change in outcomes, beyond the first year highlights the need for longer-term surveillance and monitoring of children following stroke. The change in outcomes between 12 months and 5 years also suggests that outcomes at 12 months may not adequately capture the full extent of impairments, therefore children who appear to be doing well on their assessment at 12 months should still be routinely followed up long term to ensure the full extent of their difficulties are identified.

The efficacy of the use of the PSOM as an early neurology screen tool to predict longer-term outcome is promising, particularly in children over 5 years old. A clinical neurological examination, that could be done routinely at 1 month post stoke onset to help identify children at risk of longer term motor impairments would assist in targeting early intervention to maximize motor and functional outcomes. Further, it would help to provide children and their families with a prognosis so that they have an understanding of what to expect long term.

Motor impairments were associated with a vast array of functional difficulties, which suggest that in addition to routine motor or neurological screening, it is important to include functional assessments in routine follow-up, to ensure that the extent of difficulties experienced in this population is captured. Identifying the individual needs and priorities of children needs to be part of clinical practice.

The findings from this thesis differentiate the stroke group from other brain injury groups (such as TBI), and suggest that these children would benefit from having their own specialized medical and allied health team with an individualised rehabilitation approach.
10.8 Directions for future research

The results of this thesis clearly show us that the recovery continuum has not yet plateaued in any age group at 5 years post stroke onset. As children grow, their social and developmental demands increase, thus these outcomes are likely to change over time and a longer-term observational study is therefore warranted. Further, a larger sample size would allow greater depth of analysis between age groups and may allow identification of more subtle motor and functional changes.

The PSOM did not appear to be a sufficiently sensitive tool for children under 5, particularly the neonates. Exploring the use of a different neurological assessment that could be used with this group of children is an important area for further research.

10.9 Conclusions

Study findings demonstrate that paediatric stroke has a persisting impact on many areas of a child’s life including motor function, adaptive behaviour, fatigue, participation and QOL. Outcomes change between 12 months and 5 years post-stroke, which suggests that 12 months is too early to capture the full extent of motor and functional difficulties. Further, the recovery trajectories are not linear and differ depending on age at stroke onset. For the neonatal group, impairments emerged in the first year, whereas for children sustaining their stroke later in childhood impairments become apparent early and tended to recover over time. Stroke during the pre-school period was associated with greatest vulnerability with impairments in multiple motor and functional outcomes.

Results highlight the need for long-term clinical surveillance of motor and functional outcomes following AIS so that the breadth of impact of brain injury can be identified and early intervention and long-term rehabilitation can be targeted.
REFERENCES


Riva DCL. Late effects of unilateral brain lesions sustained before and after age one. Neuropsychologia 1986;24(3):423-8.


138. Sakzewski L, Carlon S, Shields N, Ziviani J, Ware RS, Boyd RN. Impact of intensive upper limb rehabilitation on quality of life: a randomized trial in children with
Appendix 1. Featured article in The University of Melbourne’s *Pursuit*

**CHILD STROKE SURVIVORS HAVE TIME ON THEIR SIDE**

The risk of children suffering a stroke is higher than you think, but new research is showing that with the right treatment the window for recovery is wide open.

*By Andrew Trowson, University of Melbourne*

A baby just a week old is three times more likely to suffer a stroke than an adult who smokes and suffers from diabetes and hypertension.

That makes stroke one of the top 10 killers of children, and we don’t know why.

But we do know that the window for recovering motor skills following brain damage from a stroke is open wider for children than for adults, and research at the Murdoch Childrens Research Institute and the University of Melbourne is now finding out just how wide that window is.

Children have much more time to regain motor skills after a stroke, compared to adults. Picture: Pixabay
The results so far are good news, suggesting that child-stroke victims keep recovering and benefiting from rehabilitation well after a stroke has hit, when for an adult the potential for recovery is concentrated in a narrow window of just three-to-six months. But that means children need more monitoring and long-term rehabilitation.

The longitudinal study of 64 Australian child stroke victims could for the first time provide worried parents and their health practitioners more certainty on the outlook for children recovering from stroke.

“What these results suggest is that children need an individualised approach to their care and rehabilitation, which is guided in part by their age at the time of the stroke, and they need to have their progress monitored in the long term by a multidisciplinary team,” says lead researcher, occupational therapist and PhD student Ms Anna Cooper.

The ongoing study, published in US journal *Pediatrics*, focused on children who had suffered acute ischemic stroke (AIS), which is when the blood supply to the brain is constrained by an artery blockage such as a blood clot. Strokes can also be caused by a ruptured blood vessel. The risk of AIS is about 1 in 4,000 for babies less than 30 days old, falling to 2-to-8 in every 100,000 in older children.

The researchers found that the children in the study were continuing to show signs of recovery 12 months on from the stroke.

For babies however the extent of any impairment was still emerging because before four months of age babies move largely by reflex. That means that any damage affecting motor skills may not be observable until they are older.

“Children are continuously developing and changing, and they are experiencing environmental and social changes in their lives that can all affect the trajectory of their recovery from stroke,” says Ms Cooper who is based at MCRI and the University of Melbourne, and works at the Royal Children’s Hospital.
The researchers are continuing to track the 64 children to further monitor their recovery trajectory and the factors that may influence it.

The children in the study, who had all been diagnosed with acute ischemic stroke, were recruited between December 2007 and November 2013. Of these, 27 were aged less than 30 days, a further 19 were preschoolers, and 18 were school-aged.

Ms Cooper says the study will help shed light on how well babies recover from stroke compared to older children. In many cases, older children face having to relearn various motor skills impaired by the stroke. However in babies these skills won’t have been learned before the stroke.

“A six year-old who suffers a stroke may have to be relearning how to walk, whereas a baby has to recover from an impairment that will affect their walking without knowing how to walk in the first place. So they may be having to learn from a compromised position.”

Researchers are still debating how babies recover from a stroke. Picture: Pixabay
But alternatively being so young may help. Ms Cooper says there is debate over whether the greater “plasticity” of a baby’s brain, which makes it easier to adapt, may actually help them overcome a stroke impairment in learning motor skills compared to older children relearning those skills.

The results of the study so far suggest that preschoolers may have the best combination of plasticity and learned behaviour for recovery.

“They may be the age group where there is an optimal balance between greater brain plasticity and less vulnerability,” the researchers say in their paper.

Ms Coopers say she hopes the results will inform guidelines now being developed to better inform health practitioners and parents by giving them more idea of what sort of impairment they can expect to see in children as they grow, and what their trajectory for recovery is likely to be.

“At the moment, when a child has a stroke we can’t tell the parents what is going to happen in terms of motor function because it is really unclear. But with this research we hope to eventually be in a position to tell parents what they can anticipate,” says Ms Cooper.

“I think that will be really helpful and empowering for parents.”

Banner image: US Air Force photo/Staff Sgt Taylor L. Marr

First published on 19 July 2017 in Health & Wellbeing

Featured academic

Anna Cooper
PhD Candidate, Murdoch Childrens Research Institute, The Royal Melbourne Hospital, and University of Melbourne; Occupational Therapist

Share:  

Media and republication | Terms of use
Author/s: Cooper, Anna Nicole

Title: Motor outcomes and their impact on activities of daily living, following paediatric arterial ischemic stroke

Date: 2017

Persistent Link: http://hdl.handle.net/11343/212079

File Description: Motor outcomes and their impact on activities of daily living, following paediatric arterial ischemic stroke

Terms and Conditions: Copyright in works deposited in Minerva Access is retained by the copyright owner. The work may not be altered without permission from the copyright owner. Readers may only download, print and save electronic copies of whole works for their own personal non-commercial use. Any use that exceeds these limits requires permission from the copyright owner. Attribution is essential when quoting or paraphrasing from these works.