Physical activity participation in preschool age children born very preterm

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Doctor of Philosophy

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ABSTRACT

Participation in physical activity (PA) is associated with wide ranging health benefits at preschool age and across the lifespan, including favourable cardiometabolic and psychosocial outcomes. Many typically developing preschool age children are not meeting 24-hour movement guidelines in Australia and internationally. Children born very preterm (VP; <32 weeks’ gestation) may be at higher risk of physical inactivity due to myriad comorbidities associated with preterm birth, including adverse respiratory, neurological and motor outcomes. However, studies investigating PA participation in preschool age VP and term-born (born ≥37 weeks’ gestation) children are sparse. This thesis used the International Classification of Functioning, Disability and Health children and youth version (ICF-CY) framework to compare PA participation and motor outcomes of children born VP with term-born children at preschool age over four studies.

Study one was a systematic review and meta-analysis investigating motor outcomes of 3- to 6-year-old VP and term-born children within the ICF-CY framework. Children born VP had poorer outcomes than their term-born peers within the body structure and function and activity domains. However, no data on participation domain outcomes were identified.

The second study examined the agreement between parent-reported and accelerometer-measured 24-hour movement behaviour in 4- to 5-year-old children. Agreement between the two measures of sleep was moderate, but poor for PA and stationary duration. Parents under-reported PA and stationary behaviour relative to the accelerometer, and VP birth, higher social risk and male sex were associated with the difference between the two measures.

Study three compared motor outcomes within the ICF-CY body structure and function, activity and participation domains by examining grip strength, motor competence (MC) and PA
participation in 98 VP and 84 term-born 4- to 5-year-old children. Children born VP had poorer preferred and non-preferred grip strength than term-born children, but there was little difference in bimanual grip strength between the groups. Motor competence was poorer for children born VP than term-born children as measured by the Movement Assessment Battery for Children, second edition and the Little Developmental Coordination Disorder Questionnaire. Using accelerometer data, children born VP completed less PA and more stationary time, and VP parents reported less unstructured PA and more minutes of screen time per day than parents of term-born children. Although adherence to the Australian 24-hour Movement Guidelines was poor for both groups, a lower proportion of VP children met the PA and screen time recommendations than their term-born peers.

Study four examined the relationships between ICF-CY domains by investigating associations between grip strength, MC and PA levels at 4 to 5 years of age, determining if associations differed between VP and term-born children. Irrespective of birth group, more PA and less stationary behaviour were associated with better MC, and better MC was associated with greater grip strength. For children born VP, more PA was associated with better balance skills, and better balance skills were associated with greater grip strength. Physical activity levels did not appear to be associated with grip strength in 4- to 5-year-old children.

Overall this thesis demonstrates that preschool age children born VP experience poorer motor outcomes than term-born children within all ICF-CY domains. The studies within this thesis form the foundation for future research of PA participation in VP preschool age children, and contribute to a deeper understanding of the PA participation trajectory in this population. These findings have substantial implications for allied health clinicians involved in the management and developmental follow-up of children born VP, as well as for early educators and the design of PA promotion strategies.
DECLARATION

This is to certify that:

I. The thesis comprises only my original work towards the Doctor of Philosophy;

II. Due acknowledgement has been made in the text to all other materials used;

III. The thesis is less than 100,000 words in length, exclusive of tables, figures, references and appendices.

Tara Louise FitzGerald

January 2019
PREFACE

Author contributions for each published paper or manuscript in preparation for publication are detailed within the preface of the relevant chapters (Chapters 3 and 5). The PhD candidate collected the data included in this thesis, completed the statistical analyses, and wrote the first draft of each manuscript and chapter. The publication status of each study is as follows:

Study 1 (Chapter 3): Published in *Physical Therapy*, April 2018:


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young age, thank you for teaching me the value of hard work and persistence. To my partner
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doubted me and I’ve never once doubted your love. Thank you from the bottom of my heart.

Finally, I would like to acknowledge the children and their families who generously gave their
time to participate in the research within this thesis.
PUBLICATIONS & PRESENTATIONS DURING PhD CANDIDATURE

Publications


* Publication involving participants/data from studies within this thesis
Conference Presentations


**FitzGerald, T. L.,** Kwong, A. K., Cheong, J. L. Y., McGinley, J. L., Doyle, L. W., & Spittle, A. J (2018, November). *Body structure, function, activity and participation in 3- to 6-year-old children born very preterm: An ICF-based systematic review and meta-analysis.* Paper presented at The University of Melbourne School of Health Sciences Graduate Research Colloquium, Melbourne, Australia. (Poster Presentation)


* Presentation of data from studies within this thesis
SCHOLARSHIPS AND AWARDS

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Travel Scholarship

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Travel Scholarship

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## GLOSSARY OF ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA</td>
<td>Corrected age</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence interval</td>
</tr>
<tr>
<td>CP</td>
<td>Cerebral Palsy</td>
</tr>
<tr>
<td>DCD</td>
<td>Developmental Coordination Disorder</td>
</tr>
<tr>
<td>ELBW</td>
<td>Extremely low birth weight</td>
</tr>
<tr>
<td>EP</td>
<td>Extremely preterm</td>
</tr>
<tr>
<td>FT</td>
<td>Full term</td>
</tr>
<tr>
<td>GEEs</td>
<td>Generalised estimating equations</td>
</tr>
<tr>
<td>GMFCS</td>
<td>Gross Motor Function Classification System</td>
</tr>
<tr>
<td>HRPF</td>
<td>Health-related physical fitness</td>
</tr>
<tr>
<td>ICF-CY</td>
<td>International Classification of Functioning, Disability and Health children &amp; youth version</td>
</tr>
<tr>
<td>LBW</td>
<td>Low birth weight</td>
</tr>
<tr>
<td>Little DCD-Q</td>
<td>Little Developmental Coordination Disorder Questionnaire</td>
</tr>
<tr>
<td>LOA</td>
<td>Limits of agreement</td>
</tr>
<tr>
<td>MABC-2</td>
<td>The Movement Assessment Battery for Children, Second edition</td>
</tr>
<tr>
<td>MC</td>
<td>Motor competence</td>
</tr>
<tr>
<td>MLP</td>
<td>Moderate to late preterm</td>
</tr>
<tr>
<td>MND</td>
<td>Minor neurological dysfunction</td>
</tr>
<tr>
<td>MVPA</td>
<td>Moderate-vigorous physical activity</td>
</tr>
<tr>
<td>n</td>
<td>Number</td>
</tr>
<tr>
<td>NBW</td>
<td>Normal birth weight</td>
</tr>
<tr>
<td>NASPE</td>
<td>National Association for Sport and Physical Education</td>
</tr>
<tr>
<td>OR</td>
<td>Odds ratio</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>PA</td>
<td>Physical activity</td>
</tr>
<tr>
<td>PAEC-Q</td>
<td>Physical Activity and Exercise for Children Questionnaire</td>
</tr>
<tr>
<td>Pre-PAQ</td>
<td>Preschool-age Children’s Physical Activity Questionnaire</td>
</tr>
<tr>
<td>SD</td>
<td>Standard deviation</td>
</tr>
<tr>
<td>VP</td>
<td>Very preterm</td>
</tr>
<tr>
<td>VIBeS2</td>
<td>The Victorian Infant Brain Study-2</td>
</tr>
<tr>
<td>VLBW</td>
<td>Very low birth weight</td>
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This thesis uses the International Classification of Functioning, Disability and Health children and youth version (ICF-CY) framework (World Health Organisation, 2007) to comprehensively examine the physical activity (PA) and motor outcomes of preschool age children born very preterm (VP; <32 weeks' gestational age) compared with their term-born peers. The research examines the measurement of PA levels at preschool age, and investigates correlates of PA in a sample of VP and term-born 4- to 5-year-old children.

Physical activity is considered any bodily movement produced by skeletal muscles resulting in the expenditure of energy (Caspersen, Powell, & Christenson, 1985). Physical activity participation is associated with wide ranging health benefits, including improved physical fitness, mental health, bone health and cardiometabolic outcomes (Okely et al., 2012; Poitras et al., 2016). Preschool age is a crucial time to establish optimal PA behaviours for lifelong health, as PA levels have been shown to track from early to middle childhood, into adolescence and adulthood (Jones, Hinkley, Okely, & Salmon, 2013; Telama et al., 2014). However, PA research in VP populations at preschool age is sparse, and the trajectory of participation is therefore not fully understood for these children.

1.1 Statement of the problem

Preterm birth is defined as birth before 37 weeks of completed gestation, and infants can be categorised as extremely preterm (EP), VP, or moderate to late preterm (MLP) as outlined in Table 1.1. Infants can also be categorised by birth weight: extremely low birth weight (ELBW; <1000 g), very low birth weight (VLBW; <1500 g) and low birth weight (LBW; <2500 g).
Chapter One: Introduction

However, these categorisations cannot be used interchangeably, as there is a range of acceptable weights for specific gestational ages (World Health Organisation, 2012). Moreover, infants who are growth restricted in utero may be more mature than their birth weight range might suggest.

Table 1.1 Categories of birth according to gestational age in weeks and birth weight

<table>
<thead>
<tr>
<th>Preterm Category</th>
<th>Gestational Age (weeks)</th>
<th>Birth Weight Category</th>
<th>Birth Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extremely Preterm (EP)</td>
<td>&lt;28</td>
<td>Extremely low birth weight</td>
<td>&lt;1000 g</td>
</tr>
<tr>
<td>Very Preterm (VP)</td>
<td>28 to &lt;32</td>
<td>Very low birth weight</td>
<td>&lt;1500 g</td>
</tr>
<tr>
<td>Moderate-Late Preterm (MLP)</td>
<td>32 to &lt;37</td>
<td>Low birth weight</td>
<td>&lt;2500 g</td>
</tr>
<tr>
<td>Term</td>
<td>37 to &lt;42</td>
<td>Normal birth weight</td>
<td>2500 to 4500 g</td>
</tr>
</tbody>
</table>

Advances in neonatal and obstetric care have improved the survival rate of infants born preterm, especially those born at younger gestational ages (Saigal & Doyle, 2008). An estimated 15 million infants are born before 37 weeks’ gestation globally, contributing to a substantial international burden on healthcare, education and social services (Blencowe et al., 2013). The majority of preterm births are attributed to MLP births (Australian Institute of Health and Welfare, 2017; Hamilton, Martin, & Osterman, 2016): however, healthcare costs for infants born at younger gestational ages are considerably higher than those born MLP (Jacob et al., 2017; Johnston et al., 2014; Soilly, Lejeune, Quantin, Bejean, & Gouyon, 2014). As well as affecting economic outcomes, lower gestational age at birth is well recognised as having the greatest influence on morbidity for preterm infants (Saigal & Doyle, 2008).

Motor impairment is a common co-morbidity of VP birth throughout childhood (de Kieviet, Pick, Aarnoudse-Moens, & Oosterlaan, 2009), and children can present on a spectrum from mild gross motor delay to more severe conditions such as cerebral palsy (CP) (Spittle & Orton, 2014). Cerebral palsy is an umbrella term for a group of disorders affecting the development of
movement and posture and causing activity limitation, due to non-progressive disturbances occurring in the fetal or infant brain (Bax et al., 2005). The prevalence of CP increases with decreasing gestational age (Himpens, Van den Broeck, Oostra, Calders, & Vanhaesebrouck, 2008). Non-CP minor neurological dysfunction (MND) is also more frequently observed in children born VP than in those born at term (Arnaud et al., 2007), and is even more prevalent than CP in preterm-born children. Developmental Coordination Disorder (DCD) is an umbrella term used to describe a heterogenous group of children who experience impaired motor coordination, which occurs early in the developmental period and interferes with activities of daily living, academic performance, leisure and play (Vaivre-Douret, Lalanne, & Golse, 2016). There is increasing awareness of DCD in preterm populations, as gestational age at birth is inversely associated with risk of DCD (Zhu, Olsen, & Olesen, 2012).

The motor difficulties faced in early childhood by children born VP are multidimensional and can be complexly intertwined. The ICF-CY framework (Figure 1.1) is a valuable method of conceptualising the motor challenges experienced by children born VP across the domains of body structure and function, activity and participation (World Health Organisation, 2007). Using these domains, the ICF-CY framework comprehensively describes disability and health alongside environmental and personal factors. This framework represents a shift from the biomedical model towards holistically describing the influence of disability on individual functioning and on life experiences, with recognition that optimising participation is often the fundamental goal of rehabilitation (Vargus-Adams & Majnemer, 2014). In this thesis, the ICF-CY framework provides a common language and structure to explore physical activity and motor outcomes for preschool age children born VP. There is inevitable overlap between ICF-CY domains due to the dynamic process of child development and functioning; however, this chapter will explore some key body structure and function, activity and participation domain challenges for children born VP.
Chapter One: Introduction

1.1.1 Body structure and function impairments

The World Health Organisation defines body structures as ‘anatomical body parts’, while body functions are the body’s physiological processes; deficits are labelled as impairments (World Health Organisation, 2007). The body structure and function domain includes structural impairments such as joint contracture and muscle atrophy, and functions including exercise capacity, muscle strength, gait patterns and control of voluntary movement. Three conditions which are common comorbidities of preterm birth and are characterised by body structure and function impairments, include CP, non-CP MND and DCD.

1.1.1.1 Cerebral palsy

Cerebral palsy is one of the most common causes of childhood physical disability (Oskoui, Coutinho, Dykeman, Jetté, & Pringsheim, 2013). Children with CP experience a variety of clinical impairments (Spittle & Orton, 2014), and condition-specific classification methods

Figure 1.1 The International Classification of Functioning, Disability and Health Framework

(World Health Organisation, 2007)
(Table 1.2) are based on type, topography (McIntyre, Morgan, Walker, & Novak, 2011) and severity using the Gross Motor Function Classification System (GMFCS) (Palisano et al., 1997). The GMFCS classifies children based on their motor abilities from GMFCS I (least impaired) to GMFCS V (most impaired) (Palisano et al., 1997).

Table 1.2 Condition-specific classifications for cerebral palsy (McIntyre et al., 2011)

<table>
<thead>
<tr>
<th>Classification Method</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td>Spastic</td>
</tr>
<tr>
<td></td>
<td>Dyskinetic</td>
</tr>
<tr>
<td></td>
<td>Ataxic</td>
</tr>
<tr>
<td></td>
<td>Hypotonic</td>
</tr>
<tr>
<td>Topography/Distribution</td>
<td>Hemiplegia (unilateral)</td>
</tr>
<tr>
<td></td>
<td>Diplegia (bilateral)</td>
</tr>
<tr>
<td></td>
<td>Quadriplegia (bilateral)</td>
</tr>
</tbody>
</table>

The prevalence of CP has been reported as 2.11 per 1,000 live births in the general population (Oskoui et al., 2013). The prevalence of CP for infants at different gestational ages is presented in Table 1.3. The spastic type and bilateral topography (diplegia/quadriplegia) is most predominant in preterm infants, with spastic diplegia occurring in 60% of preterm-born children with CP (Himpens et al., 2008). Studies often classify children using descriptors such as ‘mild’, ‘moderate’ or ‘severe’ CP. If using these categories, the majority of preterm-born children with CP can be described as having mild to moderate disability (Spittle & Orton, 2014).
Chapter One: Introduction

Table 1.3 Prevalence of cerebral palsy per 1,000 live births by gestational age (Oskoui et al., 2013)

<table>
<thead>
<tr>
<th>Preterm Birth Category</th>
<th>Prevalence</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>EP</td>
<td>111.8</td>
<td>69.5, 179.8</td>
</tr>
<tr>
<td>VP</td>
<td>43.2</td>
<td>32.7, 56.9</td>
</tr>
<tr>
<td>MLP</td>
<td>6.75</td>
<td>4.59, 9.94</td>
</tr>
<tr>
<td>Term</td>
<td>1.35</td>
<td>1.15, 1.59</td>
</tr>
</tbody>
</table>

CP, cerebral palsy; EP, extremely preterm; MLP, moderate to late preterm; VP, very preterm

1.1.1.2 Non-cerebral palsy minor neurological dysfunction

Central to the diagnosis of non-CP MND is the presence of ‘clusters’ of neurological signs, including abnormalities in body function outcomes such as posture, muscle tone, reflexes and coordination (Hadders-Algra, Huisjes, & Touwen, 1988). Using the Modified Touwen Examination, children can be classified as having simple MND (1 or 2 abnormal clusters) or complex MND, which involves 3 or more abnormal clusters (Peters, Maathuis, Kouw, Hamming, & Hadders-Algra, 2008). In a large population-based cohort study, 46% of 5-year-old children born VP experienced simple MND compared with 23% of their term-born peers (Arnaud et al., 2007). Higher rates of MND in VP compared with term-born children have similarly been found in smaller studies of preschool age children (Fallang, Oien, Hellem, Saugstad, & Hadders-Algra, 2005; van Hus, Potharst, Jeukens-Visser, Kok, & Van Wassenaer-Leemhuis, 2014).

1.1.1.3 Developmental coordination disorder

Although children with DCD experience motor difficulties across the ICF-CY domains (Spittle, FitzGerald, Mentiplay, Williams, & Licari, 2018), the condition is characterised by marked impairment in the development of motor coordination (a body function outcome).
The diagnostic criteria for DCD are outlined in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (American Psychiatric Association, 2013), and are presented in Figure 1.2. Children born VP and VLBW have over six times the likelihood of developing DCD compared with term-born children by school age (Edwards et al., 2011) and decreased gestational age at birth by one week is associated with 19% increased risk of the disorder (Zhu et al., 2012). In a geographical cohort of EP/ELBW children in Victoria, Australia, rates of DCD were 16% compared with 5% in the term-born comparison group (Roberts et al., 2011a). Other body structure and function impairments associated with DCD include poor cardiorespiratory fitness and reduced muscle power (King-Dowling, Rodriguez, Missiuna, Timmons, & Cairney, 2018), and altered gait characteristics (Rosengren et al., 2009).

**Figure 1.2** Diagnostic criteria for Developmental Coordination Disorder (American Psychiatric Association, 2013).

A. Acquisition and execution of coordinated motor skills are below expected at a given chronological age and opportunity for skill learning and use, with difficulties manifesting as clumsiness (e.g. dropping or bumping into objects), slowness and inaccuracy of performance of motor skills (e.g. catching an object, using scissors, handwriting, riding a bike, or participating in sports).

B. The motor skill deficit significantly or persistently interferes with activities of daily living appropriate to the chronological age (e.g. self-care and self-maintenance), and impacts academic/school productivity, prevocational and vocational activities, leisure and play.

C. The onset of symptoms occurs in the early developmental period.

D. The motor skill deficits cannot be better explained by intellectual disability or visual impairment, and are not attributable to a neurological condition affecting movement (e.g. cerebral palsy, muscular dystrophy, or a degenerative disorder).
1.1.4 Other impairments

An important body function impairment is muscle weakness. Muscle weakness is an indicator of adverse health outcome, and is associated with functional impairment (Al Snih, Markides, Ottenbacher, & Raji, 2004), poorer mental health (Norio et al., 2015), cardiovascular disease and all-cause mortality (Leong et al., 2015). Children born preterm are often also born with LBW. A systematic review and meta-analysis investigating the associations between birth weight and muscle strength found a positive association between these two outcomes across the lifespan (Dodds et al., 2013). However, only one study included in the review investigated the association in early childhood (Ford, Kitchen, & Doyle, 1988). Recent studies examining strength in preschool aged children born VP or with VLBW compared with term-born controls are lacking and updated research is needed.

Alongside motor difficulties, children born VP are at higher risk of non-motor comorbidities within the body structure and function domain. In a comprehensive systematic review and meta-analysis, VP birth was associated with increased risk of wheezing disorders in childhood (Been et al., 2014). The strength of the association was found to be similar in early childhood (under age 5) as in older children. Given this respiratory morbidity, it is not surprising that children born preterm also experience decreased exercise capacity when compared with term-born children. Exercise capacity, measured by oxygen uptake at maximal exercise, was found to be 13% lower for VP participants compared with term-born controls in a systematic review and meta-analysis of participants ranging from 5 to 21 years of age (Edwards et al., 2015). However, subgroup analyses based on gestational age or age at assessment were not completed and the authors acknowledge group differences in oxygen uptake at maximal exercise were small (Edwards et al., 2015).
1.1.2 Activity limitations

Activities are defined as ‘the execution of a specific task or action’, and restrictions within this domain are described as activity limitations (World Health Organisation, 2007). Activity limitations are often characterised by gross or fine motor deficits, and the poorer motor performance of children born VP compared with term-born children is well recognised in the literature.

De Kieviet and colleagues (2009) completed a systematic review and meta-analysis of VP and VLBW children’s motor performance on three standardised assessment tools; the Bayley Scales of Infant Development 2nd edition, the Movement Assessment Battery for Children and the Bruininks-Oseretsky Test of Motor Proficiency (de Kieviet et al., 2009). Psychomotor development, measured in 1- to 42-month-old children using the Bayley Scales of Infant Development 2nd edition, was poorer for VP and VLBW children compared with normative data (effect size -0.88, 95% confidence interval [CI] -0.96, -0.80; p<0.001). Similarly, in children aged 5 to 15 years the overall motor impairment scores were significantly higher in VP and VLBW children compared with their term peers on the Movement Assessment Battery for Children (effect size -0.65, 95% CI -0.70, -0.60, p<0.001). Motor proficiency was poor for 8- to 15-year-old VP/VLBW children according to the Bruininks-Oseretsky Test of Motor Proficiency using normative values (effect size -0.57, 95% CI -0.68, -0.46, p<0.001). It is important to note that rather than including studies with a term-born control group, de Kieviet and colleagues (2009) included studies using normative data for two out of three assessment tools (Bayley Scales of Infant Development 2nd edition and Bruininks-Oseretsky Test of Motor Proficiency). Using test norms rather than a term comparison group may underestimate developmental delays; e.g. the Bayley Scales of Infant Development 3rd edition seriously underestimates developmental delay in EP and/or ELBW children (Anderson et al., 2010).
1.1.3 Participation restrictions

Participation is broadly described by the World Health Organisation as involvement in a life situation, and the term ‘participation restriction’ denotes limitation within this domain (World Health Organisation, 2007). Participation is considered a key goal of intervention and can be conceptualised as an entry point for changes at the body structure and function, and activity levels (Imms et al., 2016b). It is a multidimensional and evolving concept involving myriad personal and environmental factors (Willis et al., 2017), and disability research in this field has recently been prolific. However, the language used to describe participation in the literature is often inconsistent (Imms et al., 2016a), and the ICF-CY does not clearly distinguish between activity and participation domain outcomes (FitzGerald et al., 2018; Imms et al., 2016b). Coster and Khetani (2008) recognised that the lack of distinction between activity and participation in the ICF-CY hindered the interpretation and measurement of participation, and proposed that ‘life situations’ involve sets of activities directed towards a personally or socially meaningful goal (Coster & Khetani, 2008).

A recent systematic review including language analysis identified two key elements of participation for 5- to 18-year-old children with disability; attendance and involvement (Imms et al., 2016a). Related themes include activity competence, preferences and sense of self (Imms et al., 2016a). Research has been furthered by the recent development of a conceptual framework (Figure 1.3; see permission to reproduce in Appendix A) involving the key elements of participation and related themes, which is applicable to children with various health conditions (Imms et al., 2016b). The Family of participation-related constructs model proposed by Imms and colleagues (2016) involves intrinsic factors that are influenced by previous participation experiences, and which similarly affect future participation (Imms et al., 2016b). Intrinsic factors include: (i) activity competence: the ability to execute an activity to a specific standard; (ii) sense of self: intrapersonal factors related to confidence/self-esteem/satisfaction and self-
determination; and; (iii) preferences: interests or activities that hold meaning or are valued. The environment can influence the individual either directly or indirectly (Imms et al., 2016b). The Family of Participation-Related Constructs model is dynamic, and involves potential uni- or bi-directional processes highlighted by the arrows in Figure 1.3 (Imms et al., 2016b).

**Figure 1.3** Family of participation-related constructs: (a) person and (b) environment based processes (Imms et al., 2016b)

In this thesis, the primary participation-based outcome is PA. To date, there has been limited research of motor participation outcomes for children born VP compared with term-born children at preschool age. It is unknown whether the body structure and function, and activity domain deficits experienced by preschool age children born VP influences their PA participation.

**1.2 Knowledge gaps in the literature**

This thesis addresses some of the many knowledge gaps in the literature related to motor outcomes of preschool age children born VP compared with their term-born peers. The ICF-CY
framework has been used to comprehensively describe outcomes for various paediatric conditions, such as DCD (Magalhaes, Cardoso, & Missiuna, 2011), CP (McGinley et al., 2012) and traumatic brain injury (Ciccia & Threats, 2015). However, the ICF-CY framework has not been used to categorise motor outcomes for children born VP compared with their term-born peers at preschool age. Within the body structure and function domain, recent studies comparing grip strength in children born VP with term controls are lacking. Poor methodological quality and inconsistent use of standardised motor assessment tools have limited the comparison of activity domain outcomes for children born VP with their term-born peers (FitzGerald et al., 2018), and further high-quality research is warranted. However, the limited understanding of participation in this population is the most glaring gap in the current evidence base.

There is a paucity of studies investigating PA participation in VP preschool age children compared with their term-born peers. A single study, published in 1998 (Keller, Ayub, Saigal, & Bar-Or, 1998), has examined PA patterns in VLBW and normal birthweight (NBW; 2500 – 4500g) children, and is limited by a small sample size and subjective assessment methods. There is limited research examining the validity of subjective assessment of PA in VP compared with term-born children at preschool age, and despite recent research examining predictors and correlates of PA in typically developing populations, research examining such associations for VP children is lacking. Most PA research in VP or VLBW populations has occurred later in childhood and adolescence (Lowe, Cousins, Kotecha, & Kotecha, 2017), meaning the trajectory of PA participation from preschool age is unknown for these children.

1.3 Significance of the research

The importance of PA participation in youth and adolescence is well recognised in the literature. Higher levels of PA are associated with several health benefits, including positive cardio-
metabolic, musculoskeletal, mental health, weight and cardiorespiratory fitness outcomes (Okely et al., 2012). There is emerging evidence suggesting that higher duration or frequency of PA may also have benefits for cognitive development (Carson et al., 2016). Preschool age is a period when children develop life-long PA behaviours (Carson et al., 2016; Okely, Trost, Steele, Cliff, & Mickle, 2009), and establishing optimal early habits is vital for positive long-term health outcomes (Tucker, 2008).

It has been established that typically developing preschool aged children are currently not meeting PA guidelines internationally (Berglind, Hansson, Tynelius, & Rasmussen, 2017; Hinkley, Salmon, Okely, Crawford, & Hesketh, 2012; Pate et al., 2015; Vanderloo & Tucker, 2017). Children born VP may be at higher risk of inactivity compared with their term-born peers due to the varied motor, as well as non-motor, comorbidities associated with prematurity. It is critical to further understand the risk at preschool age, as this an important period for the development of motor competencies (Ferrari et al., 2012) and healthy PA behaviours (Carson et al., 2016; Okely et al., 2009). Given the associations between PA and multiple health benefits, understanding PA behaviours in VP preschool age populations and identifying opportunities for early intervention are crucial to optimise health, development and lifelong PA levels for those born VP.

This thesis will contribute to the understanding of PA trajectories throughout childhood in VP populations, and will examine several associations at preschool age. This work will establish a foundation for PA research in VP populations in early childhood, which is currently a significant gap in our knowledge. Outcomes have the potential to guide early PA intervention for children born VP, which may improve self-reported reductions in PA participation later in life. Targeting early PA behaviours in children born VP may have wide reaching economic, health and quality of life benefits.
1.4 Research aims

The aims of this research are as follows:

1. To systematically review the current evidence of motor outcomes at 3 to 6 years of age in children born VP compared with their term-born peers using the ICF-CY framework.

2. To evaluate the agreement between a parent-report diary and accelerometer-measured PA in preschool aged children.

3. To compare strength, motor competence and PA levels in 4- to 5-year-old children born VP with term-born peers.

4. To investigate the associations between strength, motor competence and PA in 4- to 5-year-old children, determining if associations differ for children born VP compared with term-born peers.

1.5 Research overview

The research in this thesis involves a subgroup of participants from a National Health and Medical Research Council-funded longitudinal research project titled ‘Neurobehavioural development of infants born <30 weeks’ gestational age and their parents’ psychological wellbeing between birth and five years of age’. The project is known as the Victorian Infant Brain Study-2 (VIBeS2). The VIBeS2 project was conducted in Melbourne, Australia and involves a cohort of infants born <30 weeks’ gestational age and their full-term peers born >36 weeks’ gestation with a birthweight ≥2500g (Spittle et al., 2016). Infants were serially assessed
from birth to 4 to 5 years of age, and the 4- to 5-year-old data are presented in this thesis. The VIBeS2 protocol paper is included in Appendix B.

Four studies contributed to this thesis. The first study (Chapter 3) is an ICF-CY based systematic review and meta-analysis investigating motor outcomes of preschool age children born VP compared with term-born children. In this paper, the age range of 3 to 6 years was chosen to systematically examine outcomes for children throughout the preschool period. The studies presented in Chapters 5, 6 and 7 involve data from a subgroup of the VIBeS2 cohort. The thesis overview is presented in Figure 1.4.
1.6 Thesis outline

**Chapter One**

**Introduction:** statement of the problem, knowledge gaps in the literature, significance of the research, aims & thesis overview.

Background information regarding preterm birth within the ICF-CY framework, physical activity participation knowledge gaps, thesis significance and aims, overview of the research and thesis concept map.

**Chapter Two**

**Background:** Physical activity participation in preschool age children.

Reviewed physical activity participation in preschool age children, assessment methods and measurement considerations.

**Chapter Three**

**Study 1:** Body structure, function, activity and participation in 3- to 6-year-old children born preterm: An ICF-based systematic review and meta-analysis.

Published systematic review and meta-analysis investigating motor outcomes of VP and term-born preschool age children within the ICF-CY framework.

**Chapter Four**

**Methods:** background of VIBeS2, participants and study design, study protocol, data collection, management and timeline, general statistical methods and ethics.

A detailed background of the VIBeS2 study which forms the basis of studies 2, 3 and 4.

**Chapter Five**

**Study 2:** Physical activity: Parent-report compared with accelerometry in 4- to 5-year-old children.

Examined the agreement between a parent-report diary and accelerometer-measured physical activity in a subgroup of the VIBeS2 cohort.

**Chapter Six**

**Study 3:** Strength, motor competence and physical activity in very preterm and term-born preschool age children.

Investigated group differences between VP and term-born children in grip strength, motor competence and physical activity in a subgroup of VIBeS2 participants.

**Chapter Seven**

**Study 4:** Associations between strength, motor competence and physical activity in very preterm and term-born preschool age children.

Explored the relationship between grip strength and physical activity, motor competence and physical activity, and grip strength and motor competence in a subgroup of the VIBeS2 cohort.

**Chapter Eight**

**Discussion and future directions:** Thesis summary, implications of research findings, strengths and limitations, future research directions and conclusions.

Synthesised key findings within the ICF-CY in context with previous studies, discussed the clinical and public health implications of the research, considered strengths and weaknesses and recommendations for future research.

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**Figure 1.4** Concept map showing the thesis structure

ICF-CY, The International Classification of Functioning, Disability and Health children and youth version framework; VIBeS2, The Victorian Infant Brain Study-2; VP, very preterm
Chapter Two: Physical activity participation in preschool age children

CHAPTER TWO

PHYSICAL ACTIVITY PARTICIPATION IN PRESCHOOL AGE CHILDREN

2.1 Introduction

Participation in PA has an important influence on health outcomes across the lifespan, and the associated benefits of higher PA levels can reduce the financial burden on health and social services (Department of Health, 2011). As outlined in Chapter 1, preschool age is a critical time for the development of optimal PA behaviours and motor skills, which are the foundation of participation in varied physical activities (Henrique et al., 2016). Physical activity has been defined in Chapter 1 as ‘any bodily movement produced by skeletal muscles resulting in the expenditure of energy’ (Caspersen et al., 1985). The need for consistent terminology in research has been highlighted by the Sedentary Behaviour Research Network, who have recently developed consensus definitions for sedentary-related terms (Tremblay et al., 2017a). Sedentary behaviour is distinct from physical inactivity and is characterised by any waking energy expenditure less than or equal to 1.5 metabolic equivalents in a seated, reclined or supine position (Tremblay et al., 2017a). Conversely, the term physical inactivity is used in research to describe failure to meet PA guidelines (Tremblay et al., 2017a). The Sedentary Behaviour Research Network sedentary definitions will be used throughout this thesis unless otherwise specified.

This chapter will focus on the PA participation of 3- to 6-year-old children by exploring adherence to international guidelines and correlates/determinants of PA participation. Further, the trajectory of PA participation in VP populations from preschool age to adulthood will be reviewed, and methodological considerations for PA monitoring will be discussed. The age range
of 3 to 6 years was chosen to capture the period prior to school commencement in Australia, as formal schooling becomes compulsory at 6 years of age in all states and territories (Australian Curriculum Assessment and Reporting Authority, 2018).

2.2 Adherence to international physical activity guidelines

Adherence to international PA and sedentary behaviour guidelines at preschool age has been a recent focus of research. Most PA guidelines for the preschool years do not specify intensity, however, the recently developed 24-hour Movement Guidelines for the early years advocate for at least one hour of ‘energetic play’ as part of the recommended three hours of PA per day (Okely et al., 2017; Tremblay et al., 2017b). Canada was the first country to develop the 24-hour Movement Guidelines for school age children in 2016 (Tremblay et al., 2016), and the Canadian and Australian 24-hour Movement Guidelines for the early years were concurrently released one year later (Okely et al., 2017; Tremblay et al., 2017b). The full-day, integrated approach to monitoring movement is based on the understanding that PA, sedentary and sleep behaviours should be considered in relation to one another, and that meeting recommendations in all three domains has the strongest association with health benefits (Okely et al., 2017). The 24-hour Movement Guidelines represent a shift from considering each behaviour in isolation, to conceptualising daily movement on a spectrum from sleep to vigorous PA (Tremblay et al., 2017b).

Guidelines from Australia, Canada, the United Kingdom and the United States of America are outlined in Table 2.1 (American Academy of Pediatrics, 2016; Department of Health, 2011; National Association for Sport and Physical Education, 2011; Okely et al., 2017; Tremblay et al., 2017b). Although the American PA guidelines were recently updated (US Department of Health and Human Services, 2018), specific quantities of daily PA were not provided for preschool age
children. Many research studies have been published using the National Association for Sport and Physical Education (NASPE) guideline (National Association for Sport and Physical Education, 2011), which is therefore included in Table 2.1.

Table 2.1 International daily physical activity, sedentary, and screen time guidelines for preschool age children

<table>
<thead>
<tr>
<th></th>
<th>Australia a</th>
<th>Canada b</th>
<th>United Kingdom c</th>
<th>USA d</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age range (years)</strong></td>
<td>3 - 5</td>
<td>3 - 4</td>
<td>&lt;5</td>
<td>3 - 5 #</td>
</tr>
<tr>
<td><strong>Physical activity (hours)</strong></td>
<td>≥3</td>
<td>≥3</td>
<td>≥3</td>
<td>1-3 *</td>
</tr>
<tr>
<td><strong>Age range (years)</strong></td>
<td>3 - 5</td>
<td>3 - 4</td>
<td>-</td>
<td>3 - 5 #</td>
</tr>
<tr>
<td><strong>Sedentary time (hours)</strong></td>
<td>≤1**</td>
<td>≤1**</td>
<td>NS</td>
<td>≤1**</td>
</tr>
<tr>
<td><strong>Age range (years)</strong></td>
<td>3 - 5</td>
<td>3 - 4</td>
<td>-</td>
<td>2 - 5 ^</td>
</tr>
<tr>
<td><strong>Screen time (hours)</strong></td>
<td>≤1</td>
<td>&lt;1</td>
<td>NS</td>
<td>≤1</td>
</tr>
</tbody>
</table>

a Okley et al., 2017; b Tremblay et al., 2017; c Department of Health, Physical Activity, Health Improvement and Protection, 2011; d National Association for Sport and Physical Education, 2002; American Academy of Pediatrics, 2016. *at least 1 up to several hours per day, ** no more than 1 hour at a time, # National Association for Sport and Physical Education guideline, ^ American Academy of Paediatrics guideline, NS; not specified.

Table 2.2 summarises adherence to international PA guidelines at preschool age. Poor adherence to the Australian 24-hour Movement Guidelines has recently been reported in preschool age children, although the proportion of children meeting the PA and sleep recommendations in isolation was higher than the screen time portion (Cliff et al., 2017). The authors found that adhering to all three domains was associated with higher social-cognitive development than any other combination of adherence in 3- to 6-year-old children (Cliff et al., 2017). Studies involving the Canadian 24-hour Movement Guidelines have similarly found poor adherence to the three domains combined in preschool age children (Berglind, Ljung, Tynelius, & Brooke, 2018; Chaput et al., 2017).
### Table 2.2 Studies investigating adherence to physical activity guidelines in typically developing preschool age children

<table>
<thead>
<tr>
<th>Study†</th>
<th>Region</th>
<th>Number of Participants</th>
<th>Age (years)</th>
<th>Outcome Measures</th>
<th>Guideline</th>
<th>Participants Meeting Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berglind et al., 2018</td>
<td>Sweden</td>
<td>830</td>
<td>[4 - 5]</td>
<td>Accelerometer (ActiGraph GT3X+), parent report</td>
<td>Canadian 24-h Movement Guidelines (school age)*</td>
<td>Combined 153 (18); MVPA 257 (31); screen 523 (63); sleep 813 (98)</td>
</tr>
<tr>
<td>Berglind et al, 2017</td>
<td>Sweden</td>
<td>540</td>
<td>4.2 (0.1)</td>
<td>Accelerometer (ActiGraph GT3X+)</td>
<td>NASPE (MVPA)b</td>
<td>178 (33)</td>
</tr>
<tr>
<td>Chaput et al, 2017</td>
<td>Canada</td>
<td>803</td>
<td>3.5, [3 - 4]</td>
<td>Accelerometer (Actical), parent report</td>
<td>Canadian 24-h Movement Guidelines (early years)c</td>
<td>Combined 104 (13); PA 498 (62); screen 193 (24); sleep 675 (84)</td>
</tr>
<tr>
<td>Cliff et al., 2017</td>
<td>Australia</td>
<td>248</td>
<td>4.2 (0.6)</td>
<td>Accelerometer (ActiGraph GT3X+), parent report</td>
<td>Australian 24-h Movement Guidelines (early years)d</td>
<td>Combined 37 (15); PA 231 (93); screen 43 (17); sleep 221 (89)</td>
</tr>
<tr>
<td>Ellis et al., 2016</td>
<td>Australia</td>
<td>233</td>
<td>4.1 (0.6), [3 - 5.9]</td>
<td>Accelerometer (activPAL)</td>
<td>Institute of Medicinee</td>
<td>PA 169 (16); sedentary 130 (56)</td>
</tr>
<tr>
<td>Hinkley et al., 2012</td>
<td>Australia</td>
<td>703</td>
<td>4.5, [3 - 5]</td>
<td>Accelerometer (ActiGraph GT1M), parent report</td>
<td>Australian guideline (2014)f</td>
<td>PA 35 (5); screen 155 (22)</td>
</tr>
<tr>
<td>Okely et al., 2009</td>
<td>Australia</td>
<td>266</td>
<td>4.0 (0.8)</td>
<td>Accelerometer (ActiGraph MTI)**, PAEC-Q</td>
<td>NASPE (total PA)b</td>
<td>Weekdays: PA 149 (56); screen 194 (73); Weekends: PA 210 (79); screen 186 (70)</td>
</tr>
<tr>
<td>Pate et al., 2015</td>
<td>USA</td>
<td>C1: 286, C2: 337</td>
<td>C1: 4.2 (0.7), C2: 4.5 (0.3)</td>
<td>Accelerometer (ActiGraph)</td>
<td>Institute of Medicinee</td>
<td>C1: 120 (42); C2: 168 (50)</td>
</tr>
</tbody>
</table>

*Studies ordered alphabetically by first author; †Tremblay et al., 2016; ‡National Association for Sport and Physical Education, 2002; ³Tremblay et al., 2017b; ⁴Okely et al., 2017; ⁵Institute of Medicine, 2011; ⁶Commonwealth of Australia Department of Health, 2014; ⁷combined PA, screen and sleep time recommendation; ⁸accelerometer for 36 participants only. C1, cohort 1; C2, cohort 2; MVPA, moderate to vigorous physical activity; n, number; NASPE, National Association for Sport and Physical Education; PA, physical activity; PAEC-Q, Physical Activity and Exercise Questionnaire for Children; SD, standard deviation; USA, United States of America
Chapter Two: Physical activity participation in preschool age children

An Australian study investigating the adherence of preschool age children to the NASPE PA and American Academy of Pediatrics screen time recommendations found that 56% of children met the PA guidelines on weekdays; however, this number rose to 79% on weekends (Okely et al., 2009). Seventy to 73% of participants complied with screen time guidelines on weekends and weekdays (Okely et al., 2009). However, the study largely relied on questionnaire data, with only 36 children wearing accelerometers from a total of 266 participants. A more recent Australian study with a larger sample size (n=1,004) found poor adherence in preschool age children using parent-report and accelerometer measures combined (Hinkley et al., 2012). The study by Hinkley and colleagues (2012) found adherence to the 2014 Australian guideline (≥3 hours of PA and ≤1 hour of screen time) was poorer than the American guidelines (NASPE: defined as ≥2 hours of PA; American Academy of Pediatrics 2001 guideline: ≤2 hours screen time) (Hinkley et al., 2012). A large population-based study of 4-year-old children in Sweden has also reported poor adherence, with only 33% of children meeting the NASPE PA guideline over a 7-day period (Berglind et al., 2017).

In addition to the guidelines presented in Table 2.1, specific recommendations for PA and sedentary behaviour in the childcare or preschool setting have been developed in America by the Institute of Medicine (Institute of Medicine, 2011). The Institute of Medicine guideline recommends that sedentary bouts should be limited to 30 minutes at a time, and that children should participate in PA for at least 15 minutes per hour. Poor adherence to the Institute of Medicine guideline has been reported in American (Pate et al., 2015) and Australian (Ellis et al., 2017) preschool age children (Table 2.2). Pate and colleagues (2015) reported that around 50% of participants met the PA recommendation, with more males complying than females (Pate et al., 2015), while Ellis and colleagues (2017) reported better adherence to the sedentary bout recommendation than the PA aspect of the guideline (Ellis et al., 2017).
2.3 Correlates and determinants of physical activity

As multiple studies have shown that preschool age children are physically inactive in various geographical regions (Table 2.2), evidence of modifiable correlates and determinants of PA is needed to guide intervention. In this chapter, the term ‘correlate’ is used to describe the association between an independent variable and PA without causality, whereas determinants of PA are identified through longitudinal studies establishing temporal associations over time (Bingham et al., 2016).

Successful participation in sports and unstructured play-based PA demands a specific level of fundamental motor skill competence (Robinson, 2015); however, further research is needed to determine underlying causal pathways (Figueroa & An, 2017). Fundamental motor skills include object control skills (e.g. throwing, catching, kicking) and locomotor skills such as running, jumping and hopping (Logan, Robinson, Wilson, & Lucas, 2012). A recent systematic review found evidence of a significant relationship between motor skill competence and PA in preschool age children, although the specific nature and strength of this relationship varied according to sex, type of motor skill and weekday versus weekend day (Figueroa & An, 2017). As the latter review predominately included cross sectional studies, motor skill competence can be viewed as a potential correlate of PA in preschool age populations. However, there is emerging evidence of positive associations between motor skill competence and PA outcomes throughout childhood (Cohen, Morgan, Plotnikoff, Barnett, & Lubans, 2015; King-Dowling et al., 2016; Robinson, 2015).

Environmental and social correlates and determinants are often incorporated into intervention and health promotion strategies. A systematic review of correlates and determinants in early childhood found time spent in outdoor play spaces and attendance at preschool or childcare
were positively correlated with total PA, although the methodological quality of some included studies were low (Bingham et al., 2016). Weather has similarly been identified as a determinant of PA, with preschool age children participating in more PA during warmer weather (Li, Kwan, King-Dowling, & Cairney, 2015). A study in the United Kingdom found that social and family demographic factors (e.g. family structure and parental PA) had strong associations with sedentary behaviour and PA in 3- to 4-year-old children, suggesting that social correlates may be vital to optimise PA participation in the home environment (Hnatiuk, Hesketh, & van Sluijs, 2016). Positive associations have also been found between parental perceptions of neighbourhood traffic safety with PA outcomes on weekdays and weekends (Eichinger, Schneider, & De Bock, 2017).

Sex is a strong biological variable, acting as both a correlate and determinant of total PA at preschool age. Males have been found to participate in higher levels of PA than females at preschool age (Bingham et al., 2016; Hinkley, Crawford, Salmon, Okely, & Hesketh, 2008) and although participation tends to decline with age in both sexes, the reduction is reported to occur more rapidly for females (Edwards et al., 2013). Evidence of sex discrepancy in early childhood PA, and recognition of the more rapid PA decline in female populations, suggests sex-specific interventions and health promotion strategies may be needed as early as preschool age.

### 2.4 The physical activity trajectory in very preterm populations

It is well established that a large proportion of typically developing preschool age children are not meeting current PA guidelines; however, children born VP may be at even higher risk of inactivity due to the various comorbidities associated with preterm birth. Physical activity participation in children born VP at preschool age is not well understood, as most research has occurred in later childhood and adolescence (Lowe et al., 2017). Studies examining PA
throughout the lifespan for children born VP or with VLBW are outlined in Table 2.3.

The youngest VLBW preterm cohort to be studied to date included 34 five- to seven-year-old children and 24 children born with NBW (Keller et al., 1998). Using a questionnaire to assess PA patterns and factors influencing participation, the authors suggested that there were no differences in PA participation between VLBW children and controls. However, no questionnaire data were presented in the results, and attempts to contact the authors have been unsuccessful (FitzGerald et al., 2018). Other methodological limitations with the study include the small sample sizes of both groups, the non-representative VLBW sample and poor comparability of VLBW and term cohorts, as well as the subjective PA assessment tool (questionnaire only). To date, there are no further studies investigating PA participation in preschool age children who were born VP or VLBW.

Studies of VP/VLBW children and adolescents are largely limited to self-report methods of assessment; however, a recent study of a geographically representative cohort in the UK investigated PA in 7-year-old children using accelerometers (Lowe, Watkins, Kotecha, & Kotecha, 2016). Lowe and colleagues (2017) concluded that VP born boys participated in less MVPA compared with their term-born peers, and results were not mediated by wheezing symptoms that have been found to be associated with preterm birth (Been et al., 2014). Although Lowe and colleagues (2017) found no associations between gestational age and PA participation in female participants, a lower proportion of females adhered to the British MVPA guidelines (Department of Health, 2011) than males (Table 2.3; Lowe et al., 2016).
Chapter Two: Physical activity participation in preschool age children

Table 2.3 Studies investigating physical activity in very preterm and very low birth weight children compared with term controls

<table>
<thead>
<tr>
<th>Study*</th>
<th>Design</th>
<th>Number of Participants</th>
<th>Age (years)</th>
<th>Outcome measures</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keller et al.,</td>
<td>Longitudinal</td>
<td>VP/VLBW: 34, NBW: 24</td>
<td>6.5 (0.1)</td>
<td>Modified Canada Fitness Survey</td>
<td>No difference between VLBW &amp; NBW children</td>
<td>No questionnaire data in results</td>
</tr>
<tr>
<td>1998</td>
<td>cohort</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Low sample size of both groups</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Poor comparability of cohorts</td>
</tr>
<tr>
<td>Lowe et al.,</td>
<td>Longitudinal</td>
<td>VP: 79, FT: 5,949</td>
<td>VP: 7.3 (0.3), FT: 7.2 (0.2)</td>
<td>Accelerometer (ActiGraph)</td>
<td>VP males less physically active than FT males, no difference for females Adherence to MVPA guideline* - males: 55% preterm, 63% FT; females: 34% preterm, 36% FT</td>
<td>Low VP sample size Accelerometer: model unclear, uniaxial measurement, 10 hours valid wear/day</td>
</tr>
<tr>
<td>2016</td>
<td>cohort</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Welsh et al.,</td>
<td>Longitudinal</td>
<td>EP: 31, FT: 30</td>
<td>EP: 11.1 (0.4), FT: 11.0 (0.5)</td>
<td>Accelerometer (ActiGraph GT1M), self-report diary, VAS of exercise perception</td>
<td>Accelerometer: no differences between EP &amp; FT VAS: exercise capability lower for EP than FT</td>
<td>Low sample size of both groups Uniaxial accelerometer, lack of accelerometer protocol information</td>
</tr>
<tr>
<td>2010</td>
<td>cohort</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clem et al.,</td>
<td>Cohort</td>
<td>EP: 81, FT: 75</td>
<td>C1: EP 10.5 (0.4), FT 10.6 (0.4), C2: EP 17.5 (1.1), FT 17.7 (1.2)</td>
<td>Demographic questionnaire (two PA questions)</td>
<td>EP participants had lower levels of PA</td>
<td>Didn’t use validated PA questionnaire, EP cohort were not a representative sample</td>
</tr>
<tr>
<td>2012</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 2.3 continued. Studies investigating physical activity in very preterm and very low birth weight children compared with term controls.

<table>
<thead>
<tr>
<th>Study*</th>
<th>Design</th>
<th>Number of Participants</th>
<th>Age (years)</th>
<th>Outcome measures</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lowe et al., 2015</td>
<td>Longitudinal cohort</td>
<td>VP: 72 FT: 6,854</td>
<td>VP: [11.6] IQR 11.4 - 11.7 &amp; [15.4] IQR 15.3 - 15.5 FT: [11.5] IQR 11.4 - 11.7 &amp; [15.5] IQR 15.3 - 15.5</td>
<td>Accelerometer (ActiGraph MTI)</td>
<td>No difference between VP &amp; FT</td>
<td>Low VP sample size Low follow up rates Participants lost to follow up had lower SES &amp; maternal education Accelerometer: long epoch length</td>
</tr>
<tr>
<td>Rogers et al., 2005</td>
<td>Longitudinal cohort</td>
<td>ELBW: 53 FT: 31</td>
<td>ELBW: 17.3, range 16.3 - 19.7 FT: 17.8, range 16.5 - 19.0</td>
<td>Sport participation questionnaire</td>
<td>ELBW: less frequent PA and sports than FT controls No difference in PA enjoyment</td>
<td>Self-report measured PA Low sample size of both groups Low follow up rate Excluded participants with major neurosensory impairment</td>
</tr>
<tr>
<td>Kajantie et al., 2010</td>
<td>Cohort</td>
<td>VLBW: 163 FT: 188</td>
<td>22.3, range 18.5 - 27.1</td>
<td>Self-report questionnaire</td>
<td>VLBW: lower frequency, intensity &amp; average exercise duration</td>
<td>Self-report measured PA Participation bias</td>
</tr>
<tr>
<td>Kaseva et al., 2015</td>
<td>Cohort</td>
<td>VLBW: 57 FT: 47</td>
<td>VLBW: 24.6 (2.0) FT: 24.9 (2.2)</td>
<td>Accelerometer (Actiwatch)</td>
<td>No difference between VLBW and FT</td>
<td>Accelerometer: long epoch, cut points used not validated Low sample size of both groups</td>
</tr>
</tbody>
</table>

Studies are ordered chronologically by age; “adherence not presented according to gestational age; preterm participants born <37 weeks’ gestation. C1, cohort 1; C2, cohort 2; ELBW, extremely low birthweight; EP, extremely preterm; FT, full term; IQR, interquartile range (25th and 75th centiles); NBW, normal birth weight; PA, physical activity; SD, standard deviation; SES, socio-economic status; VAS, visual analogue scale; VLBW, very low birthweight; VP, very preterm
Conversely, studies of accelerometer-measured PA in older children and young adults have reported no differences between VP/EP participants and their term-born peers (Kaseva et al., 2015; Lowe et al., 2015; Welsh et al., 2010). However, such studies should be interpreted with caution due to important methodological limitations. Lowe and colleagues (2016) suggest that the overall low levels of PA found in their 2015 study may have masked the effect of preterm birth on PA levels, and highlight several accelerometer-related methodological limitations, including epoch length (time interval over which activity counts are accumulated) and acceleration threshold (Lowe et al., 2016). The small VP sample size (n=79), poor follow-up rate (48% VP, 40% term-born) and lower socio-economic status and maternal education of participants lost to follow-up are also limitations of the study, which limit the generalisability of their findings. The study of 11-year-old EP and term-born children by Welsh and colleagues (2010) is similarly limited by small sample size (n=31 EP; n=30 controls) and lack of accelerometer protocol information, including epoch length, management of non-wear, monitor placement and valid wear time (Welsh et al., 2010). Kaseva and colleagues’ (2015) study of VLBW and term-born 25-year-olds excluded participants with developmental delay, CP and vision or hearing impairment, which reduces the representativeness of the VLBW sample (Kaseva et al., 2015). Their study also used a long accelerometer epoch length and cut points which are validated in 8- to 10-year-old children, rather than in adults.

Despite studies reporting no objective difference, adolescents and young adults born VP/VLBW consistently report participating in fewer sports and PA compared with their term-born peers (Clemm et al., 2012; Dahan-Oliel, Mazer, & Majnemer, 2012; Kajantie et al., 2010; Rogers, Fay, Whitfield, Tomlinson, & Grunau, 2005). High quality research combining self-report measures with objective accelerometer data is needed, as even perceived deficits in PA participation might be a useful a target of intervention for VP/VLBW adolescents and young adults (Lowe et al., 2017).
The motor comorbidities of preterm birth and the increased risk of DCD in VP populations are well established and are described in Chapter 1 of this thesis. Children with DCD, a proportion potentially born preterm, are less physically active than their unaffected peers. A systematic review of 40 studies found poorer motor proficiency was associated with lower levels of PA and participation in organised/free play in children with DCD (Rivilis et al., 2011). Magalhaes and colleagues (2011) similarly found that children with DCD have limited participation in organised sports (Magalhaes et al., 2011). Consistent with these results, a cross-cultural study of children in the United States and Israel found children with DCD participated in less PA, more sedentary behaviour and enjoyed PA less than their more motor proficient peers (Cermak et al., 2015).

Most research of PA in DCD populations is cross-sectional and occurs in middle childhood; however, a longitudinal study with baseline measures in the preschool period is underway (Cairney et al., 2015).

### 2.5 Physical activity monitoring in early childhood

Children’s PA patterns are uniquely characterised by frequent, short bursts of activity at varying intensities (Ekelund, Tomkinson, & Armstrong, 2011; Migueles et al., 2017). Physical activity largely involves active play in preschool age populations, which is defined as ‘a form of gross motor or total body movement in which young children exert energy in a freely chosen, fun and unstructured manner’ (Truelove, Vanderloo, & Tucker, 2017). The unique characteristics of preschool age children’s PA participation are important to consider when selecting assessment tools to accurately quantify PA levels. Accurate measurement is essential to inform community health initiatives (Hnatiuk, Salmon, Hinkley, Okely, & Trost, 2014), and to identify children at risk of adverse health outcomes (Cancela, Ayán, & Castro, 2013).
2.5.1 Subjective measures

Self-report measures are generally not suitable for preschool age children, due to the limited ability to accurately report duration and intensity of physical activities at this age (Cancela et al., 2013). However, parent or proxy-report measures of PA are widely used in research. Questionnaires and diaries provide useful information, including the type of PA and the environmental context within which the participation occurs (Ekelund et al., 2011), and can also be used to aid accelerometer data interpretation. Reliable and valid questionnaires for measuring PA in young children are more limited than in older populations (Cancela et al., 2013); however, some established measures are detailed in Table 2.4.

Another less frequently used means of measuring PA in preschool age populations is direct observation (Adamo, Prince, Tricco, Connor-Gorber, & Tremblay, 2009). Direct observation is a method of observing children and coding PA over a pre-defined period of time. The Children’s Activity Rating Scale has been used in research as a criterion measure for accelerometer validation in preschool age children (Oliver, Schofield, & Kolt, 2007), and involves activity coding in five different categories: resting, low, medium, medium-to-high and vigorous PA (Puhl, Greaves, Hoyt, & Baranowski, 1990). The Observational System for Recording Physical Activity in Children – Preschool Version is a modified version of the Children’s Activity Rating Scale and is designed to provide researchers with more detailed contextual information, including activity type, location and social environment (Brown et al., 2006). However, children may alter their behaviour when being observed and direct observation data collection is time consuming and therefore costly, making it unfeasible for large studies or data collection over extended periods of time (Oliver et al., 2007).
### Chapter Two: Physical activity participation in preschool age children

<table>
<thead>
<tr>
<th>Outcome measure*</th>
<th>Description</th>
<th>Age (years)</th>
<th>Psychometric properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young Children’s Participation and Environment Measure</td>
<td>Sections for home, day care/preschool &amp; community. Measures participation and barriers/facilitators.</td>
<td>0 - 5</td>
<td>Consistent &amp; stable estimates of participation in 0-5-year-old children (Khetani, Graham, Davies, Law, &amp; Simeonsson, 2015).</td>
</tr>
<tr>
<td>Preschool-age Children’s Physical Activity Questionnaire</td>
<td>Measures physical activity &amp; sedentary behaviour within the home environment. Includes items such as parenting style, parental physical activity &amp; home/neighbourhood environment.</td>
<td>3 - 5</td>
<td>Acceptable validity &amp; reliability for measuring PA in preschool age children, but poor measure of sedentary behaviour (Dwyer, Hardy, Peat, &amp; Baur, 2011).</td>
</tr>
<tr>
<td>Children’s Leisure Activities Study Survey, parent version</td>
<td>7-day survey of frequency &amp; duration of participation. Check-list of 30 activities, targets primary school children.</td>
<td>5 - 6</td>
<td>Reliable estimate of physical activity but poor validity (Telford, Salmon, Jolley, &amp; Crawford, 2004).</td>
</tr>
<tr>
<td>Physical Activity Level in Young Children Questionnaire</td>
<td>1-day recall of physical activity preferences, quantity compared with peers &amp; minutes of physical activity.</td>
<td>6 - 7</td>
<td>Validated using accelerometers in 21 school-aged children (Sekine et al., 2002).</td>
</tr>
<tr>
<td>Netherlands Physical Activity Questionnaire</td>
<td>Designed to establish patterns of physical activity behaviour over 6-months.</td>
<td>4 - 7</td>
<td>Acceptable validity (with accelerometers) &amp; reliability (Cancela et al., 2013).</td>
</tr>
<tr>
<td>Physical Activity for Children</td>
<td>5-day questionnaire with 3 options: parent, preschool teacher &amp; school teacher report.</td>
<td>4 - 8</td>
<td>Valid for assessing moderate to vigorous physical activity (validated using heart rate monitors &amp; accelerometers) (Harro, 1997).</td>
</tr>
</tbody>
</table>

* Measures listed chronologically by upper age limit
2.5.2 Objective measures: accelerometers

Accelerometers are the most commonly used direct measure of children’s PA in research (Adamo et al., 2009). Accelerometers measure acceleration of a specific body part through one, two or three axes (uni-axial, bi-axial and tri-axial, respectively), and are usually worn on the hip, wrist or ankle in research studies. Advances in accelerometer technology mean that devices are now able to store continuous data, rather than just sampling in specific epochs (Fairclough et al., 2016). However, most research continues to use epoch-based methods which reduce data to activity counts, rather than interpreting raw acceleration data (Janssen & Cliff, 2015).

Using epoch-based methods, accelerations are filtered to remove movements that are inconsistent with human mobility and pre-processed to obtain activity counts (Migueles et al., 2017). To obtain a count, the raw acceleration signal is digitised and integrated over a defined epoch, for example 60 seconds (Rowlands & Stiles, 2012), meaning the exact value of a given activity count will depend on the frequency and intensity of the underlying raw acceleration. Due to proprietary algorithms used by many accelerometer manufacturers, little further information about count derivation is publicly available (Fairclough et al., 2016) and activity counts are therefore not easily interpreted by clinicians or researchers unfamiliar with epoch-based accelerometer methodology. The amount and intensity of PA can be calculated using activity counts over the recording epoch, and by applying specific cut points. For example, MVPA has been defined as ≥133 counts per 5 seconds (vertical axis) for 4- to 6-year-old children using hip mounted ActiGraph GT3X accelerometers (Jimmy, Seiler, & Mäder, 2013). Algorithms can also be applied to detect accelerometer non-wear and sedentary time. However, the lack of public availability of such algorithms limits the comparison of outcomes between different accelerometer models and between studies (Migueles et al., 2017).
Conversely, using raw accelerometer data in research allows for more transparent reporting. Recording and collecting raw, unfiltered accelerations means that data can be managed using researcher-driven processing procedures (Fairclough et al., 2016), and methods can be clearly outlined in publication. Physical activity is measured in this thesis using Axivity AX3 tri-axial accelerometers (Axivity, Newcastle Upon Tyne, United Kingdom). Axivity AX3 accelerometers collect raw acceleration data and use an open-source firmware platform, which further facilitates transparent data processing (Doherty et al., 2017). Other accelerometers which produce raw data output include GENEActiv (Activinsights, Cambs, UK) and ActiGraph GT3X+ (ActiGraph, Pensacola, FL, USA) accelerometers. Irrespective of the choice of accelerometer, the rapid development of technology and research has resulted in myriad data collection and processing decisions without consensus (Migueles et al., 2017), which is a limitation of PA research.

2.6 Measurement considerations

Despite recent progress in the technology and design of PA assessment tools, limitations still exist and are amplified in children (Ekelund et al., 2011). Accelerometers are becoming increasingly feasible to include in large research studies. However, the interpretation of accelerometer data is challenging (Ekelund et al., 2011), and data collection and processing criteria directly affect data interpretation (Migueles et al., 2017). There is lack of consensus regarding accelerometer data collection and processing protocols in preschool age populations, with variation issues such as epoch length, management of non-wear, valid monitoring times, and site for monitor placement (Janssen & Cliff, 2015; Migueles et al., 2017). Variability in cut points used to determine sedentary time, light PA and MVPA also limits comparability between studies (Brazendale et al., 2016).
Considering the intermittent nature of preschool age children’s PA, epoch decisions for researchers using count-based accelerometers are crucial for accurate data interpretation. Migueles and colleagues (2017) illustrate this point by explaining that the choice of 1 second epochs versus 60 second epochs results in a difference of 45 minutes of MVPA per day (Migueles et al., 2017). The exact epoch length that is most suitable for preschool age populations is unclear; however, shorter epoch lengths may be most appropriate to capture bursts of activity that are characteristic at this age (Migueles et al., 2017).

Choice of cut points also affects data interpretation and can result in wide ranging estimates of sedentary behaviour and PA, depending on the applied cut point (Janssen & Cliff, 2015). In a systematic review of preschool aged children’s PA and sedentary time, cut points for moderate intensity PA varied widely from ≥154 counts/15 seconds to 1,002 counts/15 seconds (Hnatiuk et al., 2014). The authors of the review concluded that the considerable variability in intensity estimates precluded the determination of true PA and sedentary time in preschool age children (Hnatiuk et al., 2014). Management of non-wear similarly affects data interpretation, as inaccurate identification leads to incorrect categorisation of sedentary behaviour (Migueles et al., 2017).

Despite the feasibility and low cost, parent-report measures of PA are also associated with limitations, including recall bias, and over-estimation of the duration and intensity of PA (Ekelund et al., 2011). As different intensities tend to co-occur during physical activities, all intensities are prone to misreporting when using parent-report measures (Sprengeler, Wirsik, Hebestreit, Herrmann, & Ahrens, 2017). Comprehensive, reliable and valid parent-report questionnaires for use in preschool age populations are limited (Cancela et al., 2013), and these measures inherently only account for the time parents are with their child, unless the tool is being completed by childcare or preschool staff. It is therefore difficult to capture the true
volume of PA using subjective tools. Diary and questionnaire measures may be less accurate than objective methods; however, these tools can provide a unique insight into PA type, preference and the environmental context.

Physical activity research has been limited by lack of transparent and consistent data management and processing protocols. However, recent advances in accelerometer technology have resulted in the ability to process raw data via open source platforms. Several important methodological decisions need to be considered when measuring PA in preschool age populations, and future research should strive for clear methodological reporting and consistency to facilitate comparison of outcomes between studies and geographical cohorts.

2.7 Conclusions

Many preschool age children are not meeting PA guidelines internationally, which may result in later adverse health and developmental outcomes. Recent study of correlates and determinants of PA in typically developing populations has been prolific, and outcomes can be used to inform intervention and health promotion strategies. However, studies investigating PA participation in preschool age children born VP are limited, and the trajectory of PA participation throughout childhood and into adulthood is not well established. Further, it is unknown whether PA intervention and promotion strategies being implemented in typically developing populations are suited to preschool age children born VP. Chapter 3 will compare motor outcomes between VP and term-born 3- to 6-year-old children within the ICF-CY framework and identify multiple possible entry points for intervention.
CHAPTER THREE

BODY STRUCTURE, FUNCTION, ACTIVITY AND PARTICIPATION IN 3- TO 6-YEAR-OLD CHILDREN BORN VERY PRETERM: AN ICF-BASED SYSTEMATIC REVIEW AND META-ANALYSIS.

3.1 Preamble

The systematic review and meta-analysis was accepted for publication on 17th April 2018 and is reprinted from Physical Therapy with permission from Oxford University Press (Appendix C). The manuscript is presented in the format it in which it was published. Chapter 3 includes the published manuscript and online supplementary material.


Author contributions for this chapter are as follows: study conception and design TF, AS, JC, LD, JM; data-base searching TF; screening, data extraction and quality assessment TF, AK, AS; analysis and interpretation of the data TF, AS, JC, JM, LD; drafting the manuscript TF, AS, JC, JM, LD, AK. All authors approved the final manuscript as submitted.

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Excellence in Newborn Medicine. Ms. Amanda K.L. Kwong's PhD candidature is supported by The Australian Government Research Training Program Scholarship, the Centre of Research Excellence in Newborn Medicine and the National Health and Medical Research Council of Australia. The funding sources had no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.
3.2 Published manuscript

Body Structure, Function, Activity, and Participation in 3- to 6-Year-Old Children Born Very Preterm: An ICF-Based Systematic Review and Meta-Analysis
Tara L. FitzGerald, Amanda K.L. Kwong, Jeanie L.Y. Cheong, Jennifer L. McGinley, Lex W. Doyle, Alicia J. Spittle

Background. The World Health Organization's International Classification of Functioning, Disability, and Health framework, Children and Youth Version (ICF-CY), provides a valuable method of conceptualizing the multidomain difficulties experienced by children born very preterm (VP). Reviews investigating motor outcomes at preschool age across ICF-CY domains are lacking.

Purpose. The purpose of this review is to identify and compare motor outcomes of 3- to 6-year-old children born VP and children born full-term (FT) within the ICF-CY framework.

Data Sources. Four electronic databases and reference lists of included and key articles were searched.

Study Selection. Studies comparing motor outcomes of 3- to 6-year-old children born VP (<32 weeks' gestation or birth weight <1500 g) with peers born FT were included.

Data Extraction. Two independent authors extracted data and completed quality assessments.

Data Synthesis. Thirty-six studies were included. Activity motor performance of children born VP was consistently poorer compared with peers born FT; standardized mean difference (SMD) was -0.71 (95% CI = -0.80 to -0.61; 14 studies, 2056 participants). Furthermore, children born VP had higher relative risk (RR) of motor impairment (RR = 3.39; 95% CI = 2.68 to 4.27; 9 studies, 3466 participants). Body structure and function outcomes were largely unable to be pooled because assessment tools varied too widely. However, children born VP had higher RR of any neurological dysfunction (Touwen Neurological Examination) (RR = 4.55; 95% CI = 1.20 to 17.17; 3 studies, 1363 participants). There were no participation outcome data.

Limitations. Limitations include the lack of consistent assessment tools used in VP follow-up at preschool age and the quality of the evidence.

Conclusions. Children born VP experience significant motor impairment across ICF-CY activity and body structure and function domains at preschool age compared with peers born FT. Evidence investigating participation in VP preschool-age populations relative to children born at term is sparse, requiring further research.
Chapter Three: Very preterm motor outcomes within the ICF-CY

Very Preterm Motor Outcomes Within the ICF

Advances in neonatal and obstetric care have improved the survival rate of infants born preterm, especially those born at younger gestational ages. Despite these advances, preterm birth remains an important international concern due to short- and long-term morbidity. Children born very preterm (<32 weeks’ gestation) experience motor impairment from infancy to adolescence, with a prevalence of cerebral palsy (CP) alone of 43 per 1000 live births in those born very preterm (VP). There is increasing awareness of mild to moderate subsequent motor impairment in this population, and appreciation that even minor motor impairments can have implications for other areas of functioning, including cognition, academic ability, and behavior.

Recent guidelines for the follow-up of children and young people born preterm highlight the importance of the multidisciplinary team in developmental surveillance, and specify the involvement of physical therapists. Physical therapists have an important role in identifying and treating the motor impairments of children born VP, and in developmental surveillance from infancy to preschool age. However, the difficulties faced by these children can be complexly intertwined; consistent and detailed classification of outcomes is needed in this population.

The World Health Organization's International Classification of Functioning, Disability, and Health, Children and Youth Version (ICF-CY) framework, provides an established and valuable method of conceptualizing the multidimensional difficulties faced by children born VP across the domains of body structure and function, activity, and participation. The ICF-CY uses these domains, alongside environmental and personal factors, to holistically describe the impact of disability on individual functioning and on life experiences. Body structures are defined as anatomical body parts, and body functions include the body's physiological processes, with deficits labelled as impairments. Activity and Participation domains are grouped together in the ICF-CY, with activity defined as the execution of a specific task or action, whereas participation is broadly described as involvement in a life situation. Difficulties in the activity and participation domains are expressed as activity limitations and participation restrictions.

Prior to our review, the most recent systematic review and meta-analysis of motor outcomes for infants born VP or with very low birth weight (<1500 g) was published in 2009. The review by de Kleijve et al focused on motor outcomes using meta-analysis of only 3 standardized assessment tools, but did not include other commonly used measures such as the Peabody Developmental Motor Scales and the Touwen Neurological Examination. Moreover, additional studies have been reported since 2009. Using the ICF-CY framework, our review provides a comprehensive synthesis of updated evidence and presents a uniquely holistic overview of the motor functioning at preschool age of children born VP.

The ICF has been increasingly used to categorize outcomes for various pediatric conditions, including developmental coordination disorder (DCD), CP, and congenital hemiplegia, as well as traumatic brain injury. However, this framework has yet to be used to describe motor outcomes for children born VP compared with term-born peers at preschool age. Our study aims to identify motor outcomes of children born VP between 3 to 6 years of age, and compare these outcomes with children born FT. Our second aim is to describe motor outcomes within the ICF-CY domains of body structure and function and of activity and participation.

Methods
Our study was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, and the study protocol is published in PROSPERO International Prospective Register of Systematic Reviews (CRD 42016037753).

Data Sources and Searches
We identified relevant studies by searching 4 electronic databases (Medline, Cinahl, Embase, and PsycINFO) between March 20 and April 14, 2016, with results limited to year of publication (from 1990) and restricted to the English language. Database searching was updated on January 10, 2017. We conducted 3 discrete searches for each database using search terms specific to motor body structure or function, activity, and participation. The full search strategy is provided in Appendix 1. Where appropriate, we used subject thesauri to map keywords to subject headings and exploded relevant terms.

Two independent authors (T.F. and A.K.) removed duplicates, screened the titles and abstracts of retrieved articles, and obtained full text articles when necessary. The same 2 authors manually screened the reference lists of 3 key articles, and the first author (T.F.) screened the reference lists of included studies. An independent third author (A.S.) resolved disagreements during the screening process. When 2 articles reporting results for the same study met inclusion, the most recently published article or the article with the most complete sample was included. Multiple articles for the same study were included if different motor outcomes were presented in each publication. The flow chart of searched, identified, and included studies is outlined in Figure 1.

Study Selection
Studies met inclusion criteria if they compared motor outcomes of 3- to 6-year-old children born VP (<32 weeks’ gestational age) or with very low birth weight (<1500 g) with their peers born FT (≥37 weeks’ gestation and ≥2500 g). Studies defined by very low birth weight were included as a proxy for <32 weeks’ gestation since some would have involved cohorts where gestational age was more uncertain, but birth weight was known. Term participants also met inclusion criteria if they were only described as “full-term” (FT) or “term-born.” To fulfill inclusion, motor outcomes needed to be consistent with preselected ICF-CY body structure, body function, activity, or participation code-sets. Children born before 1980 were excluded due to...
Figure 1.
Flow chart of the searched, identified, and included studies. * = some studies satisfied more than 1 criterion. FT = full term; VP = very preterm.
Chapter Three: Very preterm motor outcomes within the ICF-CY

Very Preterm Motor Outcomes within the ICF

reported separately for those born <32 weeks’ gestation. Authors were contact-
ed to determine inclusion criteria when necessary, and responses were consid-
ered until January 30, 2017. Systematic or other reviews of the literature, non-
peer-reviewed literature, and studies published in languages other than Eng-
lish were excluded.

Data Extraction and Quality Assessment
Two independent authors (T.F. and A.K.) extracted data using a template created for our review. These 2 authors inde-
pendently assessed the methodological quality of included studies using the Newcastle-Ottawa Quality Assessment Scale (NOS) for cohort studies.20 This method of quality assessment is recom-
mended for nonrandomized studies by the Cochrane Collaboration21 and con-
tains 3 categories of items: selection, comparability, and outcome.20 A star rating provides an assessment of study quality, with a maximum rating of 9 stars indicating the highest methodological quality. For quality assessment, we con-
sidered that subjects lost to follow-up were unlikely to introduce bias when follow-up rates were ≥85%, or between 75% and 85% with an accompanying statement indicating no substantial dif-
ferences between nonparticipants and participants within the study. A third author (A.S.) resolved disagreements during data extraction and quality assessment.

Data Analysis
When outcome data were unable to be provided by individual authors or authors were unable to be contacted, values were obtained from published figures using an online data extraction tool where possible.22 Median values were used as the best estimate of the mean23 when sample sizes were larger than 25 participants, as recommend-
ed by Hozo et al.24 When outcomes matched ICF-CY10 code-sets equally in multiple domains, the data were linked to all relevant domains. During this pro-
cess, existing guidelines for ICF code-
set linking8,26 and participation frameworks17-19 were considered. Overall test scores were used in meta-analysis; however, where only subscale data were
presented, ICF-CY10 code-sets were used to decide which subscales best represented the domain being analyz-
ed. When studies assessed children using more than 1 instrument within the same ICF-CY domain, studies present-
ing overall test scores or those with the most complete sample sizes if overall score was not available were included in the meta-analysis. We excluded out-
comes from quantitative analysis when only individual item data from a stand-
ardized assessment were presented. Corrected age is calculated by subtract-
ing the number of weeks a child was born preterm from his or her chronolo-
gical age, and is commonly used in research settings.20 If both uncorrected and corrected scores were presented, we preferentially used data that were corrected for prematurity in analysis to avoid introduction of bias caused by under-
estimating performance of children born preterm.26 When studies present-
ed cohort data at multiple time points within the preschool period, outcomes for the older age only were included.

Data were analyzed using Stata version 14.2 (StataCorp, Texas, United States of America), and meta-analysis was conducted with studies grouped by outcome. Statistical heterogeneity was assessed using the F statistic and ana-
lyzed by a fixed effects model (Mantel and Haenszel)27 if F < 50%. A ran-
don model was used to determine the method of DerSimonian and Laird28 when the F statistic exceeded 50%. All meta-analysis data are presented alongside study weight (%), 95% CI, F values, and F statistics, and expressed as standardized mean difference (SMD) or risk ratio. When necessary, mean values were multiplied by –1 to adjust scale direction; this applied to scores for the Movement Assessment Battery for Children, first edition (MABC-1) and measures of speed, where a high score indicated worse function. A sensitivi-
ity analysis was completed, excluding data obtained from published figures, raw data, and studies with uncertain sample sizes. Data that were unable to be pooled for meta-analysis were qua-
nitatively analyzed to produce SMDs (95% CI) and graphically presented in forest plots.

Role of Funding Source
This work is supported by grants from the National Health and Med-
ical Research Council of Australia (Centre of Research Excellence, ref. no. 1060773; Early Career Fellowship, ref. no. 1053787 to J.L.Y. Cheong; Career Development Fellowship, ref. no. 1108714 to A.J. Spittle) and from the Victorian Government’s Operational Infrastructure Support Program. The funding sources had no role in the study design; in the collection, analysis, and interpretation of data; in the writ-
ing of the report; and in the decision to submit the paper for publication.

Results
Identified Studies and Study Characteristics
We identified 2812 articles from elec-
tronic database and reference list searching after removing duplicates (Fig. 1). After excluding articles based on title and abstract, 89 full text arti-

cles were screened for eligibility. Thir-
ty-eight articles representing 36 studies met inclusion criteria, and 22 of these studies23,32-52 were pooled in 2 me-
ta-analyses.

The characteristics of included studies and the perinatal characteristics of VP participants are detailed in the Table. Included studies are of cohort design, except 2 which are follow-up studies of randomized control trials, with results compared with term reference groups at follow-up.53,55 Included studies were conducted in Europe (n = 21),23,33-36,38,39,44,47,49,50,54-60,58 North and South America (n = 10),52,57,61-62,66,68,71,53,62-65,67 Australasia (n = 3),53,60,55 and the Mid-
dle East (n = 2),53,68 and involved 8409 participants (excluding unclear participant numbers).53,64 Studies investigated children throughout the preschool period: 3 to 4 years (n = 19)23,32,33,35,37,39,41,43,45-48,50,53,56-59,61,64,67 and 5 to 6 years (n = 15),34-36,38,40,42,44,49,52,54,55,60,62,65,66,68 Two studies reported data for children at multiple time points within the preschool period;51,65 however, only outcome data for the oldest age were included in our analysis. Nine studies presented outcome data which were corrected for prematuri-

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### Table
Characteristics of Included Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Region</th>
<th>Study Design</th>
<th>Very Preterm Birth Characteristics</th>
<th>Sex (% Male)</th>
<th>Follow-Up</th>
</tr>
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### Table.

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<th>Follow-Up</th>
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<td>Gestational Age (wk)</td>
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### Table

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<th>Study</th>
<th>Region</th>
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<th>Very Preterm Birth Characteristics</th>
<th>Sex (% Male)</th>
<th>Follow-Up</th>
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<td>Range</td>
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<td>27.5&lt;sup&gt;d&lt;/sup&gt;</td>
<td>2.3&lt;sup&gt;e&lt;/sup&gt;</td>
<td>1040&lt;sup&gt;f&lt;/sup&gt;</td>
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<td>Tornelli et al., 2000&lt;sup&gt;c&lt;/sup&gt;</td>
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<td>26–34</td>
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<td>van Hus et al., 2014&lt;sup&gt;d&lt;/sup&gt;</td>
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<td>29.8&lt;sup&gt;e&lt;/sup&gt;</td>
<td>2.2&lt;sup&gt;e&lt;/sup&gt;</td>
<td>1269&lt;sup&gt;d&lt;/sup&gt;</td>
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<td>Vohr et al., 1992&lt;sup&gt;f&lt;/sup&gt;</td>
<td>USA</td>
<td>✓</td>
<td>28.9&lt;sup&gt;e&lt;/sup&gt;</td>
<td>2.0&lt;sup&gt;e&lt;/sup&gt;</td>
<td>1137&lt;sup&gt;h&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>A = activity; AGTE = Ankara-Gelisim-Tarama-Envanteri (Ankara Developmental Screening Inventory); ASQ = Ages and Stages Questionnaire; B = body structure or function; BSID-II = Bayley Scale of Infant Development; Dev = developmental; DCDQ = Developmental Coordination Disorder Questionnaire; exam = examination; FTFQ = Five to Fifteen Questionnaire; GDS = Griffiths Developmental Scales, second edition; HSCS-FS = Health Status Classification System—Preschool Version; ICF = International Classification of Functioning, Disability and Health; IQR = interquartile range; ITQol = Infant Toddler Quality of Life Questionnaire; KT1 = Koerperskoordinationstest fuer Kinder (Whole-Body Coordination Test for Children); L = longitudinal; MABC-T = Movement Assessment Battery for Children, first edition; MABC-2 = Movement Assessment Battery for Children, second edition; MC = Developmental Test of Motor Coordination; MD = manual dexterity; MSA = McCarthy Scales of Children's Abilities; Neuro = neurological; NR = not reported; PDMS = Peabody Developmental Scales; PEDT = Paediatric Evaluation of Disability Inventory; Pop = population based; PSQ = Performance Skills Questionnaire; ROM = range of movement; Touwen = Touwen Neurological Examination; USA = United States of America; UK = United Kingdom; VMI = Beery-Buktenica Developmental Test of Visual Motor Integration; VP = very preterm; WanT = Wingate Anaerobic Test; Wee-FIM = Functional Independence Measure for Children.

<sup>b</sup>Pooled data.

<sup>c</sup>Data obtained from authors.

<sup>d</sup>Motor items or subscales.

<sup>e</sup>Touwen (s) = short version of the Touwen Neurological Examination.

<sup>f</sup>Corrected for prematurity.

<sup>g</sup>Longitudinal follow-up of VP cohort only.

<sup>h</sup>Median.

<sup>i</sup>Not provided for total cohort.

<sup>j</sup>Younger cohort.

<sup>k</sup>Older cohort.
Chapter Three: Very preterm motor outcomes within the ICF-CY

Very Preterm Motor Outcomes Within the ICF

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>VP Age</th>
<th>FT Age</th>
<th>n/N VP</th>
<th>n/N FT</th>
<th>RR (95% CI)</th>
<th>% Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSID-II: Motor Chen 2004</td>
<td>308</td>
<td>3</td>
<td>3</td>
<td>36/225</td>
<td>1/93</td>
<td>13.28 (1.65 to 95.32)</td>
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<tr>
<td>Singer 1995</td>
<td>263</td>
<td>3</td>
<td>3</td>
<td>26/168</td>
<td>1/95</td>
<td>14.70 (2.03 to 106.63)</td>
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<td>Subtotal (I-squared = 0.0%, P = .943)</td>
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<td></td>
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<td>13.94 (3.45 to 56.42)</td>
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<td>MABC-1 Erikson 2003</td>
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<td>5.5</td>
<td>5.5</td>
<td>60/165</td>
<td>19/124</td>
<td>2.37 (1.50 to 3.76)</td>
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<td>Fallang 2005</td>
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<td>18/52</td>
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<td>5.9</td>
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<td>1/23</td>
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<td>ASQ: GM &amp; FM Kerstjens 2011</td>
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<td>3.5-4</td>
<td>3.5-4</td>
<td>60/503</td>
<td>16/535</td>
<td>3.99 (2.33 to 6.83)</td>
<td>17.3</td>
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<td>HSCS-PS: mobility Schiarti 2007</td>
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<td>3.5</td>
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<td>8/393</td>
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<td>AGTE: FM Skills Ozbek 2005</td>
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<td>5/36</td>
<td>2.40 (0.81 to 7.09)</td>
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<td>FTFQ: motor Rautava 2010</td>
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<td>5</td>
<td>200/588</td>
<td>25/176</td>
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<td>Test of RR: 1: z= 10.3; P&lt;.001 Overall (I-squared = 40.9%, P = .094)</td>
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<td>3.39 (2.68 to 4.27)</td>
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</table>

![Figure 2.](image)

Activity domain and relative risk (RR) of activity limitation for children born very preterm compared with full-term (FT) controls. * = term data obtained from online data extraction tool.° AGTE: FM skills = Ankara Gelimis Tarama Envanteri (Ankara Developmental Screening Inventory) fine motor subscale; ASQ: GM & FM = Ages and Stages Questionnaire gross and fine motor domains; BSID-II: motor = Bayley Scales of Infant Development second edition motor subscale; FTFQ: motor = Five to Fifteen Questionnaire motor domain; HSCS-PS mobility = Health Status Classification System-Preschool Version mobility subscale; MABC-1 = The Movement Assessment Battery for Children first edition; N = number of participants; n/N = number of events/total participant number; VP = very preterm.

Quality Assessment

The highest NOS rating was 8 stars, achieved by 4 studies33,34,38,57 (Appendix 2), and the median score was 6 stars (ranging from 8 down to 3). Based on participant inclusion and exclusion criteria, the VP participants were generally representative of the average preterm child in the community (n = 32, 84%), and term controls were mainly selected from the same community as VP participants (n = 32, 84%). Birth status was determined from neonatal records for all but 1 study, which was inadequately described.62 All 36 studies demonstrated that outcomes of interest were not known at study commencement, while the comparability of cohorts on basis of design or analysis was inconsistently reported across articles: 12 (32%) controlled for age and any other variable, 19 (50%) for one variable only, and 7 (18%) did not control for any variable. Outcome assessment was completed poorly, with 25 (66%) articles providing no description of independent or blind assessment, and a further 3 studies reporting blinded assessment.38,49,52 Follow-up length was adequate for outcomes to occur in all studies; however, follow-up rates were poor overall. The majority of articles (n = 25, 66%) received zero stars for this criterion; <85% follow-up without accompanying statement indicating if substantial differences between non-participants and participants existed within the study (n = 22), absent statement of follow-up rate (n = 3).56,63,64 In addition to formal quality assessment, several studies excluded data from analysis based on unfavorable outcome (eg, CP).32,36-38,40,42,49,50,55,59,62

Body Structure and Function Domain

Fourteen different outcome measures were used to investigate body structure
Chapter Three: Very preterm motor outcomes within the ICF-CY

**Very Preterm Motor Outcomes Within the ICF**

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>VP Aps</th>
<th>FT Aps</th>
<th>H VP</th>
<th>N FT</th>
<th>VP Mean (SD)</th>
<th>FT Mean (SD)</th>
<th>SMR (95% CI)</th>
<th>% Weight</th>
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<td>3.7</td>
<td>60</td>
<td>58</td>
<td>34.8(17.5)</td>
<td>104.8(14.3)</td>
<td>-0.92(0.86 - 1.91)</td>
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<td>Yashar 2012</td>
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<td>3.7</td>
<td>3.7</td>
<td>104</td>
<td>102</td>
<td>100.6(13.6)</td>
<td>103.4(12.5)</td>
<td>-2.40(0.87 to 3.93)</td>
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<tr>
<td>Yashar 2012</td>
<td>181</td>
<td>3.7</td>
<td>3.7</td>
<td>104</td>
<td>102</td>
<td>100.6(13.6)</td>
<td>103.4(12.5)</td>
<td>-0.19(0.78 to 0.30)</td>
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<tr>
<td>Halliday 2017</td>
<td>81</td>
<td>4</td>
<td>4</td>
<td>108</td>
<td>106</td>
<td>74.6(6.6)</td>
<td>103.6(6.8)</td>
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<td>Sullivan 2007 b</td>
<td>205</td>
<td>4</td>
<td>4</td>
<td>173</td>
<td>172</td>
<td>66.5(14.4)</td>
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**Figure 3.**

Activity domain and motor skills of children born very preterm compared with full-term (FT) controls. * = outcome included in meta-analysis, 1 = locomotor subscale, 2 = self-care subscale (functional skills). Note: higher MABC-1 scores indicate poorer performance. BSDS-II: motor = Bayley Scales of Infant Development second edition motor subscale; GDS-II: motor = Griffiths Developmental Scales second edition motor subscale; MABC-1 = The Movement Assessment Battery for Children first edition; MABC-2 = The Movement Assessment Battery for Children second edition; MSCA: motor = McCarthy Scales of Children's Abilities motor subscale; N = number of participants; PDOMS = Peabody Developmental Motor Scales; PEDI = Paediatric Evaluation of Disability Inventory; SMD = standardized mean difference; VMI = Beery-Buktenica Developmental Test of Visual Motor Integration; VP = very preterm; Wee-FIM = Functional Independence Measure for Children.

and function, with several of these outcomes also linked to the activity domain, including the Beery-Buktenica Developmental Test of Visual Motor Integration (VMI) and the McCarthy Scales of Children's Ability (MSCA) motor subscale. The only outcome solely measuring body structure and function, and able to be pooled in meta-analysis, was the Touwen Neurological Examination.69 Children born VP had higher relative risk (RR) of any neurological dysfunction, as assessed by the Touwen Neurological Examination (eAppendix 3) (RR = 4.55%, 95% CI = 1.20 to 17.17; P = 0.02); 62 participants), and performance of children born VP on the VMI was poorer than their peers born FT (SMD = -0.66; 95% CI = -0.98 to -0.34; P = 0.007; 71.5%; 5 studies; 739 participants). Motor coordination was assessed with 2 tools, the Motor Coordination subtest of the VMI50 and Koerperkoordinationstest fuer Kinder (whole body coordination test for children).69 Children born VP had poorer coordination compared with their peers born FT (SMD = -0.47; 95% CI = -0.76 to -0.17; P = .002; 21.6%; 2 studies; 249 participants). The MSCA motor subscale also measures upper and lower limb coordination, and performance of children born VP was again poorer than children born FT (SMD = -0.98; 95% CI = -1.38 to -0.58; P < .001; 53.8%; 2 studies; 336 participants).

We were unable to complete meta-analysis of other outcomes within the body structure and function domain, as assessment tools varied too widely. We contacted several authors for data to include in the body structure and function meta-analysis; however, authors were unable to provide data or were unable to be contacted.59,60 Individual SMD values for outcomes that were unable to be pooled in meta-analysis are presented in eAppendix 4; the SMD for individual items ranged from 0 to -2.14.

**Activity Domain**

Seven standardized assessment tools were pooled in the activity domain for meta-analysis of continuous outcome data, while 6 were pooled in meta-analysis of binary outcome data (Fig. 2). Figure 3 shows the individual SMD values for outcomes within the activity domain, and indicates which outcomes were pooled to obtain an overall SMD (95% CI). Motor performance of children born VP within the activity domain was consistently poorer when compared with peers born FT (SMD = -0.71; 95% CI = -0.80 to -0.62; P < .001; 39.4%; 16 studies; estimated 2432 participants). A sensitivity analysis excluding raw data and unclear participant

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numbers yielded very similar results (SMD = -0.71; 95% CI = -0.80 to -0.61; \( P < .001 \); 14 studies; 2056 participants). The overall test of heterogeneity produced an \( F \) statistic of 32% for this sensitivity analysis of continuous activity outcome data.

Children born VP had a higher RR of activity limitation (RR = 3.39; 95% CI = 2.68 to 4.27; \( P < .001 \); \( P = 40.9\% \); 9 studies; 3466 participants) (Fig. 3). A sensitivity analysis excluding term data obtained from a published figure demonstrated little change to RR of activity limitation in children born VP (RR = 3.71; 95% CI = 2.84 to 4.85; \( P < .001 \); \( P = 40.4\% \); 8 studies; 3177 participants).

Outcome measures that were unable to be pooled in the activity domain meta-analysis (n = 8 studies) are presented in eAppendix 5, with SMD ranging from -0.38 to -1.64. A subgroup analysis comparing studies which corrected test scores for prematurity with studies using chronological age at assessment did not alter the activity domain results (eAppendix 6).

**Participation Domain**

None of the identified outcome measures were able to be linked to participation code-sets using the definitions of participation and “life situations” proposed by Coster and Khetani. One study used a fitness questionnaire to describe participant physical activity; however, this questionnaire was not reported in the results and authors of the study were uncontactable.

Two outcome measures include individual items that were linked to participation: the Five to Fifteen (FTF) Questionnaire and the Infant Toddler Quality of Life (ITQoL) Questionnaire. The FTF Questionnaire includes 1 question (out of 17 items) regarding sports participation: “Has difficulties or does not like to participate in game sports such as soccer/football, land hockey,” whereas the ITQoL physical abilities domain includes play participation among questions of activity limitation. However, authors did not have access to participation data or were unable to provide individual item data by completion of analysis for our study. As both the FTF Questionnaire and ITQoL Questionnaire items were predominantly linked to code-sets in the activity domain, we did not consider these questionnaires as measures of participation.

**Discussion**

Our study found that children born VP have poorer motor outcomes at preschool age compared with children born FT. This is evident within the body structure and function and activity domains. Within the body structure and function domain, children born VP have an almost 5-fold increased risk of neurological dysfunction, poorer performance on measures of visual-motor integration, and poorer measures of coordination compared with their peers born FT. Children born VP also have increased risk of activity limitation and poorer performance on measures of motor activity than children born at term; however, there was a lack of data in the participation domain. Awareness of motor difficulties within multiple ICF-CY domains is particularly pertinent for physical therapists and other pediatric clinicians to ensure comprehensive motor assessment, treatment, and appropriate referral for preschool-aged children born VP. Physical therapists need to not only consider body structure and function impairments, and activity limitations, but also participation. Participation is considered the ultimate outcome of rehabilitation, as well as an entry point for changes at the body structure and function and activity levels. We need to better understand participation in children born VP to guide intervention. Clinicians should also note that we found clear evidence of poorer motor performance for children born VP within the activity domain despite inclusion of studies correcting test scores for prematurity (6 out of 14 studies and 3 out of 9 studies in the meta-analysis of continuous and binary outcome data, respectively; see Table). Our results are consistent with existing literature concerning motor skill performance in other stages of childhood; however, we present several important points of difference. Our study comprehensively synthesizes updated evidence of motor outcomes within the important preschool period, presents the current evidence within each ICF-CY domain, and highlights the clear knowledge gap of participation for this population.

Our results add to the current body of evidence by using the ICF-CY to describe outcomes across the domains of body structure and function, activity, and participation. The ICF is a dynamic and reciprocal model, which reflects the nature of individual functioning and child development. By categorizing outcomes into ICF domains, we present a holistic and comprehensive overview of the motor function of children born VP at preschool age. The ICF allows us to highlight the most researched domains and the wide variety of assessment tools used within these domains. A consideration for researchers using the ICF to categorize outcomes is that many assessment tools were created prior to wider adoption of the ICF and the structured approach to holistically describing the impact of disability on individual functioning and on life experiences. Although the inevitable overlap of outcomes between domains prevents distinct classification, it illustrates the dynamic process of child development and function within environmental contexts, and highlights evidence gaps.

A strength of our study is the focus on preschool age. Understanding the motor outcomes at preschool age of children born VP is important, as it is a time of rapid sensory and musculoskeletal development characterized by the increasing complexity of motor tasks. Children develop major motor competencies and physical activity behaviors at preschool age. By presenting motor outcomes within the body structure and function and activity domains for children born VP, our study highlights multiple entry points for intervention, particularly within the health and education sectors.

Our review provides a comprehensive overview of motor outcomes in children who were born VP and/or with very low birth weight, adding to the previous systematic review and meta-analysis in this population, which used only 3 standardized assessments.
In our review, we include 12 additional studies that were published from 2009 onward, highlighting the important role our work has in updating the evidence concerning motor outcomes for children born VP. Due to different inclusion criteria, we present results from a diverse group of studies compared with the 2009 review. Moreover, rather than including studies with a group of participants born FT, de Kieviet and colleagues stipulated inclusion of studies using normative data for 2 out of 3 assessment tools. Using test norms rather than a term comparison group may underestimate developmental delays; for example, the Bayley-III underestimates developmental delay in children who were extremely preterm and/or had extremely low birth weight. In addition to providing updated evidence of the preschool-age motor skill proficiency of children born VP compared with children born FT (activity domain), we also include body structure and function outcomes, such as neurological dysfunction, and highlight important gaps in our knowledge of participation in this population.

Despite evidence of body structure and function impairments, and activity limitations for children born VP, we did not identify any outcomes fully measuring participation. Activities and participation are grouped together in the ICF-CY, and the framework does not provide a clear method of distinguishing between the 2 constructs. This issue is compounded by ongoing debate regarding the definition of participation and “life situations.” A recent systematic review investigating definitions of participation, and language used within this construct, highlights the disconnect between language and outcome measures used in research. We chose to use the definition of participation proposed by Coster and Khetani, which is considered in other studies of participation. However, we acknowledge that participation is an evolving construct, and that using alternative approaches may result in different outcome linking within the participation domain. The unclear distinction between activities and participation in the ICF-CY is a limitation for research using this framework.

A limitation of our study is that the large variation in outcome measures impeded comprehensive meta-analysis, especially in the body structure and function domain. Excluding outcomes that were also linked to the activity domain, only 3 studies used a consistent outcome, the Touwen Neurological Examination, and had sufficient data to be pooled. Despite outcome measure consistency, the heterogeneity of these 3 studies was high once pooled and required random effects meta-analysis (eAppendix 3). The pooled results of other outcomes within the body structure and function domain (coordination and MSCA) should be interpreted with caution, due to the wide age range of participants, limited number of studies (n = 2 for each outcome), limited number of participants, and the statistical heterogeneity. Inaccessible data and differing methodologies also precluded pooled meta-analysis of exercise and postural control outcomes. More consistency can be seen within the activity domain, with multiple studies using the MABC-1, MABC-2, the Movement Assessment Battery for Children second edition (MABC-2), and the Peabody Developmental Scales but however, the range of outcomes assessing activity is still large. A total of 19 different outcomes were identified within the activity domain, and several studies also used individual items of assessment tools rather than administering the entire standardized assessment. When comparing between studies, the lack of consistent assessment tools used in follow-up at preschool age is a considerable limitation. Future research in VP populations should ensure consistent use of standardized motor assessment tools to facilitate comparison of outcomes between eras and geographical cohorts.

The methodological quality and study design of included studies should also be considered. Studies differed in respect to correcting test scores for prematurity, with 9 out of 36 studies using corrected age at assessment. This methodological variation is an important limitation to consider. However, a subgroup analysis comparing studies using corrected versus chronological age did not alter our overall conclusion regarding motor performance (eAppendix 6). Cohort size, follow-up, and outcome measurement are noticeably disparate for included studies. Sample size at follow-up varied greatly (range 21 to 1168), and the comparability of VP and term cohorts was inconsistent. Independent blind assessment was poorly reported across studies, while follow-up rates were also low (eAppendix 2). A limitation of the NOS for cohort studies is that study designs including longitudinal follow-up of VP participants with later recruitment of term controls (n = 16) generally obtained a higher follow-up rate than those longitudinally designed. Another important trend to note is that multiple studies excluded participants based on unfavorable outcomes, and exclusion of these data may over-estimate the motor performance of all children born VP compared with controls born FT.

We found that preschool-aged children born VP have poorer motor outcomes compared with children born FT within the ICF-CY domains of body structure and function and activity. However, participation of children born VP compared with peers born FT at preschool age is not well described. Evidence of poorer motor outcomes for older children born VP compared with peers born FT is well documented; however, we comprehensively highlight outcomes within the important preschool period and present the current evidence within each ICF-CY domain.

Research and Clinical Implications

Further research is needed to investigate participation in VP populations at preschool age, and to decrease the gap between theoretical frameworks and participation assessment tools. Understanding participation in this population, and whether known body structure and function impairments and activity limitations ultimately influence participation, is needed to guide targeted intervention studies in the future. Researchers should continue to use the ICF-CY framework to examine outcomes in VP populations, due to the myriad comorbidities associated with...
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prematurity; however, more work is needed to distinguish between activity and participation domains. Greater outcome measure consistency in research of VP populations at preschool age is required across ICF-CY domains. Clinically, physical therapists should consider all ICF domains when assessing and treating preschool-aged children born VP, and advocate for developmental surveillance into preschool age.

Author Contributions and Acknowledgments

Concept/idea/research design: T.L. FitzGerard, J.L.Y. Cheong, J.L. McGinley, L.W. Doyle, A.J. Spittle
Fund procurement: J.L.Y. Cheong, L.W. Doyle, A.J. Spittle
Providing facilities/equipment: A.J. Spittle
Providing institutional liaisons: A.J. Spittle

T.L. FitzGerard conceptualized the research question, completed database searching, screening, data extraction, and quality assessment; drafted the manuscript; and approved the final manuscript as submitted. A.K.L. Kwong independently completed database screening and quality assessment, revised the manuscript, and approved the final manuscript as submitted. J.L.Y. Cheong, J.L. McGinley, and L.W. Doyle conceptualized the research question, revised the manuscript, and approved the final manuscript as submitted. A.J. Spittle conceptualized the research question; resolved conflicts during database searching, data extraction, and quality assessment; revised the manuscript; and approved the final manuscript as submitted.

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Disclosures and Presentations

The authors completed the ICMJE Form for Disclosure of Potential Conflicts of Interest. They reported no conflicts of interest.

This manuscript was adapted in part from the following: an oral presentation given at the 12th International Conference on Developmental Coordination Disorder, Fremantle, Western Australia, July 7, 2017; a scientific poster presentation at the 71st Annual Meeting of the American Academy for Cerebral Palsy and Developmental Medicine (AACPDM), Montreal, Quebec, Canada, September 2017; and an oral presentation given at the 9th Biennial AUSCAPDM conference, Auckland, New Zealand, March 22, 2018.

DOI: 10.1093/ptij/pzy050

References

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3.3 Online supplementary material

e-Appendix 1: Detailed search strategy

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<td>physical activity+ OR &quot;physical activity, capacity and performance&quot; OR physical capacity OR exercise+ OR leisure+ OR life+ OR play+ OR recreation+ OR sport+ OR &quot;International Classification of Functioning, Disability and Health&quot;</td>
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EMBASE
Chapter Three: Very preterm motor outcomes within the ICF-CY

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<th>ICF-CY Domain</th>
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<th>Intervention Terms</th>
<th>Outcome Terms</th>
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Population, intervention and outcome terms combined with ‘AND’. * Truncator used in database searching, + search term exploded. OR; Boolean operator used in database searching
### e-Appendix 2: Quality Assessment – ranked by total score; then alphabetically by first author

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<tr>
<th>Author &amp; Year</th>
<th>Representative *</th>
<th>Selection †</th>
<th>Exposure ‡</th>
<th>Outcome 1 §</th>
<th>Age #</th>
<th>Other ††</th>
<th>Outcome 2 ‡‡</th>
<th>Follow up ††</th>
<th>Adequacy ‡‡</th>
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**NOS criteria:**
- *: Representativeness of the exposed cohort
- †: Selection of controls
- ‡: Ascertainment of exposure
- §: Demonstration that the outcome of interest was not present at the start of the study
- #: Comparability of cohorts: study controls for age
- ||: Comparability of cohorts: additional factor
- ††: Assessment of outcome
- ‡‡: Was the follow up long enough for outcomes to occur
- ‡‡: Adequacy of the follow up of cohorts
- §§: Total star rating. Black circle: (a) star, highest rating, gray circle: (b) star, second highest rating, white circle: Zero stars, lowest rating
Chapter Three: Very preterm motor outcomes within the ICF-CY

### e-Appendix 3: Body Structure and Function Domain, relative risk of neurological dysfunction measured by the Touwen Neurological Examination.

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>VP Age</th>
<th>Term Age</th>
<th>n/N VP</th>
<th>n/N Term</th>
<th>RR (95% CI)</th>
<th>% Weight</th>
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<td>408/881</td>
<td>65/287</td>
<td>2.04 (1.63, 2.56)</td>
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<td>Fallang 2005</td>
<td>64</td>
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<td>5.8</td>
<td>23/52</td>
<td>0/12</td>
<td>11.53 (0.75, 177.59)</td>
<td>16.2</td>
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<td>131</td>
<td>5.2</td>
<td>5.2</td>
<td>16/58</td>
<td>2/73</td>
<td>10.07 (2.41, 42.03)</td>
<td>32.5</td>
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</table>

Test of RR=1: z = 2.23; p = 0.026
Overall (I-squared = 67.3%, p = 0.047) 4.55 (1.20, 17.17) 100.00

NOTE: Weights are from random effects analysis

N; number of participants, VP; preterm, n/N; number of events/total number of participants, RR; relative risk, CI; confidence interval
Chapter Three: Very preterm motor outcomes within the ICF-CY

### e-Appendix 4: Body Structure and Function Domain, outcomes unable to be pooled in meta-analysis

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>N VP</th>
<th>FT VP Age</th>
<th>FT Age Outcome</th>
<th>VP Mean (SD)</th>
<th>FT Mean (SD)</th>
<th>SMD (95% CI)</th>
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<td>8.2 (14.3)</td>
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<td>Verhulst 1992</td>
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<td>151</td>
<td>40</td>
<td>3.7</td>
<td>88.9 (17)</td>
<td>94.7 (12.9)</td>
<td>-0.36 (-0.71, 0.01)</td>
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<td>44</td>
<td>22</td>
<td>22</td>
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<td>772 (474)</td>
<td>479 (240)</td>
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<td>36</td>
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<td>3.4 (0.9)</td>
<td>2.8 (0.6)</td>
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<td>Sagot 2007</td>
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<td>11</td>
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<td>26.2 (3.1)</td>
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## e-Appendix 5: Activity Domain, outcomes unable to be pooled in meta-analysis.

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<th>FT</th>
<th>Mean (SD)</th>
<th>VT Mean (SD)</th>
<th>SMD (95% CI)</th>
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<td>4.6 (1.9)</td>
<td>5.3 (1.8)</td>
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<td>40</td>
<td>83</td>
<td>3.1 (1.3)</td>
<td>4.1 (1.3)</td>
<td>-0.77 (-1.16, -0.38)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MD: cutting zigzag</td>
<td>113</td>
<td>3.8</td>
<td>3.8</td>
<td>40</td>
<td>83</td>
<td>17.2 (10.1)</td>
<td>7.2 (7.3)</td>
<td>-1.22 (-1.66, -0.78)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MD: cutting circle</td>
<td>105</td>
<td>3.8</td>
<td>3.8</td>
<td>40</td>
<td>83</td>
<td>13.6 (7.6)</td>
<td>7.5 (5.8)</td>
<td>-1.04 (-1.49, -0.59)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MD: building</td>
<td>123</td>
<td>3.8</td>
<td>3.8</td>
<td>40</td>
<td>83</td>
<td>7.2 (2.3)</td>
<td>9.1 (2.3)</td>
<td>-0.83 (-1.22, -0.43)</td>
<td></td>
</tr>
<tr>
<td>Schiavelli 2007</td>
<td>ITQoL: physical abilities</td>
<td>644</td>
<td>3.5</td>
<td>3.5</td>
<td>251</td>
<td>393</td>
<td>90.4 (22.9)</td>
<td>97.2 (13.3)</td>
<td>-0.38 (-0.54, -0.22)</td>
<td></td>
</tr>
<tr>
<td>Sagnol 2007</td>
<td>Aiming performance: time</td>
<td>22</td>
<td>5</td>
<td>5</td>
<td>11</td>
<td>11</td>
<td>1620 (335)</td>
<td>1116 (276)</td>
<td>-1.64 (-2.62, -0.66)</td>
<td></td>
</tr>
<tr>
<td>Kerstjens 2011</td>
<td>ASQ: GM &amp;FM</td>
<td>1038</td>
<td>3.5-4</td>
<td>3.5-4</td>
<td>503</td>
<td>535</td>
<td>79 (24.4)</td>
<td>94.9 (19.2)</td>
<td>-0.72 (-0.85, -0.60)</td>
<td></td>
</tr>
<tr>
<td>Gaddlin 2006</td>
<td>GDS: assessment</td>
<td>142</td>
<td>4</td>
<td>4</td>
<td>63</td>
<td>79</td>
<td>69.8 (20)</td>
<td>87.2 (26)</td>
<td>-0.74 (-1.08, -0.40)</td>
<td></td>
</tr>
<tr>
<td>Oliveira 2011</td>
<td>DCDQ</td>
<td>46</td>
<td>5.8</td>
<td>5.9</td>
<td>23</td>
<td>23</td>
<td>54 (11.3)</td>
<td>63 (7.5)</td>
<td>-0.94 (-1.55, -0.33)</td>
<td></td>
</tr>
<tr>
<td>Andersson 2016</td>
<td>PSQ Motor</td>
<td>259</td>
<td>5.8</td>
<td>5.7</td>
<td>35</td>
<td>224</td>
<td>5.3 (0.5)</td>
<td>5.5 (0.5)</td>
<td>-0.57 (-0.93, -0.21)</td>
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</tr>
</tbody>
</table>

Chapter Three: Very preterm motor outcomes within the ICF-CY

### e-Appendix 6: Activity Domain, subgroup analysis comparing studies using corrected versus chronological age.

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>VP Age</th>
<th>FT Age</th>
<th>N</th>
<th>VP</th>
<th>Mean (SD)</th>
<th>FT Mean (SD)</th>
<th>SMD (95% CI)</th>
<th>% Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Results corrected for prematurity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baron 2011</td>
<td>150</td>
<td>3.6</td>
<td>60</td>
<td>90</td>
<td>96.6 (17.5)</td>
<td>104.8 (14.3)</td>
<td>-0.52 (-0.86, -0.19)</td>
<td>8.08</td>
<td></td>
</tr>
<tr>
<td>Verkerk 2012</td>
<td>191</td>
<td>3.7</td>
<td>151</td>
<td>40</td>
<td>100.9 (13.8)</td>
<td>106.4 (13)</td>
<td>-0.40 (-0.75, -0.05)</td>
<td>7.23</td>
<td></td>
</tr>
<tr>
<td>van Hus 2014</td>
<td>165</td>
<td>5.2</td>
<td>81</td>
<td>84</td>
<td>8.4 (3.3)</td>
<td>10 (2.6)</td>
<td>-0.56 (-0.87, -0.25)</td>
<td>9.19</td>
<td></td>
</tr>
<tr>
<td>Singer 1997</td>
<td>263</td>
<td>3</td>
<td>168</td>
<td>95</td>
<td>89.8 (26)</td>
<td>103 (15)</td>
<td>-0.59 (-0.85, -0.33)</td>
<td>13.52</td>
<td></td>
</tr>
<tr>
<td>Stjernqvist 1995</td>
<td>4</td>
<td>4</td>
<td>16</td>
<td>20</td>
<td>103.1 (15.5)</td>
<td>114.9 (11)</td>
<td>-0.90 (-1.59, -0.20)</td>
<td>1.87</td>
<td></td>
</tr>
<tr>
<td>Esbjorn 2006</td>
<td>266</td>
<td>5.1</td>
<td>190</td>
<td>76</td>
<td>10.7 (5.8)</td>
<td>5.5 (7.8)</td>
<td>-0.85 (-1.12, -0.57)</td>
<td>11.72</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-0.62 (-0.75, -0.49)</td>
<td>51.61</td>
</tr>
<tr>
<td><strong>Results not corrected for prematurity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vohr 1993</td>
<td>62</td>
<td>5</td>
<td>46</td>
<td>16</td>
<td>8.5 (2.5)</td>
<td>9 (2)</td>
<td>-0.19 (-0.76, 0.38)</td>
<td>2.74</td>
<td></td>
</tr>
<tr>
<td>Halsey 1993</td>
<td>81</td>
<td>4</td>
<td>51</td>
<td>30</td>
<td>7.6 (2.6)</td>
<td>10.4 (2.6)</td>
<td>-1.08 (-1.56, -0.60)</td>
<td>3.85</td>
<td></td>
</tr>
<tr>
<td>Sullivan 2007</td>
<td>255</td>
<td>4</td>
<td>173</td>
<td>82</td>
<td>96.3 (16.7)</td>
<td>112.5 (14.4)</td>
<td>-1.01 (-1.29, -0.73)</td>
<td>11.60</td>
<td></td>
</tr>
<tr>
<td>De Rose 2013</td>
<td>210</td>
<td>3.4</td>
<td>105</td>
<td>105</td>
<td>7.1 (3.7)</td>
<td>10 (3.1)</td>
<td>-0.84 (-1.12, -0.55)</td>
<td>11.18</td>
<td></td>
</tr>
<tr>
<td>Lee 2004</td>
<td>111</td>
<td>5.9</td>
<td>42</td>
<td>69</td>
<td>317.8 (21.8)</td>
<td>326.9 (10)</td>
<td>-0.59 (-0.98, -0.19)</td>
<td>5.81</td>
<td></td>
</tr>
<tr>
<td>Kilbride 2004</td>
<td>44</td>
<td>5</td>
<td>22</td>
<td>22</td>
<td>79 (11.1)</td>
<td>93.2 (16.7)</td>
<td>-1.00 (-1.63, -0.37)</td>
<td>2.26</td>
<td></td>
</tr>
<tr>
<td>Evensen 2009</td>
<td>98</td>
<td>5.8</td>
<td>25</td>
<td>73</td>
<td>100.6 (11.5)</td>
<td>105.9 (5.4)</td>
<td>-0.72 (-1.18, -0.25)</td>
<td>4.11</td>
<td></td>
</tr>
<tr>
<td>Maggi 2014</td>
<td>124</td>
<td>4</td>
<td>4-4y</td>
<td>4-4y11m4-4y11m62</td>
<td>37.8 (10.3)</td>
<td>44 (9.1)</td>
<td>-0.64 (-1.00, -0.28)</td>
<td>6.83</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-0.80 (-0.94, -0.66)</td>
<td>48.39</td>
</tr>
</tbody>
</table>

Test of SMD=0; z=14.67; p <0.0001
Overall (I-squared = 32.0%, p = 0.119) -0.71 (-0.80, -0.61) 100.00

N: number of participants, VP: very preterm, FT: full term, SD: standard deviation, SMD: standardized mean difference, CI: confidence interval, v: year, m: month.
3.4 Summary of systematic review findings

The systematic review and meta-analysis presented in Chapter 3 compared the motor outcomes of 3- to 6-year-old children born VP with their term-born peers within the ICF-CY framework. Children born VP had poorer motor outcomes than term-born children within the body structure and function and activity domains. However, participation in VP children compared with their term-born peers is poorly understood and it is unknown whether body structure and function impairments and activity limitations ultimately affect participation in these children. Increased awareness of multi-domain motor difficulties for VP children at preschool age is needed in clinical practice, and future research should continue to use the ICF-CY framework to examine VP outcomes due to the complex comorbidities associated with preterm birth.

The remaining studies in this thesis build on the findings from the systematic review and meta-analysis in Chapter 3, and begin to address the substantial evidence gap concerning participation in VP preschool age children relative to term-born controls. Chapter 4 outlines the general methods for VIBeS2 which are relevant to the studies presented in Chapters 5, 6 and 7.
CHAPTER FOUR

GENERAL METHODS FOR VIBeS2

As outlined in Chapter 1, the research in this thesis is nested within a National Health and Medical Research Council funded longitudinal research project known as VIBeS2 (Appendix B, (Spittle et al., 2016)). This thesis includes the first 182 participants assessed during the most recent VIBeS2 follow-up timepoint (4 to 5 years of age) and involves a portion of the overall outcome data from the larger study. Data collection for this thesis was limited by the PhD candidature timeline, as VIBeS2 recruitment occurred over a three year period. This chapter outlines the general methods of VIBeS2, while specific methods for each study are detailed in Chapters 5, 6 and 7.

4.1 Background of VIBeS2

The increased risk of motor impairment for children born VP has been comprehensively described in Chapters 1 and 3 of this thesis. Motor impairment is one of the most common adverse consequences of preterm birth, although the underlying mechanisms of motor impairment and the motor developmental trajectory for infants born preterm are unclear (Spittle et al., 2016). A Cochrane Review investigating the efficacy of early intervention for preterm infants found that motor benefits of current interventions are observed in infancy, but do not extend to school age (Spittle, Orton, Anderson, Boyd, & Doyle, 2015). Understanding the full neurodevelopmental trajectory and early indicators of impairment may help to guide intervention by determining which preterm infants will benefit most from targeted treatment (Spittle et al., 2016).
The overall aims of VIBeS2 are as follows:

1. To compare the prevalence of motor impairment from birth to 5 years of age between children born <30 weeks’ gestation and term-born children, and to examine whether abnormal motor assessments in the newborn period among those born <30 weeks’ gestation predict abnormal motor functioning at age 5 years.

2. To determine whether there are novel early Magnetic Resonance Imaging biomarkers detectable in the neonatal period that can predict motor impairments at 5 years, and whether these relationships differ between children born <30 weeks’ gestation and those born at term.

3. To investigate the association between motor impairments and concurrent deficits in body structure and function at 5 years of age, using a combination of standardised and innovative tests of gait, postural control and strength, and to determine whether these relationships differ between children born <30 weeks’ gestation and those born at term.

4. Explore how motor impairments at 5 years, including abnormalities of gait, postural control and strength, are related to concurrent functional outcomes including physical activity, cognitive and learning ability, behavioural and emotional problems, and whether these relationships differ between children born <30 weeks’ gestation and those born at term.
4.2 Subjects and study design

VIBeS2 is a prospective observational cohort study conducted in Melbourne, Australia. Study participants have been comprehensively assessed from birth until 3 years’ corrected age (CA) and were reassessed between 4- to 5-years’ CA. Corrected age is calculated by subtracting the number of weeks a child was born preterm from his or her chronological age. Although the age at which age correction should cease varies greatly in the literature and in clinical practice, CA is commonly used in research settings to avoid introduction of bias caused by underestimating performance of children born preterm (Wilson-Ching, Pascoe, Doyle, & Anderson, 2014). Age correction for prematurity in research should therefore continue into late childhood to eliminate a known bias in test scores and for consistency (Doyle & Anderson, 2016).

4.2.1 Subject recruitment

Very preterm and term-born infants were recruited between January 2011 and December 2013 from nurseries within the Royal Women’s Hospital (one of four tertiary Neonatal Intensive Care Units in Victoria, Australia). Research nurses recruited infants between birth and 2 weeks of age, and written parental consent was obtained for all participants at the time of recruitment. The study was approved by the Human Research and Ethics Committees at the Royal Women’s Hospital and the Royal Children’s Hospital in Melbourne, Australia. The study initially recruited 150 VP and 151 term-born infants.

4.2.2 Inclusion and exclusion criteria

Infants admitted to, or born at, the Royal Women’s Hospital were eligible for recruitment, and those born <30 weeks’ gestation were eligible for the VP cohort. Term-born infants were born >36 weeks’ gestation with a birthweight ≥2500 g. Participants diagnosed with congenital abnormalities known to affect neurodevelopment, and those with non-English speaking parents
were excluded (due to questionnaires needing to be completed in English). An additional exclusion criterion for term-born infants was any admission to a neonatal intensive care unit or a special care nursery. For this thesis, participants assessed between April 2016 and July 2018 were included.

### 4.2.3 Participant characteristics

The characteristics of the VIBeS2 participants are outlined in Table 4.1.

#### Table 4.1 Characteristics of the VIBeS2 participants

<table>
<thead>
<tr>
<th></th>
<th>VP Infants (n=149)</th>
<th>Term Infants (n=151)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gestational age</strong> (w), mean (SD) [range]</td>
<td>27.7 (1.5), [23.5 - 29.9]</td>
<td>39.8 (1.2), [37 - 42]</td>
</tr>
<tr>
<td><strong>Birth weight</strong> (g), mean (SD) [range]</td>
<td>1021 (261), [517 - 1638]</td>
<td>3503 (438), [2592 - 4744]</td>
</tr>
<tr>
<td>Small for gestational age, n (%)</td>
<td>16 (11)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>74 (50)</td>
<td>76 (50)</td>
</tr>
<tr>
<td>Multiple births n, (%)</td>
<td>65 (44)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Higher social risk n, (%)</td>
<td>63/139 (45)</td>
<td>36/135 (27)</td>
</tr>
<tr>
<td>Grade III/IV IVH, n (%)</td>
<td>5 (3)</td>
<td>N/A</td>
</tr>
<tr>
<td>PVL, n (%)</td>
<td>1 (0.7)*</td>
<td>N/A</td>
</tr>
</tbody>
</table>

* Infant also had grade III/IV IVH, g, grams; IVH, intraventricular haemorrhage; n, number; N/A, not applicable; PVL, periventricular leukomalacia; SD, standard deviation; VP, very preterm; w, weeks

### 4.2.4 Follow-up assessments from birth

Of the VP infants recruited (n=150), one was diagnosed with Trisomy 21 postnatally and was excluded, and 6 subsequently died in the neonatal period, leaving 143 VP infants in the study. Follow up rates and the assessment tools for each time-point are detailed in Figure 4.1.

Very preterm infants were assessed as inpatients weekly from birth until 32 weeks’ postmenstrual age, then fortnightly until hospital discharge. At term-equivalent age, both VP and term-born infants attended the Murdoch Children’s Research Institute (Melbourne, Australia) for a follow-up appointment, and optional Magnetic Resonance Imaging scans were offered to all families. For those who consented, Magnetic Resonance Imaging scans were completed during sleep.
(without anaesthesia or sedation) between 38-44 weeks’ gestational age on the same day as the neurobehavioral assessment at the Murdoch Children’s Research Institute.

After the term age assessments, participants were followed up at 1, 2 and 3 years’ CA (Figure 4.1). At each timepoint, assessments were completed by trained assessors who were blinded to previous assessment results and gestational age at birth, and parents completed questionnaires relating to parental mental health and child development. Detailed descriptions of the questionnaires administered in the VIBeS2 follow-up can be found in Appendix B (Spittle et al., 2016).

Figure 4.1 VIBeS2 follow-up from birth

* neurobehavioral assessments were the same as those completed weekly; PMA, post-menstrual age; n, number; VP, very preterm; FT, full-term; MRI, magnetic resonance imaging; GMA, Prechtl’s General Movements Assessment; NNNS, Neonatal Intensive Care Unit Network Neurobehavioural Scale; HNNE, Hammersmith Neonatal Neurological Examination; AIMS, Alberta Infant Motor Scale; NSMDA, Neurological, Sensory, Motor Developmental Assessment; TINE, Touwen Infant Neurological Examination; SOMA, Schedule for Oral-Motor Assessment; Bayley-III, Bayley Scales of Infant and Toddler Development third edition; EAS, Emotional Availability Scale
Chapter Four: General methods

4.3 Study protocol

4.3.1 Assessment procedure
Participants attended the Murdoch Children’s Research Institute for the assessments relevant to this thesis between 4- to 5-years’ CA, and efforts were made to assess children before they commenced formal schooling. The assessment procedure included motor and cognitive testing; however, only the motor protocol will be detailed in this chapter. Cognitive assessments and non-motor parent questionnaires are detailed in the VIBeS2 4- to 5-year protocol (Appendix B).

The motor assessments were completed by trained physiotherapists and an exercise scientist, who were blinded to medical history (including gestational age at birth) and previous assessment results. When families were unable to attend an appointment, a home visit was completed using a modified protocol as some equipment could not be transported. As part of the doctoral candidature, the author assessed 141 of the 182 participants included in this thesis.

4.3.2 Outcome measurement
Outcome measures were selected using the ICF-CY framework (World Health Organisation, 2007) to provide a comprehensive overview of VP children’s function at preschool age. The outcomes which are relevant to the studies in this thesis and their corresponding ICF-CY two-level classifications are detailed below.

4.3.2.1 Body structure and function domain outcomes
Outcomes within the body structure and function domain included anthropometric measures and hand grip strength.
• Anthropometric measures were collected for each participant during the follow-up appointment. Height, weight and lower limb length were measured using the same standardised and calibrated equipment and procedures for each participant. Lower limb length was measured bilaterally from the anterior superior iliac spine to the medial malleolus.
  
  o ICF-CY s 750 structure of the lower extremity; b 530 weight maintenance functions (World Health Organisation, 2007).

• Grip strength (force in kg) was measured using a digital dynamometer with the child seated, with the shoulder adducted and neutrally rotated, elbow flexed at 90° and the forearm and wrist in a neutral position. Grip strength of the preferred and non-preferred hands was measured, as well as bilateral grip strength. A practice phase preceded three formal trials of each condition, with the maximum value for each condition recorded.
  
  o ICF-CY b 730 muscle power functions

4.3.2.2 Activity domain outcomes

Activity domain outcomes included two standardised assessment tools.

• The Movement Assessment Battery for Children, 2nd Edition (MABC-2) consists of three subscales: manual dexterity, aiming and catching, and balance (Henderson, Sugden, & Barnett, 2007). It is a reliable and valid tool for the assessment of motor development in children from 3 to 16 years of age, and is considered the gold standard for determining motor impairment.
  
  o ICF-CY d 440 fine hand use; d 445 hand and arm use; d 455 moving around.
The Little Developmental Coordination Disorder Questionnaire (Little DCDQ) is a parent report measure consisting of 15 items describing specific motor abilities (Wilson et al., 2015). The Little DCDQ has been recommended for children aged 3 to 4 years, and has concurrent validity with the MABC-2; Pearson correlation between Little DCDQ and MABC-2 total score: \( r = 0.3; \) p<0.01 (Wilson et al., 2015).

- ICF-CY \( d\ 415 \) maintaining a body position; \( d\ 435 \) moving objects with lower extremities; \( d\ 440 \) fine hand use; \( d\ 445 \) hand and arm use; \( d\ 455 \) moving around; \( d\ 550 \) eating; \( d\ 560 \) drinking.

### 4.3.2.3 Participation domain outcomes

As the ICF-CY provides little guidance in distinguishing participation from activity domain tasks (FitzGerald et al., 2018), this thesis operationalises participation as involvement in ‘sets of organised activities directed towards a personally or meaningful goal’ (Coster & Khetani, 2008). The primary participation domain outcome is PA over a six-day period. Physical activity was measured objectively using an accelerometer and subjectively using a parent-report diary.

- A tri-axial accelerometer (Axivity AX3, Newcastle Upon Tyne, United Kingdom) was placed inside a band (Axivity Wrist Band, Newcastle Upon Tyne, United Kingdom) and fitted to each participant’s right ankle during their follow-up appointment at the Murdoch Children’s Research Institute (Figure 4.2). The participants wore the accelerometer for the next six consecutive days before the family returned it by mail in a pre-paid envelope. The AX3 accelerometer is water resistant to 1.5 metres, and parents/caregivers were instructed to not remove it during swimming and bathing where possible.
During the same six days that the accelerometer was worn, parents/caregivers completed a physical activity diary (Appendix D). The diary was returned by mail alongside the accelerometer, and was created specifically for VIBeS2 as existing parent-report measures did not capture the desired PA participation data. The diary included daily sleep and wake time, accelerometer non-wear time, and time spent in stationary and physical activities. The first day of the diary was completed by the assessors as a written example of how to best complete the diary and parents were instructed to only account for the time they spent with their child each day (i.e. not to be completed by childcare/preschool staff). To minimise recall bias, parents/caregivers were instructed to complete the diary at the end of each day.
Chapter Four: General methods

4.4 Data collection, management and timeline

4.4.1 Data collection & management

Data collection for VIBeS2 commenced in April 2016. Questionnaires were sent to parents via e-mail and were completed online using a link to the VIBeS2 REDcap database. When families had difficulty accessing e-mail or internet, paper questionnaires were completed and entered manually into REDcap by study research assistants. All data collected during the assessment protocol were scored by trained, blinded assessors and entered into REDcap.

Accelerometers were initialised using the open source OmGui software (Open Movement, United Kingdom) to capture tri-axial accelerations at 50 Hz with a dynamic range of +/- 8 g. Once an accelerometer was returned by mail, the participant data were downloaded using the same OmGui software and stored within a secure server.

Data, excluding accelerometer data, were cleaned, edited and analysed using Stata statistical software version 14.2 (StataCorp, Texas, USA). Accelerometer data were converted from Continuous Wave Accelerometer (CWA) files to Wave Sound (WAV) files and processed using a program designed for VIBeS2 according to a pre-determined guideline (see Appendices E and F).
4.4.2 Victorian Infant Brain Study 2 timeline

The overall VIBeS2 timeline is outlined in Figure 4.3.

<table>
<thead>
<tr>
<th>Protocol development &amp; ethics approval</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data collection</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statistical analysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Publication &amp; translation of research</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 4.3 VIBeS2 timeline

4.5 General Statistical Methods and Ethics

4.5.1 General statistical methods

The sample size of the VIBeS2 follow-up study was determined by the size of the existing cohort (n=252). VIBeS2 data collection concluded in January 2019, with an overall follow-up rate of 86%. The VIBeS2 cohort includes a large number of multiple births (Table 4.1), therefore all linear and logistic regression models were fitted with generalised estimating equations (GEEs) to allow for clustering of multiple births within a family.

4.5.2 Ethics

The VIBeS2 4- to 5-year follow up project has ethical clearance from the Human Research and Ethics Committees at the Royal Children’s Hospital (Reference Number: 34147D, Appendix G) and external ethics registration with the University of Melbourne. No further ethics applications were required, as studies included in this thesis fall within the existing ethics clearance.
4.6 Summary

This chapter provides background information for the VIBeS2 study and outlines the 4 to 5 year follow-up assessment and data management procedures, which are relevant to studies 2, 3 and 4 (Chapters 5 – 7). More detailed methods are reported for each study within the relevant chapter. A subgroup of the overall thesis sample is included in Chapter 5 to examine the agreement between parent-reported and accelerometer-measured physical activity.
CHAPTER FIVE

PHYSICAL ACTIVITY: PARENT REPORT COMPARED WITH ACCELEROMETRY IN 4-5-YEAR-OLD CHILDREN

5.1 Preamble

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Author contributions for this manuscript are as follows: study conception and design AS, JC, LD, JM, RC, TF; data collection TF, BM; accelerometer processing TF; technical expertise RC; statistical expertise KL; analysis and interpretation of the data TF, AS, JC, JM, LD, RC KL; drafting the manuscript TF, AS, JC, JM, LD, RC, KL, BM. All authors approved the final version of the manuscript.

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The funding sources had no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication. The authors have no conflicts of interest to declare.
5.2 Abstract

**Purpose:** To examine the agreement between parent-reported and accelerometer-measured physical activity (PA) levels in preschool age children, and to determine if agreement differs according to birth group [very preterm (VP); <30 weeks’ gestational age vs. full-term (FT)], sex of the child, social risk, or days of valid data.

**Methods:** Eighty 4- to 5-year-old children (44 VP, 36 FT) wore an Axivity AX3 accelerometer and parents completed a diary for 7 days. Participants with at least one 24-hour period of data were included in the analyses. Bland-Altman plots were used to assess the agreement between the diary and two accelerometer measures of PA (1-minute and stepping) and stationary (1-minute and 5-minute) durations, and sleep durations. Linear regression was used to examine associations between participant characteristics and the differences between the diary and accelerometer measures.

**Results:** Agreement between parent-reported and accelerometer-measured activity was poor for both PA and stationary durations, but better for sleep duration. VP birth was associated with smaller differences between parent-reported and accelerometer-measured 1-minute PA than FT birth. Higher social risk was associated with larger differences between the diary and accelerometer for 1-minute PA, both stationary durations, and sleep duration than lower social risk. There was little evidence for associations between the difference in the two measures with sex or days of valid data.

**Conclusions:** Parent-report diaries may be useful to measure sleep duration in preschool age children, but the large discrepancy between parent-reported and accelerometer-measured PA and stationary durations suggests that the two report different aspects of PA. Future research should
combine parent-reported diaries with accelerometers to provide contextual information of preschool age children’s daily movement behavior obtained alongside the more objective accelerometer measurement.

**Key words:** MOVEMENT BEHAVIOR, SEDENTARY, PRESCHOOL AGE CHILDREN, VERY PRETERM BIRTH, ACCELEROMETRY, PARENT-REPORT DIARY
5.3 Introduction

Participation in physical activity (PA) is recognized as a critical component of health promotion and development in childhood (Ross, Case, & Leung, 2016); it is associated with multiple health benefits (Okely et al., 2012), and is essential for chronic disease prevention (Poitras et al., 2016). However, childhood PA is an international concern, with many children failing to meet established PA guidelines across a number of regions (Berglind et al., 2017; Hinkley et al., 2012; Pate et al., 2015). Until recently, PA guidelines have focused on moderate to vigorous PA (MVPA) which comprises only a small portion of total daily movement (Berglind et al., 2018). In contrast, recent publication of the Canadian 24-hour Movement Guidelines has highlighted the importance of a whole day approach to monitoring movement (Tremblay et al., 2017b). Rather than recommending specific minutes of daily PA or sedentary behavior in isolation, the 24-hour Movement Guidelines integrate recommendations for daily sleep, PA and sedentary time during the preschool years for a healthy 24-hour period. Recent research has found that better adherence to the daily sleep, PA and sedentary/screen time recommendations was associated with higher social-cognitive development in 3- to 6-year-old children (Cliff et al., 2017), although the percentages of children meeting these daily targets were low (Cliff et al., 2017). With researchers beginning to compare the potential health benefits of specific combinations of sleep, PA and sedentary behaviors in preschool children, investigating the validity of subjective and objective measures of 24-hour movement behavior is warranted in this population.

Self or parent-report diaries and questionnaires are commonly used to measure PA in research as they are easily administered and inexpensive (Fukuoka, Haskell, & Vittinghoff, 2016). However, subjective assessment tools can typically overestimate PA participation and are subject to recall bias (Ekelund et al., 2011). With advances in technology, accelerometers are feasible to include in research, and are increasingly used as an objective measure of PA (Migueles et al., 2017).
However, accelerometers cannot provide information regarding the environmental and behavioral context of PA participation, which is useful when designing interventions to improve outcomes (Schnurr et al., 2017). Understanding specific health-related behaviors, such as time spent in screen-based activities, is also important and cannot be ascertained by accelerometers (Dwyer et al., 2011). Incorporating objective measurements of PA alongside self- or parent-report instruments allows researchers to capture the volume, duration and frequency of PA within the context in which it occurs (Ekelund et al., 2011; Truelove et al., 2017). However, understanding the agreement between subjective and objective measures is crucial when choosing or combining PA assessment tools in research to identify potential adverse health outcomes and when deciding if intervention may be indicated. This is particularly important at preschool age, which may be a key period for PA interventions, as children develop major motor competencies during this time (Ferrari et al., 2012) and establish foundations of lifelong PA participation (Henrique et al., 2016). Importantly, determining the efficacy of intervention strategies over time relies on accurate measurement of PA (Fukuoka et al., 2016), which is vital to inform community health initiatives (Hnatiuk et al., 2014).

Children born very preterm (VP; <32 weeks’ gestational age) may have increased risk of physical inactivity and greater sedentary behavior than term-born children due to the multidimensional comorbidities associated with preterm birth, including reduced exercise capacity (Edwards et al., 2015), respiratory morbidity (Been et al., 2014) and poor motor skills (FitzGerald et al., 2018). Yet despite this risk, evidence of compliance with PA guidelines and studies of PA (Lowe et al., 2017), stationary and sleep behavior in preschool age children born VP are lacking. Studies investigating relationships between questionnaire or diary and accelerometer-measured PA, sedentary behavior (Adamo et al., 2009; Dwyer et al., 2011; Nascimento-Ferreira et al., 2018) and sleep (Nascimento-Ferreira et al., 2016) in term-born children have been conducted and found moderate to strong validity of sleep questionnaires with accelerometers, but weaker agreement
between subjective and objective measures of PA and sedentary time. However, similar data are not available for VP children. It is also important to identify other participant characteristics that may affect the agreement between diary and accelerometer-measured PA, sedentary and sleep duration, so that researchers can make evidence-based decisions regarding which assessment tool to select according to the characteristics of their sample.

In order to fill the current gaps in the literature, the primary aim of this study was to examine the agreement between a parent-report diary and accelerometer-measured sleep, PA and stationary duration in 4- to 5-year-old children. The secondary aim was to determine if the agreement between the two measures differed for children born VP and at term, or with sex of the child, higher social risk, or the number of days of recorded data.

5.4 Methods

5.4.1 Study design and participants

Participants were 4- to 5-year-old children recruited into a prospective longitudinal cohort study examining the motor development of children born VP compared with their term-born peers (Spittle et al., 2016). Infants born <30 weeks’ gestation (VP) and at full term (FT) (>36 weeks’ gestation with birthweight ≥2500 g) were recruited between 2011 and 2013 from the Royal Women’s Hospital in Melbourne, Australia. Infants with congenital conditions known to affect neurodevelopment and non-English speaking parents were excluded. Children attended a follow-up appointment between 4- to 5-years’ corrected age. For the purposes of this study, we included a subgroup of the total cohort; the sample size of the subgroup was determined by feasibility and is in line with recent recommendations for stable estimation of agreement between subjective and objective measurement of PA (Nascimento-Ferreira et al., 2018). The inclusion
criteria for this sub-study were participants assessed between April 8 2016 and April 16 2018 with at least one 24-hour period of accelerometer and parent-reported diary data. As we instructed parents to complete the diary based on just the time that they spent with their child, we excluded days when parents reported attendance at childcare, preschool or school to minimize gaps in the diary data. We also excluded non-ambulatory participants as accelerometers were worn on the ankle, precluding obtaining useful data from such participants.

Informed, written consent for the original study and the sub-study was obtained from parents/caregivers for all participants and both were approved by Human Research Ethics Committees at the University of Melbourne and the Royal Children’s Hospital.

5.4.2 Measures

During the follow-up appointment, participants were fitted with a small, water resistant to 1.5 m, tri-axial accelerometer (Axivity AX3, Newcastle Upon Tyne, United Kingdom). This accelerometer was chosen because of its high resolution, sampling rate and bandwidth. The accelerometer was placed inside a removable band (Axivity Wrist Band, Newcastle Upon Tyne, United Kingdom) fitted to the right ankle, and families were provided with written information about the accelerometer. The ankle was chosen due to its logical reflection of gait, and it is well established in research as the optimal position for detecting stepping movements across a range of devices (Korpan, Schafer, Wilson, & Webber, 2015; Storm, Heller, & Mazzà, 2015; Treacy et al., 2017). The participants were asked to wear the accelerometer on their ankle for the next six consecutive days (seven days in total), before returning it by mail in a pre-paid envelope.

At the same appointment, parents/caregivers were provided with a PA diary to be completed for the same seven days that their child wore the accelerometer. The first day (day of the appointment) was completed by the assessor as an example of how to best fill in each section. As
the data entry for the first day was completed before the end of the day and was not estimated by parents, it was incomplete and was therefore excluded from the analysis, leaving a maximum of six days of parent-report. The diary was developed specifically for use in our study (see Supplemental Digital Content 1, parent-report diary), and includes daily sleep and wake times, accelerometer non-wear time, stationary time (screen-based and other stationary activities), and time spent in unstructured and structured PA. We were required to create a custom diary as existing parent-report measures were too lengthy for our study or did not capture certain aspects of PA participation, such as active transport to preschool, school or childcare. We instructed parents/caregivers to complete the diary at the end of each day but did not specifically instruct them to ensure their responses summed to 24-hours. Although not modelled on any existing parent-report tool, aspects of the diary used in our study were similar to the Physical Activity and Exercise for Children Questionnaire (PAEC-Q) which has been validated using accelerometers in preschool age children (Okely et al., 2009). Specifically, the instructions advising parents to only account for the time they spent with their child, the non-screen stationary behaviors and unstructured PA sections of our diary are similar to the PAEC-Q.

Consistent with the Sedentary Behavior Research Network consensus terminology (Tremblay et al., 2017a), we measured stationary behavior as any waking behavior completed while lying, reclining, sitting or standing with no ambulation regardless of energy expenditure. Sedentary behavior (waking behavior characterized by energy expenditure ≤1.5 metabolic equivalents while in a sitting, reclining or lying posture) (Tremblay et al., 2017a) was not directly measured in this study as it is not possible to determine these data from ankle-mounted accelerometers.

Social risk status was obtained using parent questionnaires administered birth/term-equivalent age. When birth/term equivalent age data were incomplete, we used social risk data collected during the one or two-year follow-up appointments. Social risk was assessed using a composite
measure (Roberts et al., 2008) of six aspects of social status: family structure, education of primary caregiver, occupation of primary income earner, employment status of primary income earner, language spoken at home and maternal age at birth. Scores for each item were 0, 1 or 2, with higher social risk categorized as ≥2 overall.

5.4.3 Data management

Variables of interest from the accelerometer and diary data were (all in minutes per day): (1) time spent in PA; (2) stationary duration; and (3) sleep duration. To be included in the analysis, a valid day consisted of 24-hour accelerometer wear (no detectable non-wear), diary completion of the sleep, stationary and PA sections, and an answer of ‘no’ to the attendance at preschool, school or childcare question for the same 24-hour period that the accelerometer was worn. Each variable was averaged across the valid days of accelerometer and diary data for individual participants. The first day of accelerometer data (the day of the participant’s assessment) was removed from analysis, as it did not capture a full 24-hour period. This left a maximum of six days of data for each individual.

Accelerometers were initialized using open source OmGui software (Open Movement, United Kingdom) and set to record for seven days from the time of each participant’s appointment. A sampling rate of 50 Hz, dynamic range of ±8 g and 13-bit analogue to digital conversion were used. Data were downloaded to a specialized analysis program created for our study (by author R.A.C), and high pass filtered from 12.5 Hz to 25 Hz using a Symlet-8 wavelet filter. Each axis was then summed at each time interval. A 200 ms windowed moving average filter was then applied to the data, which effectively transformed the data into a cyclical wave pattern when a stride occurred. A threshold of 0.5 g was then used to identify a step on that limb, with stride thresholds set between 0.5 Hz to 3.33 Hz to remove movements deemed unfeasible for human gait (i.e. too slow or fast to reflect a typical gait-related step).
Accelerometer non-wear was defined as 20 consecutive minutes of no accelerations or angle changes during waking hours. Waking hours were determined by visual inspection of raw accelerometer data. During visual data inspection, the first author (T.L.F) identified periods of non-wear which were confirmed using an automated non-wear algorithm. To improve the accuracy of non-wear time from the accelerometer data, it was pre-processed using the Teager Keiser Energy Operator technique to attenuate signal noise and augment real signal. This approach has been shown to improve the accuracy of manual and automated timing assessments of other physiological signals such as electromyography (Heywood et al., 2018; Solnik, Rider, Steinweg, DeVita, & Hortobágyi, 2010). After this pre-processing, cursors were manually moved to a single location on the data trace which represented non-wear time (if this existed). The cursors were set at the start and end of the period, from which the maximum value was obtained and multiplied by five. This created a non-wear acceleration threshold. The acceleration trace was then iteratively examined to identify any periods of 20 or more consecutive minutes where no data exceeded this threshold, with the entire period deemed non-wear. A semi-automatic method was used to identify the sleep and wake times in accordance with the criterion-reference recommendations of prior research (Tudor-Locke, Barreira, Schuna Jr, Mire, & Katzmarzyk, 2013). When a participant’s sleep or wake times were unclear during visual accelerometer data inspection, we used the average parent-reported sleep or wake time for the whole sample (n=80) to assist with setting accelerometer sleep or wake time.

Due to the lack of consensus regarding accelerometer data management procedures (Migueles et al., 2017), we chose to investigate the relationship between the parent-report diary and two different methods of accelerometer determined PA and stationary duration which are reported separately. Time spent in PA or stationary was first calculated using a minute-by-minute approach (1-minute PA/1-minute stationary), where each non-stationary minute during waking hours was classified as PA and each minute with no recorded steps was classified as stationary.
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An alternative definition of PA was minutes spent stepping (stepping PA), which was calculated as the total time per day performing actual stepping movements during waking hours. An alternative measure of stationary duration was using a 5-minute cut off (5-minute stationary), whereby stationary minutes were only recorded after 5 consecutive minutes in which no steps had been performed during waking hours. There was no equivalent 5-minute PA outcome. The primary PA outcome was 1-minute PA and the primary stationary outcome was 1-minute stationary duration. Sleep duration (minutes per night) was the time between accelerometer determined sleep onset and waking. Summing daily accelerometer 1-minute PA, 1-minute stationary and sleep values per day equates to a full 24-hour period in situations where the accelerometer was worn all the time.

Accelerometer data were processed by the first author (T.L.F) using processing guidelines developed for the current study, and a second author (R.A.C) was consulted when any participant data were unclear. Accelerometer data were processed independently to individual diary data, with the first author blinded to parental responses at the time of accelerometer data processing.

5.4.4 Statistical analysis

Stata (Version 14.2) and Minitab® statistical software were used to analyze these data. As we only included days with full 24-hour accelerometer wear, there were no accelerometer non-wear data. However, as parent-reported non-wear was not an exclusion criterion, we described the proportion of the sample with parent-reported non-wear and the median non-wear duration. Descriptive statistics were calculated using either two-sample t-tests or Chi-square tests to assess differences between included and excluded participant characteristics.
Bland–Altman plots (Bland & Altman, 1986) were used to assess the agreement between diary and accelerometer-measured PA, stationary and sleep duration. The mean differences between the two measures and the 95% limits of agreement (LOA) were calculated. Next, linear regression was used to assess the relationships of the differences between the parent-reported and accelerometer data with birth group (VP vs. FT), sex (male vs. female), social risk (higher vs. lower), and days of valid data (dichotomized at the median; ≤2 vs. >2 days) (independent variables) in both univariable and multivariable models. All linear regression models were fitted using generalized estimating equations (GEEs) to allow for potential clustering between multiple births within a family.

5.5 Results

5.5.1 Participant characteristics

One hundred and forty-five participants were assessed between April 8 2016 and April 16 2018. One hundred and thirty-two participants (91%) returned the accelerometer and parent-report diary by mail. Of these, 16 were excluded due to no 24-hour periods of accelerometer data, including one participant whose accelerometer malfunctioned, 22 were excluded due to no 24-hour periods of diary completion, and 7 were excluded due to no 24-hour periods of both the diary and accelerometer. A further 6 participants were excluded as they attended preschool, school or childcare on days of full diary completion and accelerometer wear. One additional participant was non-ambulant at the time of assessment and was therefore excluded, leaving 80 for analysis (61%). The perinatal characteristics of excluded participants were similar to those included in the study, with the exception of social risk for term-born participants (Table 5.1).
Table 5.1 Participant characteristics

<table>
<thead>
<tr>
<th></th>
<th>Very Preterm</th>
<th>Term-born</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Included (n=44)</td>
<td>Excluded (n=31)</td>
</tr>
<tr>
<td><strong>Gestational age (weeks), mean (SD)</strong></td>
<td>27.8 (1.5)</td>
<td>27.8 (1.3)</td>
</tr>
<tr>
<td><strong>Birthweight (g)</strong></td>
<td>1035 (249)</td>
<td>997 (243)</td>
</tr>
<tr>
<td><strong>Multiple births, n (%)</strong></td>
<td>20 (45)</td>
<td>9 (29)</td>
</tr>
<tr>
<td><strong>Male sex, n (%)</strong></td>
<td>24 (55)</td>
<td>14 (45)</td>
</tr>
<tr>
<td><strong>Higher social risk, n (%)</strong></td>
<td>17 (39)</td>
<td>15 (48)</td>
</tr>
<tr>
<td><strong>Age (years), mean (SD)</strong></td>
<td>4.7 (0.1)</td>
<td>4.7 (0.1)</td>
</tr>
</tbody>
</table>

* Difference between included & excluded participants, p = 0.02. n; number, SD; standard deviation.

In the 80 included participants, the median number of days included in the analysis was 2 per participant (interquartile range (IQR) 2 - 3). Most of the sample was assessed during non-holiday periods (73%; n=58) and were attending preschool (96%; n=77). Seasons varied, with 30% (n=24) assessed during autumn, 29% (n=23) during summer, 21% (n=17) during spring and 20% (n=16) during winter. Ten (13%) parents (3 VP; 7 FT) reported accelerometer non-wear and the median (IQR) duration was 16 (6 - 30) minutes per day. Of the 10 parents who reported accelerometer non-wear, six parents reported fewer than 20 minutes (below the threshold for our definition of non-wear), three parents reported 30 minutes of non-wear and one participant had non-wear time subjectively reported but none observed in the accelerometer trace.

**5.5.2 Agreement between the diary and accelerometer data**

Bland-Altman plots showing the agreement between parent-reported and accelerometer-measured PA, stationary, and sleep duration (minutes per day) for the whole cohort are presented in Figure 5.1. Agreement between parent-reported PA and accelerometer-measured 1-minute PA was poor, with wide LOAs. Moreover, parent-reported PA was consistently lower than accelerometer-measured 1-minute PA values (mean difference -340 minutes). Agreement between parent-reported and accelerometer-measured 1-minute stationary duration was similarly
poor, with most parents under-reporting stationary duration relative to the accelerometer (mean difference -118 minutes). There was better agreement between parent-reported and accelerometer-measured sleep than for 1-minute PA/stationary, as demonstrated by the tighter LOA. However, it was the longest of the three activities, and there was still a tendency for parents to over-report sleep duration relative to the accelerometer by an average of 51 minutes.

With regards to stepping PA, the overall level of agreement was the closest to zero of all the measures (mean difference -37 minutes). Of note, there appeared to be a slight trend for parents to under-report stepping in children with low levels of activity, and over-report stepping in children with higher levels of activity compared with the accelerometer. Using 5-minute stationary duration, the mean difference between the diary and accelerometer was smaller than for 1-minute stationary duration, although LOA were wide for both of these measures.

5.5.3 Associations between participant characteristics and the difference between the diary and accelerometer data

Results from the univariable and multivariable models were similar (see Supplemental Digital Content 2, figure of mean differences from univariable models). We therefore present results from multivariable models for brevity.

There was little evidence that the difference in the diary and accelerometer measures was associated with sex or the number of days of available data for most outcomes (Figure 5.2; see Supplemental Digital Content 3, data table). In contrast, there was evidence that VP birth was associated with smaller differences between parent-reported PA and accelerometer-measured 1-minute PA compared with the term-born group (VP mean difference -289 minutes compared with FT mean difference -346 minutes, p = 0.04, Figure 5.2-a). There was also evidence of larger differences between these two measures of PA in the higher social risk compared with the lower
social risk group (Figure 5.2-a). Similarly, there were larger differences between parent-reported stationary and accelerometer-measured 1-minute stationary duration in the higher social risk than the lower social risk group (Figure 5.2-c). There was evidence that female sex and higher social risk were associated with larger differences in parent-reported stationary and accelerometer-measured 5-minute stationary duration (Figure 5.2-d). Higher social risk was also associated with larger differences in parent-reported and accelerometer-measured sleep duration compared with the lower social risk group (Figure 5.2-e).
Figure 5.1 Bland-Altman plots demonstrating the agreement (average minutes per day) between the parent-report diary and the accelerometer

LLA, lower limits of agreement (-1.96 standard deviations below the mean difference); Mins, minutes; ULA, upper limits of agreement (+1.96 standard deviations above the mean difference)
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Figure 5.2 Mean difference between diary and accelerometer measures by birth group, sex, social risk and available days of data

VP, very preterm; Mean difference (diary minus accelerometer time in minutes); 95% confidence interval (from the regression model including all four independent variables in a single model, values for each subgroup represent the mean difference in that subgroup when all covariates are in the reference (first) group)
5.6 Discussion

The agreement between parent-reported and accelerometer-measured 1-minute PA and stationary duration in 4- to 5-year-old children was poor, with the parent-report diary consistently under-reporting relative to the accelerometer. However, our results show that the parent-report diary more closely agreed with the stepping PA and 5-minute stationary duration than the 1-minute PA and 1-minute stationary duration, suggesting that the shorter duration intermittent activity and stationary behavior may be more difficult to capture subjectively. There was greater agreement between parent-reported and accelerometer-measured sleep than for 1-minute PA and 1-minute stationary duration; however, there was a tendency for parents to over-report sleep duration relative to the accelerometer.

Considering whether the agreement between the two measures was associated with participant characteristics, we found that VP birth was associated with smaller differences in parent-reported PA and accelerometer-measured 1-minute PA; however, there was little evidence of associations between birth group and the agreement between any of the other measures. Higher social risk was associated with greater differences between the parent-report and accelerometer measures of stationary duration and sleep duration, while female sex was associated with larger differences between parent-reported stationary and accelerometer-measured 5-minute stationary duration. Having ≤2 days of complete data compared with >2 days did not appear to be associated with the difference between the parent-report and accelerometer measures for all outcomes.

The results of our study are largely consistent with previous research in typically developing children. A systematic review and meta-analysis investigating the criterion validity of sleep time questionnaires in children and adolescents reported moderate to strong correlation with accelerometers (Nascimento-Ferreira et al., 2016). A more recent systematic review found poor
to moderate correlation between diaries or logs and accelerometer-measured PA duration (Nascimento-Ferreira et al., 2018). However, this study included participants aged 2 to 19 years and did not present results for the preschool age period in isolation. As movement patterns in early childhood are distinct from patterns of older children/adolescents (usually occurring in frequent short bouts of varying intensity (Migueles et al., 2017)) this may explain the differences with our results. Adjusting for participant age has been shown to diminish associations between questionnaire and accelerometer measures, especially for sedentary behavior (Bringolf-Isler et al., 2012), highlighting the need for age-based subgroup analyses in future systematic reviews.

A study investigating the reliability and validity of the Preschool-age Children’s Physical Activity Questionnaire (Pre-PAQ) reported acceptable agreement between Pre-PAQ and accelerometer for total PA (Dwyer et al., 2011). The authors reported mean differences ranging from 21 to 45 minutes for total PA; however, LOA were wide and correlation between the questionnaire and the accelerometer was weak (Pearson’s r 0.05 to 0.16). Agreement between the Pre-PAQ and accelerometer for sedentary behavior was poor (mean differences -208 to -235 minutes) and parents tended to over-report sedentary time on the Pre-PAQ relative to the accelerometer. Mean differences were minimal when investigating stationary time; however, the authors acknowledge clear limitations in their methods of determining accelerometer stationary time which limits comparability of findings to our study.

The considerable methodological variability and lack of transparent reporting of data processing decisions have historically affected comparison of PA and sedentary outcomes between studies (Hnatiuk et al., 2014; Janssen & Cliff, 2015). A key issue is that many of the commercial systems are not suitable for assessment of activity in children. For example, the commonly used ActivPAL3 (PAL Technologies Ltd, Glasgow, UK) has poor validity for assessing fast walking and running in children (Aminian & Hinckson, 2012), which is likely due to the
combination of its low resolution (8-bit), bandwidth (±2g) and sampling frequency (20Hz). A strength of our study lies in using Axivity AX3 accelerometers with an open-source firmware platform. By collecting and processing raw acceleration data, we were able to clearly report data management decisions and algorithms. As specific algorithms used by manufacturers are often not publicly available (Janssen & Cliff, 2015), our approach to accelerometer data management promotes reproducibility and facilitates comparability of our findings. A limitation of the current evidence base is that there is lack of consensus in accelerometer non-wear algorithms and data processing protocols at preschool age (Migueles et al., 2017). We believe that our method of identifying accelerometer non-wear time is a strength, as we combined visual inspection of the raw data with a data de-noising algorithm to ensure accurate detection. We similarly address absence of evidence-based data management recommendations by investigating two different methods of identifying PA (stepping PA and 1-minute PA) and stationary time (1-minute and 5-minute stationary time) and analyzing the relationship between each of these two measures and the parent-report diary separately.

By examining the agreement between subjective and objectively measured PA, stationary and sleep behaviors recorded concurrently, our study is consistent with a recent shift to considering integrated daily movement behaviors, rather than focusing on PA or sedentary duration in isolation. A systematic review investigating associations between 24-hour movement behaviors and health outcomes in 5- to 17-year-old children/adolescents found the most optimal combination was high PA, high sleep and low sedentary time (Saunders et al., 2016). Participants achieving this combination had positive adiposity and cardiometabolic outcomes compared with those who did not meet all three criteria. Subsequently, research investigating associations between different combinations of daily behaviors and health benefits in early childhood is emerging (Berglind et al., 2018; Cliff et al., 2017). For high quality future intervention and
systematic review studies of 24-hour movement patterns, understanding the agreement between subjective and objectively measured PA, sleep and stationary/sedentary time is crucial.

To our knowledge, this is the first study to examine agreement between parent-reported and accelerometer-measured 24-hour movement behaviors in VP populations compared with FT controls. Physical activity participation in children born VP at preschool age is not well understood, as most research has occurred in later childhood and adolescence (Lowe et al., 2017). Children born VP are at higher risk of neurological dysfunction, poorer motor skills and respiratory morbidity when compared with their term-born peers (Been et al., 2014; FitzGerald et al., 2018), all of which may result in less optimal 24-hour movement behaviors. Our findings regarding the agreement between parent-reported and accelerometer-measured PA, stationary and sleep duration specifically for VP participants is the foundation for much needed future research in this population. We also highlight how factors such as social risk and sex may affect the validity of parent-report measures.

Despite the strengths, several methodological limitations of the current study must be acknowledged. A shortcoming of the parent-report diary used in our study is that parents only accounted for the time that their child was with them, and therefore we excluded days when children attended preschool, school or childcare to ensure more accurate comparison of parent-report and 24-hour accelerometer data. Excluding days of preschool, school or childcare attendance reduced the number of available days for analysis. We were, however, unable to determine if children were out of their parent’s care due to other circumstances (for example in the care of grandparents). Parents were also not specifically instructed to ensure their responses summed to 24-hours, which may account for the consistent under-reporting of PA and stationary outcomes in our study. We also acknowledge the limitations which are inherent in parent-report measures, including parental understanding of ‘unstructured play’ compared with
Chapter Five: Physical activity: Parent report compared with accelerometry in 4- to 5-year-old children

'Structured PA' and recording the times children get into or out of bed, as opposed to actual time spent sleeping as is measured by the accelerometer.

Another limitation is that the agreement between parent-reported and accelerometer-measured non-wear was not examined in our study, as we restricted our analysis to days where there was no accelerometer non-wear. We therefore cannot comment on the validity of the non-wear aspect of the parent-report diary, although it is important to note that 13% (n=10) of parents in the study reported accelerometer non-wear which we did not detect when processing the accelerometer data. Of those: (a) six parents reported fewer than 20 minutes, meaning that accelerometer non-wear periods were too short to be defined as non-wear based on our algorithm; (b) three parents reported 30 minutes of non-wear which may have been overestimated and therefore actually below our 20 minute threshold; and (c) one participant had non-wear time subjectively reported but none observed in the accelerometer trace; however, on a different day the opposite occurred and therefore this may have been a subjective recall error. Nevertheless, given the prescribed 24-hour wear time these relatively small non-wear periods would have had minimal impact on the results of this study. It is also worth noting that we were only able to analyze data from 60% of participants, and the median number of included days in analysis were 2 from a maximum of 6 days per participant. However, our results show that having ≤2 days of complete data compared with >2 days was weakly associated with the difference between the diary and accelerometer measures. Furthermore, as study participants wore the accelerometer on their ankle, we were unable to capture upper limb exercise and activity. One final limitation of our study is the representativeness of our study sample. According to the inclusion criteria, our sample comprised families with at least one 24-hour period of parent-report and accelerometer data meaning our results may not be generalizable to those with poorer compliance.
In conclusion, we found that the parent-report diary may be useful in measuring sleep duration in preschool age children. However, the large discrepancy between parent-reported and accelerometer-measured PA and stationary outcomes suggests the subjective measure recorded by parents should be used with caution to capture duration of movement behavior in this population. Our study also highlights how birth group, participant social risk status and sex may influence parent-reporting of 24-hour movement behaviors relative to accelerometers in preschool age populations. Future research should focus on studying VP preschool age children and strive to combine parent-report diaries with accelerometry to obtain contextual information alongside objective measurement of preschool age children’s daily movement behavior. Studies using accelerometers should ensure transparent reporting of accelerometer methodology to facilitate comparison between studies, and further study of relationships between subjective and objective accelerometer non-wear detection is warranted.
5.7 Supplementary material

**Supplemental Digital Content 1**

**PHYSICAL ACTIVITY DIARY**

<table>
<thead>
<tr>
<th>Study number:</th>
<th>Day 1 date: ____________________</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 1</td>
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<tr>
<td>Day 1</td>
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<td>Day 2</td>
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<td>Day 4</td>
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<td>Day 5</td>
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<tr>
<td>Day 6</td>
<td></td>
</tr>
<tr>
<td>Day 7</td>
<td></td>
</tr>
</tbody>
</table>

Please answer the following questions as best as you can for the time your child was with you each day. Estimate any times in hours, including decimals.

**Sleep time last night**

- Time: __________ : __________ : __________

**Wake time this morning**

- Time: __________ : __________ : __________

**Did you child take off the activity monitor today?**

- Yes/No

**If yes, record time with monitor off (hours)**

- Time: __________

**Time watching TV/videos/playing computer/video games/playing on smart phones or tablets (hours)**

- Time: __________

**Time spent in quiet play e.g. reading/being read to/drawing/painting/puzzles/games (hours)**

- Time: __________

**Did your child attend childcare/kinder/school today?**

- Yes/No

**If yes, did they travel by active transport?**

- Please circle type of active transport if applicable.

  - Walk/Bike/Scooter

**Time spent participating in active unstructured play e.g. playground, climbing, running, skipping, hula hoops (hours)**

- Time: __________

**Did your child participate in active structured play today?**

- Yes/No

**If yes, please tick type of activity**

- Swimming
- Football
- Dance/Gymnastics
- Trampolining
- Athletics
- Walking (e.g. walking the dog)
- Bike riding
- Tennis
- Cricket
- Netball/Basketball
- Soccer
- Martial arts
- Other

**If yes, record time spent in total (hours)**

- Time: __________
**Supplemental Digital Content 2**

Figure. Mean difference between diary and accelerometer measures for birth group, sex, social risk and available days of data

VP, very preterm; * Mean difference (diary minus accelerometer time in minutes); ** 95% confidence interval (from univariable model); ¹ significant difference between the groups
**Supplemental Digital Content 3**

Table. Associations between birth group, sex, social risk, and available days of data with difference between diary and accelerometer measures (diary minus accelerometer time in minutes) – results from multivariable analyses

<table>
<thead>
<tr>
<th>Multivariable Analysis</th>
<th>State</th>
<th>Independent variables</th>
<th>Mean difference, (95% CI) P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sleep</td>
<td>VP</td>
<td>-14.7 (-33.0, 3.6) p = 0.12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Male sex</td>
<td>2.2 (-14.7, 19.1) p = 0.80</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Higher social risk</td>
<td>31.7 (11.0, 52.4) p = 0.003</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≤2 days of data</td>
<td>6.1 (-10.1, 22.4) p = 0.46</td>
</tr>
<tr>
<td></td>
<td>1-minute PA*</td>
<td>VP</td>
<td>56.8 (17.6, 96.0), p = 0.004</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Male sex</td>
<td>-4.5 (-45.9, 37.0), p = 0.83</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Higher social risk</td>
<td>-44.0 (-87.6, 0.4), p = 0.048</td>
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<tr>
<td></td>
<td></td>
<td>≤2 days of data</td>
<td>-16.8 (-59.3, 25.7), p = 0.44</td>
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<tr>
<td></td>
<td>1-minute stationary*</td>
<td>VP</td>
<td>-18.8 (-67.6, 30.0), p = 0.45</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Male sex</td>
<td>50.6 (-0.2, 101.5), p = 0.051</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Higher social risk</td>
<td>-72.2 (-131.4, -13.0) p = 0.02</td>
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<tr>
<td></td>
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<td>≤2 days of data</td>
<td>26.4 (-23.4, 76.3), p = 0.30</td>
</tr>
<tr>
<td></td>
<td>Stepping PA*</td>
<td>VP</td>
<td>15.5 (-27.3, 58.4) p = 0.48</td>
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<td></td>
<td>Male sex</td>
<td>-12.0 (-53.2, 29.1) p = 0.57</td>
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<td></td>
<td></td>
<td>Higher social risk</td>
<td>-18.2 (-61.6, 25.1), p = 0.41</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≤2 days of data</td>
<td>-10.6 (-53.4, 32.2) p = 0.63</td>
</tr>
<tr>
<td></td>
<td>5-minute stationary*</td>
<td>VP</td>
<td>-17.4 (-66.18, 31.9), p = 0.49</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Male sex</td>
<td>53.1 (1.6, 104.7), p = 0.04</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Higher social risk</td>
<td>-60.2 (-120.2, -0.2) p = 0.049</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≤2 days of data</td>
<td>23.5 (-26.8, 73.8) p = 0.40</td>
</tr>
</tbody>
</table>

* Indicates negative mean difference between diary and accelerometer values. CI, confidence intervals; PA, physical activity; VP, very preterm
CHAPTER SIX

STRENGTH, MOTOR COMPETENCE AND PHYSICAL ACTIVITY IN VERY PRETERM AND TERM-BORN PRESCHOOL AGE CHILDREN

Chapter 6 is formatted as a manuscript in preparation for submission to Pediatrics:

Strength, motor competence and physical activity in very preterm and term-born preschool age children

When submitted, the final manuscript will include data for all participants who attended the VIBeS 4- to 5-year follow-up. The manuscript presented in this chapter includes data for 72% of the final cohort.
6.1 Abstract

Strength, motor competence and physical activity in very preterm and term-born preschool age children

**Background:** Preschool age children born very preterm (<32 weeks’ gestation; VP) experience poorer motor outcomes and higher rates of neurological impairment than full-term (FT) children, but little is known about physical activity (PA) participation. This study aimed to compare motor outcomes across the ICF-CY framework body structure and function, activity and participation domains between VP and FT preschool age children.

**Methods:** Ninety-eight VP and 84 FT children were assessed at 4 - 5 years. Outcomes were: grip strength (kg), the Movement Assessment Battery for Children 2nd edition (MABC-2), the Little Developmental Coordination Disorder Questionnaire (Little DCDQ), accelerometer-measured PA and a parent-completed PA diary. Linear regression and mixed effects models were used to examine differences between VP and FT children.

**Results:** Children born VP had poorer grip strength (e.g. preferred hand mean difference 95% confidence interval [CI] -0.6 kg [-1.1, -0.04], p= 0.04) and poorer motor competence (MC) (MABC-2 standard score mean difference -2.3 [-3.4, -1.2], p<0.001; Little DCDQ total score mean difference -5.0 [-8.7, -1.3], p=0.01). VP children completed fewer minutes of accelerometer-measured PA (mean difference -45 minutes, [-71, -19], p= 0.001), more minutes of accelerometer-measured stationary behavior (mean difference 43 minutes, [17, 70], p= 0.001), and more parent-reported screen time (mean difference 20 minutes, [7, 33], p= 0.003) per day.
Conclusions: Preschool age children born VP had poorer outcomes than FT children within all ICF-CY domains. Differences in PA between VP and FT children emerge in early childhood, which suggests enhanced surveillance and promotion of PA in VP populations is warranted at preschool age.

What’s known on the subject: Preschool age children born very preterm (VP) experience diverse motor challenges compared with their term-born peers. However, research into physical activity (PA) participation is sparse in this age group and there have been few recent studies examining strength outcomes.

What this study adds: Children born VP had poorer grip strength and motor skills than term-born children. In this novel study using accelerometry and parent-report, preschool age children born VP participated in less PA and had more screen and stationary behaviors than term-born children.
6.2 Introduction

Preterm birth is a substantial cause of global mortality and morbidity in childhood (Blencowe et al., 2013). Survivors of preterm birth are at higher risk of adverse respiratory health (Been et al., 2014; Edwards et al., 2015), poorer cognitive performance (Bhutta, Cleves, Casey, Cradock, & Anand, 2002) and impaired neurodevelopment (Olsen et al., 2018). Preschool age children born very preterm (VP; <32 weeks’ gestational age) also experience diverse motor challenges compared with their term-born peers, including higher risk of neurological dysfunction and poorer performance on standardized motor assessment (FitzGerald et al., 2018). The International Classification of Functioning, Disability and Health children and youth version (ICF-CY) framework (World Health Organisation, 2007) is a comprehensive method of conceptualizing the varied motor comorbidities associated with preterm birth across body structure and function, and activity and participation domains. Within the ICF-CY framework, preschool age children born VP experience greater body structure and function impairment and activity limitation compared with term-born children (FitzGerald et al., 2018).

Muscle strength is classified as a body function outcome within the ICF-CY (World Health Organisation, 2007), and at preschool age, greater muscle strength has been shown to have a beneficial effect on skeletal development (Herrmann et al., 2015). In adulthood, grip strength can be used as an indicator of health, as poorer grip strength has been associated with functional impairment (Al Snih et al., 2004), poorer mental health (Norio et al., 2015), cardiovascular disease, and all-cause mortality (Leong et al., 2015). Children born VP may experience poorer grip strength compared with their term-born peers due to a range of factors associated with prematurity and intra-uterine development (Inskip et al., 2007). An adverse fetal environment, as indicated by low birth weight (LBW; <2500 g), has been linked with alterations in muscle fiber composition and size (Jensen, Storgaard, Madsbad, Richter, & Vaag, 2007). A systematic review
and meta-analysis found a positive association between birth weight and muscle strength (measured predominantly by grip strength) across the lifespan (Dodds et al., 2013). However, only one study in the review investigated the association between birth weight and grip strength in early childhood (Ford et al., 1988) and was not included in the meta-analysis.

Within the activity domain, the term ‘motor competence’ (MC) encompasses concepts such as motor proficiency and fundamental motor skill performance, and is used to describe goal-directed movement (Robinson, 2015). Evidence of poorer MC in VP populations compared with term-born controls is widely reported in the literature (FitzGerald et al., 2018). However, there are several important methodological limitations within the current evidence base at preschool age, including widely varying assessment tools, variable age correction for prematurity and exclusion of children with more severe impairments such as CP (FitzGerald et al., 2018). Preschool age is an important study time point, as development of MC in early childhood forms the foundation for successful participation in a wide variety of physical activities (Henrique et al., 2016).

Physical activity (PA) is a key participation domain outcome in early childhood, as higher PA levels are associated with various physical and mental health benefits (Okely et al., 2012). Poor compliance to existing PA guidelines by typically developing preschool age children has been reported in the literature (Berglind et al., 2017; Ellis et al., 2017; Hinkley et al., 2012). The Australian physical activity guidelines (Okely et al., 2017) were recently updated to integrate recommendations for PA, sedentary behavior and sleep to form an ideal 24-hour period. A healthy 24-hour period for 3- to 5-year old children should include at least 180 minutes of PA (of which at least 60 minutes is energetic play), no more than 60 minutes of sedentary behavior at a time, screen time limited to no more than 60 minutes per day, and 10 to 13 hours of sleep (Okely et al., 2017). Recent studies have reported poor compliance with these recommendations.
in Australia (Cliff et al., 2017; Santos et al., 2017) and with similar 24-hour guidelines internationally (Chaput et al., 2017). Despite extensive PA research in typically developing children, the PA participation of children born VP compared with term-born controls at preschool age is poorly understood.

The current study addresses several important gaps in the literature. There has been limited recent research of grip strength in preschool age VP and/or VLBW children compared with term-born controls, and further high-quality study of motor competence in VP populations at preschool age is warranted. Despite clear evidence of body structure and function impairment, and activity domain limitations in VP populations at preschool age, there has been limited research into participation outcomes (FitzGerald et al., 2018), especially PA (Lowe et al., 2015). Thus, the aims of this study are to compare motor outcomes across the ICF-CY domains of body structure and function, activity and participation by examining grip strength, MC and the PA levels of preschool age children born VP with their term-born peers.

6.3 Methods

6.3.1 Participants and study design

Participants in this study were a subset of the Victorian Infant Brain Study-2 (VIBeS2) cohort; a prospective longitudinal cohort study of infants born VP and term-born controls. The VIBeS2 methods have been comprehensively reported elsewhere (Spittle et al., 2016). Very preterm (n=149) and term-born (n=151) infants were recruited between 2011 and 2013 from the Royal Women’s Hospital in Melbourne, Australia. Very preterm infants were born <30 weeks’ gestation and term-born infants were >36 weeks’ gestation with birthweight ≥2500 g. Exclusion criteria included congenital abnormalities known to affect neurodevelopment, non-English speaking parents (due to questionnaires needing to be completed in English), and term-born
participants admitted to a neonatal intensive care unit or a special care nursery. Participants were serially assessed from birth to 3 years of age, and those attending the 4- to 5-year follow up time-point were included in the current study. The study was approved by the Human Research and Ethics Committees at the Royal Children’s Hospital in Melbourne, Australia, and parents gave written informed consent for their child to participate.

6.3.2 Procedures and assessment tools

Data collection for the VIBeS2 4- to 5-year follow-up assessment commenced on April 8 2016 and ceased for the current study on June 15 2018, with a total of 182 participants (98 VP, 84 FT). Participants attended follow-up appointments between 4- and 5-years’ corrected age (CA) and were preferentially assessed before they commenced formal schooling (which is usually the year when the child turns 5 by the 30th of April in Melbourne, Australia). Age was corrected for prematurity to avoid introduction of bias caused by underestimating the performance of children born preterm (Wilson-Ching et al., 2014). The motor assessments were completed by trained physiotherapists and an exercise scientist, who were blinded to medical history (including gestational age) and previous assessment results. When families were unable to attend the outpatient setting, a home visit was completed using a modified protocol as some equipment could not be transported.

During the assessment, height and weight were recorded using the same standardized procedure and a calibrated seca 284 stadiometer (seca gmbh & co. kg., California, USA) for each participant. Lower limb length was measured bilaterally from the anterior superior iliac spine to the medial malleolus. Grip strength (force in kg) was measured using a calibrated Smedley digital hand dynamometer (Model: 12-0286, Baseline® New York, USA) with the child seated, the shoulder adducted and neutrally rotated, elbow flexed at 90° and the forearm and wrist in a neutral position. The preferred hand of each participant was recorded during the assessment.
When hand preference was unclear, the hand used to draw during the manual dexterity component of the motor assessment was recorded as the preferred hand. Grip strength of the preferred and non-preferred hands were measured, as well as bilateral grip strength. A practice phase preceded three formal trials of each condition and the maximum value of each trial was recorded.

Motor competence was assessed using the Movement Assessment Battery for Children, 2nd Edition (MABC-2), a reliable and valid tool for the assessment of motor development in children aged 3- to 16-years (Henderson et al., 2007). Participants were also assessed with the Little Developmental Coordination Disorder Questionnaire (Little DCDQ), a parent report measure of 15 items describing fine and gross motor abilities (Wilson et al., 2015). The Little DCDQ was developed to screen 3- to 4-year-old children who may be at risk of a formal Developmental Coordination Disorder (DCD) diagnosis at school age and is a reliable and valid measure for early identification of motor difficulties (Wilson et al., 2015).

Physical activity was measured objectively using an accelerometer and subjectively with a parent-report diary. A tri-axial accelerometer (Axivity AX3, Newcastle Upon Tyne, United Kingdom) was placed inside a band (Axivity Wrist Band, Newcastle Upon Tyne, United Kingdom) and fitted to each participant’s right ankle during the follow-up appointment. The ankle was chosen due to its logical reflection of gait, and it is well established in research as the optimal position for detecting stepping movements across a range of devices (Korpan et al., 2015; Storm et al., 2015; Treacy et al., 2017). The participants wore the accelerometer for the next 6 consecutive days before the family returned it by mail in a pre-paid envelope. The AX3 accelerometer is water resistant to 1.5 m, and parents were instructed to not remove it during swimming and bathing where possible.
During the same seven days that the accelerometer was worn, parents completed a PA diary (Appendix D). The first day (day of the appointment) was completed by the assessor as an example of how to best fill in each section, leaving six days of parent-report. The diary was returned by mail alongside the accelerometer and was created specifically for VIBeS2. The diary included daily sleep and wake times, accelerometer non-wear duration, time spent in stationary activities (screen-based or other stationary activities) and physical activities. We instructed parents to complete the diary at the end of each day, based on just the time that they spent with their child. Parents were not specifically instructed to ensure their responses summed to 24-hours.

Consistent with the Sedentary Behavior Research Network consensus terminology (Tremblay et al., 2017a), we measured stationary behavior as any waking behavior completed while lying, reclining, sitting or standing with no ambulation regardless of energy expenditure. Sedentary behavior defined as waking behavior characterized by energy expenditure \( \leq 1.5 \) metabolic equivalents while in a sitting, reclining or lying posture (Tremblay et al., 2017a) was not measured in this study. Social risk status was obtained using parent questionnaires administered at birth/term-equivalent age, one or two years of age. Social risk was assessed using a composite measure (Roberts et al., 2008) of six aspects of social status: family structure, education of primary caregiver, occupation of primary income earner, employment status of primary income earner, language spoken at home and maternal age at birth. Scores for each item were 0, 1 or 2, with higher social risk categorized as \( \geq 2 \) overall. When birth/term equivalent age data were incomplete, we used social risk data collected during the one or two-year follow-up appointments.
6.3.3 Data management

All data collected during the assessment protocol were scored by trained, blinded assessors and entered into the VIBeS2 REDcap database, except the Little DCDQ which was completed online by parents using a link to the REDcap database. Participants who were unable to complete the MABC-2 due to motor impairment (e.g. CP) were given the lowest possible standard score (1) and percentile (0.1). However, participants who did not complete the assessment due to behavior (e.g. task refusal) or cognitive impairment were treated as missing data.

Accelerometers were initialized using open source OmGui software (Open Movement, United Kingdom) and set to record for seven days from the time of each participant’s appointment. The first day of accelerometer data (the day of the participant’s assessment) was removed from analysis, as it did not capture a full 24-hour period. This left a maximum of six days of accelerometer data for analysis. A sampling rate of 50 Hz, dynamic range of +/- 8 g and 13-bit analogue to digital conversion were used. Data were downloaded to a specialized analysis program created for our study. Further accelerometer processing technical information is detailed in Appendix E. Accelerometer data were processed according to a pre-determined guideline (Appendix F). Accelerometer non-wear was defined as 20 consecutive minutes of no accelerations or angle changes during waking hours. During visual raw data inspection, periods of non-wear were identified and confirmed using an automated non-wear algorithm. Days of data containing accelerometer non-wear were excluded from the primary analysis. Participants with accelerometer non-wear overnight were included in secondary analysis if \( \geq 12 \) hours of accelerometer wear were recorded during waking hours.

Accelerometer-determined outcomes were obtained using different methods to capture the spectrum of daily movement behaviors and results are reported separately for each outcome.
A detailed summary of each accelerometer and diary outcome is presented in Appendix H. Time spent in PA was calculated using a minute-by-minute approach (1-minute PA), where each non-stationary minute was calculated during waking hours. A subset of 1-minute PA duration was minutes spent stepping each day (Stepping PA). Time spent in ‘fast steps’ was calculated as another subgroup of 1-minute PA and was used as a proxy measure of moderate to vigorous PA (MVPA) in the study. The modal stride rate over the days of accelerometer wear (Hz) was multiplied by 1.31 to identify a threshold for fast gait for each individual participant (Lim et al., 2016). The number of steps above the fast gait threshold were recorded per day (number of fast steps), and the time each child spent stepping above this threshold was then summed to obtain minutes per day spent in fast gait (minutes of MVPA). The duration of stationary behavior was obtained by summing each minute with no recorded steps during waking hours. Stationary bouts during waking hours were also calculated for each participant and were defined as >5 consecutive minutes of no steps being recorded during times when the accelerometer was worn. Minutes of sleep duration were identified from sleep onset to waking each night of accelerometer wear (see Appendix E for further technical information regarding accelerometer identification of sleep and wake times).

To summarize, accelerometer outcomes included in the study were: (a) minutes per day: total PA (1-minute PA), stepping PA, MVPA, stationary duration, sleep duration; and (b) number per day: total steps, fast steps and stationary bouts. Parent-reported outcomes were all measured in minutes per day, and were: total PA, unstructured PA, structured PA, screen time, total stationary duration (screen plus non-screen stationary activities) and sleep duration.

6.3.4 Statistical analysis

Data were analyzed using Stata (Version 14.2, StataCorp, Texas, USA). Associations between VP birth and grip strength (kg) were examined using separate univariable linear regression models
for bimanual, preferred and non-preferred hand conditions. Multivariable analysis was completed combining birth group (VP vs. term-born), sex (male vs. female) and body weight (kg) (independent variables). Body mass index and height (cm) were added to the multivariable analysis; however, body weight (kg) had the strongest relationship with grip strength and was therefore included in the final model. Each linear regression model was fitted with generalized estimating equations (GEEs) to allow for clustering of multiple births within a family.

Univariable linear regression models fitted with GEEs were used to investigate associations between VP birth and MABC-2 total standard scores, MABC-2 subscale standard scores (manual dexterity, aiming and catching, and balance subscales), and Little DCDQ total scores.

Univariable logistic regression models, again fitted with GEEs, were used to examine associations between VP birth and MABC-2 and Little DCDQ cut-off scores. Cut-off scores were defined as ≤5\(^{th}\) percentile and <16\(^{th}\) percentile overall for the MABC-2. Little DCDQ cut-off scores for children falling in the ‘suspect for DCD’ category were defined as ≤67 for males and ≤68 for females (Wilson et al., 2015). Linear and logistic regression models were repeated combining birth group, sex, social risk (higher vs. lower) and CA at assessment (independent variables) in multivariable analysis. As the Little DCDQ is designed for children aged 3 to 4 years, sensitivity analyses were completed excluding participants older than 4 years 11 completed months at the time of assessment. When GEE models could not be fitted correctly, linear and logistic regression analyses clustering for twins were completed and reported with robust standard errors.

Compliance with the accelerometer and the diary was examined by the number (%) of full days of accelerometer wear (days without detectable non-wear) and full diary completion (answers to all sleep, PA and stationary questions). Mixed effects models were used to examine associations between VP birth and accelerometer and diary outcomes, allowing for the differing number of
included days between participants. Mixed effects models were repeated combining birth group, sex, social risk, data from weekend or holiday periods (yes vs. no), the day of data (day 1 to 6), attendance at preschool, school or childcare (yes vs. no) and season (daylight saving vs. non-daylight saving periods). In Melbourne, Australia, daylight saving fell between the first Sunday of October and the first Sunday of April during the data collection period of this study. The independent variables ‘attendance at preschool, school or childcare’ and ‘data from weekend or holiday periods’ were distinct from one another, as there were non-holiday weekdays when children were not attending preschool, school or childcare. Mixed effects models examining the association between VP birth and accelerometer-measured number of fast steps and minutes of MVPA were both adjusted for average lower limb length (cm), as individual stride rates were used to determine the fast gait cut off threshold. Descriptive statistics were calculated using either two-sample t-tests or Chi-square tests to assess differences between included participants and those with missing accelerometer and diary data.

Adherence to the Australian 24-hour Movement Guidelines (Okely et al., 2017) was examined by calculating the mean minutes of accelerometer-measured stepping PA, MVPA, sleep and parent-reported screen time over the available days of data for each participant. The proportion of VP and term-born children meeting or exceeding the recommendations was calculated for PA, MVPA, sleep and screen time duration separately and repeated to assess compliance with all four recommendations combined. Stepping PA was chosen as the accelerometer measure of PA as it was deemed a more accurate method of assessment than 1-minute PA (Appendix E). This study did not examine compliance with the overall sedentary behavior recommendation, as the exact lengths of accelerometer-measured stationary bouts were not recorded. Furthermore, multiple comparisons were not adjusted for because the analyses were considered to be exploratory only, and would need confirmation in subsequent studies.
6.4 Results

6.4.1 Participant characteristics

One hundred and eighty-two participants were included in the analysis (98 VP, 84 term-born). The characteristics of the sample are presented in Table 6.1. Forty-two percent of VP participants were twins/triplets, while all term-born participants were singletons. There was an even spread of males and females in both groups and most participants were attending preschool at the time of the assessment. A greater proportion of VP participants was of higher social risk status than term-born participants. On average, children born VP were shorter and lighter than their term-born peers, although BMI was similar between the groups (Table 6.1). At the time of assessment, six children born VP had a diagnosis of CP. Of those with CP, 5 were classified as Gross Motor Function Classification System (GMFCS) level I and one was classified as GMFCS level IV.

Table 6.1 Characteristics of included participants (n=182)

<table>
<thead>
<tr>
<th></th>
<th>Very preterm n=98</th>
<th>Term-born n=84</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age (weeks), mean (SD) [range]</td>
<td>27.9 (1.5) [24.1 – 29.9]</td>
<td>40 (1.2) [37 – 42]</td>
</tr>
<tr>
<td>Birthweight (g), mean (SD) [range]</td>
<td>1037 (259) [529 – 1613]</td>
<td>3532 (431) [2700 – 4744]</td>
</tr>
<tr>
<td>Multiple births, n (%)</td>
<td>41 (42)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Sex (male), n (%)</td>
<td>50 (51)</td>
<td>41 (49)</td>
</tr>
<tr>
<td>Higher social risk, n (%)</td>
<td>40 (42)</td>
<td>20 (25)</td>
</tr>
<tr>
<td>Attending preschool, n (%)</td>
<td>88 (90)</td>
<td>79 (94)</td>
</tr>
<tr>
<td>CA at assessment (years), mean (SD) [range]</td>
<td>4.7 (0.1) [4.4 – 5.0]</td>
<td>4.8 (0.1) [4.3 – 5.2]</td>
</tr>
<tr>
<td>Weight at assessment (kg), mean (SD) [range]</td>
<td>17.4 (3.0) [11.9 – 34.5]</td>
<td>19.2 (2.3) [14.9 – 25.0]</td>
</tr>
<tr>
<td>Height at assessment (cm), mean (SD) [range]</td>
<td>106.2 (5.1) [93.0 – 118.4]</td>
<td>109.7 (4.5) [97.9 – 117.4]</td>
</tr>
<tr>
<td>Body mass index, mean (SD) [range]</td>
<td>15.3 (1.6) [12.5 – 24.6]</td>
<td>15.9 (1.2) [13.6 – 20.4]</td>
</tr>
</tbody>
</table>

* data for 96 VP and 80 term-born participants; † data for 97 VP & 82 term-born participants; ¤ data for 82 term-born participants; CA, corrected age; cm, centimeters; kg, kilograms; n, number; SD, standard deviation
6.4.2 Grip strength of VP and term-born children

One hundred and sixty-two participants (79 VP, 83 term-born) completed at least one grip strength condition (preferred hand, non-preferred hand or bimanual conditions). Of the 20 (19 VP, 1 term-born) participants with missing grip strength data, 17 were unable to complete the assessment as the dynamometer was unavailable (delay in equipment delivery). Of the remaining 3 participants, one was unable to be assessed due to behavior (task refusal), one due to cognitive impairment and one due to dynamometer equipment failure.

There was evidence that children born VP had lower peak grip strength compared with term-born controls on both preferred and non-preferred hands, but evidence for a difference in peak bimanual grip strength between the groups was weaker (Figure 6.1-a, Table 6.2). When combined with body weight (kg) and sex in multivariable analyses, the evidence for the association between VP birth and grip strength weakened for all conditions.

Body weight had the strongest association with peak grip strength for preferred hand (mean difference 0.3 kg per kg increase in body weight, 95% confidence interval [CI] 0.2, 0.4, p<0.001) and non-preferred hand (mean difference 0.2 kg per kg increase in body weight, 95% CI 0.1, 0.3; p<0.001). However, evidence of an association was weak for the bimanual condition (mean difference 0.2 kg per kg increase in body weight, 95% CI -0.03, 0.4; p= 0.09). There was little evidence for associations between male sex and any of the grip strength conditions (all p values >0.05).
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Figure 6.1 Differences between very preterm and term-born children across ICF-CY domains

A&C, aiming and catching subscale; DCD, Developmental Coordination Disorder; Kg, kilograms; Little DCDQ, Little Developmental Coordination Disorder Questionnaire; MABC-2, The Movement Assessment Battery for Children second edition; MD, manual dexterity subscale; PA, physical activity; ss, standard score. * Note: outcome not shown: accelerometer-measured stationary bouts per day
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Table 6.2 **Body Structure and Function Domain:** Grip strength (peak value in kg)\(^*$\) of children born very preterm compared with their term-born peers

<table>
<thead>
<tr>
<th>Grip strength condition</th>
<th>Very Preterm n= 78</th>
<th>Term-born n= 83</th>
<th>Univariable analysis</th>
<th>Multivariable analysis**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean difference(^*) (95% CI), p value</td>
<td>Mean difference(^*) (95% CI), p value</td>
</tr>
<tr>
<td>Preferred hand</td>
<td>6.6 (1.6)</td>
<td>7.2 (1.7)</td>
<td>-0.6 (-1.1, -0.04), p= 0.04</td>
<td>0.1 (-0.4, 0.6), p= 0.80</td>
</tr>
<tr>
<td>Non-preferred hand</td>
<td>6.3 (1.6)</td>
<td>6.9 (1.8)</td>
<td>-0.6 (-1.2, -0.1), p= 0.02</td>
<td>-0.1 (-0.7, 0.4), p= 0.58</td>
</tr>
<tr>
<td>Bimanual</td>
<td>11.0 (2.9)</td>
<td>11.7 (3.3)</td>
<td>-0.8 (-1.8, 0.1), p= 0.09</td>
<td>-0.4 (-1.4, 0.6), p= 0.40</td>
</tr>
</tbody>
</table>

* Peak values of three trials per condition; ** independent variables in multivariable analysis: VP birth (mean difference values shown); body weight (kg) and male sex; \(^*\) mean differences are from linear regression with models fitted using generalized estimating equations to allow for clustering of twins; \(^\sim\) data for 82 term-born participants. CI, confidence interval; kg, kilograms; n, number; SD, standard deviation
6.4.3 Motor competence of VP and term-born children

One hundred and seventy-eight children completed the MABC-2 assessment (95 VP, 83 term-born). Of those without MABC-2 data (3 VP, 1 term-born), one participant was unable to complete the assessment due to significant motor impairment (GMFCS IV CP) and was given the lowest possible MABC-2 standard score and percentile overall and for all subscales. One participant was unable to complete the MABC-2 due to cognitive impairment, and two owing to behavior (task refusal); all three participants were treated as missing data. However, Little-DCDQ data were obtained for the three participants who did not complete the MABC-2.

On univariable analysis, there was strong evidence that VP birth was associated with lower MABC-2 total standard scores and Little DCDQ total scores compared with term-born children (Figure 6.1-b, Table 6.3), which remained strong when combined with sex, social risk and CA in multivariable analyses. Very preterm birth was also associated with lower MABC-2 standard scores within the manual dexterity, aiming and catching and balance subscales. Evidence for the associations between VP birth and poorer performance on MABC-2 subscales persisted in multivariable analyses for aiming and catching, and balance, but became weaker for manual dexterity (Figure 6.1-b, Table 6.3). Higher social risk was not strongly associated with MABC-2 scores (mean difference: -1.0 to -0.3, p= 0.09 to 0.6) or Little DCDQ total scores (mean difference: -2.9, 95% CI 7.7, 1.7; p= 0.5) in linear multivariable analysis. Similarly, CA was not substantially associated with MABC-2 scores (mean difference: 0.2 to 2.0, p= 0.4 to 0.9) or Little DCDQ scores (mean difference: -5.1, 95% CI -20.1, 10.7; p= 0.5).
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Table 6.3 **Activity Domain:** Motor competence of children born very preterm compared with their term-born peers

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Very Preterm n=96</th>
<th>Term-born n=83</th>
<th>Univariable Analysis Mean difference (95% CI), p value**</th>
<th>Multivariable analyses Mean difference (95% CI), p value**</th>
</tr>
</thead>
<tbody>
<tr>
<td>MABC-2 standard score</td>
<td>8.9 (3.3)</td>
<td>11.0 (3.5)</td>
<td>-2.3 (-3.4, -1.2), p &lt; 0.001</td>
<td>VP birth -2.0 (-3.2, -0.7), p= 0.002</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Male sex -1.7 (-2.6, -0.7), p= 0.001</td>
</tr>
<tr>
<td>MABC-2 MD standard score^</td>
<td>9.2 (3.7)</td>
<td>11.0 (3.6)</td>
<td>-1.8 (-3.0, -0.7), p= 0.001</td>
<td>VP birth -1.3 (-2.6, .03), p= 0.055</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Male sex -2.2 (-3.2, -1.2), p&lt;0.001</td>
</tr>
<tr>
<td>MABC-2 A&amp;C standard score^^</td>
<td>9.7 (3.3)</td>
<td>11.0 (3.1)</td>
<td>-1.3 (-2.2, -0.3), p= 0.01</td>
<td>VP birth -1.2 (-2.4, -0.06), p= 0.04</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Male sex -0.1 (-1.1, 0.9), p= 0.84</td>
</tr>
<tr>
<td>MABC-2 Bal standard score</td>
<td>8.4 (2.9)</td>
<td>10.5 (3.5)</td>
<td>-2.2 (-3.2, -1.2), p&lt; 0.001</td>
<td>VP birth -1.9 (-3.1, -0.7), p= 0.002</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Male sex -1.5 (-2.4, -0.5), p= 0.002</td>
</tr>
<tr>
<td>Little DCDQ total score^+</td>
<td>63.3 (12.4)</td>
<td>68.2 (8.4)</td>
<td>-5.0 (-8.7, -1.3), p= 0.01 ++</td>
<td>VP birth -5.2 (-9.7, -0.7), p= 0.02 ++</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Male sex -0.7 (-4.5, 3.1), p= 0.72 ++</td>
</tr>
</tbody>
</table>
**Table 6.3 continued. Activity Domain: Motor competence of children born very preterm compared with their term-born peers**

<table>
<thead>
<tr>
<th>Cut off scores</th>
<th>Very Preterm n=95</th>
<th>Term-born n=83</th>
<th>Univariable Analysis</th>
<th>Multivariable analyses †</th>
<th>Independent variables</th>
<th>p value †</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%) below cut off</td>
<td>n (%) below cut off</td>
<td>OR (95% CI), p value †</td>
<td>OR (95% CI), p value †</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MABC-2 ≤5th percentile</td>
<td>18 (19)</td>
<td>4 (5)</td>
<td>4.5 (1.4, 14.2), p= 0.01</td>
<td>VP</td>
<td>2.1 (0.6, 7.4), p= 0.23</td>
<td></td>
</tr>
<tr>
<td>MABC-2 &lt;16th percentile</td>
<td>24 (25)</td>
<td>11 (13)</td>
<td>2.3 (1.0, 5.1), p= 0.052</td>
<td>VP</td>
<td>1.4 (0.6, 3.5), p= 0.42</td>
<td>Male sex</td>
</tr>
<tr>
<td>'Suspect for DCD' ^ ^</td>
<td>44 (50) #</td>
<td>30 (41) # #</td>
<td>1.4 (0.7, 2.6), p= 0.40</td>
<td>VP</td>
<td>1.4 (0.7, 3.1,) p= 0.38</td>
<td>Male sex</td>
</tr>
</tbody>
</table>

† Independent variables in multivariable models: VP birth, male sex, higher social risk and corrected age. † † Mean differences from linear regression with models fitted using generalized estimating equations (GEEs) to allow for clustering of multiple births within the same family, † † n= 97 VP and 84 term-born participants, † † † n= 98 VP and 84 term-born participants, † † † † n=88 VP and n=74 term-born participants, † † † † † mean differences from linear regression models clustering for twin births and reported with robust standard errors as GEE models did not fit, † † † † † † odds ratios from logistic regression models fitted with GEEs to allow for clustering of multiple births within the same family, † † † † † † † Cut off scores on Little DCDQ for females ≤68; cut off scores for males ≤67, # data for n=88 VP participants, # # data for 74 term-born participants. A&C, aiming and catching subscale; Bal, Balance subscale; CI, confidence interval; DCD, Developmental Coordination Disorder; Little DCDQ, Little Developmental Coordination Disorder Questionnaire; MABC-2, The Movement Assessment Battery for Children, 2nd edition; MD, manual dexterity subscale; n, number; SD, standard deviation.
Very preterm birth was associated with greater odds of scoring ≤5th percentile and scoring <16th percentile on the MABC-2 compared with term-born participants (Figure 6.1-c, Table 6.3). However, evidence for associations between VP birth and scoring below the cut-off scores weakened when combined with sex, social risk and CA in multivariable analysis. Consistent with linear regression results, CA was not strongly associated with scoring ≤5th percentile (OR 0.04, 95% CI 0.001, 3.6; p = 0.2) and <16th percentile (OR 0.2, 95% CI 0.01, 4.0; p = 0.3). Higher social risk was also not strongly associated with scoring ≤5th percentile (OR 2.6, 95% CI 0.9, 7.3; p = 0.08) or <16th percentile (OR 1.6, 95 % CI 0.7, 3.6; p = 0.3).

Logistic regression models examining the odds of being classified as ‘suspect for DCD’ by the Little DCDQ showed little difference between the groups (Figure 6.1-c, Table 6.3). Higher social risk (mean difference 1.7, 95% CI 0.8, 3.4; p = 0.2) and CA (mean difference 2.6, 95% CI 0.2, 31.6, p = 0.5) were not strongly associated with being classified as ‘suspect for DCD’. Sensitivity analyses removing nine participants who were older than 4 years 11 completed months’ CA from the DCDQ analyses did not change the between group conclusions from the linear (mean difference -5.4, 95% CI -10.0, -0.8; p = 0.02) or logistic regression outcomes (OR 1.6, 95% CI 0.7, 3.5; p = 0.3).

6.4.4 Physical activity participation of VP and term-born children

6.4.4.1 Accelerometer-measured physical activity participation

Of the 182 participants included in the study, 7 lost or did not return the accelerometer and 25 returned the accelerometer without any acceptable days for analysis (19 VP, 13 term-born). Perinatal and demographic characteristics were similar between the included and excluded groups (Supplementary Table 1). One hundred and thirty-eight participants (76%; 72 VP, 66 term-born) returned the accelerometer with at least one full 24-hour period of wear and were
included in the primary analysis. An additional 12 participants had accelerometer non-wear overnight but \( \geq 12 \) hours wear during the day and were included in the secondary analysis (total \( n = 150; 82\% \)). Of those included in the primary analysis, 39\% (\( n = 54 \)) wore the accelerometer for the full six days without detectable non-wear. The mean (SD) number of days included in the primary analysis was 4.5 (1.3) days. A summary of accelerometer outcomes for VP and term-born participants is shown in Table 6.4.

Very preterm birth was associated with less daily PA on all accelerometer measures, except for minutes spent in MVPA (Figure 6.1-d, Table 6.5). Children born VP participated in fewer minutes of PA per day (1-minute & stepping PA) and took fewer steps per day than their term-born peers. Evidence for the associations between VP birth and 1-minute PA, stepping PA and steps per day remained strong in multivariable analyses. Despite weak evidence for the association between VP birth and minutes of MVPA per day, evidence for an association with the number of fast steps per day strengthened in multivariable analysis, with fewer fast steps per day for children born VP. Average lower limb length (cm) was not strongly associated with minutes of MVPA (mean difference: -0.5 minutes, 95 \% CI -0.9, 0.03; \( p = 0.06 \)) or number of fast steps (mean difference: -74 steps, 95 \% CI -158, 11; \( p = 0.09 \)). Very preterm birth was associated with more minutes of stationary behavior (Figure 6.1-d, Table 6.5) and a higher number of stationary bouts per day, although the mean difference in bouts between the groups was minimal. Evidence for the association between VP birth and stationary minutes per day persisted when analyzed in multivariable analysis but weakened for stationary bouts (Table 6.5). Associations between VP birth and accelerometer outcomes were not attributed to any difference in accelerometer-measured waking hours between the groups (sleep duration: mean difference 2.2 minutes, 95 \% CI -10.3, 14.6; \( p = 0.7 \)).
Chapter Six: Group differences within ICF-CY domains

Table 6.4 **Participation Domain**: Summary of accelerometer and diary outcomes for children born very preterm and their term-born peers

<table>
<thead>
<tr>
<th>Accelerometer outcome</th>
<th>VP n=72</th>
<th>Term-born n=66</th>
<th>Diary outcome</th>
<th>VP</th>
<th>Term-born</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>minutes per day</td>
<td>n Mean (SD)</td>
<td>n Mean (SD)</td>
</tr>
<tr>
<td>1-minute PA, minutes</td>
<td>482.8 (118.2)</td>
<td>531.2 (91.8)</td>
<td>Total PA</td>
<td>69</td>
<td>154.5 (100.3)</td>
</tr>
<tr>
<td>Stepping PA, minutes</td>
<td>182.7 (63.2)</td>
<td>204.4 (59.9)</td>
<td>Unstructured PA</td>
<td>76</td>
<td>120.8 (84.5)</td>
</tr>
<tr>
<td>MVPA, minutes</td>
<td>21.2 (13.2)</td>
<td>22.8 (9.3)</td>
<td>Structured PA</td>
<td>74</td>
<td>28.5 (51.1)</td>
</tr>
<tr>
<td>Stationary, minutes</td>
<td>352.1 (115.6)</td>
<td>307.1 (85.5)</td>
<td>Total stationary</td>
<td>76</td>
<td>214.8 (119.4)</td>
</tr>
<tr>
<td>Sleep time, minutes</td>
<td>605.2 (58.4)</td>
<td>601.7 (51.0)</td>
<td>Screen time</td>
<td>77</td>
<td>95.5 (57.6)</td>
</tr>
<tr>
<td>Steps per day, n</td>
<td>13,451 (5,108)</td>
<td>15,370 (4,556)</td>
<td>Sleep time</td>
<td>67</td>
<td>655.8 (59.0)</td>
</tr>
<tr>
<td>Fast steps per day, n</td>
<td>4,602 (2,540)</td>
<td>4,987 (1,874)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stationary bouts, n</td>
<td>23.9 (7.0)</td>
<td>22.1 (6.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MVPA, moderate to vigorous physical activity; n, number; PA, physical activity; SD, standard deviation; VP, very preterm
### Table 6.5 Participation Domain: Accelerometer-determined physical activity levels of children born very preterm and their term-born peers

<table>
<thead>
<tr>
<th>Univariable Analysis</th>
<th>Multivariable analyses</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean difference (95% CI), p value</td>
</tr>
<tr>
<td>Outcome</td>
<td>VP birth</td>
</tr>
<tr>
<td>(per day)</td>
<td>VP birth</td>
</tr>
<tr>
<td>1-minute PA, minutes</td>
<td>-45.2 (-71.3, -19.1), p&lt;0.001</td>
</tr>
<tr>
<td>Stepping PA, minutes</td>
<td>-25.5 (-37.5, -7.4), p=0.002</td>
</tr>
<tr>
<td>MVPA, minutes**</td>
<td>-1.8 (-5.1, 1.5), p=0.28</td>
</tr>
<tr>
<td>Stationary minutes</td>
<td>43.1 (16.7, 70.0), p=0.001</td>
</tr>
<tr>
<td>Sleep, minutes</td>
<td>2.2 (-10.3, 14.6), p=0.73</td>
</tr>
<tr>
<td>Steps, n</td>
<td>-2005 (-3230, -780), p=0.001</td>
</tr>
<tr>
<td>Fast steps, n**</td>
<td>-452 (-1063, 159), p=0.15</td>
</tr>
<tr>
<td>Stationary bouts, n</td>
<td>1.8 (0.2, 3.3), p=0.03</td>
</tr>
</tbody>
</table>

* Mean differences from mixed effects models, ** average lower limb length (cm) included as a covariate in the multivariable model. CI, confidence interval; n, number; PA, physical activity; VP, very preterm
Children were more physically active on weekends or during holiday periods than non-holiday weekdays for all measures of PA, but evidence was weak for stationary duration (Table 6.5). Conversely, children participated in less PA (as measured by 1-minute PA, stepping PA and total steps per day) and more minutes of stationary behavior during periods of non-daylight saving compared with daylight saving periods. Attendance at preschool, school or childcare was associated with more 1-minute PA time and less stationary time than days of non-attendance. As indicated by the day of data, children tended to be more active towards the end of the monitoring period, although the mean difference (minutes) was low. There was weak evidence for a difference in PA or stationary outcomes between the sexes, except for higher stepping PA and total steps per day in males. Higher social risk was not associated with any accelerometer PA or stationary outcomes.

The secondary analysis including participants with accelerometer non-wear overnight, but with ≥12 hours wear during the day (n=12 additional participants), had minimal effect on accelerometer results (Supplementary Table 2). Evidence for an association between VP birth and minutes of MVPA strengthened in the secondary multivariable analysis. However, the mean difference in minutes of MVPA was small (-4.3 minutes, 95% CI -8.3, -0.3; p= 0.04).

6.4.4.2 Parent-reported physical activity participation

The parent-report diary was returned for 153 participants (84%; 80 VP, 73 term-born). The perinatal characteristics of participants with missing parent-report data were similar to the included participants; however a larger proportion of term-born children with missing data was of higher social risk (p= 0.02; Supplementary Table 1). The number of VP and term-born participants with data for each part of the parent-report diary fluctuated and is reported in Table 6.4 alongside mean (SD) values for each parent-reported outcome. Of the 153 participants included in analysis, only 33% (n=51) had 6 complete days of diary data.
Very preterm birth was associated with less unstructured PA and more screen time per day in both the univariable and multivariable analyses (Figure 6.1-d, Table 6.6). Very preterm birth was associated with less parent-reported total PA; however, evidence for the association weakened in the multivariable analysis. There was weak evidence for associations between VP birth and parent-reported structured PA participation and total stationary duration in univariable and multivariable analysis. Consistent with the accelerometer results, the associations between VP birth and daily unstructured PA and screen time were not attributable to differences in parent-reported waking hours between the groups (sleep duration: mean difference 5.5 minutes, 95% CI -6.1, 16.9; p= 0.4).

Male sex and higher social risk status were associated with more and fewer minutes of total and unstructured PA respectively, but associations were weak for stationary outcomes (Table 6.6). Weekends and holiday periods were associated with fewer minutes of screen time and total stationary duration, and more unstructured and total PA per day compared with non-holiday weekdays. Attendance at preschool, school or childcare was similarly associated with less screen time, total stationary and structured PA per day than on non-attending days, but evidence for associations with other PA outcomes were weak. Non-daylight saving periods were associated with more minutes of screen time and stationary behavior, but evidence for associations with PA outcomes was weak.
### Table 6.6 Participation Domain: parent-reported physical activity levels of children born very preterm and their term-born peers

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Univariable Analysis</th>
<th>Multivariable analyses</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean difference (95% CI), p value</td>
<td>Mean difference (95% CI), p value</td>
</tr>
<tr>
<td></td>
<td>VP birth</td>
<td>Male sex</td>
</tr>
<tr>
<td>Total PA</td>
<td>-34.0 (-63.3, -4.7), p = 0.02</td>
<td>-26.6 (-54.5, 1.2), p = 0.06</td>
</tr>
<tr>
<td>Unstructured PA</td>
<td>-33.5 (-56.9, -10.0), p = 0.005</td>
<td>-24.0 (-46.3, -1.8), p = 0.03</td>
</tr>
<tr>
<td>Structured PA</td>
<td>8.1 (-5.3, 21.4), p = 0.24</td>
<td>8.3 (-5.6, 22.2), p = 0.24</td>
</tr>
<tr>
<td>Total Stationary</td>
<td>17.9 (-11.2, 47.1), p = 0.20</td>
<td>12.5 (-15.2, 40.2), p = 0.38</td>
</tr>
<tr>
<td>Screen time</td>
<td>19.6 (6.6, 32.6), p = 0.003</td>
<td>17.4 (4.3, 30.6), p = 0.01</td>
</tr>
<tr>
<td>Sleep</td>
<td>5.4 (-6.1, 16.9), p = 0.35</td>
<td>3.5 (-7.9, 14.9), p = 0.55</td>
</tr>
</tbody>
</table>

* Minutes per day; **mean differences from mixed effects models. CI, confidence interval; n, number; PA, physical activity; VP, very preterm
6.4.4.3 Adherence to Australian physical activity guidelines

Figure 6.2 shows the adherence of 72 VP and 66 term-born participants to the Australian 24-hour Movement Guidelines using accelerometer data, and adherence of 77 VP and 73 term-born children to the screen time recommendation using parent-report data. A higher proportion of term-born children (n=49, 74%) achieved the recommended ≥180 minutes of PA per day compared with children born VP (n= 41, 57%). Only one VP participant, and none of the term-born participants, met the recommended ≥60 minutes of MVPA per day. One additional VP participant completed 59.3 minutes of MVPA per day (Figure 6.2). The proportion of VP and term-born children meeting the daily screen time recommendations was low for both groups (term-born 40%, n=29), but lower for VP born children (n=16, 21%). The recommended 10-13 hours of sleep was achieved by half of VP (n=38, 53%) and term-born (n=34, 52%) children.

One hundred and thirty (94%; 66 VP, 64 term-born) participants had data for accelerometer PA, MVPA, sleep duration and parent-reported screen time combined. As only one participant achieved the recommended minutes of MVPA per day, <1% participants met the combined Australian 24-hour Movement Guidelines. Combining the PA, screen and sleep recommendations, only 12% (n=16) complied. The proportion of VP and term-born participants adhering to the PA, screen and sleep guidelines were low but similar (VP 11%, n=7, term-born 14%, n=9).
Chapter Six: Group differences within ICF-CY domains

Figure 6.2 Proportion of very preterm (n=72) and term-born (n=66) children meeting or exceeding the Australian 24-hour Movement Guidelines

- Mean values over available days of monitoring for each participant, red line representing recommended minutes per day for each activity, low minutes per day due to participant who was non-ambulant at the time of the assessment, green shaded box: participants meeting/exceeding recommendation, red shaded box: participants who did not meet recommendation.

* for parent-reported screen time: VP n=73, FT n=77. FT, term-born participants; Min, minutes; VP, very preterm participants; Data points jittered: ‘jitter(10)’. 
6.5 Discussion

This study found that preschool age children born VP have poorer motor outcomes than their term-born peers within multiple ICF-CY domains. Within the body structure and function domain, children born VP had lower grip strength than term-born children on preferred and non-preferred hands. However, group differences diminished when adjusted for body weight and sex. Children born VP performed more poorly on activity domain outcome measures than their term-born peers, with lower MABC-2 standard scores and total Little DCDQ scores. Within the participation domain, children born VP were less physically active and participated in more stationary behavior than term-born children as indicated by all accelerometer measures, except for minutes of MVPA. Parents of children born VP also reported fewer minutes of total and unstructured PA, and more minutes of screen time per day than parents of term-born children. Adherence to the Australian 24-hour Movement Guidelines was poor for both groups, although a smaller proportion of VP born children met PA and screen time recommendations than term-born children.

Prior to this study, the most recent work examining grip strength in VP/VLBW preschool age children was published in 1988 (Ford et al., 1988). Ford and colleagues (1988) compared the grip strength of 24 VLBW and 18 normal birthweight children at 5 years of age, finding a 12-15% reduction for VLBW participants relative to controls. These authors used a different grip strength testing procedure than implemented in the current study, and in contrast to our findings, reported that reduced grip strength for VLBW participants persisted even when adjusted for body weight. Within the VLBW group, Ford and colleagues (1988) found no relationship between grip strength and birthweight, gestational age or sex. However, Dodds and colleagues (2013) reported a 0.9 kg increase in muscle strength per additional kilogram of birthweight when adjusted for age, gender and height in a meta-analysis (Dodds et al., 2013). The
youngest participants included in the meta-analysis were 9 years of age, highlighting the paucity of studies investigating grip strength for VP/VLBW children in early childhood. Further study of grip strength at preschool age is required to examine how early in life group differences may emerge.

The results of the current study are consistent with existing literature examining the motor competence of preschool age children born VP compared with term-born peers measured by a range of assessment tools (FitzGerald et al., 2018). In line with our findings, others have reported that preschool age children born VP perform more poorly on the MABC-2 overall than term-born children, as well as within the manual dexterity (De Rose et al., 2013; van Hus et al., 2014) and aiming and catching subscales (De Rose et al., 2013). At 4 years of age, children born VP have demonstrated poorer postural control and performance on balance tasks than term-born controls (Lorefice et al., 2015), which is consistent with our finding of lower MABC-2 balance subscale standard scores for VP participants.

To our knowledge, this is the first study to investigate accelerometer-measured and parent-reported PA participation in children born VP compared with their term-born peers at preschool age. Prior to the current study, the youngest cohort to be studied were 34 VLBW and 24 NBW 5- to 7-year old children (Keller et al., 1998). Using a parent questionnaire to investigate PA patterns and factors influencing participation, the authors found no differences between the groups. Research of PA participation in preterm populations has otherwise occurred in older children and adolescents, and has relied of self-report measures rather than accelerometry (Lowe et al., 2015). Our study is also the first to examine VP preschool age children’s adherence to the Australian 24-hour Movement Guidelines (Okely et al., 2017). Overall, the proportion of children in the current study who met the movement guidelines was consistent with recent
reports of poor compliance in typically developing preschool age children (Chaput et al., 2017; Cliff et al., 2017).

The current study contributes to a greater understanding of the trajectory of PA participation in VP populations by demonstrating that differences between VP and term-born children emerge as young as 4 years of age on both objective and subjective measures of PA. A major strength lies in combining the accelerometer and parent-report diary to comprehensively measure PA participation. Our previous work investigating the agreement between the parent-report diary and the accelerometer highlights that such tools capture different aspects of 24-hour movement behaviour in preschool age populations and should be used in combination in research (FitzGerald et al, Chapter 5). Objectively collecting minutes of PA and stationary behavior alongside environmental and contextual factors from the parent-report diary, may lead to more opportunities for translation and implementation of the research than if each tool were collected in isolation. For example, combining minutes of stationary behavior with parent-reported screen time, and minutes of PA per day with participation in unstructured or structured PA, has the potential to inform intervention studies and public health initiatives. Further, by collecting data over full 24-hour periods, this study adds to the growing evidence base examining adherence to integrated 24-hour Movement Guidelines both in Australia (Cliff et al., 2017; Santos et al., 2017) and internationally (Berglind et al., 2018; Chaput et al., 2017). By demonstrating that adherence to the Australian 24-hour Movement Guidelines are poor, we highlight that targeted intervention and health promotion strategies are warranted at preschool age, especially for children born VP.

The transparent accelerometer data management and processing protocol used in this study is another strength, as it facilitates reproducibility and comparison of outcomes. Physical activity research has been limited by lack of consistent accelerometer data management procedures and clear methodological reporting (Hnatiuk et al., 2014), as algorithms used by manufacturers are
often not available to the public (Janssen & Cliff, 2015). However, Axivity AX3 accelerometers enable researcher-driven data processing protocols and detailed reporting of data management decisions due to an open-source firmware platform and unforced sampling of raw acceleration data (Doherty et al., 2017). Processing raw acceleration data in the current study made it possible to combine visual data inspection with a de-noising algorithm (Appendix E) to detect participant non-wear. The rigorous approach to accelerometer non-wear detection, as well as inclusion of participants with full 24-hour periods of accelerometer wear in the primary analysis, ensures that minutes of non-wear were unlikely to be categorized as stationary behavior and introduce bias to the study. Collecting raw data in the current study also facilitated an individualized approach to determining PA intensity, by using each participant’s cadence cut points to determine time spent in MVPA and the number of fast steps per day.

Despite the strengths of the study, several limitations must be acknowledged. Excluding participants with accelerometer non-wear during waking hours affects the generalizability of results to those with poor compliance. A larger proportion of children with missing accelerometer and/or parent-report data was of higher social risk than included participants, most noticeably for term-born controls, which affects the representativeness of the sample. However, the sample was more complete for grip strength and motor competence outcomes. The current study included all available participants in grip strength and motor competence analysis regardless of their level of motor impairment, therefore avoiding the trend within the wider evidence base of excluding VP children from analysis based on unfavorable outcome, and subsequent overestimation the VP group’s performance (FitzGerald et al., 2018).

A shortcoming of the parent-report diary used in the study is that parents did not account for the time that their child was at preschool, school or childcare, and therefore the diary did not capture a full 24-hour period on those days. Subsequently, the parent-report diary did not
capture qualitative information of PA, stationary and screen behaviors in the preschool, school or childcare context. As the current study found attendance at preschool, school or childcare to be associated with more minutes of PA and less stationary time, obtaining contextual information alongside the objective data would be useful to examine potential environmental predictors of PA. Finally, despite the benefit of individualizing the measurement of MVPA in this study, participants with a higher modal stride rate may have been disadvantaged by a high fast gait threshold, with less opportunity to accumulate steps (and minutes) above the fast gait cut off.

6.6 Conclusions

The current study found that children born VP have poorer outcomes within the body structure and function, activity and participation domains of the ICF-CY compared with their term-born peers. To our knowledge, this study is the first to examine group differences between VP and term-born preschool age children within the participation domain. Children born VP participate in less PA and more stationary behavior than their term-born peers. Given the clear associations between higher PA levels and multiple health benefits (Carson et al., 2017; Poitras et al., 2016) and recognition that PA levels can track from early childhood into adulthood (Telama et al., 2014), our study highlights the need for enhanced surveillance and promotion of PA in VP populations at preschool age.

Future research should continue to investigate PA participation in VP populations at preschool age, and combine subjective measures with accelerometry to comprehensively assess daily movement behavior. Studies using accelerometers should ensure transparent reporting of accelerometer methodology to facilitate comparison of outcomes between studies. As preschool age children born VP are less physically active, and a higher proportion are failing to meet
Australian 24-hour Movement Guidelines than term-born children, researchers should begin to examine potentially modifiable predictors of low PA levels in VP children to identify opportunities for early intervention.
### 6.7 Supplementary material

#### Supplementary Table 1 Characteristics of included vs. excluded participants: accelerometer and parent-report data

<table>
<thead>
<tr>
<th></th>
<th>Very preterm</th>
<th></th>
<th>Term-born</th>
<th></th>
<th>Very preterm</th>
<th>Missing data</th>
<th>Term-born</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Included</td>
<td>Excluded</td>
<td>Included</td>
<td>Excluded</td>
<td>Included</td>
<td>Missing data</td>
<td>Included</td>
<td>Missing data</td>
</tr>
<tr>
<td>n</td>
<td>n= 79</td>
<td>n=19</td>
<td>n=71</td>
<td>n=13</td>
<td>n= 80</td>
<td>n= 18</td>
<td>n= 73</td>
<td>n=11</td>
</tr>
<tr>
<td>Gestational age (weeks), mean (SD)</td>
<td>27.9 (1.5)</td>
<td>27.9 (1.3)</td>
<td>40.0 (1.2)</td>
<td>40.2 (1.5)</td>
<td>27.9 (1.5)</td>
<td>27.7 (1.4)</td>
<td>40.0 (1.2)</td>
<td>39.9 (1.5)</td>
</tr>
<tr>
<td>Birthweight (grams), mean (SD)</td>
<td>1025 (253)</td>
<td>1089 (279)</td>
<td>3556 (415)</td>
<td>3406 (516)</td>
<td>1028 (250)</td>
<td>1078 (298)</td>
<td>3559 (418)</td>
<td>3354 (500)</td>
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<tr>
<td>Multiple births, n (%)</td>
<td>35 (44)</td>
<td>6 (32)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>34 (43)</td>
<td>7 (39)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Sex (male), n (%)</td>
<td>38 (48)</td>
<td>12 (63)</td>
<td>35 (49)</td>
<td>6 (46)</td>
<td>40 (50)</td>
<td>10 (56)</td>
<td>37 (51)</td>
<td>4 (36)</td>
</tr>
<tr>
<td>Higher social risk, n (%)</td>
<td>32 (41)</td>
<td>8 (47)^[a]</td>
<td>15 (22)^[#]</td>
<td>5 (45)^</td>
<td>34 (43)^[^^]</td>
<td>6 (35)^[+]</td>
<td>15 (21)^[++]</td>
<td>5 (56)^[&amp;]</td>
</tr>
<tr>
<td>Attending preschool, n (%)</td>
<td>70 (89)</td>
<td>18 (95)</td>
<td>68 (96)</td>
<td>11 (85)</td>
<td>72 (90)</td>
<td>16 (89)</td>
<td>70 (96)</td>
<td>9 (81)</td>
</tr>
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<td>CA at assessment (years), mean (SD)</td>
<td>4.6 (0.1)</td>
<td>4.6 (0.1)</td>
<td>4.8 (0.1)</td>
<td>4.9 (0.1)</td>
<td>4.7 (0.1)</td>
<td>4.6 (0.1)</td>
<td>4.8 (0.1)</td>
<td>4.9 (0.1)</td>
</tr>
</tbody>
</table>

* Participants included in primary and secondary analysis, ^ data for 17 very preterm participants, # data for 69 term-born participants, * data for 79 very preterm participants, + data for 17 very preterm participants, ++ data for 71 term-born participants, & data for 9 term-born participants. CA, corrected age; n, number, SD, standard deviation. Note two-sample $t$-tests or Chi-square tests were used to compare characteristics between included and excluded participants: all $p$ values $\geq0.05$ except higher social risk for term-born participants ($p= 0.02$).
### Supplementary Table 2 Secondary analysis: Accelerometer-determined physical activity levels of children born very preterm and term-born (n=150)

<table>
<thead>
<tr>
<th>Univariable Analysis</th>
<th>Multivariable analyses</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outcome</strong></td>
<td>Mean difference (95% CI), p value**</td>
</tr>
<tr>
<td><strong>Mean difference</strong></td>
<td><strong>Mean difference</strong></td>
</tr>
<tr>
<td><strong>PA</strong> min</td>
<td><strong>Stationary</strong> min</td>
</tr>
<tr>
<td>VP birth</td>
<td>Male sex</td>
</tr>
<tr>
<td>-41.7 (-67.4, -16.0), p=0.001</td>
<td>-38.4 (-64.0, -12.7), p=0.003</td>
</tr>
<tr>
<td>Stepping</td>
<td>-22.6 (-37.4, -7.9), p=0.003</td>
</tr>
<tr>
<td>PA min</td>
<td>-2.0 (-5.1, 1.6), p=0.22</td>
</tr>
<tr>
<td>MVPA min</td>
<td>36.7 (0.5, 62.8), p=0.006</td>
</tr>
<tr>
<td>Stationary min</td>
<td>0.1 (-12.4, 12.6), p=0.99</td>
</tr>
<tr>
<td>Steps, n</td>
<td>-1944 (-3131, -757), p=0.001</td>
</tr>
<tr>
<td>Fast steps, n</td>
<td>-429 (-1015, 156), p=0.15</td>
</tr>
<tr>
<td>Stationary bouts, n</td>
<td>1.6 (0.1, 3.1), p=0.04</td>
</tr>
</tbody>
</table>

* Per day, **mean differences from mixed effects models, ^average lower limb length (cm) included as a covariate in the multivariable model. CI, confidence interval; min, minutes; MVPA, moderate to vigorous physical activity; n, number; PA, physical activity; VP, very preterm
CHAPTER SEVEN

ASSOCIATIONS BETWEEN GRIP STRENGTH, MOTOR COMPETENCE AND PHYSICAL ACTIVITY IN VERY PRETERM AND TERM-BORN PRESCHOOL AGE CHILDREN

Chapter 7 is formatted as a manuscript in preparation for submission to Developmental Medicine and Child Neurology:

Associations between grip strength, motor competence and physical activity in very preterm and term-born preschool age children

When submitted, the final manuscript will include data for all participants who attended the VIBeS2 4- to 5-year follow-up. The manuscript includes data for 72% of the final cohort and the participants and outcomes presented in this chapter are the same as the ones which appear in Chapter 6.

Additional background information has been included in the preamble prior to the manuscript to expand on theoretical frameworks underpinning the research presented in this chapter, and to discuss the research in context with the previous thesis chapters.
7.1 Preamble

The ICF-CY framework underpins the research in this thesis and has been comprehensively described in Chapter 1. A second framework (Figure 7.1; see Appendix J for permission to reproduce) which is integral to the research presented in Chapter 7, describes the developmental mechanisms influencing PA trajectories in children (Stodden et al., 2008). The model hypothesises dynamic relationships depending on the developmental period, and includes perceived motor competence and health-related physical fitness (HRPF) as potential mediators on the central relationship between MC and PA. Stodden and colleagues (Stodden et al., 2008) suggest that high actual and perceived MC, PA participation and HRPF lead to healthy weight status which positively feeds back into the model. This process is conceptualised as a 'positive spiral of engagement'. Conversely, a ‘negative spiral of disengagement’ occurs as a result of lower levels of MC, PA and HRPF leading to overweight and obesity.

![Figure 7.1 Developmental mechanisms influencing physical activity trajectories of children (Stodden et al., 2008)](image)

EC, early childhood; LC, late childhood; MC, middle childhood
Chapter Seven: Associations between ICF-CY domains at preschool age

Preschool age is a ‘window of opportunity’ for motor development (Barnett, Ridgers, Zask, & Salmon, 2015), as children begin to learn fundamental motor skills consisting of object control skills (throwing, catching, kicking), and locomotor skills (running, jumping, hopping) during this time (Logan et al., 2012). Stodden and colleagues hypothesise that in early childhood (2 to 5 years of age), participation in PA drives the development of MC (Stodden et al., 2008). Motor competence is proposed to promote HRPF in early childhood, as the time spent learning fundamental motor skills places higher demand on the neuromuscular system (Stodden et al., 2008). Health-related physical fitness, which includes cardiorespiratory fitness, flexibility and muscular strength and endurance (King-Dowling et al., 2018), is in turn developed by participation in PA in the early childhood period. The relationships presented in the theoretical model are hypothesised to be weak in early childhood, and to strengthen with age.

As outlined in Chapter 6, preschool age children born VP have poorer motor outcomes than their term-born peers within the ICF-CY body structure and function, activity and participation domains. However, Chapter 3 highlights that due to the paucity of participation research in VP preschool age populations, little is known about whether established body structure and function impairments and activity limitations ultimately influence participation outcomes. This chapter will investigate the associations between ICF-CY domains by examining grip strength (body structure and function), motor competence (activity) and PA (participation) in 4- to 5-year-old children, determining if associations differ for children born VP compared with term-born controls.
Chapter Seven: Associations between ICF-CY domains at preschool age

7.2 Abstract

Associations between grip strength, motor competence and physical activity in very preterm and term-born preschool age children

**Aim:** To investigate associations between International Classification of Functioning, Disability and Health children and youth version (ICF-CY) framework domains by examining grip strength, motor competence (MC) and physical activity (PA) in 4-5-year-old children, determining if associations differ between very preterm (VP; <32 weeks’ gestation) and term-born children.

**Method:** One hundred and eighty-two children (98 VP, 84 term-born) were assessed at 4-5 years’ corrected age. Outcomes were: peak bimanual grip strength, the Movement Assessment Battery for Children, 2nd edition (MABC-2), the Little Developmental Coordination Disorder Questionnaire (Little DCDQ) and 7-day accelerometry. Associations between outcomes were examined using regression and mixed effects models.

**Results:** PA was positively associated with Little DCDQ total score (minutes per unit increase in total score; 2.3, 95% confidence interval [CI] 1.0, 3.5; p<0.001), and negatively associated with stationary behaviour: (minutes per unit increase in total score; -1.5, 95% CI -2.9, -0.2; p= 0.03). MC was positively associated with grip strength (p<0.05). Positive associations for PA with MABC-2 balance standard score, and balance standard score with grip strength, were stronger for VP children than term-born children. There was little evidence for associations between PA and grip strength.
**Interpretation:** Associations were found between PA and MC, and MC and grip strength in 4-5-year-old children. Associations between PA and balance, and balance and grip strength were stronger for VP than term-born children.

**Shortened title:** Associations between ICF-CY domains at preschool age

**What this paper adds:**

- More physical activity is associated with higher motor competence in 4-5-year-old children, with little difference between VP and term-born children.
- Greater grip strength is associated with higher motor competence in 4-5-year-old children, with little difference between VP and term-born children.
- More physical activity is associated with better balance, and better balance is associated with greater grip strength in VP children.
7.3 Introduction

Higher levels of physical activity (PA) in early childhood have been consistently linked with improved psychosocial and cardiometabolic health, as well as cognitive and motor development (Carson et al., 2017). The foundation of lifelong optimal PA participation begins in early childhood, as PA levels have been shown to track from preschool age throughout childhood (Jones et al., 2013), and into adulthood (Telama et al., 2014). However, the proportion of preschool age children meeting international 24-hour movement guidelines is low (Chaput et al., 2017; Cliff et al., 2017). Evidence-based PA intervention approaches are needed at preschool age, and there is a growing body of intervention studies being conducted in typically developing populations, with mixed results (De Craemer et al., 2017; Tucker et al., 2017).

The International Classification of Functioning, Disability and Health, children and youth version (ICF-CY) framework is a useful method of investigating predictors of PA in preschool age children. The ICF-CY framework presents bi-directional relationships between health conditions, body structures and functions, activities and participation, reflecting the dynamic process of child development (World Health Organisation, 2007). Within the body structure and function domain, the term health-related physical fitness (HRPF) describes outcomes such as muscle strength and power (King-Dowling et al., 2018; World Health Organisation, 2007). Studies examining the associations between HRPF, including grip strength and PA participation are limited at preschool age (Fang et al., 2017). However, emerging research (Potter, Spence, Boulé, Stearns, & Carson, 2018) has found weak evidence of an association between HRPF and PA participation. Conversely, the evidence base examining associations between the activity and participation domains in early childhood is more established. Since Stodden and colleagues’ (Stodden et al., 2008) proposal of a model conceptualising the developmental mechanisms influencing PA trajectories throughout childhood in 2008, many studies have investigated the
associations between PA and motor competence (MC) (Robinson, 2015). In early childhood, studies have consistently reported associations between the two outcomes, although the relationship varies in strength and nature during the preschool period (Figueroa & An, 2017). Conversely, most studies examining the associations between strength and MC have been in older typically developing children and children with Developmental Coordination Disorder (DCD). Those studies have found consistent positive associations between the body structure and function and activity domain outcomes (Cattuzzo et al., 2016; Comeau et al., 2017; Rivilis et al., 2011).

Preschool age children born very preterm (VP; <32 weeks’ gestational age) experience poorer motor outcomes within ICF-CY body structure and function, and activity domains than their term-born peers (FitzGerald et al., 2018). However, due to the paucity of participation-based research in VP preschool age populations, it is unclear if body structure and function impairments and activity limitations ultimately influence participation (FitzGerald et al., 2018). Preschool age children born VP may be at even higher risk of physical inactivity than their term-born peers due to the short- and long-term morbidities associated with preterm birth, including respiratory morbidity (Been et al., 2014), neurological dysfunction and poor motor skills (FitzGerald et al., 2018). Yet research of PA participation in VP preschool age populations compared with term-born controls is sparse (Lowe et al., 2017), meaning that the trajectory of PA participation throughout childhood and into adolescence is not fully understood.

Given the poor adherence to existing PA guidelines and the paucity of PA research in VP populations, further study of potentially modifiable predictors of PA participation is warranted at preschool age to inform future intervention studies and PA promotion strategies. Thus, the primary aim of this study was to examine the associations between grip strength, MC and PA
levels in 4- to 5-year-old children. The secondary aim was to determine if the associations differed between children born VP and term-born controls.

7.4 Method

7.4.1 Participants
Children in the study were a subgroup of a prospective longitudinal cohort study of infants born <30 weeks’ gestation (VP) and term-born controls, for which methods have been reported elsewhere (Spittle et al., 2016). Very preterm and term-born infants (>36 weeks’ gestation with birthweight ≥2500 g) were recruited between 2011 and 2013 from the Royal Women’s Hospital, Melbourne, Australia. Infants with congenital abnormalities known to affect neurodevelopment, non-English speaking parents and term-born infants who were admitted to a neonatal intensive care unit or special care nursery were excluded. Participants were assessed from birth to 3 years of age. Participants who attended follow-up appointments at 4- to 5-years’ corrected age (CA) between April 2016 and June 2018 were included in the current study. Written informed consent was obtained at the 4- to 5-year follow-up assessment and the study was approved by the Human Research and Ethics Committees at the Royal Children’s Hospital. Melbourne Australia.

7.4.2 Procedures and assessment tools
Children were preferentially assessed before they commenced formal schooling to ensure the majority of participants were within the preschool period, and age was corrected for preterm birth to avoid introducing bias due to underestimating the performance of children born preterm (Wilson-Ching et al., 2014). Assessors were unaware of medical and birth history, as well as results from previous assessments. Body weight (kg) was recorded using a calibrated stadiometer (seca gmbh & co. kg., California, USA) and lower limb length (cm) was measured from the anterior superior iliac spine to medial malleolus for each child.
Bimanual handgrip strength (force in kg) was measured using a calibrated Smedley digital hand dynamometer (Model: 12-0286, Baseline® New York, USA) with the participant seated. The participant was instructed to maintain shoulder adduction with the elbow flexed at 90 degrees and the forearm and wrist in a neutral position. A practice trial preceded three formal trials, and the maximum value was recorded.

The Movement Assessment Battery for Children, 2nd Edition (*MABC-2*) (Henderson et al., 2007) the parent-completed Little Developmental Coordination Disorder Questionnaire (*Little DCDQ*) (Wilson et al., 2015) were used to assess motor competence. Physical activity was measured using a water-resistant tri-axial accelerometer (Axivity, Newcastle Upon Tyne, United Kingdom). The accelerometer was placed inside a band (Axivity Wrist Band, Newcastle Upon Tyne, United Kingdom) and fitted to each child’s right ankle on the day of their appointment. The ankle was chosen due to the logical reflection of gait and stepping movements (Storm et al., 2015). The children wore the accelerometer for the next six consecutive days before families returned it by mail in a pre-paid envelope. Social risk status was obtained using parent questionnaires administered at birth/term-equivalent age and was assessed using a composite measure (Roberts et al., 2008) of six aspects of social status. When birth/term equivalent age data were incomplete, we used social risk data collected during the one or two-year follow-up appointments.

### 7.4.3 Data collection and management

Children who were unable to complete the *MABC-2* due to motor impairment (e.g. CP) were given the lowest possible standard score (1) and percentile (0.1). Consistent with the Sedentary Behaviour Research Network consensus terminology (Tremblay et al., 2017a), accelerometer-measured stationary behaviour was defined as any waking behaviour completed while lying, reclining, sitting or standing without ambulation regardless of energy expenditure. Sedentary behaviour defined as waking behaviour characterised by energy expenditure ≤1.5 metabolic
equivalents while in a sitting, reclining or lying posture (Tremblay et al., 2017a) was not measured in this study.

Accelerometers were initialised using open source OmGui software (Open Movement, United Kingdom) and set to record for seven days from the time of each child’s appointment. The first day of accelerometer data (the day of the assessment) did not capture a full 24-hour period and was therefore removed from analysis, leaving a maximum of six days of accelerometer data. Accelerometer data were downloaded using a specialised analysis program created for the study (Appendix E) and processed using guidelines developed for the current study (Appendix F).

Accelerometer non-wear was defined as 20 consecutive minutes of no accelerations or angle changes during waking hours, and days of data containing accelerometer non-wear were excluded from the analysis. Periods of non-wear were visually identified and confirmed using an automated non-wear algorithm. Participants with ≥1 full 24-hour period without detectable accelerometer non-wear were included in the analysis.

A detailed summary of each accelerometer and diary outcome is included in Appendix H.

Accelerometer-determined PA was obtained using different methods and results are reported separately for each outcome. Total time spent in PA was calculated using a minute-by-minute approach (1-minute PA), where each non-stationary minute was calculated during waking hours. Minutes spent stepping each day (stepping PA) was used as a subset of total PA. Time spent in ‘fast steps’ was calculated as a measure of moderate to vigorous PA (MVPA). Fast steps were identified using the modal stride rate (Hz) for each child over the days of accelerometer wear. The modal stride rate was then multiplied by 1.31 to identify a threshold for fast gait for each individual (Lim et al., 2016), and the time spent stepping above this threshold was summed to obtain minutes per day spent in fast gait (minutes of MVPA). A minute-by-minute approach was
used to determine the duration of stationary behaviour, whereby each minute with no recorded steps was categorised as stationary.

Physical activity outcomes in the current study were chosen to represent differing levels of movement behaviour and were all measured in minutes per day: total PA (1-minute PA), stepping PA, MVPA and stationary duration. As 1-minute PA and stepping PA outcomes were only moderately correlated in our sample (Pearson’s $r=0.62; p<0.001$), we chose to report associations for both outcomes.

7.4.4 Statistical analysis

Data were analysed using Stata (version 14.2, StataCorp, Texas, USA).

Physical activity and grip strength

Univariable associations between PA and peak bimanual grip strength (independent variable) were examined using separate mixed effects models for each PA outcome to account for the multiple days of PA data, adjusted for VP birth. The models were repeated in a multivariable analysis to include the following independent variables: birth group (VP vs. term-born), body weight at assessment (kg), sex (male vs. female), social risk (higher vs. lower), data from weekend or holiday periods (yes vs. no), season (daylight saving vs. non-daylight saving periods), attendance at preschool, school or childcare (yes vs. no) and days of data (1-6). For analyses involving MVPA, models were also adjusted for lower limb length (cm). In Melbourne, Australia, daylight saving fell between the first Sunday of October and the first Sunday of April during the data collection period of the study. Birth group was also fitted as an interaction term with the other main independent variables in each multivariable model to examine if associations between dependent and independent variables differed between birth groups.
Physical activity and motor competence

The associations between PA and MC outcomes were analysed using separate mixed effects models to account for the multiple days of PA data, and each model was adjusted for VP birth for each combination of outcome and predictor. Continuous MC independent variables were MABC-2 total standard score, MABC-2 manual dexterity, aiming and catching and balance subscale standard scores and Little DCDQ total score and a binary independent variable of either scoring ≤5th MABC-2 percentile overall or being ‘suspect for DCD’ on the Little DCDQ (yes vs. no). Little DCDQ ‘suspect’ scores were defined as ≤67 for males and ≤68 for females (Wilson et al., 2015). Mixed effects models were repeated combining birth group, sex, social risk, data from weekend or holiday periods, season, attendance at preschool, school or childcare, day of data and CA at assessment. Analyses involving MVPA were additionally adjusted for lower limb length. VP birth was again fitted as an interaction term in each model to assess if the relationships differed between birth groups.

Motor competence and grip strength

Linear and logistic regression models fitted with generalised estimating equations (GEEs), to allow for clustering of multiple births within a family, and adjusted for VP birth, were used to investigate associations between MC outcomes and peak bimanual grip strength. MC outcomes were the same as in the PA and MC analyses: MABC-2 total standard score, MABC-2 manual dexterity, aiming and catching and balance subscale standard scores, Little DCDQ total score and scoring ≤5th MABC-2 percentile overall and/or ‘suspect for DCD’. Linear and logistic regression models with GEEs were repeated combining birth group, body weight (kg), sex, social risk and CA at assessment (independent variables). VP birth was fitted as an interaction term in each linear and logistic regression model, and repeated combining the same independent variables as in the full multivariable analysis. When GEE models could not be fitted correctly to
continuous data, linear regression models clustering for twins were completed and reported with robust standard errors.

Multiple comparisons were not adjusted for in the current study because the analyses were considered to be exploratory only, and would need confirmation in subsequent studies.

7.5 Results

7.5.1 Participant characteristics

One hundred and eighty-two children were included in the analysis (98 VP, 84 term-born).

Forty-two percent of VP children were born twins or triplets, but all term-born children were singletons (Table 7.1). The majority of children were attending preschool at the time of the assessment and there was an even spread of males and females in both groups. A larger proportion of VP children was of higher social risk compared with term-born children. The study sample included six VP children with a diagnosis of CP (n=5 Gross Motor Function Classification System (GMFCS) level I and n=1 GMFCS level IV).

<table>
<thead>
<tr>
<th></th>
<th>Very preterm n=98</th>
<th>Term-born n=84</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gestational age (weeks), mean (SD) [range]</strong></td>
<td>27.9 (1.5) [24.1 – 29.9]</td>
<td>40 (1.2) [37 – 42]</td>
</tr>
<tr>
<td><strong>Birthweight (g), mean (SD) [range]</strong></td>
<td>1037 (259) [529 – 1613]</td>
<td>3532 (431) [2700 – 4744]</td>
</tr>
<tr>
<td>Multiple births, n (%)</td>
<td>41 (42)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Sex (male), n (%)</td>
<td>50 (51)</td>
<td>41 (49)</td>
</tr>
<tr>
<td>Higher social risk, n (%)</td>
<td>40 (42)</td>
<td>20 (25)</td>
</tr>
<tr>
<td>Attending preschool, n (%)</td>
<td>88 (90)</td>
<td>79 (94)</td>
</tr>
<tr>
<td><strong>CA at assessment (years), mean (SD) [range]</strong></td>
<td>4.7 (0.1) [4.4 – 5.0]</td>
<td>4.8 (0.1) [4.3 – 5.2]</td>
</tr>
<tr>
<td><strong>Weight at assessment (kg), mean (SD) [range]</strong></td>
<td>17.4 (3.0) [11.9 – 34.5]</td>
<td>19.2 (2.3) [14.9 – 25.0]</td>
</tr>
<tr>
<td><strong>Height at assessment (cm), mean (SD) [range]</strong></td>
<td>106.2 (5.1) [93.0 – 118.4]</td>
<td>109.7 (4.5) [97.9 – 117.4]</td>
</tr>
</tbody>
</table>

Table 7.1 Characteristics of included participants (n=182)

* data for 96 VP and 80 term-born participants, † data for 97 VP & 82 term-born participants, # data for 82 term-born participants. CA, corrected age; cm, centimetres; g, grams; kg, kilograms; n, number, SD, standard deviation
7.5.2 Associations between physical activity and grip strength

Of the 138 children who met the accelerometer data inclusion criterion, a further 13 VP children had missing peak bimanual grip strength data, leaving n=125 included in the analysis (59 VP, 66 term-born).

Social risk and the day of data demonstrated little influence on the overall associations for each PA outcome with grip strength and were removed from the final multivariable model. Similarly, lower limb length (cm), day of data, season and attendance at preschool, school or childcare did not influence the overall association between grip strength and minutes of MVPA, and were removed from the final model. Data from the full models (including all covariates) and the final (simplified) models are presented in Appendix SI.

Evidence for the associations between 1-minute PA, stepping PA, MVPA and stationary duration with grip strength, was weak in the adjusted and multivariable analyses (Appendix SII). There was also little evidence of an interaction of birth group on the associations between grip strength and 1-minute PA (p=0.49), stepping PA (p=0.28), MVPA (p=0.46) and stationary duration (p=0.72).

7.5.3 Associations between physical activity and motor competence

The day of data and social risk were removed from all final models, and CA was removed from the multivariable model involving the ≤5th percentile on the MABC2 and/or ‘suspect for DCD’ predictor, as they had little influence on the associations between MC and PA outcomes. Data from the full models including all covariates are presented in Appendix SIII.

There was little evidence of associations of PA outcomes with MABC-2 standard scores, or with scoring ≤5th percentile/ ‘suspect for DCD’, in both the adjusted and full multivariable analyses.
There was little evidence of interaction effects of birth group on the associations between PA outcomes with MC predictors (Appendix SIII), except for the relationship between 1-minute PA and MABC-2 balance subscale (Figure 7.2; p = 0.03). A strong positive association between 1-minute PA and MABC-2 balance subscale standard score was found for VP children (minutes per unit increase in balance standard score: 8.1, 95% CI 2.2 to 14.1; p = 0.008), but evidence was weak for term-born children (minutes per unit increase in balance standard score: -0.2, 95% CI -5.1 to 4.6; p = 0.92). There was little evidence for group differences in associations between the other MC predictors and PA outcomes (p value for interaction all >0.05).
<table>
<thead>
<tr>
<th>PA outcome, minutes/day</th>
<th>MABC-2 standard score</th>
<th>MABC-2 MD standard score</th>
<th>MABC-2 A&amp;C standard score</th>
<th>MABC-2 Balance standard score</th>
<th>Little DCDQ score</th>
<th>≤5th percentile/ ‘suspect for DCD’ **^</th>
<th>( p ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-minute PA</td>
<td>0.6 (-3.2, 4.3), ( p = 0.77 )</td>
<td>0.1 (-3.6, 3.7), ( p = 0.98 )</td>
<td>1.1 (-2.8, 5.1), ( p = 0.57 )</td>
<td>1.6 (-2.4, 5.6), ( p = 0.43 )</td>
<td>2.1 (0.8, 3.3), ( p = 0.001 )</td>
<td>-17.0 (-43.4, 9.4), ( p = 0.21 )</td>
<td>0.04</td>
</tr>
<tr>
<td>Stepping PA</td>
<td>-0.2 (-2.5, 2.1), ( p = 0.85 )</td>
<td>-1.1 (-3.3, 1.1), ( p = 0.32 )</td>
<td>1.5 (-0.9, 3.9), ( p = 0.22 )</td>
<td>0.3 (-2.2, 2.7), ( p = 0.83 )</td>
<td>0.5 (-0.2, 1.3), ( p = 0.18 )</td>
<td>-1.1 (-17.3, 15.0), ( p = 0.89 )</td>
<td>0.03</td>
</tr>
<tr>
<td>MVPA</td>
<td>-0.02 (-0.5, 0.5), ( p = 0.95 )</td>
<td>-0.1 (-0.6, 0.4), ( p = 0.68 )</td>
<td>0.1 (-0.4, 0.6), ( p = 0.66 )</td>
<td>0.1 (-0.5, 0.6), ( p = 0.84 )</td>
<td>0.1 (-0.1, 0.3), ( p = 0.19 )</td>
<td>-0.8 (-4.1, 2.6), ( p = 0.65 )</td>
<td>0.19</td>
</tr>
<tr>
<td>Stationary</td>
<td>-1.1 (-4.8, 2.7), ( p = 0.58 )</td>
<td>0.1 (-3.6, 3.8), ( p = 0.96 )</td>
<td>-2.0 (-6.0, 2.0), ( p = 0.33 )</td>
<td>-1.9 (-5.9, 2.2), ( p = 0.37 )</td>
<td>-1.5 (-2.8, -0.2), ( p = 0.02 )</td>
<td>18.0 (-8.6, 44.7), ( p = 0.19 )</td>
<td>0.03</td>
</tr>
</tbody>
</table>

**Adjusted Analyses **^ **

Change in minutes for each unit increase in independent variable (95% CI), \( p \) value.

<table>
<thead>
<tr>
<th>PA outcome, minutes/day</th>
<th>MABC-2 standard score</th>
<th>MABC-2 MD standard score</th>
<th>MABC-2 A&amp;C standard score</th>
<th>MABC-2 Balance standard score</th>
<th>Little DCDQ score</th>
<th>≤5th percentile/ ‘suspect for DCD’ **^</th>
<th>( p ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-minute PA</td>
<td>2.2 (-1.6, 5.9), ( p = 0.25 )</td>
<td>1.8 (-1.9, 5.5), ( p = 0.34 )</td>
<td>1.7 (-2.2, 5.6), ( p = 0.38 )</td>
<td>3.1 (-0.8, 7.0), ( p = 0.12 )</td>
<td>2.3 (1.0, 3.5), ( p &lt; 0.001 )</td>
<td>-18.7 (-44.2, 6.9), ( p = 0.15 )</td>
<td>0.04</td>
</tr>
<tr>
<td>Stepping PA</td>
<td>1.1 (-1.1, 2.3), ( p = 0.32 )</td>
<td>0.4 (-1.7, 2.6), ( p = 0.70 )</td>
<td>2.1 (-0.1, 4.3), ( p = 0.07 )</td>
<td>1.3 (-1.0, 3.6), ( p = 0.26 )</td>
<td>0.5 (-0.3, 1.3), ( p = 0.19 )</td>
<td>-3.3 (-18.2, 11.6), ( p = 0.66 )</td>
<td>0.03</td>
</tr>
<tr>
<td>MVPA</td>
<td>0.1 (-0.4, 0.6), ( p = 0.62 )</td>
<td>0.07 (-0.4, 0.6), ( p = 0.76 )</td>
<td>0.2 (-0.3, 0.7), ( p = 0.51 )</td>
<td>0.2 (-0.4, 0.7), ( p = 0.54 )</td>
<td>0.1 (-0.03, 0.3), ( p = 0.11 )</td>
<td>-1.2 (-4.5, 2.2), ( p = 0.50 )</td>
<td>0.03</td>
</tr>
<tr>
<td>Stationary</td>
<td>-2.2 (-6.1, 1.6), ( p = 0.26 )</td>
<td>-1.3 (-5.2, 2.5), ( p = 0.51 )</td>
<td>-2.4 (-6.4, 1.7), ( p = 0.25 )</td>
<td>-3.1 (-7.1, 1.0), ( p = 0.14 )</td>
<td>-1.5 (-2.9, -0.2), ( p = 0.03 )</td>
<td>-19.0 (-7.6, 45.6), ( p = 0.16 )</td>
<td>0.03</td>
</tr>
</tbody>
</table>

* \( n = 137 \) for manual dexterity subscale, \( n = 138 \) for aiming & catching subscale, \( n = 130 \) for Little DCDQ total score, \( n = 138 \) for ≤5th percentile/ ‘suspect for DCD’.

** results from mixed effects models adjusted for very preterm birth; ** significant group interaction (\( p < 0.04 \)); ** multivariable mixed effects models combining birth group, sex, weekend/holiday period data, season, attendance at preschool/school/childcare and corrected age; # significant group interaction (\( p < 0.03 \)); ## scoring ≤5th percentile on MABC-2 and/or classified as ‘suspect for DCD’ and corrected age removed from multivariable model; * MVPA analysis adjusted for birth group, sex, social risk and weekend/holiday period data and corrected age. A&C, aiming and catching; CI, confidence interval; DCD, Developmental Coordination Disorder; Little DCDQ, Little Developmental Coordination Disorder Questionnaire; MABC-2, the Movement Assessment Battery for Children, 2nd edition; MD, manual dexterity; PA, physical activity.
Figure 7.2 Associations between motor competence and physical activity

FT, term-born participants; Little DCDQ, The Little Developmental Coordination Disorder Questionnaire; MABC-2, The Movement Assessment Battery for Children, 2nd edition; PA, physical activity; VP, very preterm participants
7.5.4 **Associations between motor competence and grip strength**

The associations between continuous MC outcomes and peak bimanual grip strength are presented in Figure 7.3. There was strong evidence in the adjusted analyses of positive associations between MABC-2 total standard score, manual dexterity standard score, aiming and catching standard score, and Little DCDQ total score with peak bimanual grip strength (Table 7.3). The conclusions were unaltered in the full multivariable model adjusting for other confounders (Table 7.3). Evidence for the association between scoring ≤5th percentile/ ‘suspect for DCD’ and grip strength was weak in the adjusted analysis, but strengthened in the full multivariable analysis (Table 7.3). There was little evidence of an association between the MABC-2 balance subscale standard score and grip strength in the adjusted and full multivariable models (Table 7.3).

There was little evidence of interactions of birth group on the associations between motor outcomes and grip strength (all p values for interaction >0.05), except for the MABC-2 balance subscale (p = 0.04). For children born VP, a positive association between MABC-2 balance subscale standard score and grip strength was found (Figure 7.3, standard score per kg increase in grip strength: 0.3, 95% CI 0.1, 0.5; p = 0.001), but evidence was weak for term-born children (standard score per kg increase in grip strength: 0.01, 95% CI -0.2, 0.2; p = 0.92).
Figure 7.3 Associations between motor competence and grip strength

FT, term-born participants; kg, kilogram; Little DCDQ, The Little Developmental Coordination Disorder Questionnaire; MABC-2, The Movement Assessment Battery for Children, 2nd edition; VP, very preterm participants. Data points jittered: 'jitter(5)
## Table 7.3 Associations between motor competence and peak bimanual grip strength

<table>
<thead>
<tr>
<th>Motor competence outcome</th>
<th>Adjusted analysis</th>
<th>Multivariable analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total n</td>
<td>Change in motor competence outcome for each kg increase in grip strength</td>
</tr>
<tr>
<td>MABC-2 standard score</td>
<td>160</td>
<td>0.3 (0.2, 0.5), p&lt;0.001</td>
</tr>
<tr>
<td>MABC-2 manual dexterity standard score</td>
<td>161</td>
<td>0.3 (0.1, 0.5), p&lt;0.001</td>
</tr>
<tr>
<td>MABC-2 aiming &amp; catching standard score</td>
<td>161</td>
<td>0.4 (0.2, 0.5), p&lt;0.001</td>
</tr>
<tr>
<td>MABC-2 balance standard score</td>
<td>160</td>
<td>0.1 (-0.03, 0.3), p= 0.10</td>
</tr>
<tr>
<td>Little DCDQ total score #</td>
<td>145</td>
<td>0.8 (0.2, 1.3), p= 0.008</td>
</tr>
</tbody>
</table>

### Cut off scores

<table>
<thead>
<tr>
<th>MABC-2 ≤ 5th percentile/suspect for DCD $&amp;$</th>
<th>OR (95% CI), p value $##$</th>
</tr>
</thead>
<tbody>
<tr>
<td>160</td>
<td>0.9 (0.8, 1.0), p= 0.07</td>
</tr>
</tbody>
</table>

* Analyses adjusted for birth group, "Multivariable analyses combining birth group, body weight (kg), sex, social risk and corrected age, ¦ values from linear regression with models fitted using generalised estimating equations (GEEs) to allow for clustering of multiple births within the same family, " Significant group interaction (p 0.04), $^\#$ values from linear regression models clustering for twin births and reported with robust standard errors as GEE models did not fit, $^\#\#$ odds ratios from logistic regression models fitted with GEEs to allow for clustering of multiple births within the same family, $^\&$ cut off scores on the Little DCDQ for females $\leq 68$ and for males $\leq 67$. CI, confidence interval; DCD, Developmental Coordination Disorder; Little DCDQ, Little Developmental Coordination Disorder Questionnaire; MABC-2, the Movement Assessment Battery for Children, 2nd edition.
7.6 Discussion

This study demonstrated that PA was associated with some aspects of MC, and that MC was consistently positively associated with grip strength in 4- to 5-year-old children. More 1-minute PA and fewer minutes of stationary behaviour were associated with higher Little DCDQ total scores. Physical activity outcomes were weakly associated with scores from the MABC-2, but there were birth group differences for the association between PA the and balance subscale. For VP children, more daily 1-minute PA was associated with higher MABC-2 balance subscale standard scores, but there was little evidence of such a relationship for term-born children. Irrespective of birth group, higher MABC-2 total, manual dexterity and aiming and catching standard scores, as well as Little DCDQ total scores were associated with larger grip strength values. The association of MABC-2 balance subscale standard score with grip strength was different between the groups. For children born VP, higher balance scores were associated with larger grip strength values, while no such relationship was found for term-born children. Physical activity levels did not appear to be associated with grip strength in 4- to 5-year-old children.

Our results are consistent with previous research finding little evidence of relationships between PA levels and strength at preschool age in term-born children (Fang et al., 2017). Similarly, a recent study of typically developing preschool age children and those with DCD found that differences in HRPF between the groups were not mediated by daily PA levels (King-Dowling et al., 2018). A recent longitudinal study with baseline measures at 4.5 years of age in children born mostly at term reported participation in screen time to be negatively associated with grip strength three years later, but found no associations for PA (Potter et al., 2018).

Our findings are also consistent with a recent study of mostly term-born 5- to 6-year-old children reporting little evidence of associations between accelerometer-measured MVPA and
sedentary behaviour with objectively measured motor skills (Matarma et al., 2018). Conversely, a systematic review investigating PA and MC levels in 3- to 5-year-old typically developing children found consistent evidence of a significant positive association between the two outcomes, although the review included diary, pedometer and observational PA assessment methods alongside accelerometers (Figueroa & An, 2017). Furthermore, several randomised control trials included in the systematic review with sample sizes >200 and accelerometer-measured PA reported weak (Fisher et al., 2005) or no evidence (Bellows, Davies, Anderson, & Kennedy, 2013; Bonvin et al., 2013) of associations between PA and MC. The authors of the review (Figueroa & An, 2017) report that the strength and nature of the association between PA and MC is dependent on several variables, such as sex and day of the week (Figueroa & An, 2017). Although we adjusted for sex and weekday vs. weekend data along with other variables in our analyses, further research is needed to understand the potential role of environmental factors on the associations between PA and MC in VP and term-born preschool age children.

Studies examining associations between MC and strength at preschool age are limited, but our results are consistent with evidence of positive associations between the two outcomes in older typically developing children (Comeau et al., 2017). Similarly, research in children and adolescents with DCD has found strong evidence of positive associations between MC and strength/endurance (Cattuzzo et al., 2016).

To our knowledge, this is the first study to examine associations between grip strength, MC and objectively measured PA levels in VP and term-born children. The current study contributes to the evidence base researching predictors of low PA and poor MC in childhood, but by examining birth group differences, our work furthers the understanding of PA participation in VP preschool age children. Children born VP may be at higher risk of inactivity than term-born children due to poorer respiratory health (Been et al., 2014), adverse motor outcomes and
increased risk of neurological dysfunction (FitzGerald et al., 2018). Our work investigating differences in accelerometer-measured and parent-reported PA and stationary behaviours between VP and term-born children (FitzGerald et al., Chapter 6) has demonstrated that VP children are less physically active than their term-born peers as early as 4 years of age. Children born VP have poorer postural control and balance than term-born children (Lorefice et al., 2015), and our findings that balance skills are more strongly associated with PA and grip strength, may inform intervention studies and strategies for VP preschool age children. The current study forms the basis of objective PA research in VP preschool age populations, and contributes to understanding possible mechanisms of physical inactivity in VP populations.

Another strength of the study is the rigorous accelerometer data inclusion criterion and the transparent methods of accelerometer data management. Due to limited evidence to inform accelerometer data management for children, researchers should clearly report decisions to facilitate the evaluation and comparison of studies (Janssen & Cliff, 2015). Inclusion of detailed accelerometer technical information (Appendix E) and reporting of management protocols in our study facilitates reproducibility, appraisal and synthesis of outcomes with other studies. By processing raw acceleration data, as was possible when using Axivity AX3 accelerometers, we were able to combine visual data inspection with a non-wear algorithm and take an individualised approach to measuring MVPA in our sample. Lastly, by including participants with full 24-hour periods of accelerometer wear, we avoid misclassifying periods of non-wear as stationary behaviour.

We acknowledge several limitations of the current study. Despite the benefits of our accelerometer non-wear management approach, excluding participants with non-wear limits the generalisability of results to children with poor compliance. Another important consideration when investigating associations between ICF-CY domains is the direction of enquiry, as
participation outcomes can be conceptualised as either dependent or independent variables (Imms et al., 2016b). Physical activity was treated as the primary outcome, as prior to the current study, very little was known regarding objectively measured PA participation in VP preschool age children relative to term-born controls (Lowe et al., 2017). Research demonstrating poorer MC for children born VP compared with their term-born peers is well established (de Kieviet et al., 2009; Edwards et al., 2011; FitzGerald et al., 2018), and therefore could be a possible predictor of low PA in VP preschool age populations. However, our direction of enquiry is in contrast to the conceptual framework described by Stodden and colleagues (Stodden et al., 2008). Despite finding positive associations between PA and some MC predictors, and between MC and grip strength, the small coefficient values limit the clinical and practical relevance of our findings. Although grip strength can be considered as measure of total body strength (Johnson, Friedl, Frykman, & Moore, 1994), measurement precision can be affected by hand size, posture, effort and encouragement (Roberts et al., 2011b). Choice of a functional strength measure, such as a squat jump which is likely to be more relevant to a child’s mobility and quality of life (Edelson, Mathias, Fulgoni, & Karagounis, 2016), may show stronger associations with PA at preschool age.

This study found that irrespective of birth group, PA levels were associated with some aspects of MC, and MC was positively associated with grip strength in 4- to 5-year old children. For children born VP, more PA was associated with better balance skills, and better balance skills with greater grip strength. Further research of associations between ICF-CY domains is needed to test the bi-directionality of the framework in preschool age populations. Future studies should prioritise investigating PA levels in VP preschool age children and identifying potentially modifiable predictors of low PA to inform intervention studies and health promotion initiatives.
### Appendix SI: Associations between physical activity and peak bimanual grip strength (n=125)

<table>
<thead>
<tr>
<th>PA outcome, minutes/day</th>
<th>Adjusted analysis *</th>
<th>Full multivariable model **</th>
<th>Simplified multivariable model ^</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Change in minutes for each kg increase in grip strength (95% CI), p value ^^</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-minute PA</td>
<td>1.0 (-3.0, 5.0), p= 0.61</td>
<td>0.8 (-3.0, 4.5), p= 0.69</td>
<td>0.7 (-3.0, 4.5), p= 0.71</td>
</tr>
<tr>
<td>Stepping PA</td>
<td>0.2 (-2.4, 2.7), p= 0.91</td>
<td>0.5 (-1.8, 2.8), p= 0.69</td>
<td>0.5 (-1.8, 2.8), p= 0.70</td>
</tr>
<tr>
<td>MVPA</td>
<td>0.2 (-0.4, 0.70, p = 0.55</td>
<td>0.3 (-0.4, 0.9), p = 0.40 #</td>
<td>0.3 (-0.2, 0.8), p = 0.29 ##</td>
</tr>
<tr>
<td>Stationary</td>
<td>-0.1 (-4.0, 3.8), p= 0.96</td>
<td>0.1 (-3.8, 3.9), p= 0.98</td>
<td>0.02 (-3.8, 3.9), p= 0.99</td>
</tr>
</tbody>
</table>

* Analysis adjusted for VP birth, ** Multivariable analyses combining birth group, body weight (kg), sex, social risk, weekend/holiday period data, attendance at preschool/school/childcare, daylight savings periods and day of data, ^ Multivariable analyses combining birth group, body weight (kg), sex, weekend/holiday period data, attendance at preschool/school/childcare, daylight savings periods, ^^ mean differences from mixed effects models, # MVPA model combining birth group, body weight (kg), sex, social risk, weekend/holiday period data, attendance at preschool/school/childcare, daylight savings periods and day of data and average lower limb length (cm), ## MVPA model combining birth group, body weight (kg), sex, social risk and weekend/holiday period data. CI, confidence interval; MVPA, moderate to vigorous physical activity; PA, physical activity.
### Chapter Seven: Associations between ICF-CY domains at preschool age

**Appendix SII** Associations between physical activity and motor competence. Results from full mixed effects models combining all covariates (n=129)

#### Multivariable Analyses ""

<table>
<thead>
<tr>
<th>Outcome</th>
<th>MABC-2 standard score</th>
<th>MABC-2 MD standard score</th>
<th>MABC-2 A&amp;C standard score</th>
<th>MABC-2 Bal standard score</th>
<th>Little DCDQ score</th>
<th>≤5th percentile/ 'suspect for DCD'</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-minute PA</td>
<td>2.2 (-1.6, 5.9), p= 0.26</td>
<td>-1.8 (-1.9, 5.5), p= 0.33</td>
<td>1.8 (-2.1, 5.7), p= 0.37</td>
<td>3.1 (-0.9, 7.0), p= 0.13 **</td>
<td>2.3 (1.1, 3.6), p&lt;0.001</td>
<td>-32.4 (-76.0, 11.3), p= 0.15</td>
</tr>
<tr>
<td>Stepping PA</td>
<td>1.1 (-1.1, 3.4), p= 0.31</td>
<td>0.4 (-1.7, 2.6), p= 0.70</td>
<td>2.1 (-0.1, 4.4), p= 0.06</td>
<td>1.3 (-1.0, 3.7), p= 0.26</td>
<td>0.5 (-3.3, 1.3), p= 0.18</td>
<td>-6.3 (-31.8, 19.3), p= 0.63</td>
</tr>
<tr>
<td>MVPA +</td>
<td>0.2 (-0.4, 0.7), p= 0.58</td>
<td>0.1 (-0.4, 0.7), p= 0.62</td>
<td>0.2 (-0.3, 0.8), p= 0.41</td>
<td>0.2 (-0.4, 0.7), p= 0.56</td>
<td>0.1 (-0.1, 0.2), p= 0.32</td>
<td>-2.4 (-8.6, 3.8), p= 0.45</td>
</tr>
<tr>
<td>Stationary</td>
<td>-2.1 (-6.0, 1.7), p= 0.28</td>
<td>-1.2 (-5.0, 2.7), p= 0.56</td>
<td>-2.4 (-6.4, 1.6), p= 0.24</td>
<td>-2.9 (-6.9, 1.2), p= 0.16</td>
<td>-1.5 (-2.9, -0.1), p= 0.03</td>
<td>15.6 (-30.0, 61.2), p= 0.50</td>
</tr>
</tbody>
</table>

'n= 130 for manual dexterity subscale, n= 131 for aiming & catching subscale, n= 125 for Little DCDQ total score, n= 131 for ≤5th percentile/ ‘suspect for DCD’; ** multivariable models combining birth group, sex, social risk, weekend/holiday period data, attendance at preschool/school/childcare, season, day of data and corrected age, " mean differences from mixed effects models, " minutes per day, " scoring ≤5th percentile on MABC-2 and/or classified as ‘suspect for DCD’ according to Little DCDQ, "" significant group interaction (p= 0.03), MVPA model combining birth group, sex, social risk, weekend/holiday period data, attendance at preschool/school/childcare, season, day of data, corrected age and average lower limb length. A&C, aiming and catching; Bal, balance; CI, confidence interval; DCD, Developmental Coordination Disorder; Little DCDQ, Little Developmental Coordination Disorder Questionnaire; MABC-2, the Movement Assessment Battery for Children, 2nd edition; MD, manual dexterity; PA, physical activity
Appendix SIII Birth group differences in associations between physical activity and motor competence (n= 136 *)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>MABC-2 standard score</th>
<th>MABC-2 MD standard score</th>
<th>MABC-2 A&amp;C standard score</th>
<th>MABC-2 Bal standard score</th>
<th>Little DCDQ score</th>
<th>≤5&lt;sup&gt;th&lt;/sup&gt; percentile/ ‘suspect for DCD’</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-minute PA</td>
<td>5.3 (-1.8, 12.4), p= 0.14</td>
<td>3.1 (-4.0, 10.1), p= 0.40</td>
<td>4.9 (-2.8, 12.6), p= 0.21</td>
<td>8.3 (0.8, 15.9), p= 0.03</td>
<td>0.9 (-1.8, 3.7), p= 0.51</td>
<td>4.4 (-46.3, 55.2), p= 0.87</td>
</tr>
<tr>
<td>Stepping PA</td>
<td>2.0 (-2.2, 6.2), p= 0.35</td>
<td>1.4 (-2.7, 5.5), p= 0.51</td>
<td>2.4 (-2.0, 6.9), p= 0.28</td>
<td>3.5 (-1.0, 8.0), p= 0.13</td>
<td>0.5 (-1.2, 2.2), p= 0.56</td>
<td>-3.5 (-33.2, 26.2), p= 0.82</td>
</tr>
<tr>
<td>MVPA †</td>
<td>-0.3 (-1.2, 0.7), p= 0.59</td>
<td>-0.4 (-1.2, 0.6), p= 0.44</td>
<td>-0.1 (-1.1, 0.8), p= 0.82</td>
<td>0.4 (-0.7, 1.4), p= 0.49</td>
<td>-0.1 (-0.5, 0.3), p= 0.53</td>
<td>5.9 (-0.7, 12.6), p= 0.08</td>
</tr>
<tr>
<td>Stationary</td>
<td>-1.1 (-8.5, 6.3), p= 0.76</td>
<td>1.4 (-6.0, 8.7), p= 0.72</td>
<td>-2.1 (-10.1, 6.0), p= 0.61</td>
<td>-7.0 (-14.9, 0.9), p= 0.08</td>
<td>-2.0 (-5.0, 1.0), p= 0.19</td>
<td>16.4 (-36.3, 69.2) p= 0.54</td>
</tr>
</tbody>
</table>

* n= 137 for manual dexterity subscale, n= 138 for aiming & catching subscale, n= 130 for Little DCDQ total score, n= 138 for ≤5<sup>th</sup> percentile/ ‘suspect for DCD’; † mixed effects models combining sex, weekend/holiday period data, season, attendance at preschool/school/childcare and corrected age with very preterm birth fitted as an interaction term; †† scoring ≤5<sup>th</sup> percentile on MABC-2 and/or classified as ‘suspect for DCD’ according to Little DCDQ; ††† minutes per day, # MVPA analysis adjusted for birth group, sex, social risk and weekend/holiday period data., A&C, aiming and catching; Bal, balance; CI, confidence interval; DCD, Developmental Coordination Disorder; Little DCDQ, Little Developmental Coordination Disorder Questionnaire; MABC-2, the Movement Assessment Battery for Children, 2<sup>nd</sup> edition; MD, manual dexterity; PA, physical activity
The overall aim of this thesis was to compare PA participation and motor outcomes of preschool age children born VP with their term-born peers within the ICF-CY framework (World Health Organisation, 2007). Chapter 8 summarises the main findings, implications of the research, strengths and limitations, and future research directions.

8.1 Summary of main findings

Overall, this thesis found that preschool age children born VP experience poorer motor outcomes across all ICF-CY domains and lower PA levels compared with their term-born peers. This thesis contributes to existing knowledge of VP children’s physical functioning compared with their term-born peers at preschool age by presenting novel evidence of less parent-reported and accelerometer-measured PA participation. The thesis findings also extend existing knowledge of physical inactivity in typically developing preschool age populations to those born VP, and identify several predictors of low PA levels in VP and term-born preschool age children. The main findings of the four studies within this thesis are summarised in Figure 8.1.
Figure 8.1 Thesis findings within the ICF-CY framework (World Health Organisation, 2007)

Little DCDQ, Little Developmental Coordination Disorder Questionnaire; MABC-2, the Movement Assessment Battery for Children second edition; PA, physical activity
8.1.1 Body structure and function domain

Study 1, a systematic review and meta-analysis including 36 studies (Chapter 3), identified 14 body structure and function outcomes, and found that 3- to 6-year-old children born VP had an almost 5-fold increased risk of neurological dysfunction, poorer visual motor integration and worse coordination compared with their term-born peers. In study 1, body structure and function outcome measures varied widely which impeded comprehensive meta-analysis. Furthermore, studies investigating grip strength of VP preschool age children relative to term-born controls published after 1990 were lacking. Study 3 (Chapter 6) investigated motor outcomes of 4- to 5-year-old VP children in each ICF-CY domain compared with their term-born peers. Within the body structure and function domain, children born VP had poorer grip strength on their preferred and non-preferred hands than term-born children. However, group differences diminished when adjusted for body weight and sex, and there was little difference in bimanual grip strength between the groups.

8.1.2 Activity domain

In study 1 (Chapter 3), 19 different outcomes were linked to the activity domain, and 6 binary and 7 continuous outcomes were combined in meta-analysis. Children born VP had almost 3.5 times increased risk of activity limitation compared with term-born controls, and scored below term-born children on activity domain standardised assessment tools. Consistent with study 1 results, study 3 (Chapter 6) found that 4- to 5-year-old children born VP had higher odds of scoring ≤5th percentile on the MABC-2 and achieved lower scores on the MABC-2 overall and within each MABC-2 subscale than term-born children. For children born VP, poorer performance within the MABC-2 balance subscale was associated with poorer body function and participation outcomes (see section 8.1.4). However, evidence for group differences in the MABC-2 manual dexterity subscale and the odds of scoring ≤5th MABC-2 percentile weakened when adjusted for sex, social risk and CA at assessment. Little DCDQ total scores were also
poorer for VP children compared with their term-born peers, but there was little difference in the odds of being classified as 'suspect for DCD' between the groups.

8.1.3 Participation domain

Study 1 (Chapter 3) found no participation outcome data and highlighted that future research was needed to understand participation in VP preschool age populations. Study 2 (Chapter 5) began to address this knowledge gap by investigating the agreement between parent-reported and accelerometer-measured 24-hour movement behaviours in VP and term-born 4- to 5-year-old children, determining if agreement was affected by participant characteristics, including birth group, sex, social risk status and days of valid data. There was moderate agreement between parent-reported and accelerometer-measured sleep, but poor agreement between the two measures of PA and stationary duration. Very preterm birth, higher social risk status and male sex influenced parent-reporting of 24-hour movement behaviours relative to the accelerometer. Based on the results from study 2, parent-report diaries and accelerometers should be used in combination to obtain contextual information about participation alongside objective measurement of 24-hour movement behaviours.

Therefore, both parent-report and accelerometer data were used to compare the PA levels of VP and term-born 4- to 5-year-old children in study 3 (Chapter 6). Children born VP completed fewer total steps, fast steps and minutes of PA, and more stationary behaviour per day than term-born children as measured by accelerometry. Parents of VP children reported fewer minutes of unstructured play-based PA participation and more minutes of screen time per day than parents of term-born children. Adherence to the Australian 24-hour Movement Guidelines (Okely et al., 2017) was poor for both groups, with only 11% of VP and 14% of term-born participants meeting the PA, screen and sleep recommendations combined. However, the VP group had poorer adherence to the PA and screen aspects of the guideline. Fifty-seven percent
of VP children adhered to the PA recommendation compared with 74% of term-born children, and 21% of VP children adhered to the screen time recommendations compared with 40% of term-born children.

8.1.4 Relationships between ICF-CY domains

Study 1 (Chapter 3) emphasised that it was unclear whether known motor body structure and function impairments and activity limitations ultimately influenced participation in 3- to 6-year-old children born VP. Study 4 (Chapter 7) aimed to investigate the relationship between ICF-CY domains by examining associations between grip strength, MC and PA levels in 4- to 5-year-old children. Irrespective of birth group, consistent positive associations between MC (measured by the MABC-2 and Little DCDQ) and peak bimanual grip strength were found. A stronger positive association between MABC-2 balance subscale standard score and grip strength was found for VP children than for term-born controls. For both VP and term-born children, PA was positively associated, and stationary duration was negatively associated with Little DCDQ total score. Physical activity was positively associated with MABC-2 balance subscale standard score in the VP group, but there was little evidence of such an association in the term-born group. Physical activity levels did not appear to be associated with peak bimanual grip strength in 4- to 5-year old children.

8.1.5 Thesis summary in context with previous work

Prior to study 1 (Chapter 3), studies of preschool age children born VP compared with term-born controls had not synthesised motor outcomes within the ICF-CY framework. Although evidence of poorer motor skills and increased risk of neurological dysfunction in VP children compared with their term-born peers is well recognised in the wider literature (de Kieviet et al., 2009; Edwards et al., 2011; van Hus et al., 2014), studies investigating PA participation at preschool age are sparse.
Conversely, PA participation in typically developing children has been well researched, including study of adherence to international guidelines and correlates of PA levels at preschool age. Consistent with recent work in typically developing children (Chaput et al., 2017; Cliff et al., 2017), this thesis found poor adherence to the Australian 24-hour Movement Guidelines (study 3, Chapter 6). However, this thesis also presents novel findings of lower parent-reported and accelerometer-measured PA levels in children born VP compared with their term-born peers. Studies of typically developing children and DCD populations have reported similar findings to those in study 4 (Chapter 7), with weak associations between PA levels and strength (Fang et al., 2017) and little evidence that differences in HRPF were mediated by daily PA levels (King-Dowling et al., 2018). Furthermore, associations between objectively measured PA and motor skills have been reported to be weak at preschool age (Matarma et al., 2018). Studies in older children and children with DCD support the finding in this thesis of positive associations between MC and muscle strength (Cattuzzo et al., 2016; Comeau et al., 2017). The studies within this thesis form the foundation of PA participation-based research for VP preschool age children, and future research directions will be explored in section 8.4.

8.2 Implications of the research findings

Findings from this thesis contribute to a deeper understanding of motor outcomes for preschool age children born VP, and there are several important clinical and broader health implications of the research.

8.2.1 Clinical implications

Overall, this thesis extends prior understanding of VP outcomes by showing that children born VP experience multidomain motor difficulties compared with their term-born peers at preschool age. In line with similar recommendations from the American Academy of Pediatrics (Wang et
al., 2006), the recently published National Institute of Health and Care Excellence guideline for the follow-up of children and young people born preterm in the United Kingdom (National Institute of Health Care and Excellence, 2017) focuses on the early detection of developmental issues in preterm populations. The NICE guideline (National Institute of Health Care and Excellence, 2017) recognises that certain developmental disorders may not be detectable, or cannot be diagnosed, until later in childhood such as DCD (Spittle & Orton, 2014). The findings from this thesis support the need for developmental surveillance of children born VP by allied health clinicians and paediatricians throughout the preschool period. Awareness of multidomain motor challenges is especially pertinent for clinicians to ensure they look beyond solely assessing and treating body structure and function impairments or activity limitations, to evaluating and optimising age-appropriate participation in VP populations.

Specifically, this thesis highlights the importance of PA participation in the preschool period. The public health implications of the research findings are discussed in section 8.2.2, however there are several key implications for clinicians and other professionals working with young children. Greater awareness that preschool age children born VP may be at risk of less optimal 24-hour movement behaviours than their term-born peers is needed in clinical practice. Clinicians working with children born VP should incorporate assessment of 24-hour movement behaviours into clinical practice, ideally using questionnaires or diaries with accelerometers to understand environmental factors, and barriers/facilitators of participation alongside objectively measured PA levels. The cost of accelerometers and resources required to handle data have been identified as barriers to monitoring PA by health care professionals (Shelley et al., 2018). However, recent technological advances have resulted in cheaper consumer-grade wearable devices equipped with modern accelerometer technology and simple data display, which may address such barriers in clinical practice. However, further validation studies involving commercially available wearable devices are needed (Kim & Lochbaum, 2018). By
comprehensively monitoring of 24-hour movement behaviours in clinical practice, individualised strategies to enhance PA participation can be incorporated into a holistic treatment plan.

Young children also need support from parents and caregivers to achieve an active lifestyle, including opportunities for participation in varied, age-appropriate structured and unstructured activities within diverse environmental contexts. Therefore, clinicians working with VP children and their families can play an important role in delivering education to parents/caregivers regarding daily 24-hour movement targets and the benefits of PA participation. The findings in this thesis are pertinent not only for clinicians, but also for early educators. In this thesis, attendance at preschool, school or childcare was associated with more accelerometer-measured PA and fewer minutes of stationary behaviour than non-attendance (Chapter 6), which suggests early educators may have an important role in facilitating optimal PA participation at preschool age.

As presented in Chapter 7, PA was positively associated, and stationary duration was negatively associated with Little DCDQ total score. For children born VP, PA was positively associated with MABC-2 balance subscale standard score. These findings suggest that evidence-based motor skill interventions should be implemented by clinicians working with preschool age children born VP with motor impairments. Task specific and participation-oriented approaches involving goal setting and family/teacher support is recommended for children with motor impairments, such as DCD (Blank et al., 2019). Similarly, teacher-led interventions have been associated with improved fundamental motor skills and trends towards increased PA levels in typically developing preschool age children (Engel, Broderick, van Doom, Hardy, & Parmenter, 2018). Although such evidence can be extrapolated to children born VP, further research is needed to examine the efficacy of interventions to improve MC and PA levels specifically for VP preschool age children.
8.2.2 Public health implications

Given that higher PA levels are associated with various health and developmental benefits in the early years (Carson et al., 2017) and throughout childhood (Okely et al., 2012), this thesis contains several important implications for the public health sector and for PA promotion initiatives.

Many preschool age children are failing to adhere to 24-hour Movement Guidelines in Australia and internationally (Chaput et al., 2017; Cliff et al., 2017). Only 12% of 4- to 5-year-old children included in this thesis met all three recommendations (PA, sedentary and sleep; Chapter 6), and adherence was even lower when MVPA recommendations were included. Physical inactivity in childhood is a substantial public health concern, as adhering to the combined PA, sedentary and sleep recommendations has been found to be associated with more favourable social-cognitive development at preschool age (Cliff et al., 2017), and with lower levels of obesity and cardiometabolic risk factors in older children (Katzmarzyk & Staiano, 2017).

The preschool period is a crucial time to promote optimal PA behaviours due to several key characteristics inherent in this age group. At preschool age, children rapidly develop fundamental motor skills which facilitate participation in a wide range of physical activities (Stodden et al., 2008). Developmentally, young children have limited ability to accurately perceive their own motor skill competence (Stodden et al., 2008) and perceptions are generally positive even when actual motor skill levels are low (LeGear et al., 2012). Positive self-perception during the time of rapid motor development could be used as an opportunity to enhance motor skills and PA participation at preschool age, as children may engage and persist longer in challenging motor activities than older children (LeGear et al., 2012). Evidence suggests that a physically active lifestyle begins in early childhood (Telama et al., 2014), which further strengthens the argument that PA promotion strategies should target the preschool period for lifelong health.
Targeted PA promotion at preschool age may be even more important for children born VP due to the varied comorbidities associated with prematurity. Children born VP /VLBW have higher risk of adverse respiratory health throughout childhood (Been et al., 2014) and poorer cardiovascular outcomes later in life (Hovi et al., 2016) than their term-born peers. As children and adolescents participating in optimal 24-hour movement behaviours (i.e. high PA, low sedentary and high sleep) have more favourable cardiometabolic and adiposity outcomes than those who do not (Saunders et al., 2016), optimising healthy movement behaviours may be even more important in VP preschool age populations. As this thesis demonstrated that preschool age children born VP are less physically active than their term-born peers, increased efforts to implement PA promotion strategies in VP populations are warranted.

8.3 Strengths and limitations of the research

The methodological strengths and limitations of each individual study have been discussed within the relevant thesis chapters. Therefore, this section will discuss the strengths and limitations of the PhD research as a whole.

The most substantial strength is the novel contribution to understanding the trajectory of PA participation in VP populations. To the author’s knowledge, the studies in this thesis are the first to investigate PA levels using parent-report and accelerometers in VP preschool age children and their term-born peers. This thesis demonstrates that preschool age children born VP are less physically active, more stationary and participate in more screen time per day than term-born children, findings that have important clinical and public health implications as discussed in section 8.2. The studies in this thesis will inform future research of PA participation in VP preschool age populations.
A second major strength of this thesis is the consistent use of the ICF-CY (World Health Organisation, 2007) as a framework underpinning the research. By categorising outcomes within each ICF-CY domain in study 1 (Chapter 3), a substantial evidence gap surrounding participation in VP children compared with term-born peers was identified at preschool age. This evidence gap began to be addressed by investigating PA measurement in study 2 (Chapter 5), which subsequently informed the methodology of study 3 (Chapter 6). After identifying body structure and function impairments, activity limitations and participation restrictions for VP children relative to term-born controls in study 3, the dynamic nature of the ICF-CY framework was then investigated in study 4 (Chapter 7). By using the ICF-CY framework, this thesis identified multiple assessment and intervention entry points, deepening the understanding of physical functioning in preschool age children born VP compared with term-born peers.

The comprehensive PA measurement and data management approach used in this thesis is a further strength of the research. As highlighted in Chapter 2, high quality studies combining self or parent-report measures with accelerometry are lacking in the existing VP and/or VLBW evidence base. Including parent-report data alongside the accelerometer enabled collection of contextual information (such as screen time and participation in structured activities) with objectively measured minutes of PA, stationary behaviour, and sleep. Combining subjective and objective assessment tools meant that adherence to the PA, sedentary and screen time aspects of the Australian 24-hour Movement Guidelines was able to be investigated, maximising research translation opportunities to clinicians, health services and the broader community.

Some existing studies using accelerometers to measure PA in older VP/VLBW populations lack detailed accelerometer protocol information and several accelerometer-related methodological limitations are highlighted in Chapter 2. The accelerometer data management protocol used in this thesis is a strength and was clearly reported, which facilitates reproducibility and comparison of outcomes with existing literature. Using Axivity AX3 accelerometers enabled the collection
and processing of raw acceleration data, and meant researcher driven data management decisions could be implemented due to lack of manufacturer proprietary algorithms and the open-source firmware platform. For example, visual raw data inspection was able to be combined with an algorithm, detailed in Appendix E, for comprehensive detection of accelerometer non-wear. In the absence of evidence-based accelerometer data management protocols for preschool age children (Migueles et al., 2017), clear methodological reporting is crucial to facilitate synthesis of study findings and further the field of PA research.

Despite these strengths, there are several methodological considerations which warrant discussion. The parent-report diary used in studies 2 and 3 (Appendix D) was created specifically for use in the VIBeS2 study, as existing tools were too lengthy or did not capture the desired aspects of PA participation in the sample. Therefore, the diary has not been validated for use in preschool age children. As parents or caregivers were asked to complete the PA diary only for the time they were with their child each day, information regarding PA participation in the preschool, school or childcare context was not recorded, and full 24-hour periods of diary data were not captured on days when children were out of parental care. Similarly, including days of accelerometer data with full 24-hour wear, or ≥12 hours of daytime wear, may limit the generalisability of the study findings to those with poor compliance.

Although grip strength is a useful measure which can be used as an indicator of later health outcomes (Cheung, Nguyen, Au, Tan, & Kung, 2013; Norio et al., 2015), it may not be as relevant to physical functioning in 4- and 5-year-old children. It is possible that using a more functionally relevant strength measure, or a measure of lower limb strength such as a standing broad jump (Fernandez-Santos, Ruiz, Cohen, Gonzalez-Montesinos, & Castro-Piñero, 2015), may be more strongly associated with PA levels at preschool age.
A further limitation is that the social risk index, which was used to ascertain social risk status (studies 2, 3 and 4), was not administered at the time of the 4- to 5-year assessment. As social risk status can change over time, using data from earlier assessment timepoints may mean social risk status was misclassified for some participants at 4 to 5 years of age. Lastly, a diagnosis of DCD was unable to be made in this thesis due to recommendations that formal diagnosis should not occur before 5 years of age (Blank, Smits-Engelsman, Polatajko, & Wilson, 2012). Early identification of DCD and subsequent targeted intervention is crucial to prevent sequelae such as limited PA participation (Cairney, Hay, Veldhuizen, Missiuna, & Faught, 2010; Spittle et al., 2018). However, the Little DCDQ (Wilson et al., 2015) can be used to identify preschool age children who are at risk of diagnosis at school age, and should be incorporated into future studies to more comprehensively understand DCD risk at preschool age in VP populations.

8.4 Future research directions

This thesis addresses many gaps in the current evidence base, but further research is needed to comprehensively understand the PA participation of children born VP compared with their term-born peers at preschool age. Two key areas for future research are detailed below.

8.4.1 Studies of physical activity participation

To the author’s knowledge, only one other study (Keller et al., 1998) has examined PA in preschool age VP/VLBW children and term-born/NBW controls, meaning the evidence is limited to outcomes for just one cohort in Canada and one in Australia. Consistent with much of the research completed in older children born preterm (Lowe et al., 2017), the study by Keller and colleagues (1998) relied on subjectively reported PA data alone. Further studies combining parent-report with accelerometers in different geographical regions are needed to more fully understand PA in VP populations at preschool age. Longitudinal cohort studies of PA are
similarly needed to further appreciate the PA trajectory throughout childhood for those born preterm, including whether this trajectory is vastly different to term-born children. Transparent reporting of accelerometer data management protocols in future studies is also essential to facilitate comparison and synthesis of accelerometer-measured PA data.

8.4.2 Predictors and determinants of physical activity participation

Future research should build on the data presented in study 4 of this thesis to further identify possibly modifiable predictors of PA. Identifying environmental/societal barriers and facilitators of PA participation alongside accelerometer-measured PA levels is also required to inform VP intervention studies, as well as guide clinical management and PA promotion strategies.

Stodden and colleagues’ conceptual model (Stodden et al., 2008), which hypothesises developmental mechanisms influencing PA trajectories, has been increasingly studied in typically developing children (Robinson, 2015). However, there are limited studies investigating the central relationship between MC and PA in VP and term-born preschool age children. Similarly, the role of potentially mediating factors (HRPF and perceived MC) and weight status as an either positive or negative influence on the relationship between MC and PA have not been explored.

Although hand grip strength was treated as a component of HRPF in this thesis, other outcomes such as cardiorespiratory fitness may be more important to study in VP preschool age children. The lower levels of PA observed in VP children compared with term-born controls in this thesis may be explained by the increased prevalence of respiratory morbidity and poor exercise capacity observed in VP populations (Been et al., 2014; Lowe et al., 2017). Exercise capacity may have an important mediating role in the relationship between MC and PA for VP children, or be more strongly associated with PA levels. However, further research is needed to confirm such hypotheses at preschool age.
8.5 Conclusions

This thesis builds on existing knowledge of body structure and function impairments and activity limitations in VP preschool age children by comprehensively examining PA participation compared with term-born children. Physical activity participation in the preschool years is crucial for optimal health, development and an active lifestyle into adulthood. Many preschool age children are not sufficiently active, and preschool age children born VP appear to be at higher risk of physical inactivity than their term-born peers. The four studies in this thesis provide in-depth understanding of VP children’s physical functioning at preschool age, by highlighting that children born VP experience motor deficits within all ICF-CY domains compared with their term-born peers. This thesis emphasises that future high-quality research combining subjective and objective measures of PA participation in VP children at preschool age is greatly needed. Results from this thesis will inform future PA research, clinical management and PA promotion strategies at preschool age for children born VP.


References

questionnaire to accelerometer data and diaries. Pediatric Exercise Science, 24, 229-245. doi:10.1123/pes.24.2.229


References


References


References


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References


APPENDICES

APPENDIX A: Copyright permission for chapter one

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Original Wiley figure/table number(s) Figure 1: Family of participation-related constructs: (a) person-focused processes, (b) environment-focused processes.
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Appendix B: VIBeS2 protocol

APPENDIX B: Victorian Infant Brain Study 2 protocol publication

Motor trajectories of children born <30 weeks' gestation from birth to five years: early predictors and functional implications - protocol for a prospective cohort study

Alicia J Spittle¹,²,³, Jennifer L McGinley¹, Ross Clark²,³,⁴, Deanne Thompson⁵,⁶, Tara L FitzGerald¹,², Benjamin F Mentiplay²,⁴, Katherine Lee²,⁵, Joy E Olsen²,³, Alice Burnett², Karli Treyvaud²,³, Elisha Josev², Bonnie Alexander², Claire E Kelly²,⁴, Lex W Doyle²,³,⁷, Peter J Anderson²,⁵ and Jeanie LY Cheong²,³,⁷

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Introduction

Due to advances in medical care, younger and more vulnerable children born preterm are surviving.¹ The earlier a baby is born the greater the risk of long-term consequences, with over 50% of children born <30 weeks facing motor, cognitive and behavioural impairments.²,⁴ The neurodevelopmental deficits resulting from early birth may compromise academic achievement, physical function and other health outcomes.¹,⁵ Motor difficulties in children born <30 weeks are a particular concern, and can range from a mild impairment to the most severe developmental motor impairment of childhood, cerebral palsy (CP).⁶ A recent systematic review reported the rate of CP to be approximately 15% for children born <28 weeks and 6% for those born between 28-31 weeks, which is in stark contrast to expected rates of 0.1% in term-born children.⁷ Deficits in gross and fine motor control, balance and coordination in preterm children without CP are even more common and occur in up to 50% of children born <30 weeks.⁸

A recent Cochrane review by our group of early developmental interventions for preterm infants demonstrated the importance of intervening early to improve cognitive and motor outcomes.⁹ However, current interventions have failed to improve long-term motor outcome...
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at school age. The reasons for this are likely to be multifactorial, including: (a) a lack of understanding of the trajectory of motor impairment, i.e. whether early motor delay is associated with long-term motor impairment; (b) inability to detect possible motor deficits in the neonatal intensive care unit (NICU), which means intervention is not commenced during this key period of brain plasticity and musculoskeletal development; (c) poor understanding of the nature and consequences of motor deficits, i.e. whether the target of intervention should focus on general gross motor skills, gait training, postural control, muscle strengthening, or a combination, or on other functional limitations; and (d) a lack of knowledge of co-morbidities, i.e. the extent to which particular motor deficits are related to cognitive or behavioural problems and other non-motor difficulties.

Determining the trajectory of motor development in preterm children will help differentiate developmental delay from impairment in the clinical setting, which has traditionally been difficult. There are considerable clinical implications from knowing early in life which children are likely to: 1) have persistent motor impairments; 2) catch-up and be free of later motor impairment; and 3) develop later motor impairment. Unfortunately, there is limited understanding about the evolution of motor difficulties up to school age, due to the lack of prospective longitudinal studies with an adequate sample size. Our research team has been pivotal in revealing the strong associations between early motor assessments in the first year post-term equivalent age and later motor functioning in preterm children. However, identifying children most at risk earlier in their NICU course is crucial to ensure interventions are targeted to children most in need and to optimise the benefits of early intervention during a time of maximal brain plasticity and musculoskeletal development.

A substantial evidence base has been established for the risk factors, causal pathways and neurological mechanisms for CP, but there has been little research into the non-CP motor impairments, which affect a much larger number of preterm children. Whilst early measures of motor functioning in the neonatal period offer opportunities for early detection of motor impairment, combining these assessments with magnetic resonance imaging (MRI) at term equivalent age offers a unique opportunity to strengthen our prediction and understanding of the development of motor impairment. Our group has used MRI to identify how brain injury and altered brain development relates to motor impairment in children born preterm, such as changes in brain tissue volumes and structures and white matter microstructure. The

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neuroimaging field is expanding rapidly, with many exciting technological advancements occurring in the past few years that provide us with the opportunity to better understand large-scale (whole-brain network) to small-scale (microstructural) brain characteristics. Thus, these new MRI analytic techniques may hold the key to a more comprehensive understanding of the brain abnormalities leading to motor dysfunction in preterm populations.

To address these issues, we are extending our prospective longitudinal cohort of preterm children born <30 weeks and term-born controls already recruited for a study examining brain development and neurobehavioural impairments from birth to two years, and will comprehensively re-assess the children at five years of age. This study will utilise: (a) detailed motor assessments collected from birth to two years; (b) novel advanced brain MRI techniques to analyse previously collected neonatal images; (c) comprehensive motor assessments including novel measures of gait and postural control at five years; and (d) measures of physical activity, cognitive and learning ability, and emotional and behavioural status at five years.

The specific aims are:

**Aim 1:** To compare the prevalence of motor impairment from birth to five years of age between children born <30 weeks and term-born children, and examine whether abnormal motor assessments in the newborn period among those born <30 weeks predict abnormal motor functioning at age five years.

**Aim 2:** To determine whether there are novel early MRI biomarkers detectable in the neonatal period that can predict motor impairments at five years, and whether these relationships differ between children born <30 weeks and those born at term.

**Aim 3:** To investigate the association between motor impairments and concurrent deficits in body function and structure at five years of age using a combination of standardised and innovative tests of gait, postural control and strength, and determine whether these relationships differ between children born <30 weeks and those born at term.

**Aim 4:** Explore how motor impairments at five years, including abnormalities of gait, postural control and strength, are related to concurrent functional outcomes including physical activity, cognitive and learning ability, behavioural and emotional problems, and whether these relationships differ between children born <30 weeks and those born at term.
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Methods

Design

Prospective follow-up of a longitudinal cohort study of children born <30 weeks and term-born children recruited at birth from the Royal Women’s Hospital, Melbourne, Australia at five years of age.

Participants and Setting

Over a three-year period between 1/1/2011 to 31/12/2013 we recruited 150 preterm children (born <30 weeks) and 151 term-born children (born >36 completed weeks’ gestation and weighing ≥2500 g).\textsuperscript{15} Inclusion criteria: infants admitted to the Royal Women’s Hospital. Exclusion criteria: (i) infants with congenital abnormalities known to affect neurodevelopment; (ii) infants with non-English speaking parents due to questionnaires needing to be completed in English; and additionally for term-born infants only (iii) any admission to a neonatal intensive or special care nursery. Of the preterm children, six died in the neonatal period and one was diagnosed with Down’s Syndrome and was later excluded.

Motor assessments from birth to two years

All children in this study have had comprehensive motor assessments from birth to two years of age as previously described\textsuperscript{15} as part of a longitudinal prospective cohort study. To summarise, infants born <30 weeks had weekly assessments from shortly after birth to 32 weeks’ post menstrual age, followed by fortnightly assessments until discharge from the Royal Women’s Hospital and/or term equivalent age. At term equivalent age and at one and two years corrected age, infants from both groups attended an assessment at the Murdoch Childrens Research Institute, The Royal Women’s Hospital, or a had a home visit if unable to attend an outpatient appointment. This assessment was performed by an independent, blinded assessor, masked to previous assessment results and medical history (including preterm birth).

Procedure for five-year follow-up

The five-year follow-up will consist of a single visit to the Murdoch Childrens Research Institute at the Royal Children’s Hospital, Melbourne. Age will be corrected for prematurity...
to avoid a known bias in cognitive test scores if age is not corrected.\textsuperscript{16} The assessment will take approximately three to four hours and be conducted by an experienced physiotherapist, psychologist/research assistant and exercise scientist who will be blinded to clinical history and previous assessment results. Parents will be asked to complete a questionnaire on demographics, physical activity, activities of daily living, behaviour and additional therapy (e.g. physiotherapy, occupational therapy). Questionnaires will be sent to the primary caregiver prior to the assessment where possible, via email using REDcap. Further assessments that are not able to administered via REDcap will be administered with the caregiver during the assessment. When the child is unable to attend the hospital for follow-up, an appointment will be offered at home.

\textbf{Measurements}

Assessment measures to be collected at 5 years were selected in accordance with the World Health Organization’s International Classification of Function, Health, and Disability (known as the ICF)\textsuperscript{17} and are described below. The primary outcome is motor impairment at five years.

\textbf{Measures of Activity:} Motor development will be assessed with the: \textit{i) Movement Assessment Battery for Children – Second edition (MABC-2)}\textsuperscript{18} which consists of three subscales: manual dexterity, aiming and catching, and balance, which are summed to give a total motor score. It is reliable and valid in assessing motor development of children from three to sixteen years of age and considered the ‘gold standard’ outcome measure of motor impairment. \textit{ii) A CP diagnosis} will be made by the child's paediatrician and confirmed by the assessing physiotherapist on the basis of loss of motor function and abnormal tone and tendon reflexes at five years. The five-level \textit{Gross Motor Function Classification System (GMFCS)} will used to further classify motor function for children with CP.\textsuperscript{19}

\textbf{Measures of Body Structure and Function:} We will use a combination of clinically validated measures and new techniques to measure balance, gait and functional strength including:

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i) **Anthropometric measures** will be recorded for each child. These measures include weight, height, head circumference, lower limb length and shoe size. Lower limb length will be measured from the anterior superior iliac spine to the medial malleolus in a supine position.

ii) The GAITRite® Walkway (CIR Systems Inc., Clifton, NJ) – a 16 foot electronic carpet walkway consisting of an instrumented walking surface with an array of embedded pressure-sensitive switches used to measure gait. As a participant walks, the switches close, enabling the calculation of timing and spatial measures of the gait pattern. **Key spatiotemporal variables** will be extracted including, but not limited to, gait speed, cadence, step length, step width, and step time, and step-to-step variation of associated variables.

For all trials, children will walk between 'goal posts' placed two metres from each end of the GAITRite® Walkway, to ensure steady-state speed is captured and to minimise acceleration or deceleration phases. All assessments will be completed in bare feet, unless unsafe to do so. Gait aids or orthoses will be used, and recorded, if required for safety. A verbal and a visual demonstration, as well as a practice trial, will precede each walking condition. Six walking trials will be captured during each condition in the following sequence: (1) preferred walking speed, (2) a dual cognitive task, (3) a dual motor task, (4) a tandem line-walk and (5) running.

Dual task conditions have been shown to affect gait in both preterm and full term born children. The cognitive dual task involves walking at preferred speed while providing verbal answers within a specified category. The participant is instructed to state as many answers as possible, with the number of items recorded. Example categories for this condition include; ‘animals’, ‘things you can eat or drink’, or ‘things you can wear’. The dual motor task requires the participant to walk while balancing four table tennis balls on a 20 cm diameter plate, with the number of dropped balls recorded. In the tandem line-walk condition, participants will walk placing one foot in front of the other on a 5 cm wide non-slip line placed over the walkway, with occasions of loss of balance recorded. The running condition involves six continuous laps without stopping, at preferred running pace. Prior to the running condition, we will record resting heart rate, oxygen saturation and perceived rate of exertion using the Children’s OMNI Scale of Perceived Exertion for walking and running. These measures will be recorded again immediately after completion of the six laps.
iii) A *Microsoft Kinect*® will be used to track reflective markers placed on the sacrum and posterior calcaneus in three dimensional (3D) space during all walking and running conditions. The Kinect® includes an infrared camera (514x424) and light source used to track the location of the markers, and a depth sensing (514x424) and video camera (1920x1080) to track the body surface around the marker to allow for representation of the anatomical landmark in 3D space. The variables derived from the Kinect® at 30Hz will include (but not be limited to) those acquired from the GAITRite® and additional measures of trunk movement including vertical and medial-lateral centre of mass displacement. These trunk measures may be important, as they are known to be affected in children born preterm.²³ The participant will also complete three vertical jumps with Kinect® monitoring, with the primary outcome measure being maximum vertical jump height.

iv) *Hand grip strength* (force in kilograms) will be measured using a grip strength dynamometer in a seated position, with the shoulder adducted and neutrally rotated, elbow flexed at 90° and the forearm and wrist in a neutral position.²⁴ Children will be instructed to squeeze the dynamometer as hard as possible with verbal encouragement throughout each trial. A practice trial will be provided to ensure the child understands the contraction required. Three unilateral trials on each arm will be recorded. Three additional trials of bilateral grip strength will be performed with the participant in the same position as the unilateral test but with the shoulders internally rotated to allow the dynamometer to be positioned at the midline of the body.

**Measures of Participation:** i) A small Axivity AX3 tri-axial accelerometer-based activity monitor will be worn on the ankle over a consecutive seven day period to obtain information about the number of steps taken per day and sedentary behaviour patterns. The child and caregiver will be educated on wearing the device, and the child will wear it 24 hours a day for seven days before returning it in a pre-paid envelope.

ii) A *physical activity questionnaire* will accompany the activity monitor and will be completed by parents during the same seven-day period that the monitor is worn. This questionnaire will provide more detailed information regarding the sedentary behaviours, screen time and the types of physical activities completed by participants. This questionnaire was developed for use in this study, and is included in Appendix 1.
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iii) The PEDI-CAT (Pediatric Evaluation of Disability Inventory)\textsuperscript{25} is a questionnaire that will be used to assess abilities in three functional domains: Daily Activities (e.g. dressing, feeding), Mobility (e.g. transfers, steps and inclines, running and playing) and Social/Cognitive (e.g. interaction, communication, self-management). It provides standard and scaled scores based on normative and disability samples, and is validated for children with a range of physical and behavioural conditions, including children who use mobility devices. Caregivers will complete the PEDI-CAT on an iPad during their child’s assessment.

iv) The PedsQL 4.0\textsuperscript{26} is a 23 item questionnaire that will be used to assess child health-related quality of life. It will be completed by parents, and measures domains of physical health, emotional and social functioning.

v) The Little Developmental Coordination Disorder Questionnaire (Little DCD)\textsuperscript{27} is a parent-completed measure which is designed to identify subtle motor problems in children. This questionnaire has been revised to be appropriate for use by parents of children aged five to seven years of age and its concurrent validity has been established with the MABC-2.\textsuperscript{28}

**Measures of Personal Factors:**

i) General cognitive function will be assessed using the Wechsler Preschool and Primary Scale of Intelligence (Fourth Edition, Australian and New Zealand Standardised Edition; WPPSI-IV).\textsuperscript{29} The WPPSI-IV has Australasian norms and is the gold standard measure for assessing general intellectual ability. It provides measures of key cognitive domains: full-scale IQ, verbal comprehension, visual-spatial reasoning, fluid reasoning, working memory, and processing speed.

ii) Children’s emotional symptoms, conduct problems, hyperactivity/inattention, peer problems and prosocial behaviour will be assessed using the well-validated and widely-used parent-report of symptoms, the Strengths and Difficulties Questionnaire.\textsuperscript{30}

iv) Psychiatric disorder will also be assessed using the Developmental and Wellbeing Assessment (DAWBA). The DAWBA is a structured evaluation for assigning DSM-V psychiatric diagnoses, and demonstrates good validity and will be completed by parents via an online questionnaire.\textsuperscript{31}

v) Parent report using the validated Ages and Stages Questionnaire (ASQ-3) will screen child development in the areas of communication, gross motor skills, fine motor skills, problem solving, and personal-social skills.\textsuperscript{32}
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**Measures of Environmental Factors:** The Social Risk Index\(^{33}\) assesses six aspects of social status including family structure, education of the primary caregiver, occupation of the primary income earner, employment status of the primary income earner, language spoken at home, and maternal age at birth. It will be completed by the primary caregiver at five years.

**Predictors of motor impairment**

**Brain MRI:** Between 38 and 44 weeks’ gestational age, MRI was performed at the Royal Children’s Hospital, Melbourne on a 3T Siemens Magnetom Trio, Tim system, as previously described.\(^{15}\) As part of the current proposal, three novel advanced multi-modal MRI analyses will be applied to our previously acquired structural, functional, and diffusion images (n=110 for children born <30 weeks and n=38 for term-born controls):

i) **Infant volumetric analyses.** Morphologically Adaptive Neonatal Tissue Segmentation (MANTiS) will be used to divide \(T_2\) images into white matter, cortical grey matter, cerebrospinal fluid, deep nuclear grey matter, brainstem, hippocampus, amygdala, and cerebellum (Figure 1).\(^{34}\) Further, volumes for 100 brain regions will be quantified, including basal ganglia and thalamus, cerebellar vermis and hemispheres, and 68 cortical brain regions (based on the commonly used Desikan-Killiany adult brain atlas available in FreeSurfer software;\(^{35}\) Figure 1). This will be achieved by applying our recently developed novel infant brain atlas: the Melbourne Children’s Regional Infant Brain (M-CRIB) atlas.

![Figure 1. Morphologically Adaptive Neonatal Tissue Segmentation (MANTiS) brain tissue segmentation (A) and Melbourne Children’s Regional Infant Brain (M-CRIB) atlas infant](image)

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brain sub-regional parcellation including basal ganglia and thalamus, cerebellar vermis and hemispheres, and cortical regions (B).

ii) Connectivity analyses. Graph theoretical methods will be applied to understand the complex large-scale network of the brain, allowing the quantification of topological properties including modularity, network integration and network hierarchy. The ‘nodes’ of the graphs will include the cortical and sub-cortical grey matter regions delineated using M-CRIB. The ‘edges’ will be denoted as the white matter fiber tracts from diffusion weighted images in the case of Structural connectivity analyses. Alternatively, Functional connectivity analyses will utilise resting state images, where temporal correlations in spontaneous Blood Oxygen Level Dependent (BOLD) signal oscillations will form the ‘edges’ of the graph.

iii) White matter microstructural organisation. Advanced cutting edge models of water diffusion will be used to glean insight into microstructural characteristics of grey and white matter, including axon density and myelination. In addition to the quantification of grey and white matter complexity, diffusion models will enable the most advanced tractography methods.

Sample Size: The sample size for the study has already been determined by the size of the existing cohort (currently n=143 <30 weeks and n=151 term). Based on our past experience in assessing many similar aged cohorts over several decades, we conservatively estimate a follow-up rate of 88% overall, which will be higher for the preterm than the term group, and hence we expect approximately 130 in each group. With 130 in each group, the study will have 80% power to detect differences in means between the group as small as 0.35 standard deviation (SD), and a reduction in proportions from 50% down to 35%, with a Type-I error of 5%.

Data Management and Analysis:

Data will be collected, entered into a REDCap database, edited, and analysed using Stata, in accordance with the aims as follows:

Aim 1: The prevalence of motor impairment from birth to five years will be compared between children born <30 weeks and term-born peers using separate logistic regression models applied at each of the time points (term age, one, two and five years). Results will be
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reported as odds ratios for impairment, along with 95% confidence intervals (CI). Persistent motor impairments during the neonatal period will be assessed as a predictor of severity of motor impairment at five years of age in children born <30 weeks using linear regression. All models will be fitted using generalised estimating equations (GEEs) with results reported with robust standard errors, to allow for the clustering of multiple births. Analysis will be repeated adjusting for predictors of motor outcome, including additional therapy, sex, brain injury and chronic lung disease.

**Aim 2:** Logistic regression will be used to investigate the association between neonatal MRI biomarkers and the severity and occurrence of motor impairment at five years, again fitted using GEEs and reported with robust standard errors. Initially univariable models will be fitted for each predictor before combining important predictors into a single multivariable model to investigate independent predictors. Predictor-by-group interactions will be used to explore whether relationships differ in the two birth groups.

**Aim 3:** Linear and logistic regression will be used to investigate the association between gait, posture and strength, and the severity and occurrence of motor impairment respectively. Separate models will be fitted for each predictor using GEEs, with an interaction between each gait, posture and strength variable and group to explore whether these relationships are different in the two birth groups.

**Aim 4:** Linear and logistic regression will investigate the association between severity and occurrence of motor impairment and physical activity, cognitive and learning and behavioural outcomes, applied across all participants in a single model. Separate models will be fitted for each outcome using GEEs, with an interaction between motor impairment and group to explore whether these relationships differ in the two birth groups.

**Discussion/Significance**

The adverse social and economic impact of the impairments and subsequent health outcomes associated with preterm birth is substantial due to both direct costs (health care and educational support) and lost opportunity costs. Understanding the developmental precursors of motor impairment in children born <30 weeks is essential to minimise the negative effects of preterm birth on motor skill development, and potential secondary impacts on physical activity, participation, academic achievement, and self-esteem. Better understanding of motor skill development will enable targeting of intervention and streamlining of services to the
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individuals who are at highest risk of motor impairments. This study will enable the development of clinical practice guidelines, not only for recommendations of early assessment, but also for interventions targeting aspects of motor development, such as strength training if there is underlying weakness identified, or postural control training if balance problems are identified at the body function and structure level. Furthermore, we will be able to advise on the rates of co-morbidities and thus develop recommendations on the role of the multi-disciplinary team in the follow-up of children with motor impairments to ensure appropriate allocation of health resources.

Conflict of interest declaration:
The authors have no conflicts of interest to declare.

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References


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**APPENDIX D: Physical activity diary**

**PHYSICAL ACTIVITY DIARY**

Study number:

Day 1 date: ____________________

Please answer the following questions as best as you can for the time your child was with you each day. Estimate any times in hours, including decimals.

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<th></th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
<th>Day 7</th>
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<tr>
<td>Sleep time last night</td>
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<td>:</td>
<td>:</td>
<td>:</td>
<td>:</td>
<td>:</td>
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<tr>
<td>Wake time this morning</td>
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<tr>
<td>Did you child take off the activity monitor today?</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
</tr>
<tr>
<td>If yes, record time with monitor off (hours)</td>
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<td>Time watching TV/videos/playing computer/video games/playing on smart phones or tablets (hours)</td>
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</tr>
<tr>
<td>Time spent in quiet play e.g. reading/being read to/drawing/painting/puzzles/games (hours)</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
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<td>[ ]</td>
</tr>
<tr>
<td>Did your child attend childcare/kinder/school today?</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
</tr>
<tr>
<td>If yes, did they travel by active transport?</td>
<td>Walk/Bike/Scooter</td>
<td>Walk/Bike/Scooter</td>
<td>Walk/Bike/Scooter</td>
<td>Walk/Bike/Scooter</td>
<td>Walk/Bike/Scooter</td>
<td>Walk/Bike/Scooter</td>
<td>Walk/Bike/Scooter</td>
</tr>
<tr>
<td>Please circle type of active transport if applicable.</td>
<td>[ ]</td>
<td>[ ]</td>
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</tr>
<tr>
<td>Time spent participating in active unstructured play e.g. playground, climbing, running, skipping, hula hoops (hours)</td>
<td>[ ]</td>
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<td>[ ]</td>
<td>[ ]</td>
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<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Did your child participate in active structured play today?</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
</tr>
<tr>
<td>If yes, please tick type of activity</td>
<td>Swimming</td>
<td>Football</td>
<td>Dance/Gymnastics</td>
<td>Trampolining</td>
<td>Athletics</td>
<td>Walking (e.g. walking the dog)</td>
<td>Bike riding</td>
</tr>
<tr>
<td></td>
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<td>[ ]</td>
<td>[ ]</td>
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</tr>
<tr>
<td></td>
<td>Tennis</td>
<td>Cricket</td>
<td>Netball/Basketball</td>
<td>Soccer</td>
<td>Martial arts</td>
<td>Other</td>
<td></td>
</tr>
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<td></td>
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</tr>
<tr>
<td>If yes, record time spent in total (hours)</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
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</tr>
</tbody>
</table>
Axivity AX3 (Axivity AX3, Newcastle Upon Tyne, United Kingdom) accelerometers were initialised using open source OmGui software (Open Movement, United Kingdom) and set to record for 7 days from the time of each participant’s appointment. A sampling rate of 50 Hz, dynamic range of +/- 8 g and 13-bit analogue to digital conversion were used. Data were downloaded to a specialised analysis program. This technical document describes the analysis program and methods of accelerometer data management. A summary of accelerometer-measured outcomes and the thesis chapters which are relevant to each outcome are included in Appendix H.

General data management

Accelerometer data were high pass filtered from 12.5 Hz to 25 Hz using a Symlet-8 wavelet filter. Each axis was then summed at each time interval. A 200 ms windowed moving average filter was then applied to the data, which effectively transformed it into a cyclical wave pattern when a stride occurred. Further information about stride threshold is included below.

Physical activity outcomes

A threshold of 0.5 g was used to identify a step on that lower limb. This threshold was chosen based on visual inspection of observed gait traces collected from multiple children in each group. An example of stride detection using this algorithm is provided in Figure E.
Figure E: Visualisation of raw data from one axis of the accelerometer (white trace), with identified strides (red circles). The x-axis is shown in seconds, with B a zoomed in section of A.

Stride thresholds were set between 0.5 Hz to 3.33 Hz to remove movements deemed unfeasible for human gait (i.e. too slow or fast to reflect a typical gait-related step). Physical activity was measured using several different methods. The number of steps and the minutes spent stepping (stepping PA) were summed for each day of data. Time spent moving (1-minute physical activity) was calculated by subtracting minutes of sleep and stationary time from 24-hours for each day of data. Moderate to vigorous physical activity (MVPA) was determined for each day using individualised cadence cut points. Each participant’s habitual stride rate was determined using the modal stride rate (Hz) – i.e. the most common stride speed - over the time they wore the
accelerometer. The modal stride rate was multiplied by 1.31 to identify a threshold for ‘fast gait’, a multiplication factor based on the observed stride rate difference between fast and habitual gait in children (Lim et al., 2016). The number of fast steps and minutes spent in fast gait (minutes of MVPA) were calculated for each day of available data.

Stationary outcomes

Stationary time was measured using two different measures, which were both individualised to the waking hours on each day for each participant. Firstly, stationary duration was calculated using a minute-by-minute approach, whereby each minute with no recorded steps during waking hours was categorised as stationary behaviour. Secondly, the number of stationary bouts per day during waking hours were summed. Stationary bouts were defined as >5 consecutive minutes of no steps being recorded during times when the accelerometer was being worn.

Sleep time

A semi-automatic method was used to identify the sleep and wake times in accordance with the criterion-reference recommendations of prior research (Tudor-Locke, Barreira, Schuna, Mire, & Katzmarzyk, 2013), however the technique used in this thesis was novel. Pre-processing consisted of a nine-level discrete wavelet transform with the approximation level retained, implemented on the accelerometer data for each of the three axes using the Haar mother wavelet. This served two purposes. Firstly, it separated the accelerometer traces into the retained underlying posture of the limb (low frequency data) and excluded oscillations due to rapid movements (high frequency data). Secondly, due to the unique, square shape of the wavelet it effectively suppressed noise by converting small fluctuations about a stable mean value into a flat line with no movement. From these processed data, a summed threshold on all axes of 10
degree change over a five-minute period was set to represent a significant movement. This was assessed iteratively throughout the entire signal, and converted into a binary signal (0 = no movement in the subsequent 5-minute period, 1 = movement recorded in that period).

Consequently, the first instance in the signal for each night that scored a 0 value was deemed the onset of sleep. This was manually set, and required inspection of the trace surrounding this position to determine that it was sleep onset and not just a one-off stationary period of this duration. Wake time was determined using the opposite methodology, with the last instance of a 0 value being deemed the end of the sleep and start of movement associated with waking up. This could not be fully automated as all children showed repeated bouts of movement throughout the night associated with normal sleep posture changes and/or getting up for short periods and returning to bed.

**Non-wear time**

To improve the accuracy of non-wear time, accelerometer data were pre-processed using the Teager Keiser Energy Operator technique to attenuate signal noise and augment real signal. This approach has been shown to improve the accuracy of manual and automated timing assessments of other physiological signals such as electromyography (Heywood et al., 2018; Solnik, Rider, Steinweg, DeVita & Hortobágyi, 2010). After this pre-processing, cursors were manually moved to a single location on the data trace which represented non-wear time (if this existed). The cursors were set at the start and end of the period, from which the maximum value was obtained and multiplied by five. This created a non-wear acceleration threshold. The acceleration trace was then iteratively examined to identify any periods of 20 or more consecutive minutes where no data exceeded this threshold, with the entire period deemed non-wear.
References:


STEP 1:

- Load the .wav file for the participant data you are processing using this folder:

- Visually inspect the data for non-wear time day by day (see examples of non-wear below)

  - Non-wear = consecutive zero g’s with no angle changes for ≥20 minutes during waking hours

  - Do not count as non-wear if sleep onset can be identified, and ≥20-minute period is occurring during sleep hours

- Set non-wear algorithm cursors at a period of visually identified non-wear to check whole data set
Examples of accelerometer non-wear:

- **8 hours of non-wear**
  - Non-wear on day 1
Appendix F: Accelerometer data processing guideline

STEP 2

- Once periods of non-wear are identified and documented in the processing notes for the specific participant, click the ‘process’ button

- The green ‘wait’ button will change to a red ‘ready’ button once the data are processed

STEP 3:

- Change to the ‘Process’ tab and set sleep and wake cursors for all nights (yellow arrows) (including first sleep and last wake - orange arrows)
Appendix F: Accelerometer data processing guideline

- Zoom in to each sleep/wake section, using both top and bottom graphs in conjunction to set sleep and wake time (ensure the bottom graph reflects the exact data on the top graph)

- Click ‘Finished all’ when all full sleep/wake times are set

**STEP 4:**

- Click along each remaining tab to view the corresponding data (see screenshots below)

- Check the data have saved in the results spreadsheet
APPENDIX G: VIBeS2 ethical clearance

ETHICS APPROVAL & GOVERNANCE AUTHORISATION

15 January 2016

Dr Alicia Spittle
ViBeS
The Royal Children’s Hospital Melbourne

Dear Dr Spittle

Project Title: Neurobehavioural development of infants born <30 weeks gestational age and their parents psychological wellbeing between birth and five years of age

RCH HREC Reference Number: HREC 34147D

I am pleased to advise that the below modification has received ethical approval from The Royal Children’s Hospital Melbourne Human Research Ethics Committee (HREC). The modification has also received governance authorisation at the Melbourne Children’s Campus (Incorporating The Royal Children’s Hospital, Murdoch Children’s Research Institute and the University of Melbourne Department of Paediatrics).

The Royal Children’s Hospital Melbourne HREC is organised and operates in accordance with the National Health and Medical Research Council’s (NHRMC) National Statement on Ethical Conduct in Research Involving Humans (2007) and all subsequent updates, and in accordance with the Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95), the Health Privacy Principles described in the Health Records Act 2001 (Vic) and Section 95A of the Privacy Act 1988 (and subsequent Guidelines).

HREC Approval Date: 15 January 2016

Participating Sites:
Ethical approval for this project applies at the following sites:

<table>
<thead>
<tr>
<th>Site Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Royal Children’s Hospital and Murdoch Childrens Research Institute</td>
</tr>
</tbody>
</table>

Approved Documents:
The following documents have been reviewed and approved:

<table>
<thead>
<tr>
<th>Document</th>
<th>Version</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protocol</td>
<td>Version 6.0</td>
<td>08 December 2015</td>
</tr>
<tr>
<td>Parent / Guardian Information Statement and Consent Form</td>
<td>Version 6.0</td>
<td>08 December 2015</td>
</tr>
<tr>
<td>Ages &amp; Stages Questionnaire (60mth) (ASQ-3)</td>
<td></td>
<td>2009</td>
</tr>
<tr>
<td>PedsQL - Parent 5-7</td>
<td>4.0</td>
<td>1998</td>
</tr>
<tr>
<td>Change of Investigator – Addition of Dr Deanne Thompson, A/Prof Jennifer McGinley, Dr Ross Clark and Dr Joy Olsen.</td>
<td></td>
<td>23 December 2015</td>
</tr>
</tbody>
</table>

Conditions of Ethics Approval:
- You are required to submit to the HREC:
  - An Annual Progress Report (that covers all sites listed on approval) for the duration of the project. This report is due on the anniversary of HREC approval. Continuation of ethics approval is contingent on submission of an annual report, due within one month of the
Appendix G: VIBeS2 ethical clearance

approval anniversary. Failure to comply with this requirement may result in suspension of
the project by the HREC.

- A comprehensive Final Report upon completion of the project.
- Submit to the reviewing HREC for approval any proposed amendments to the project including any
proposed changes to the Protocol, Participant Information and Consent Form/s and the Investigator
Brochure.
- Notify the reviewing HREC of any adverse events that have a material impact on the conduct of the
research in accordance with the NHMRC Position Statement: Monitoring and reporting of safety for
clinical trials involving therapeutic products May 2009.
- Notify the reviewing HREC of your inability to continue as Coordinating Principal Investigator.
- Notify the reviewing HREC of the failure to commence the study within 12 months of the HREC
approval date or if a decision is taken to end the study at any of the sites prior to the expected date
of completion.
- Notify the reviewing HREC of any matters which may impact the conduct of the project.
- If your project involves radiation, you are legally obliged to conduct your research in accordance
with the Australian Radiation Protection and Nuclear Safety Agency Code of Practice "Exposure of
Humans to Ionizing Radiation for Research Purposes" Radiation Protection series Publication No.8
- The HREC, authorising institution and/or their delegate/s may conduct an audit of the project at
any time.

Yours sincerely

Kelly Hoffman
Research Governance Manager
Research Ethics and Governance
The Royal Children’s Hospital Melbourne
Phone: (03) 9345 5044
Email: rch.ethics@rch.org.au
Web: www.rch.org.au
Appendix H: Summary of accelerometer and diary outcomes

**APPENDIX H: Summary of accelerometer and diary outcomes**

A summary of accelerometer-measured outcomes and the thesis chapters which are relevant to each outcome are included in Table H. Detailed technical information regarding accelerometer outcomes are presented in Appendix E.

Table H Summary of accelerometer-determined and parent-reported outcomes

<table>
<thead>
<tr>
<th>Accelerometer outcome</th>
<th>Unit of measurement</th>
<th>Definition</th>
<th>Relevant thesis chapter</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-minute physical activity</td>
<td>Minutes per day</td>
<td>Each non-stationary minute during waking hours: 24-hours minus (sleep + 1-minute stationary minutes)</td>
<td>5, 6, 7</td>
</tr>
<tr>
<td>Total steps</td>
<td>Number per day</td>
<td>Total steps during waking hours</td>
<td>6</td>
</tr>
<tr>
<td>Stepping physical activity</td>
<td>Minutes per day</td>
<td>Total time per day spent performing stepping movements</td>
<td>5, 6, 7</td>
</tr>
<tr>
<td>Time in MVPA</td>
<td>Minutes per day</td>
<td>Time spent stepping above the fast gait threshold (Appendix E)</td>
<td>6, 7</td>
</tr>
<tr>
<td>Number of fast steps</td>
<td>Number per day</td>
<td>Steps taken above the fast gait threshold (Appendix E)</td>
<td>6</td>
</tr>
<tr>
<td>Stationary duration (1-minute stationary)</td>
<td>Minutes per day</td>
<td>Each minute with no recorded steps during waking hours</td>
<td>5, 6, 7</td>
</tr>
<tr>
<td>5-minute stationary duration</td>
<td>Minutes per day</td>
<td>Stationary minutes recorded after 5 consecutive minutes of no steps being recorded.</td>
<td>5</td>
</tr>
<tr>
<td>Stationary bouts</td>
<td>Number per day</td>
<td>Number of bouts &gt;5 minutes with no recorded steps</td>
<td>6</td>
</tr>
<tr>
<td>Sleep duration</td>
<td>Minutes per night</td>
<td>Minutes between sleep onset and waking</td>
<td>5, 6</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diary outcome</th>
<th>Unit of measurement</th>
<th>Definition</th>
<th>Relevant thesis chapter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total physical activity</td>
<td>Minutes per day</td>
<td>Structured + unstructured physical activity</td>
<td>5, 6</td>
</tr>
<tr>
<td>Unstructured physical activity</td>
<td>Minutes per day</td>
<td>Play-based physical activity e.g. playground, climbing, running</td>
<td>6</td>
</tr>
</tbody>
</table>
## Appendix H: Summary of accelerometer and diary outcomes

### Table H continued Summary of accelerometer-determined and parent-reported outcomes

<table>
<thead>
<tr>
<th>Diary outcome</th>
<th>Unit of measurement</th>
<th>Definition</th>
<th>Relevant thesis chapter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structured physical activity</td>
<td>Minutes per day</td>
<td>Activities in which the child is enrolled or completes on a regular basis e.g. swimming lessons, dance classes</td>
<td>6</td>
</tr>
<tr>
<td>Total stationary duration</td>
<td>Minutes per day</td>
<td>Non-screen stationary + stationary behaviour</td>
<td>5, 6</td>
</tr>
<tr>
<td>Non-screen stationary duration</td>
<td>Minutes per day</td>
<td>Time spent in stationary activities e.g. reading, drawing, puzzles</td>
<td>6</td>
</tr>
<tr>
<td>Screen time</td>
<td>Minutes per day</td>
<td>Time spent watching TV, playing computer/video games or on smart phones/tablets</td>
<td>6</td>
</tr>
<tr>
<td>Sleep duration</td>
<td>Minutes per day</td>
<td>Minutes from sleep onset to waking</td>
<td>5, 6</td>
</tr>
</tbody>
</table>

MVPA, moderate to vigorous physical activity
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Appendix J: Copyright permission for chapter seven

APPENDIX J: Copyright permission for chapter seven

Title: A Developmental Perspective on the Role of Motor Skill Competence in Physical Activity: An Emergent Relationship

Author: David F. Stodden, Jacqueline D. Goodway, Stephen J. Langendorfer, et al

Publication: Quest

Publisher: Taylor & Francis

Date: May 1, 2008

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Author/s:
FitzGerald, Tara Louise

Title:
Physical activity participation in preschool age children born very preterm

Date:
2019

Persistent Link:
http://hdl.handle.net/11343/222573

File Description:
Physical activity participation in preschool age children born very preterm

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