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The inter-relationship between physical activity, cardiorespiratory fitness, body composition and cardiometabolic risk factors in adults and children with cerebral palsy

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DECLARATION

This thesis is submitted by the undersigned to Trinity College Dublin for the examination of a doctor of philosophy. All work described herein is entirely my own work and has not been submitted as an exercise for a degree at this or any other University. I hereby agree that this thesis may be lent or copied upon request with the consent of the librarian and with the due acknowledgement of the author.

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SUMMARY OF THESIS

The association between physical activity, delayed all-cause mortality, decreased risk of hypertension, coronary heart disease, stroke and type II diabetes mellitus is well established. Physical activity has a positive effect on a number of cardiometabolic risk factors in adults and children including systolic blood pressure, triglycerides, high density lipoprotein-cholesterol, plasma glucose, insulin, and insulin resistance. It has been established that adults and children with cerebral palsy participate in less physical activity than their able-bodied peers. The aim of this thesis was to investigate the effect of reduced participation in physical activity on body composition, cardiorespiratory fitness, and cardiometabolic risk factors in adults and children with cerebral palsy.

At the time that the studies presented in this thesis commenced, there were limited methods available to measure physical activity in adults and children with cerebral palsy. The literature review presented in Chapter 3 identified three accelerometry-based devices that provided estimates of energy expenditure in intervals of 1 minute or less. These devices had not been directly compared in adults or children without cerebral palsy and therefore there was no information about the concurrent validity of them in the general population.

In study 1 the criterion and concurrent validity of these three devices, the RT3 accelerometer, the Sensewear Pro Armband (SWA) and the Intelligent Device for Energy Expenditure and Activity (IDEEA), was investigated in adults and children without cerebral palsy. The results of this study indicated that the SWA provided the best estimate of energy expenditure in adults and children without cerebral palsy. However, even when the SWA demonstrated the best agreement with a criterion measure, during running, limits of agreement ranged from -29% to 13% of the mean energy expenditure.

In study 2 the criterion and concurrent validity of the RT3, the SWA and the IDEEA was investigated in adults and children with cerebral palsy. The RT3 provided the most accurate estimation of energy expenditure in comparison to the gold standard. There was significant inter-individual variation, however, and the RT3 underestimated energy expenditure by up to 37.9% in adults and up to 26.9% in children. The results of this study indicated that caution must be used when using the RT3 to estimate energy expenditure in adults and children with cerebral palsy, particularly at an individual level.

As a result of the findings in study 2 it was hypothesised that a large proportion of the error in energy expenditure estimation was associated with the inbuilt algorithms that convert raw data to energy expenditure. The RT3 is a traditional accelerometer, which is conventionally used to quantify time spent in sedentary, light, moderate or vigorous activity by categorising raw accelerometer counts with count thresholds or 'cut-points'. In study 3 the accuracy of previously published cut-points for the RT3 at classifying physical activity intensity in adults and children with cerebral palsy was investigated. In children, the cut-points incorrectly classified moderate-to-vigorous activity as light activity 30% of the time. Published cut-points had a higher sensitivity value (83.9%) in adults, as a result of fewer incorrect classifications. A new moderate-to-vigorous cut-point of 689 counts.min^{-1} was identified for children with cerebral palsy. The sample size was insufficient to cross-validate this cut-point however, and therefore requires cross-validation in an independent sample.

In study 4 everyday levels of physical activity were compared between adults with and without cerebral palsy. Adults with cerebral palsy participated in less moderate, vigorous and total activity than adults without cerebral palsy. Gross motor function was the main determinant of physical activity levels in people with cerebral palsy, and those with the highest gross motor function achieved similar levels of moderate, vigorous, and total activity as those without cerebral palsy. Moderate physical activity was negatively associated with a number cardiometabolic risk factors.

In study 5 the prevalence of cardiometabolic risk factors in adults with cerebral palsy was investigated. More than a fifth of the relatively young cohort of adults with cerebral palsy had the metabolic syndrome and more than a third were centrally obese. The results of this study also indicated that waist circumference is a stronger predictor of cardiometabolic risk factors, including hypertension, dyslipidaemia, and insulin resistance in adults with cerebral palsy, compared to BMI, waist-hip ratio, and waist-height ratio.

In study 6 the association between physical activity, body composition and blood pressure was investigated in children with cerebral palsy. Total and central adiposity was associated with systolic blood pressure in children with cerebral palsy. Total physical activity, moderate-to-vigorous physical activity, and vigorous activity were negatively associated with high risk blood pressure values. Sedentary activity was positively associated with high risk blood pressure values.

In study 7 the association between cardiorespiratory fitness, blood pressure, and body fat was investigated in children with cerebral palsy. Cardiorespiratory fitness was negatively associated with systolic blood pressure and body fat, particularly central adiposity. A large proportion of the association between cardiorespiratory fitness and blood pressure was explained by the relationship between body fat and blood pressure. Total activity, sustained bouts of moderate-to-vigorous activity and vigorous activity alone, but not sedentary, light or moderate activity, were associated with cardiorespiratory fitness. Only vigorous physical activity differed across levels of fitness, classified according to reference curves, highlighting the need for healthcare professionals to promote participation in vigorous physical activity among children with cerebral palsy.

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Published papers

Ryan, J. and Gormley, J. (2013) Measurement of energy expenditure by activity monitors. Physical Therapy Reviews. doi:10.1179/1743288X13Y.0000000063

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Ryan, J., Walsh, M., McGahey, A., McLoughlin, B. and Gormley, J. An investigation into the ability of three accelerometry-based devices to detect the increased energy cost of locomotion in ambulatory adults and children with cerebral palsy. AACPDM (American Academy of Cerebral Palsy and Developmental Medicine) 67th Annual Meeting, Milwaukee, October 2013.

LIST OF ABBREVIATIONS

CP	Cerebral palsy
TD	Typically developing
GMFCS	Gross Motor Function Classification System
ICF	International Classification of Functioning, Disability and Health
PE	Physical education
BMI	Body mass index
CVD	Cardiovascular disease
T2DM	Type II diabetes mellitus
TC	Total cholesterol
LDL-C	Low-density lipoprotein cholesterol
HDL-C	High-density lipoprotein cholesterol
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
CRP	C-reactive protein
HbA_{1c}	Glycated haemoglobin
25OHD	25-hydroxy vitamin D
IDF	International Diabetes Federation
NHLBI	The National Heart, Lung and Blood Institute
AHA	American Heart Association
WHF	World Health Federation
ACSM	American College of Sports Medicine
WHO	World Health Organisation
NHANES	National Health and Nutrition Examination Survey
VO_2	Oxygen uptake
HR	Heart-rate
RER	Respiratory exchange rate
SRT	Shuttle run test
CDC	Centre for Disease Control and Prevention
IOTF	International Obesity Task Force
WC	Waist circumference
WHR	Waist-hip ratio
WHtR	Waist-height ratio

EE	Energy expenditure
IDEEA	Intelligent Device for Energy Expenditure and Activity
SWA	Sensewear ProArmband
MET	Metabolic equivalent
DLW	Doubly labelled water
BMR	Basal metabolic rate
LOA	Bland and Altman Limits of Agreement
CRC	Central Remedial Clinic
VM	Vector magnitude
LOA	Limits of agreement

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Chapter 1 Introduction

1.1 Definition of Cerebral Palsy

Cerebral palsy (CP) is defined as 'a group of permanent disorders causing activity limitation that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain' (Rosenbaum et al., 2007). The definition also states that 'the motor disorders of CP are often accompanied by disturbances of sensation, perception, cognition, communication, and behaviour, by epilepsy, and by secondary musculoskeletal problems'. CP is an umbrella term that encompasses a variety of motor disorders. As such it is a heterogeneous condition in terms of aetiology, type and severity of impairment. Regardless of the cause or presentation of CP abnormal fine and gross motor functioning and organisation are the core features of CP.

To be considered CP, the disturbance that leads to motor disorders must occur within a time frame that results in interruption to the development of the child. This allows CP to be distinguished from conditions with similar presentations that result from later-acquired lesions, when motor development is well established. It is usually expected that the motor impairments of CP will manifest before 18 months of age. There is no explicit upper age limit specified however, to determine when disturbances to the brain must occur in order to be considered CP.

1.1.1 Classification of cerebral palsy

Cerebral palsy covers a wide range of clinical presentations and accompanying impairments. Classification of CP into subtypes is therefore necessary for a number of reasons. Firstly, classifying CP provides a description of the nature of the problem and its severity. This allows healthcare professionals to predict the current and future service needs of individuals with CP. Without classification, comparison of individuals with CP at one time-point is impossible because of the heterogeneity of the condition. Classification also allows healthcare professionals to evaluate changes in an individual's condition across a number of time-points.

Traditionally classification schemes focused on the distribution of the affected limbs (e.g. diplegia, hemiplegia), with a description of the predominant type of tone or movement abnormality (e.g. spastic, dyskinetic). This method of classification can be considered unreliable however as it introduces a lack of precision and clarity into the extent of involvement of each limb. For example, a person whose lower limbs are affected but who has no upper limb involvement may be classified with diplegia. Similarly a person whose four limbs are affected but their arms are not as severely affected as their legs may also be considered diplegic. Without an operational definition of the characteristics included in the classification scheme examiners may not classify the same individual in the same way. In 2006 experts developed 'The Definition and Classification of Cerebral Palsy' document to provide a common conceptualisation about CP (Rosenbaum et al., 2007). This document clearly outlines the information required for classification and the four major components of classification. These components are 1) motor abnormalities, 2) accompanying impairments, 3) anatomical and neuro-imaging findings, 4) causation and timing. The definition of each of these components and instructions on how to apply them to the classification of CP will be discussed next.

1.1.1.1 The four components of classification

Motor abnormalities can be subdivided into i) the nature and typology of the motor disorder and ii) functional motor abilities. Cases of CP should be classified by the dominant type of tone or movement abnormality categorised as spasticity, dystonia, choreoathetosis, or ataxia. It is acknowledged however, that many people will have mixed presentations. It is therefore important to list any additional tone or movement abnormalities as secondary types.

Recognition and evaluation of the functional consequences of different health states has become of increasing importance to health professionals in recent years. CP is primarily defined by movement abnormalities that result in activity limitation. It is therefore important to acknowledge and classify the functional consequences of involvement of the upper and lower extremities. The Gross Motor Function Classification System (GMFCS) is widely used to classify individuals according to their functional mobility or activity limitation (Palisano et al., 1997). The GMFCS is a quick, easy-to-use, valid and reliable measure of gross motor function, which classifies children and adolescents on a scale of 1 to 5. It places a particular emphasis on truncal control and walking. The

GMFCS was initially developed for children up to 12 years of age. The categorisation of each child into level I to V is based on functional limitations and the need for assistive technology, particularly mobility devices including wheeled mobility. Children classified as level I have minimal functional limitations whereas children classified as level V would be considered severely disabled and often unable to self-mobilise even in a power wheelchair. The classification of each child into level I to V is dependent on age with separate descriptions provided for each level in age-bands of <2 years, 2-4 years, 4-6 years, and 6-12 years. In 2007 an expanded and revised version of the GMFCS was released which revised the 6-12 year age-band of the GMFCS and included a 12-18 year age-band (Palisano et al., 2008). The purpose of this was firstly to distinguish between capability (what an individual can do in a natural environment) and performance (what an individual does in his/her current environment), and secondly to integrate the perspective that environmental and personal factors influence performance of gross motor function. As a result the distinctions between levels in the 6-12 year age-band were clarified by including only the methods of mobility most representative of each level. The differences between the 6-12 year age-band and the 12-18 year age-band are not pronounced, reflecting the fact that although children will usually continue to be capable of the methods of mobility they used at younger ages, environmental and personal factors may influence their choice of method in adolescence. A full description of the expanded and revised GMFCS can be found in Appendix 1. A version of the GMFCS has not been developed to classify physical functioning in adults with CP. However, descriptors for children have been successfully used to classify adults according to the gross motor function and mobility status (McCormick et al., 2007, Sandstrom et al., 2004).

The second component of classification is accompanying impairments. The definition of CP clearly recognises that the motor disorders of CP are often accompanied by other impairments that interfere with the ability to function in daily life. It is therefore important when classifying CP to note the presence or absence of epilepsy (defined as two or more afebrile, non-neonatal seizures), IQ (as a measure of presence/absence and severity of mental retardation), visual impairments, and hearing impairments.

The third component, anatomical and neuro-imaging findings, has historically been used to classify CP. As mentioned previously however, traditional classification schemes focused on the distribution of the affected limbs. Although this is still considered a

major component of classification the terms 'diplegia', 'hemiplegia' and 'quadraplegia' fail to clearly define the level of involvement of each limb, and notably omit a description of truncal or oropharyngeal involvement. Although these terms are firmly rooted in research and clinical practice, the 2006 report recommends that the terms 'unilateral' and 'bilateral' are used instead to differentiate between patterns of involvement. It can still be difficult to obtain clarity when implementing this system as some people with unilateral CP may also have a degree of motor involvement on the other side or people with bilateral CP may have asymmetry across sides. It is therefore important to include a description of the motor abnormality and functional motor ability with a description of anatomical distribution.

Neuro-imaging findings is also part of this component. Although categorisation of CP according to neuro-imaging findings is desirable there is insufficient research to allow for classification of CP according to neuro-imaging at present.

Finally, cause and timing of the onset of motor abnormalities is the fourth component of classification. Although efforts are made to investigate the cause of CP in individual cases it is often not possible to identify a cause. This makes categorisation of CP by cause unfeasible at present. Similarly it is difficult to identify the timing of an insult, with reasonably firm evidence, in the majority of cases. While adverse events that occur prenatally, perinatally, and postnatally should be recorded it cannot be assumed that such an event directly caused CP and therefore classifying CP by the timing of insult would introduce the potential for error into the classification system.

1.1.2 Prevalence of cerebral palsy

CP is the most common form of childhood disability with prevalence rates of 2 to 3 per 1000 live births generally reported (Stanley, 2000). This figure varies between countries, birth-weights and gestational age-groups. Although the number of people with a diagnosis of CP currently living in the Republic of Ireland is unknown attempts have been made to calculate prevalence rates of CP in different parts of Ireland at different time periods. Between 1990 and 1999 the prevalence of CP was 1.88 per 1000 live births [95% confidence interval (CI): 1.5 to 2.4] in the west of Ireland (counties Galway, Mayo and Roscommon) (Mongan et al., 2006). The rate of severe CP, defined as an IQ less than 5 and an inability to walk, was 0.26/1000 live births. Of the children diagnosed with CP, 68% were male and 32% were female. The majority of children were classified as

bilateral spastic CP (51%), followed by unilateral spastic CP (32%), dyskinesia (9%), and hypotonia with ataxia (7%). Seven children (8%), all of whom were classified as quadriplegic CP died between the ages of 2 yr 11 months and 10 yr 6 months. Of the remaining children, 26% had minimal gait abnormalities, 38% were able to walk independently without a mobility aid but had some gait disturbances, 18% required a mobility aid, and 18% required wheeled mobility. Over half of the children (56%) had an intellectual impairment; 35% had an IQ less than 50, 10% had an IQ 50 to 69, 10% had an IQ 70 to 84. Only one child had both visual and hearing impairments, 12% had visual impairment and 10% had hearing impairment. Sensory impairment was present in 21% of children. Thirty-one children (46%) had experienced seizure activity, 84% of whom still had seizure activity. Only 5% of children had a known postneonatal origin of CP that occurred between 7 months and 22 months.

Data from a collaborative network of 11 CP registers and surveys across Europe indicated that the overall prevalence rate for CP in the years 1980-1990 was similar to that reported in the west of Ireland [2.08/1000 live births (95% CI 2.02 to 2.14)] (2002). Data collected from registers in Cork/Kerry and Northern Ireland indicated that the prevalence rate in these areas was 1.49 and 2.26, respectively. Similar to reports from the west of Ireland bilateral spastic CP was the largest subtype of CP across Europe (54.9%), followed by unilateral spastic CP (29.2%), dyskinesia (6.5%), ataxia (4.3%), unclassified (3.7%), and unspecified spastic CP (1.6%). The rate of severe CP in Cork/Kerry was similar to that in the west of Ireland (0.2 per 1000 live births).

1.1.3 Predictors of mortality among adults and children with cerebral palsy

It has been well reported that mortality among children with CP is related to the severity of their condition (Strauss et al., 1998, Evans and Alberman, 1991, Crichton et al., 1995, Blair et al., 2001a). Immobility, severe intellectual disability and feeding problems have all been associated with increased mortality in this population. Children without severe impairments however, are expected to live well into adulthood (Strauss et al., 1998, Blair et al., 2001a, Evans and Alberman, 1991). Less is known about the life expectancy of adults with CP. The majority of the information about mortality and causes of mortality in adults with CP has come from research conducted on a large database of adults with CP in California. Results from this database must be interpreted with caution however, as adults on the database were still receiving services. This suggests they may

have been a more severely impaired population compared to the general population of adults with CP.

As with children the most significant risk factors for mortality in adults were deficits in functional skills such as mobility and feeding (Strauss and Shavelle, 1998). Results from the Western Australia Cerebral Palsy Register, that included people aged up to 44 years, indicated that intellectual disability was the strongest predictor of mortality among adults and children with CP (Blair et al., 2001a). This study also found that severity of motor impairment increased the risk of mortality, but only up to the age of 15 years. Mortality declined thereafter and remained steady for the next 20 years. Although this suggests that mortality may not be associated with motor impairment in middle-aged adults this study was unable to speculate on the association between motor impairment and mortality in adults over 44 years of age. Strauss et al. (2004) reported that ambulatory status was strongly predictive of mortality in older adults with CP. Adults who maintained a level of independent ambulation at 70 years of age had a survival rate of 75% compared to 85% in the general population. The survival rate was only 60% in adults who were non-ambulatory at age 70.

Mortality rate among adults with CP appears to be declining only in the most severely disabled individuals. Over the 20 year period from 1983 to 2002 mortality rates amongst adults who had severe motor impairments and were gastrostomy fed, fell by 50% (Strauss et al., 2007); the life expectancy of these individuals increased by approximately 5 years. The same decline in mortality may not have been observed in the general population of adults with CP because high functioning adults with CP are reported to have a similar, albeit slightly lower, life expectancy to the general population (Strauss and Shavelle, 1998). The association between mobility and survival in older adults suggests that interventions to maintain mobility in this population may prolong the life span of people with CP.

1.2 Consequences of Cerebral Palsy

CP is considered a non-progressive condition, in so much as the pathophysiological mechanisms leading to CP are presumed to arise from a single, inciting event or discrete series of events, which are no longer active at the time of diagnosis. It is important,

however, to recognise that CP is a life-long condition and an increased number of secondary conditions can manifest over the lifespan of a person with CP. The impact of CP on children results in poorer health, in terms of physical functioning, bodily pain, general health perceptions and family activities, compared to typically developing (TD) children (Parkes et al., 2009). Other secondary conditions reported by people with CP include fatigue, musculoskeletal conditions, chronic pain, depressive symptoms, and reduced participation (Turk, 2009, Majnemer et al., 2008).

The World Health Organisation's *International Classification of Functioning, Disability and Health (ICF)* (World Health Organisation, 2001) provides a useful framework for comprehensively assessing the effect of disability on the individual. 'Impairments' are considered problems in body structures and functions, 'activity limitations' are difficulties an individual may have in the execution of a task or action, and 'participation restrictions' are the problems an individual may experience in involvement in life situations. The consequences of CP will now be discussed in relation to the ICF framework.

1.2.1 Primary impairments associated with cerebral palsy

As discussed in Section 1.1.1.1 a number of motor abnormalities, and anatomical distributions of these abnormalities, are associated with CP. Spasticity is the most common clinical subtype of motor abnormality observed in CP (2002). Spasticity is a specific form of hypertonia that results from upper motor neurone lesion. CP is the most common condition associated with upper motor neurone lesion in children (National Collaborating Centre for Women's and Children's Health UK, 2012). Spasticity is defined by the presence of one or both of the following features: 1) abnormally increased resistance to externally imposed movement, which increases with increasing speed of stretch and varies with the direction of joint movement; 2) an abnormally increased resistance to externally imposed movement which increases rapidly beyond a threshold speed or joint angle. It is presumed to be caused by a lesion of the pyramidal tract. Other motor abnormalities observed in people with CP, such as dystonia, chorea and athetosis are caused by lesions to the extra-pyramidal tract and other motor tracts (Sanger et al., 2003). As discussed in Section 1.1.1.1 many people will have a mixed pattern of motor symptoms suggesting that although the primary lesion may be in one tract it will have secondary effects on the function of other parts of the motor pathways.

Additional components of upper motor neurone lesion include reduced range of movement, muscle weakness, poor selective motor control, exaggerated deep tendon reflexes and difficulties with motor planning. Reduced range of movement, indicative of minimal fixed muscle contractures and marked spasticity, is a primary feature of CP. Stiffness is a predominant complaint amongst adults with CP (Jahnsen et al., 2004). Although clinicians often highlight reduced range of movement as a priority during rehabilitation, research suggests that muscle weakness and poor selective motor control are key contributors to activity limitation and reduced physical functioning in this population (Rose and McGill, 2005, Stackhouse et al., 2005, Ostensjo et al., 2004). Significant reductions in muscle volumes have been reported in ambulatory adolescents and young adults with spastic unilateral CP (Lampe et al., 2006, Riad et al., 2012). Muscle wasting was apparent in all lower limb muscles. On average, the percentage reduction in muscle volume (compared to the non-affected side) was larger in the lower leg muscles than the thigh musculature (Lampe et al., 2006, Riad et al., 2012). Reductions in muscle volumes were associated with lower concentric muscle work on the affected side compared to the non-affected side (Riad et al., 2012). This suggests that even people with mild CP have significant reductions in muscle volume and strength. In addition to deficits in voluntary muscle activation, increases in antagonist coactivation have been reported in children with spastic diplegia (Stackhouse et al., 2005). People with CP therefore have the additional problem of inhibiting antagonistic coactivation as well as producing voluntary contractions of an adequate force when trying to improve strength.

1.2.2 Activity limitation and cerebral palsy

Reductions in short-term muscle power and functional muscle strength have been associated with activity limitations, specifically activities in standing, walking, running and jumping, in children with minimal impairments (Verschuren et al., 2009). It is likely that this is partly due to the contribution of muscle weakness to delayed or absent balance reactions observed in children and adolescents with CP (Campbell and Ball, 1978). Poor dynamic balance is associated with a slower speed and increased metabolic cost of walking (Liao et al., 1997). Reduced muscle strength and inefficient concentric activity also have an independent effect on the normal gait cycle and gait efficiency.

It has been widely reported that the energy cost of ambulation is increased in children with CP (Unnithan et al., 1996, Waters and Mulroy, 1999, Brehm et al., 2007, Dallmeijer and Brehm, 2011, Rose et al., 1993). Energy cost, defined as the energy used per unit of the distance covered during walking, is accepted as a measure of energy efficiency (Bowen et al., 1998). When net energy cost was examined (i.e. gross energy expenditure – resting energy expenditure) the energy cost of ambulation was approximately 40% greater in children with CP (Brehm et al., 2007). Energy efficiency of gait is significantly associated with activity limitation (Kerr et al., 2008). Both energy efficiency and activity limitation differ across classifications of CP. Energy cost and activity limitation is significantly higher in children with bilateral spastic CP compared to unilateral spastic CP (Kerr et al., 2008, Rose et al., 1993, Bell and Davies, 2010), and also in children classified as level III on the GMFCS compare to levels I and II (Kerr et al., 2008).

The energy efficiency of gait also varies with age. Kerr et al. (2011) reported that among children and adolescents with CP gait was most inefficient at age 12. This coincides with deterioration in gross motor skills from age 13 (Kerr et al., 2011). Possible explanations for functional declines in early adolescence are the onset of puberty, the reduction in activity levels that is often observed in adolescence, the need to use wheeled mobility when transitioning to secondary school, and the impact of increased school work on time spent on physiotherapy interventions. As might be expected surgery can positively impact change in net energy cost over time. The strongest predictor of an improvement in energy efficiency over time however is the baseline severity of impairment (Kerr et al., 2011). Gross motor function declines more rapidly in children classified as level III or IV compared to children at level I (Kerr et al., 2011).

1.2.3 Secondary conditions associated with cerebral palsy

A predominant complaint amongst adults with CP is an awareness of premature deterioration in function compared to their able-bodied peers (Horsman et al., 2010). This is often attributed to the secondary conditions of CP. The most common conditions are fatigue, pain and stiffness (Horsman et al., 2010; Jahnsen et al., 2004; Van Der Slot et al., 2012; Sandstrom et al., 2004; Turk et al., 1997; Riquelme et al., 2011; Engel et al., 2004; Schwartz et al., 1999). The prevalence of pain reported among adults with CP ranges from 69% to 84% (Sandstrom et al., 2004; Engel et al., 2004; Turk et al., 1997; Hilberink et al., 2007). Chronic pain is reported by 28% to 75% of adults with CP and

reports suggest it is experienced daily and can be of a moderate to severe intensity (van Der Slot et al., 2012; Jahnsen et al., 2004; Engel et al., 2004; Riquelme et al., 2011; Schwartz et al., 1999). Discrepancies in reports of the prevalence of chronic pain are likely due to differences in the definition of chronic pain between studies. Even the lowest rate of 28%, however, was higher than reports in the general adult population (Jahnsen et al., 2004). Despite the high prevalence of pain among adults with CP it is poorly recognised and treated in this population (Engel et al., 2004).

Riquelme et al. (2011) reported that pain did not differ across childhood, adolescence and young adulthood in people with CP but age was a predictor of pain in able-bodied controls. In contrast Jahnsen et al. (2004) reported that the mean age of pain debut among adults with CP (age 18-72 years) was 21 ± 11 yr. The prevalence of pain also appeared to increase with age but did not differ across gender. Adults with CP report that overexertion, fatigue, inactivity and cold weather increase pain. Rest, physiotherapy, medication, movement and exercise, and warm weather are factors that reduce pain (Jahnsen et al., 2004, Schwartz et al., 1999). Pain has been found to be significantly associated with limited joint range of movement (ROM) (Jahnsen et al., 2004). Limited ROM in at least one joint was reported by 86% of adults with CP; 15% reported reduced ROM in 5 or more joints (Jahnsen et al., 2004). Even amongst high functioning adults with CP (GMFCS level I and II) 77% experienced limited ROM in the ankle joint (Sandstrom et al., 2004).

Pain is also associated with fatigue (Hilberink et al., 2007; Jahnsen et al., 2003). Chronic fatigue is higher amongst adults with CP compared to reference values for the able-bodied population and occurs in combination with chronic pain in 34% of adults with CP (van Der Slot et al., 2012; Jahnsen et al., 2003). Although one study reported that fatigue was not associated with GMFCS level (van Der Slot et al., 2012), Jahnsen et al. (2003) reported that fatigue was most prevalent amongst people with moderate motor impairments. This may be because of an imbalance between motor capacity and the work load associated with daily life. While these individuals have a greater energetic cost of locomotion than individuals with mild CP they are still trying to keep up with their able-bodied peers. Fatigue was associated with a lack of physical activity (Jahnsen et al., 2003). This is likely because reduced physical activity leads to a decline in cardiorespiratory fitness. In addition, fatigue was associated with low life satisfaction. Deterioration in functional skills with age may widen the gap between the energetic cost

of completing every day activities and the metabolic demands of daily life resulting in increased fatigue and decreased life satisfaction.

As well as the physical health consequences of CP, the physical limitations that result from CP often lead to isolation, loneliness and sometimes depression (Horsman et al., 2010). Depressive symptoms occur more frequently in adults with bilateral spastic CP than normal references and are associated with chronic fatigue (van Der Slot et al., 2012). There does not appear to be a difference in depressive symptoms amongst men and women. Participants classified as level III or IV on the GMFCS reported more depressive symptoms than adults in level I or II (van Der Slot et al., 2012). Depressive symptoms occurred in combination with chronic pain and fatigue in 16% of adults with bilateral spastic CP (van Der Slot et al., 2012). In addition, many adults with CP experience fear and frustration because of the lack of knowledge surrounding age-related secondary conditions associated with CP (Moll and Cott, 2012). Many feel that by the time they appreciate the benefits of rehabilitation for preventing further decline in function rehabilitation services are often unavailable (Moll and Cott, 2012).

1.2.4 Participation restriction and cerebral palsy

The combination of the motor impairments and secondary conditions associated with CP can result in participation restriction. Unlike activity limitation, participation restriction does not appear to be associated with energy efficiency (Kerr et al., 2008), reflecting the impact of contextual factors, i.e. personal and environmental factors, on activity performance. According to the ICF participation restriction are problems that a person may have with involvement in a particular life situation (World Health Organisation, 2001). This recognises that although a person may be capable of performing an activity in a natural environment they may not actually perform it in their current environment. A set of nine domains have been identified for recording activities and participation across different areas of life (World Health Organisation, 2001). These are learning and applying knowledge, general tasks and demands, communication, mobility, self-care, domestic life, interpersonal interactions and relationships, major life areas, and community, social and civic life. Capacity and performance can be recorded in each of these domains with much of the discrepancy between the two being explained by contextual factors. Additional impairments that accompany the motor disorders of CP

may also affect participation in everyday activities. These include intellectual impairment, epilepsy, hearing and visual impairments.

Restricted mobility is viewed as a key barrier to participation and independence by people with CP (Palisano et al., 2009). Mobility across the lifespan of individuals with CP will therefore be discussed first in detail, before returning to participation in the other domains.

1.2.4.1 Mobility and cerebral palsy

Ambulatory ability and mobility methods can vary considerably throughout the lifespan of an individual with CP in response to their motor impairments, their environment, and the demands of daily life. In a retrospective study of children who were non-ambulatory at 2 years of age 10% could walk independently at age 6 to 7 years and 17% could walk with support (Wu et al., 2004). Motor milestones at age two, in particular sitting ability and ability to pull to stand, absence of spastic quadriplegia and absence of blindness were strong predictors of ambulation at age 6. Day et al. (2007) reported that if children were able to walk and climb stairs independently by age 10 years they were very likely to remain at this level of ambulatory ability by age 25 years (77% remained at this level). Children, who walked independently but required support to climb stairs at age 10 years, were likely to remain the same by age 25 years (i.e. a 54% chance of remaining stable). They had an approximately equal chance of improving or declining in ability. Variability in the prognosis for ambulatory ability at age 25 years exists in children who require support to walk at 10 years, which can largely be explained by the choice of mobility method at baseline. Children who used a wheelchair had a 34% chance of being non-ambulatory by age 25. Children who did not use a wheelchair at 10 years had a small chance of regressing to a non-ambulatory state but had a 32% chance of improving their ambulatory ability by age 25.

Several studies have reported that the walking function of people with CP deteriorates in adulthood (Bottos et al., 2001; Sandstrom et al., 2004; Strauss et al., 2004; Opheim et al., 2009; McCormick et al., 2007). Sandstrom et al. (2004) reported that in a heterogeneous group of adults (mean age 32.9 ± 8.2 yr) a third experienced a decline in functional ability according to GMFCS level. Deterioration in mobility was predominant in GMFCS level I. This was supported by a study of 103 adults (mean age 22 yr), which reported that 60% of children who were classified as level I on the GMFCS at 12 years of

age had declined to level II by 22 years of age (McCormick et al., 2007). In general, however, if a participant was walking without mobility aids as a child (i.e. GMFCS level I or II) the likelihood of them having a similar status as a young adult was 88%. Day et al. (2007) reported that at 25 years of age, adults with CP had a greater chance of remaining at their baseline status over the following 15 years, compared to the 10 year olds. This reflected the smaller chance of improving ambulatory ability in young adulthood compared to childhood. Young adults who walked without support had a slightly greater chance of functional decline than children who walked without support. This study did not classify mobility according to GMFCS level however, so it was not reported if adults at level I would decline to level II. As with children, the choice of using a wheelchair was associated with changes in mobility status in young adults who required assistance to mobilise. Adults who used a wheelchair at 25 years of age were unlikely to improve over the following 15 years and had a greater chance of decline than those who did not use a wheelchair. Type of motor abnormality, anatomical distribution and presence of seizure activity were not associated with changes in ambulatory status over time (Day et al., 2007).

Bottos et al. (2001) reported that walking function had deteriorated in 30.5% of adults with CP (mean age 33 yr; range 19 to 65 yr). Of the people who had once been independently mobile 44.8% reported a decline in functional ability. A loss of mobility was most commonly observed between the age of 20 and 40 years (69%), with only 15% of people deteriorating after 40 years. Loss of mobility prior to age 20 years was the result of psychiatric problems or problems with surgery. The people who remained independently mobile in adulthood experienced functional deterioration, as seen by a reduction in the distance that they could walk. Diagnosis (i.e. hemiplegia, diplegia etc.) and motor impairment were related to the achievement of locomotion and its maintenance in adulthood; intellectual status was not. The majority of adults who had lost mobility reported being very frustrated at the loss, but believed that the effort in childhood and adolescence to achieve and maintain independent mobility at one time was worth it. Only 18% of adults reported being only mildly frustrated with their loss of mobility because they felt the effort to maintain walking was too high or the back pain they experienced while walking was too high.

Opheim et al. (2009) reported a higher level of deterioration in self-reported walking function (52%) in adults with CP (mean age 40 yr; range 24 to 76 yr). This rate of

deterioration had increased in the same cohort from a report 7 years previously, when 39% of participants reported deterioration. Of the adults classified in level I on the GMFCS (79% of the total sample) 25% had declined to level II. Of the adults classified in level II (10% of the total sample) 43% had improved to level I. Some of this change may be explained by error associated with self-reports of the initial GMFCS level. A decline in function was more common among people with bilateral CP. The median age for a decline in function among people with unilateral CP was 52 years; the median age of decline among people with bilateral CP was 37 years. Of the people who experienced deterioration in walking function, 65% attributed it to impaired balance, 33% reported it was a result of reduced muscle strength, 28% reported it was a result of reduced cardiorespiratory fitness and walking speed, 24% reported that spasm, stiffness, pain and reduced training contributed to the deterioration. When Opheim et al. (2012) conducted a follow-up study to objectively investigate the effect of balance on deterioration in walking function in adults with spastic bilateral CP no differences in balance confidence, fear of falling, and balance ability were observed between the adults who had or had not experienced deteriorated walking function. There was large variability in balance scores among both groups. This suggests that social roles and contextual factors contribute to the complex relationship between walking deterioration and balance, and that balance rehabilitation alone may not prevent loss of mobility.

Strauss et al. (2004) investigated walking function in three groups of young, middle-aged and older adults with CP. Although 39% of young adults (20 yr) could walk independently without support only 25% of older adults (60 yr) could walk without support. The decline in rate of independent ambulation outweighed the mortality rate in the sample, eliminating the healthy survivor effect. The older adults were followed up 15 years later and unlike the younger age groups, a dramatic decline in ambulation was noted. Out of the 70% of adults who had survived the majority were unable to walk 20 ft independently.

1.2.4.2 Participation in other domains

Imms et al. (2008) reported that children and adolescents with CP participate in a wide variety of activities at a relatively low intensity. A number of factors influence children's participation including anatomical distribution, low IQ, communication, and rehabilitation. The influence of each factor on participation depends on the domain of

the activity. Anatomical distribution of CP and cognitive impairments are associated with participation in self-care, domestic life and social activities (Ostensjo et al., 2004, Voorman et al., 2006, Majnemer et al., 2008). Communication is associated with reduced participation in formal activities and involvement in self-improvement activities in older children (Majnemer et al., 2008). Attendance at rehabilitation services is associated with increased participation in skill-based activities, although children with CP are generally less involved in these activities (Majnemer et al., 2008).

Many studies have reported that gross motor function is associated with participation in physical activities in children and adolescents with CP (Ostensjo et al., 2004, Palisano et al., 2007, Schenker et al., 2005, Majnemer et al., 2008, Voorman et al., 2006). Imms et al. (2008), however, observed a large variation in the diversity and intensity of activity amongst children classified as levels I-IV. Although only 58.8% of children with CP participated in at least one organised sport at least once a week, apart from the case of severely impaired children (level V), motor impairment did not completely explain reduced participation in physical activity. This is supported by research that found participation in the domains of mobility and social function do not decline until late adolescence despite a decline in gait efficiency and gross motor skills being evident from early adolescence (Kerr et al., 2011).

In a study of children with CP in Ireland Mc Manus et al. (2008) found that fewer children with CP play a sport 'a few times a week' compared to TD children. The number of children playing a sport declined from 52.9% of children with a mild impairment to 18.2% in moderately disabled children and 17.4% in severely disabled children. The level of participation in sport was reduced across all levels compared to TD children, of whom 79.3% of children played sport a few times a week. Interestingly, computer use was higher in children with CP with 65.4% of children with a mild disability, 73.9% of children with a moderate disability, and 60.9% of children with a severe disability using a computer a few times per week. Only 42.8% of TD children reported using a computer a few times a week. The sample of children with CP included in this study was relatively young with 40.8% of children aged 8-9 years, indicating that participation in sedentary activities was high even before adolescence, when sedentary time typically increases. Overall participation did not vary across age. Only a small proportion of children (23.5%) were 12 years of age or older however, so it is unclear if participation declined in adolescence.

Participation in physical education (PE) is generally high among children and adolescents with CP (87%) (Lauruschkus et al., 2013). Differences are observed across GMFCS level, however, with 94% of children in level I and 93% in level II participating in PE, compared to 85% in level III, 88% in level IV and 52% in level V. Although children with CP classified as level III are able to participate in PE it is clear that many do not. A lack of education among PE providers regarding appropriate activities that children with CP can participate in, lack of space, or lack of facilities are possible reasons for children being excluded from PE. Age is also significantly predictive of children participating in PE with 7-11 year olds more likely to participate than 12-17 year olds. Although this may be similar to observations in TD children maintaining physical activity levels during adolescence is particularly important in children with CP to prevent premature declines in function. If children with CP generally participate in less formal physical activities, like sport, than TD children PE may be the only opportunity they have to participate in structured physical activity.

Although gross motor function does play a role in reduced participation in physical activity among children with CP other factors clearly influence participation. It has been reported that environmental factors such as physical restrictions (e.g. stairs, uneven surfaces), transport restrictions, cultural and societal attitudes impact children's participation in community-based activities (Shikako-Thomas et al., 2008). Personal choice also appears to be a key factor in participation in physical activities (Palisano et al., 2007). Although adolescents reported that they participated in low levels of sport and play activities, they did not report that they had 'no opportunity to participate', indicating that they chose not to (Palisano et al., 2007). A recent study investigated the barriers that children and adolescents with CP (age 7-18 years), and their parents felt prevented them participating in physical activity (Verschuren et al., 2012). Personal factors for not participating in physical activity included decreased motivation of the child, feeling insecure or like an outsider, the perception that sports aren't fun, and that learning the motor skills required is too time consuming. Environmental barriers included parents' fear of their child not fitting in, parents' difficulty with watching their child struggle (i.e. losing), lack of opportunities, peers attitudes towards children with CP, sports teams not being 'open' or not having a suitable level for children with CP, and trainers not being aware of the complexity of the child.

Although the influence of age on participation restriction in leisure activities has been reported in adolescents with CP, little research has been conducted on participation restriction in adults with CP. Adults have reported that participation in physical activity is restricted by lack of knowledge, lack of access to healthcare support and rehabilitation, and social difficulties with attending gyms (Sandstrom et al., 2009). The weak relationship between motor impairments and participation restriction in adults and children with CP suggests that treatment of impairments, as is the focus of rehabilitation, may not lead to improved participation. Environmental and personal factors must be addressed simultaneously when attempting to increase participation levels in this population.

Although reduced participation in physical activity has been reported by many studies, these studies provide little information about the frequency, duration or intensity of physical activity that people with CP participate in. One would expect that as a result of the motor impairments and secondary musculoskeletal conditions, leading to deterioration in mobility, people with CP would participate in low levels of habitual physical activity at a low intensity. The next section will discuss this.

1.3 Physical Activity and Cerebral Palsy

Physical activity is defined as *'any bodily movement produced by skeletal muscle that results in energy expenditure' (Caspersen et al., 1985)*. The term physical activity therefore not only includes energy expended during exercise but also encompasses the energy cost of activities of daily living, fidgeting, spontaneous muscle contraction and maintaining posture. A useful formula to express the contribution of different components to the total energy expenditure due to physical activity is as follows:

$$kcal_{sleep}+kcal_{occupation}+kcal_{conditioning}+kcal_{household}+kcal_{other}=kcal_{total\ daily\ physical\ activity}$$

(Caspersen et al., 1985)

Many of the factors discussed already in this chapter may contribute to a reduction in habitual physical activity levels and increased sedentary behaviour in adults and children with CP. Other factors that may contribute to reduced physical activity levels and

increased sedentary time in people disabilities include: (a) the perception that physical activity should be avoided to prevent pain and fatigue; (b) assistive technologies (such as powered mobility devices); (c) overprotection of people with disabilities by family members, healthcare providers and personal assistants; (d) lack of access to exercise facilities; and (e) decreased opportunity to perform task-related physical activity such as housework or gardening (Rimmer et al., 2012).

1.3.1 Level of habitual physical activity in adults with cerebral palsy

Most information regarding physical activity levels in adults with CP is of a subjective or qualitative nature. Women with CP reported being more physically inactive than their able-bodied peers (Capriotti, 2006). Half of a sample of adults with an intellectual disability (including adults with CP) reported engaging in no exercise, and 43% reported in engaging in light exercise only (Janicki et al., 2002). Research also suggests that although adults with CP recognise the positive effect of physical activity on pain, stiffness, fatigue and general well-being they lack supportive healthcare and rehabilitation (Sandstrom et al., 2009). They therefore have little knowledge about the time, intensity and type of activities they should perform and often associate activity with pain and boredom, despite recognising the overall benefit (Sandstrom et al., 2009).

Only two studies have objectively measured habitual levels of physical activity in adults with CP. A study of 16 ambulatory adults with unilateral CP age 25-35 years and 16 age- and gender -matched control participants found no differences in the duration of dynamic activities between groups (van der Slot et al., 2007). Dynamic activities included walking, cycling and general movement e.g. moving around the kitchen during cooking. Everyday physical activity was measured with an 'Activity Monitor' for 48 hours during two randomly selected consecutive weekdays. This monitor provided information on duration, rate and moment of occurrence of activities associated with mobility (lying, sitting, standing, walking, cycling) and transitions between postures. Although the monitor has been validated in a number of populations it has not been validated in people with CP or people with other movement disorders. It was also unable to provide information about the intensity of activity that allowed comparison with physical activity guidelines.

These adults with CP were independently mobile, and did not require the use of an aid or personal assistance. They also scored highly on a measure of functional independence

and cognition. The similar duration of dynamic activities during a 24 hr period in each group (2 hr 32 min in adults with CP and 2 hr 41 min in adults without CP) may therefore be expected. Interestingly, although more participants with CP were unemployed or worked part-time (50% worked part-time, 12.5% were unemployed) compared to control participants, participation in work was not related to everyday activity. The only factor found to determine physical activity levels was participation in sport. A negative correlation was also found between satisfaction with everyday level of physical activity and mean duration of dynamic activities in a day. Although adults with CP achieved similar levels of physical activity as adults without CP they did report spending more time on non-intensive leisure activities such as watching TV.

A similar protocol was used to assess everyday physical activity levels in 56 adults with bilateral spastic CP using an Activity Monitor. Participants were 25-45 years and classified as GMFCS level I (23%), level II (50%), level III (20%) and level IV (7%). Participants classified as GMFCS level IV were non-ambulatory. Participants with CP had significantly shorter durations of dynamic activity and lower mean motility (which reflected both duration and intensity of activity) than able-bodied controls (Nieuwenhuijsen et al., 2009). Women with CP had shorter duration of activity and lower mean motility compared to control participants. Only mean motility was lower in men with CP.

A comparison of these two studies revealed that adults with bilateral spastic CP were less active than adults with unilateral CP (116 min of dynamic activities per day compared to 152 min per day). This is likely to be due to level of gross motor functioning. Adults with bilateral CP classified as GMFCS level I and II had significantly greater duration of dynamic activities and mean motility than participants classified as GMFCS level III and IV. When adults classified as GMFCS level I were compared to able-bodied adults everyday levels of physical activity were similar (mean duration of dynamic activities 10.3% vs 10.9%). Although not reported in the study by van der Slot et al. (2007), it was noted in a personal communication that adults with unilateral CP classified as GMFCS level I had similar levels of everyday activity compared to adults without CP (11.1% vs 11.2%). Only 57% of adults with bilateral spastic CP achieved at least one 5 min bout of dynamic activity and only 39% achieved one or two 10 min bouts

of dynamic activity. This would suggest that adults with bilateral CP aren't accumulating 30 min of activity in 10 min bouts as the guidelines recommend.

Using activity data from ambulatory participants in the previous study Nieuwenhuijsen et al. (2011) investigated the association between fatigue, cardiorespiratory fitness and everyday levels of physical activity in adults with bilateral spastic CP. Objectively measured physical activity was not associated with fitness in men or women. Women who self-reported higher levels of physical activity, however, had higher levels of fitness. This association was not found for men. The lack of association between physical activity and fitness may be due to the potentially low intensity at which everyday activity is performed by adults with CP. The Activity Monitor used to measure physical activity in this study did not quantify the intensity of everyday activity in terms of light, moderate or vigorous; the intensity of dynamic movement was however reported to be lower than that of able-bodied controls. If everyday activity is performed at a low intensity it is unlikely to induce changes in cardiorespiratory fitness. Further investigation into the intensity of everyday physical activity in adults with CP is required.

1.3.2 Level of habitual physical activity in children with cerebral palsy

A comprehensive review recently reported that children with CP participate in significantly less habitual physical activity than their TD peers (Carlon et al., 2012). In addition, children and adolescents with CP do not meet physical activity guidelines. Only seven studies, however, have quantitatively measured physical activity in this population. The samples included in these studies, the methods used to measure physical activity, and the parameters of physical activity that were reported varied between studies.

Three studies used a self-report measure to quantify physical activity (Zwier et al., 2010, Maher et al., 2007, Martin et al., 2012). Levels of light to moderate physical activity were similar between 11 children with CP (9-16 yr) and 11 age- and sex-matched TD children (Martin et al., 2012). Children with CP spent significantly less time in vigorous physical activity. Despite this no differences were seen in any measured indices of vascular health between groups. The questionnaire used to assess physical activity may not have been sensitive enough to determine absolute differences in time spent in each physical activity intensity.

In the study by Zwier et al. (2010) of 100 children (age 5-7 yr) with CP only 7% of children met the recommendation for physical activity. This was a relatively high functioning group of children with 56% of participants classified as level I on the GMFCS. The sample did however include children classified as level II (21%), III (17%) and IV (6%). A strength of this study was that it reported physical activity intensity. Physical activity in children with CP reached 18.1 MET.h.week^{-1}, which was significantly lower than the 31.9 MET.h.week^{-1} achieved by TD children. Soccer and horse riding were the most frequently reported activities that children with CP participated in.

Maher et al. 2007 did not report physical activity intensity in a sample of 112 adolescents with CP (11-17 yr). The sample included children in all levels of the GMFCS. As a group, children with CP participated in less physical activity than their TD peers. Gross motor function was found to be the strongest predictor of self-reported physical activity. Physical activity also declined with age. Unlike in children without CP there was no gender-difference in physical activity levels. Children with CP spent 28.49 hr per week engaging in recreational screen time. This was similar to normative values. Unlike physical activity no relationship was found between sedentary behaviour and gross motor function or age. Gender was the only significant determinant of sedentary behaviour in adolescents with CP.

The influence of GMFCS on physical activity levels was supported by a study that objectively measured physical activity in 81 children using a pedometer (Bjornson et al., 2007). When activity was averaged over five days children with CP had a lower daily walking activity than TD children. Children in level I, however, had a similar level of physical activity and intensity of physical activity as TD children. Children classified as level II and III were active at a lower intensity than their TD peers. Children in level III were the least active compared to their TD peers and peers with CP.

Stevens et al. (2010) reported an association between age and objectively measured physical activity in children with CP. Twenty-seven children (4-18 yr) wore a pedometer over four days to determine habitual physical activity levels. Young children (<10 yr) with CP had a similar number of daily steps as TD children. Older children with CP (10-18 yr) took fewer steps daily, and displayed higher levels of inactivity and low-intensity activity. They also achieved lower relative levels of high intensity activity compared to older TD children and younger children with CP. Of the sample of children included in this study

78% were classified as level I and the remainder were level II on the GMFCS. This suggests that personal and environmental factors play a role in participation in physical activity, independent of gross motor function, in adolescents with CP.

Two studies measured daily energy expenditure using the doubly labelled water method (Bell and Davies, 2010, van den Berg-Emons et al., 1995). Both studies reported that resting energy expenditure in ambulatory children with CP did not differ from that of TD children but children with CP had a lower total energy expenditure. This indicates that children with CP have a lower energy expenditure as a result of decreased activity. Although Bell and Davies (2010) noted that children with diplegia were less physically active, had a slower walking velocity, and a higher energy expenditure of walking than children with hemiplegia, they did not find a significant correlation between the energy cost of walking and activity levels. This was in contrast to the finding of Maltais et al. (2005a) who found that the net energy cost of walking could be explained by the variance in physical activity levels. Maltais et al. (2005b) also found a positive relationship between habitual levels of physical activity and biomechanical walking economy.

Only one study has objectively measured physical activity in 31 children with CP using an accelerometer, an objective measure that records duration, frequency and intensity of everyday activity. Children with CP (mean age 7.41 ± 2.48 yr; GMFCS level I-III) participated in less moderate-to-vigorous activity and spent more time in sedentary activity than a control group of TD children (Capio et al., 2012). Interestingly the authors found no association between age, BMI and total physical activity. Children with CP displayed lower scores for fundamental movement skills than TD children, which were found to be associated with lower levels of moderate-to-vigorous activity and higher levels of sedentary activity. Specifically children displayed slower running speed, shorter jumping distance, greater error in throwing at a target and fewer successful ball catches (Capio et al., 2012). Bjornson et al. (2008) also reported that walking activity is positively associated with self-reported physical function in pre-adolescent children with CP.

Physical activity is strongly associated with cardiovascular disease (CVD), type II diabetes mellitus (T2DM) and obesity. Reduced levels of physical activity may therefore not only impact physical functioning in people with CP it may increase their risk of developing

chronic disease. The next section will discuss the association between physical activity, T2DM and CVD.

1.4 Physical Activity and Cardiometabolic Risk Factors

CVD is a chronic disease that develops insidiously throughout life. CVD, especially coronary heart disease, remains the leading cause of death in Europe accounting for 42% and 38% of all premature deaths in women and men, respectively (Perk et al., 2012). It also results in mass disability, with levels of disability expected to rise significantly in coming decades (Perk et al., 2012). CVD is strongly associated with lifestyle factors, particularly smoking, diet, physical inactivity, and psychosocial stress (WHO, 2003). Modification of lifestyle factors associated with CVD therefore plays a major role in its prevention. Many of the modifiable risk factors associated with CVD can also prevent T2DM. T2DM is a metabolic disorder that is characterised by high blood glucose in the context of insulin resistance and relative insulin deficiency (Kumar, 2005). As well as having a 2 to 4 times higher risk of coronary heart disease than the rest of the population, people with T2DM have a significantly higher risk of cerebrovascular disease and peripheral vascular disease (Alberti et al., 2007). Many high-risk or 'pre-diabetic' individuals have a clustering of risk factors which are also risk factors for CVD (Alberti et al., 2009). The interrelated risk factors for CVD and T2DM are often referred to as cardiometabolic risk factors.

Cardiometabolic risk factors include age, gender, blood pressure, obesity, increased plasma cholesterol, low-density lipoprotein cholesterol (LDL-C) and trigylcerides, and low levels of high-density lipoprotein cholesterol (HDL-C). CVD and T2DM are a global problem and the prevalence of these diseases will continue to increase without effective preventive programmes (Federation, 2006). In daily practice prevention is usually targeted at middle- to older-aged men and women with established risk factors. As atherosclerosis is a progressive process, however, it has usually progressed to an advanced stage before the symptoms of CVD become apparent. Strategies to promote healthy lifestyles and prevent CVD should therefore be targeted at the general population and not just at those with established risk factors.

A recent costing report from the National Institute for Health and Clinical Excellence (NICE) (2010) stated that implementation of a population approach to the prevention of CVD would result in significant savings in healthcare costs. Halving the number of CVD events across England and Wales (a population of 50 million) would result in savings of approximately £14 billion per year. Reducing mean population cholesterol or blood pressure levels by 5% would result in savings of £0.7 billion and £0.9 billion respectively. Reducing cardiovascular risk by just 1% would result in savings of approximately £260 million per year.

Promoting participation in physical activity is a major component of preventive programmes. Regular participation in physical activity is associated with delayed all-cause mortality, and decreased risk of hypertension, coronary heart disease, stroke and T2DM (USDHHS 2008, Luke et al., 2011, Blair et al., 2001b, Camhi et al., 2011). Population-based studies have also shown that physical activity has a positive effect on many cardiometabolic risk factors. Objectively measured moderate-to-vigorous physical activity is associated with lower systolic blood pressure (SBP), BMI, waist circumference, triglycerides, and higher HDL-C (Atienza et al., 2011, Luke et al., 2011). It is also associated with lower plasma glucose, insulin, and insulin resistance (Atienza et al., 2011, Nelson et al., 2013).

In addition, associations between physical activity and less common markers of cardiometabolic disease risk, including high-sensitivity C-reactive protein (CRP), glycated haemoglobin (HbA_{1c}) and serum 25 hydroxy-vitamin D (25OHD), have been observed (Atienza et al., 2011, Loprinzi and Cardinal, 2013, Loprinzi et al., 2013, Scott et al., 2010). High-sensitivity CRP has been shown to be a risk factor that combines metabolic and low-grade inflammatory factors that underlie the development of unstable atherosclerotic plaques, with a magnitude of effect matching that of classical major risk factors (2012a). The HbA_{1c} assay reflects time averaged blood glucose during the previous 2-3 months and is used as the gold standard for long-term follow up of glycaemic control (Hanas and John, 2010). Low levels of 25OHD are associated with cardiovascular risk factors, including T2DM, dyslipidaemia, and arterial hypertension, and also predict cardiovascular events (Pludowski et al., 2013).

Reduced participation in physical activity is also associated with the metabolic syndrome, a term used to describe the presence of multiple cardiometabolic risk factors

(Loprinzi and Cardinal, 2013, Camhi et al., 2011). These risk factors include obesity, dyslipidaemia, hyperglycaemia, and insulin resistance. There has been considerable disagreement over the terminology and diagnostic criteria related to the metabolic syndrome. In 2009, a joint interim statement from the International Diabetes Federation Task Force on Epidemiology and Prevention (IDF), the National Heart, Lung, and Blood Institute (NHLBI), the American Heart Association (AHA), the World Health Federation (WHF), the International Atherosclerosis Society, and the International Association for the Study of Obesity proposed a common criteria for the clinical diagnosis of the metabolic syndrome (Alberti et al., 2009). The criteria are presented in Table 1.1. Although there is still some confusion over what waist circumference cut-off values should be used to define elevated waist circumference it is recommended that the IDF cut points of ≥94 cm for men and ≥80 cm for women, or the AHA/NHLBI cut points of ≥102 cm for men and ≥88 cm for women be used for people of European origin.

1.4.1 Physical activity and cardiometabolic risk factors in childhood

It is important to recognise that CVD is partly a paediatric condition, as the onset of atherosclerosis has been observed from early childhood (Kavey et al., 2003). Andersen et al. (2011a) reported that clustering of risk factors for CVD had developed in 13.8% of children before the age of 9 years. The retention of risk factors for CVD from childhood to adulthood predicts CVD risk factors and CVD events in young adulthood (Morrison et al., 2012, Juhola et al., 2011). In particular there is tracking between childhood and adulthood cholesterol, overweight/obesity, blood pressure and triglycerides (Juhola et al., 2011, Chen and Wang, 2008). Children who retain high blood pressure and high triglycerides from childhood to adulthood are also more likely to have adult T2DM, perhaps reflecting the presence of paediatric metabolic syndrome (Morrison et al., 2012).

Risk for CVD appears to be attenuated when childhood risk factors are not maintained into adulthood however, highlighting the need for childhood screening for CVD risk factors (Morrison et al., 2012). Screening of blood pressure measurements at any age between 6 to 18 years is predictive of hypertension in adulthood (Juhola et al., 2011). For lipid levels the age of screening does not appear to affect the predictive ability of tests in males. In females age 12 to 18 years appears to be an optimal time for screening

Table 1.1 Criteria for Clinical Diagnosis of the Metabolic Syndrome

Measure	Categorical Cut Points
Elevated waist circumference*	Population and country specific definitions
Elevated triglycerides (drug treatment for elevated triglycerides is an alternate indicator)	≥150mg/dL (1.7mmol/L)
Reduced HDL-C (drug treatment for reduced HDL-C is an alternate indicator†)	<40mg/dL (1.0 mmol/L) in males; <50mg/dL (1.3 mmol/L in females
Elevated blood pressure (antihypertensive drug treatment in a patient with a history of hypertension is an alternate indicator†)	Systolic ≥130 and/or diastolic ≥85 mmHg
Elevated fasting glucose (drug treatment of elevated of elevated glucose is an alternate indicator)	≥100 mg/dL

*It is recommended that the IDF cut points be used for non-Europeans and either the IDF or AHA/NHLBI cut points used for people of European origin until more data are available

†The most commonly used drugs for elevated triglycerides and reduced HDL-C are fibrates and nicotinic acid. A patient taking 1 of these drugs can be presumed to have high triglycerides and low HDL-C. High dose ω-3 fatty acids presumes high triglycerides. HDL-C, high-density lipoprotein cholesterol.

(Juhola et al., 2011). As with adults, intervention should occur immediately when a child of any age presents as overweight in a medical setting.

The health benefits of physical activity in children and adolescents are similar to those observed in adults. Physical activity is strongly associated with an improved metabolic profile in children (Strong et al., 2005, Guinhouya et al., 2011, Brambilla et al., 2011). Ekelund et al. (2009) found that children with the metabolic syndrome were 25% less physically active than children without the metabolic syndrome. In addition children with a low physical activity score are 5.12 times (95% confidence intervals: 1.05-49.10) more likely to develop the metabolic syndrome as adolescents (McMurray et al., 2008a).

Andersen et al. (2006) similarly reported an increase in clustered risk for CVD in children and adolescents as physical activity levels decreased. The clustered risk score included SBP, triglycerides, TC/HDL-C ratio, insulin resistance, body fat measured by skinfolds, and aerobic fitness. When physical activity levels were divided into quintiles, risk was raised in the 1st to 3rd least active quintiles compared to the most active quintile. Children in the least active quintile had a 3.26 greater risk of clustered CVD risk compared to children in the most active quintile. Nine year old children in the 4th quintile were active at a moderate-to-vigorous intensity for 116 min/day. Fifteen year old adolescents in the 4th quintile achieved 88 min of moderate-to-vigorous physical activity daily. This suggests that children and adolescents may need approximately 90 min of moderate-to-vigorous activity daily to reduce their clustered CVD risk.

Although physical activity is related to CVD risk in children many studies have reported only a modest dose-response relationship between total physical activity, moderate-to-vigorous activity, and blood pressure (Strong et al., 2005; Andersen et al., 2011b; Mark and Janssen, 2008). Physical activity appears to have a stronger effect on SBP when predicting high risk values in children within the hypertensive range (Mark and Janssen, 2008). Moderate-to-vigorous activity in particular is associated with a reduced risk of hypertension with considerably fewer minutes in moderate-to-vigorous activity, compared to time in total physical activity, required to reduce the likelihood of hypertension (Mark and Janssen, 2008). The amount of moderate-to-vigorous activity required to reduce blood pressure in children is still unclear. Some reports suggest at least 30 min of physical activity on at least 3 days per week, at an intensity sufficient enough to improve aerobic fitness, is required to reduce blood pressure in children with hypertension (Andersen et al., 2011b, Strong et al., 2005). However larger volumes of moderate-to-vigorous activity may be more beneficial. Children who are physically active at a moderate-to-vigorous intensity for 60 min daily reduce their likelihood of hypertension by a third compared to children who spend no time in moderate-to-vigorous activity (Mark and Janssen, 2008).

Interventions to increase physical activity in children who have features of the metabolic syndrome are effective at decreasing metabolic risk (Guinhouya et al., 2011). In most cases improvements in insulin dynamics, the metabolic syndrome and/or its main features are accompanied by an increase in cardiorespiratory fitness (Guinhouya et al., 2011). Although improvements may also be associated with changes in adiposity

(Guinhouya et al., 2011), physical activity can improve or maintain healthy insulin sensitivity in children and adolescents, independent of initial adiposity status or changes in adiposity for children of all ages and ethnicities (Berman 2011). Two reviews suggested that children need at least 40 min of moderate activity per day, on five days per week for at least 4 months to achieve improvements in lipid profile, specifically to increase HDL-C and decrease triglyceride levels (Andersen et al., 2006, Strong et al., 2005).

The difference in levels of physical activity associated with reduced CVD risk between cross-sectional studies and interventional studies may be because participants included in interventional studies usually have established risk factors for CVD and low levels of cardiorespiratory fitness. A smaller volume and intensity of physical activity is therefore required to improve cardiorespiratory fitness, which is a strong facilitator in the association between physical activity and CVD risk. In 2011 Resaland et al. conducted a school-based teacher-led exercise intervention to investigate the dose-response relationship between cardiometabolic risk factors and physical activity in a cohort of children from the general population. This study indicated that 60 min of physical activity daily was required to achieve benefits in the development in SBP, diastolic blood pressure, TC/HDL-C ratio, triglycerides and cardiorespiratory fitness in school children compared to a control group who received usual physical education.

1.4.2 The role of sedentary time in cardiometabolic disease risk

Sedentary behaviour has a large effect on major non-communicable diseases worldwide (Lee et al., 2012). A longitudinal study with a 21 year follow-up found that self-reported sedentary behaviour (i.e. a combination of time spent riding in a car and TV viewing) was a significant predictor of CVD mortality in men aged 20-84yrs (Warren et al., 2010). High physical activity levels were also related to lower CVD deaths regardless of time spent in inactivity. A possible explanation for not finding an independent association between sedentary behaviour and CVD mortality is that physical activity levels were assessed using a self-report measure. The differences between light physical activity and moderate-to-vigorous activity were also not examined. A large study on adults recently reported that objectively measured sedentary time was significantly associated with increased waist circumference, reduced HDL-C, and increased CRP, triglycerides, insulin, and insulin resistance, independent of exercise time (Healy et al., 2011). Breaks in

sedentary time were also associated with a lower waist circumference, lower CRP and lower glucose levels, independent of time spent in sedentary behaviour (Healy et al., 2011). This suggests that light activity may play a protective role in cardiometabolic health as it reduces time spent in inactivity.

When self-report and objective sedentary behaviour were measured in a large sample of adults, self-reported sedentary behaviour was associated with increased BMI, waist circumference, TC/HDL-C ratio, and T2DM, independent of moderate-to-vigorous activity (Stamatakis et al., 2012b). The association between objectively measured sedentary behaviour and cardiometabolic risk was found to be less consistent that that between self-reported sedentary behaviour and risk. This may be explained by the inability of accelerometers to distinguish between sitting and standing sedentary behaviour, or to identify activity behaviours. When time spent in activity domains was looked at using self-report data, TV-viewing was strongly associated with cardiometabolic risk (Stamatakis et al., 2012b). It is possible that confounding factors such as snacking while watching TV or the influence of adverts on unhealthy behaviours could explain the particularly strong association between TV-viewing and cardiometabolic risk.

This association between cardiometabolic risk and TV-viewing was also found in older adults and in children, independent of moderate-to-vigorous activity (Stamatakis et al., 2012a; Aadahl et al., 2007; Carson and Janssen, 2011). Interestingly only the type of sedentary behaviour i.e. TV-viewing, and not the volume or pattern of sedentary behaviour was related to cardiometabolic risk in children aged 6-19 years (Carson and Janssen, 2011). Unlike TV-viewing computer use was not associated with a high risk for cardiometabolic disease. This association between sedentary behaviour and cardiometabolic risk was not captured by an objective measure of sedentary behaviour. The inability of an objective measure to capture the risk associated with sedentary behaviour was supported by Ekelund et al. (2012) who did not find an association between objectively measured sedentary time and any cardiometabolic risk factor. The authors of this study did find an association between moderate-to-vigorous activity and waist circumference, SBP, insulin, triglycerides and HDL-C regardless of time spent being sedentary. As well as both having independent associations with cardiometabolic risk factors, moderate-to-vigorous activity and self-reported TV-viewing are poorly correlated (Carson and Janssen, 2011). Inactivity and moderate-to-vigorous activity

should therefore be considered as two distinct concepts that require different policy and intervention to change.

1.4.3 Physical activity guidelines for adults and children

The current American College of Sports Medicine (ACSM) and World Health Organisation (WHO) guidelines for physical activity suggest that adults should participate in 150 min of moderate intensity physical activity per week or 75 min of vigorous physical activity per week, or a combination of the two, to reduce their risk of CVD and premature mortality (Garber et al., 2011, WHO, 2010). These are also the current guidelines for Ireland (Department of Health and Children, 2009). These guidelines are based on a number of large prospective cohort studies of diverse populations that show an energy expenditure of approximately 1000 kcal.week^{-1} or 10 MET-hours per week of moderate intensity physical activity is associated with lower rates of CVD and premature mortality (Garber et al., 2011). Most of this data, however, was obtained from self-report measures of physical activity. Atienza et al. (2011) found that average daily minutes of self-reported moderate-to-vigorous activity in adults was 54.8 (SE 1.9) and average daily minutes of objectively measured moderate-to-vigorous activity was 6.7 (SE 0.3). Self-report measures clearly result in a large overestimation of time spent in physical activity. Until more studies use objective measures of physical activity to demonstrate the association between physical activity and health it is useful to equate specific amounts of physical activity to levels of cardiorespiratory fitness in order to clarify the amount of physical activity required to achieve health benefits. Results from a large study that reported the inverse association between fitness and CVD mortality rates noted that adults of a moderate fitness (the level required to reduce risk) reported a weekly energy expenditure of 8-9 MET.h.wk^{-1} (Stofan et al., 1998).

The current guidelines indicate that moderate-to-vigorous activity should be accumulated in bouts of at least 10 min. The evidence for the benefits of accumulating activity in 10 min bouts rather than shorter bouts is inconclusive however (Murphy et al., 2009). Two recent studies of over 4000 adults concluded that accumulating activity in bouts of <10 min is highly beneficial for weight gain prevention and strongly associated with several biomarkers of cardiometabolic risk (Fan et al., 2013, Loprinzi and Cardinal, 2013). This suggests that every minute counts in the prevention of CVD and weight gain, and this message should be promoted.

There are currently no physical activity guidelines for people with CP. Physical activity guidelines for adults aged over 65 years, and 50-64 years with clinically significant chronic conditions or functional limitations that affect movement ability, fitness or physical activity, are 150 min of moderate activity per week or 60 min of vigorous activity per week. It is suggested that this should be in addition to routine light activity, or moderate intensity activities that last for less than 10 min (Nelson et al., 2007). One study reported that only 2.5% of older adults met these guidelines when physical activity was objectively measured (Harris et al., 2009). This was substantially lower than the percentage of older adults who reported meeting physical activity guidelines (National Centre for Social Research, 2005). Increasing age, poor general health, disability, diabetes, higher BMI, low exercise self-efficacy and low perceived exercise control were all associated with lower levels of objectively measured physical activity (Harris et al., 2009). It's not only important for older adults to maintain high levels of physical activity to prevent chronic disease, there's also substantial evidence that physical activity reduces risk of falls and injuries from falls, and prevents or mitigates functional limitations (Nelson et al., 2007). Although there is currently no evidence into the effect of physical activity on physical functioning in adults with CP it is likely that the benefits are similar to those observed in older adults.

In 2005 Strong et al. recommended that children and adolescents get 60 min of moderate-to-vigorous activity daily following a review of the dose-response relationship between activity and cardiometabolic risk factors. This recommendation was subsequently adopted by many countries including Ireland (Department of Health and Children, 2009, US Department of Health and Human Services, 2008). In 2010 however, the WHO issued guidelines that children should achieve 90 min moderate-to-vigorous activity daily, resulting from 60 min of moderate-to-vigorous activity on top of activities of daily living (WHO, 2010). Although this has yet to be adopted as the national guideline in many countries it is likely to be a more accurate guideline as it accounts for the fact that even the most sedentary children accumulate around 30 to 40 min of moderate-to-vigorous activity a day when activity is objectively measured (Andersen et al., 2006).

1.5 Physical Activity and Obesity

Physical activity also plays an important role in weight management (Donnelly et al., 2009). Overweight and obesity are defined as abnormal or excessive fat accumulation that may impair health (WHO, 2011). Excess body fat is associated with numerous adverse health outcomes and all-cause and CVD mortality (Dudina et al., 2011, Poirier et al., 2006, Katzmarzyk et al., 2012). Between 4 and 6.5% of all deaths, 8.8-13.7% of CVD deaths and 2.4-3.9% of cancer deaths can be attributed to obesity (Faeh et al., 2011). The association between obesity and cardiovascular mortality appears to be J-shaped, in that those underweight are at higher risk than those of a normal weight, and thereon the risk of CVD increases with increasing weight (Dudina et al., 2011, Song et al., 2012). There is conflicting evidence regarding whether overweight or obesity alone is associated with increased mortality. Some studies have found that overweight is not associated with excess mortality, and in fact modestly overweight people are in the lowest risk category (Faeh et al., 2011, Dudina et al., 2011, Song et al., 2012). Other studies have found an increased risk in those with a BMI ≥ 25 kg.m^{-2} (Katzmarzyk et al., 2012). This discrepancy may be due to the relative risk of excess weight among different age groups. Being modestly overweight appears to have a protective effect against CVD in adults over 60 (Dudina et al., 2011). The relative risk associated with increased body weight is much greater in younger persons than older persons (Dudina et al., 2011, Ma et al., 2011). In addition, people who have an increased BMI in adolescence have a much greater risk of all-cause mortality and coronary heart disease morbidity in adulthood (Ruiz et al., 2009).

The relationship between body weight and CVD mortality appears to be mediated through the effect of bodyweight on blood pressure and blood lipids (Willett et al., 1999). BMI is positively associated with age, blood pressure, total blood cholesterol and the prevalence of T2DM and negatively associated with HDL-C (Dudina et al., 2011, Jousilahti et al., 1996). Weight reduction is also associated with improvements in total cholesterol, LDL-C, HDL-C, blood pressure, triglycerides, glucose, insulin and CRP (Dattilo and Kris-Etherton, 1992, Flechtner-Mors et al., 2000, Heilbronn et al., 2001, Kopp et al., 2003, Lalonde et al., 2002, Wadden et al., 1999). Reducing excess adiposity should therefore be considered a powerful non-pharmaceutical method of reducing cardiovascular risk through its effect on individual risk factors.

Physical activity is an important part of an effective weight management programme (Haskell et al., 2007, Donnelly et al., 2009). Moderate-to-vigorous physical activity is associated with BMI and abdominal fat (Strath et al., 2008, Atienza et al., 2011, Stamatakis et al., 2009). Dose-response studies suggest that 150-250 min.week^{-1} of moderate-to-vigorous activity will result in only a modest weight loss (Donnelly et al., 2009). Increasing physical activity to >250 min.week^{-1} will result in greater weight loss. Dietary intervention plays an equally important role in weight loss. The aim of any weight loss programme is to create an energy deficit. Physical activity and moderate diet restriction provide comparable weight loss if they create a similar energy imbalance. If diet restriction is severe physical activity does not appear to further increase weight loss (Donnelly et al., 2009). Randomised trials, where activity levels are increased but dietary intervention does not occur, often do not result in weight loss because increased energy expenditure is matched by increased calorific intake (Church et al., 2007, Dunn et al., 2006). Physical activity alone, however, can result in increased muscle mass, reduced total adiposity and/or altered body fat distribution (Garber et al., 2011, Ness et al., 2007). It is also important to note that physical activity can result in improvements in HDL-C, insulin resistance and triglycerides without weight loss (Kraus et al., 2002, Donnelly et al., 2000, Duncan et al., 2003).

Interestingly the association between physical activity and adiposity appears to be dependent on weight status. In a detailed meta-analysis Kay and Fiatarone Singh (2006) found limited evidence that physical activity reduces abdominal and visceral fat. It also only appeared to be effective in overweight and obese participants. Hemmingsson and Ekelund (2007) observed a stronger relationship between BMI and all aspects of physical activity in obese people compared to non-obese people. Particularly there was a strong association between vigorous activity and BMI. Although cross-sectional studies may suggest that there's a relationship between BMI and physical activity, and that this is stronger in obese people, causality cannot be inferred. A recent longitudinal study demonstrated that over a 20 month period objectively measured total physical activity and moderate-to-vigorous activity decreased more in obese women than in non-obese women (Tucker et al., 2013). Obesity therefore appears to be an independent risk factor for decreasing physical activity in middle-aged women. More longitudinal studies are required to investigate if obesity leads to a reduction in physical activity.

Not only does physical activity facilitate weight loss, it is also important for the prevention of weight gain. Over a 30 year period, persistent leisure time physical activity was found to be associated with a decreased rate of weight gain and abdominal obesity (Waller et al., 2008). The ACSM position stand suggests that 150-250 min of moderate-to-vigorous activity per week may be sufficient to prevent weight gain (Donnelly et al., 2009). Prevention of weight gain may be the easiest way to prevent the development of undesirable changes in cardiometabolic risk factors with age (Schubert et al., 2006, Lloyd-Jones et al., 2007, Norman et al., 2003).

1.5.1 Physical activity and obesity in children

The relationship between body composition and physical activity is similarly complex in children. Studies have reported conflicting results regarding differences in physical activity levels between normal weight and overweight/obese children. Some studies have reported that higher levels of physical activity are associated with lower body mass, BMI and percent body fat (Wittmeier et al., 2007, Rowlands et al., 1999, Hussey et al., 2007, Ness et al., 2007). Others have suggested that there is no consistent relationship between BMI and total activity (Vincent et al., 2003, Raustorp et al., 2004, Thompson et al., 2005). Some of this discrepancy may arise from differences observed between sexes. One study reported that physical activity and body composition were associated in boys but not girls (Hussey et al., 2007). The disagreement between studies may also result from the methods used to measure physical activity. Studies that have used pedometers to measure activity have found no association between total activity and body composition (Vincent et al., 2003; Raustorp et al., 2004). However studies that have used accelerometers to measure physical activity have reported that body composition is related to moderate-to-vigorous intensity activity, but not total activity (Ruiz et al., 2006; Trost et al., 2001; Dencker et al., 2008). Methods used to measure body composition have also varied between studies, and may impact on results, with a stronger association between body fat and physical activity being observed in comparison to BMI (Ness et al., 2007; Ruiz et al., 2006). This may be expected because of the strong positive association between lean muscle mass and activity in children (Ness et al., 2007).

There is consistent evidence that vigorous physical activity is negatively associated with abdominal adiposity, and total body fat (Ruiz et al., 2006; Dencker et al., 2008; Hussey et

al., 2007). Ruiz et al. (2006) reported that this association was not present for total physical activity, moderate physical activity or moderate-to-vigorous activity. Children who spent >40 min in vigorous physical activity per day had significantly lower body fat than children who spent 10-18 min in vigorous activity. When patterns of activity are examined in depth obese children exhibit fewer bouts of moderate-to-vigorous and vigorous physical activity and this predicts greater weight gain over time (Trost et al., 2001; Dorsey et al., 2011; Janz et al., 2009). In addition overweight/obese children perform a smaller proportion of moderate-to-vigorous and vigorous physical activity bouts in consecutive clusters (Dorsey et al., 2011). A greater number of vigorous physical activity bouts are associated with lower BMI scores (Dorsey et al., 2011). This may be as a result of physical deconditioning. Overweight/obese children who are unable to perform continuous bouts of vigorous intensity activity are likely to be less fit, and being less fit is associated with a larger fat mass and larger gains in fat over time (Janz et al., 2002; Pate et al., 2006; Ruiz et al., 2006).

Trost et al. (2001) found that as well as participating in less moderate-to-vigorous activity obese children had significantly lower physical activity self-efficacy scores compared to non-obese children. This indicates that obese children are significantly less confident in their ability to overcome barriers to physical activity, ask parents to provide opportunities for physical activity, and choose physically active pursuits over sedentary ones. It is important to consider the impact of this when prescribing exercise programmes. The effect of exercise interventions on body composition is still unclear. Some studies have reported that exercise programmes resulted in reduced BMI while others reported that it resulted in increased muscle mass but no changes in waist circumference or BMI (Carrel et al., 2009, Resaland et al., 2011).The importance of reducing body fat and increasing lean muscle mass in children through physical activity without changing BMI, should however be emphasised.

Strategies to prevent obesity should begin as early as preschool age. A longitudinal study following children from birth to 11 years demonstrated that by age 11 the most active children had lower BMIs and less subcutaneous fat than children in the lower activity categories (Moore et al., 2003). Although some decline in physical activity was observed over the 11 years children who remained most active had much less body fat by the time they reached early adolescence. In a study of children aged 6-10 years, physical activity did not predict BMI at follow up (duration of follow up: median 532 days) A large

study of pooled activity data from 14 studies on children aged 4-18 years indicated that neither moderate-to-vigorous activity nor sedentary behaviour predicted waist circumference at follow-up (Ekelund et al., 2012). This may be explained by a sex difference in the influence of habitual physical activity on weight status. McMurray et al. (2008b) found that moderate physical activity and vigorous physical activity declined in children from age 9-11 years to 14-16 years by 67% and 70%, respectively. This decline in physical activity was only associated with changes in weight status in girls. Girls who became overweight during the follow-up period displayed greater declines in moderate and vigorous activity. Similarly girls who normalised their weight status over time had less of a decline in moderate and vigorous activity.

1.5.2 Obesity and CP

It may be expected that because of their reduced levels of physical activity (see sections 1.3.1 and 1.3.2) adults and children with CP are particularly vulnerable to developing obesity. Although historically children with CP were considered short and light for their age clinical observations suggest that the number of overweight or obese people with CP is increasing. Despite this few studies have investigated the prevalence of obesity in people with CP. To provide a context for the following information the prevalence of obesity in the general population will be given.

As part of the National Health and Nutrition Examination Survey (NHANES) conducted in the United States the prevalence of overweight and obesity was reported in children, adolescents and adults over a number of years. The prevalence of overweight/obesity and obesity, respectively, from 2009-2010 data was 68.8% and 35.7% among adults (Flegal et al., 2012). This was higher than the prevalence of obesity reported in 1999-2000 (30.5%) (Hedley et al., 2004) The prevalence of obesity was higher among women than men (35.8% vs 35.5%, respectively). For men, but not women, there was a significant linear increase in the prevalence of obesity over a 12 year period from 1999-2010. There was a similar increase in the prevalence of obesity between 1999-2000 and 2009-2010 in male children and adolescents (2 to 19 years) but not in females (Ogden et al., 2012). In 2009-2010 the prevalence of overweight and obesity in children and adolescents was 31.8% and the prevalence of obesity was 16.9%. The prevalence of obesity was higher in boys than girls (18.6% vs 15.0%).

The prevalence of obesity amongst adults in Ireland was reported in the 2007 *Survey of Lifestyle, Attitudes and Nutrition in Ireland*. Thirty-six percent of adults were classified as overweight and 14% were obese. Overweight and obesity were more prevalent in men than in women. Forty-three percent of men had a BMI ≥ 25 $kg.m^{-2}$ compared to 28% of women. Sixteen percent of men had a BMI ≥ 30 $kg.m^{-2}$ compared to 13% of women (Morgan K and R, 2008). In 2009 the *Growing up in Ireland* National Longitudinal Study reported that 19% of 9 year old children were overweight and 7% were obese (2009).

Using data collected in 2003-2004, Rogozinski et al. (2007) reported the prevalence of obesity in children with CP was 16.5%. This was a significant increase from a rate of 7.7% observed in 1994-1997. An increase in height, weight, and percentage of children with unilateral CP accompanied this rise in obesity. When sorted for age there was an increase in obesity among children who were less than 8 years and who were between 8 and 10 years, but not among children greater than 10 years. An increase in obesity was observed in both males and females. The prevalence increased over time in children classified as level I and II on the GMFCS but not III. This resulted in a prevalence of 16.0% in the level I group and 21.1% in the level II group and 7.6% in the level III group in 2003-2004.

A retrospective study of children and adolescents with CP seen over 3 months in 2007 found that 10.9% of children were overweight and 18.2% of children were obese (Hurvitz et al., 2008). The prevalence of overweight/obesity was higher among ambulatory children than non-ambulatory children, with 33%, 29% and 21% of children classified as level I-II, III, and IV-V, respectively, classified as overweight or obese. Sex was not associated with obesity. There was a trend towards a greater risk of overweight among older children.

In a study of adolescents with intellectual disabilities the prevalence of obesity among adolescents with CP was 4.0% and overweight was 18.8%. This was lower than all other disability types. Overweight youths with CP had a significantly higher prevalence of hypertension, compared with their counterparts who fell into the normal weight category. The lower level of obesity reported in this study may be because of the relationship between severity of CP and intellectual disability. Children with moderate-to-severe CP are more likely to have an intellectual disability. They are also likely to be

non-ambulatory and have low muscle mass. Therefore BMI may not be an accurate indicator of weight-related health status in this population.

There is no information on the prevalence of obesity in adults with CP. Hombergen et al. (2012) conducted a systematic review of the effect of CP on health-related fitness, including body composition. Conflicting evidence regarding body composition in adults compared to able-bodied peers was reported by four studies, of poor methodological quality, and therefore no conclusions could be drawn.

1.6 Physical activity and cardiorespiratory fitness

Physical activity and cardiorespiratory fitness are strongly interlinked. Cardiorespiratory fitness is a component of health-related physical fitness. It is often referred to as 'aerobic endurance' or 'aerobic capacity'. In combination with the other health-related components of physical fitness, i.e. body composition and muscular fitness, cardiorespiratory fitness allows an individual 'to carry out everyday tasks with vigor and without (undue) fatigue' (Caspersen et al., 1985). Cardiorespiratory fitness is related to 'the ability of the circulatory and respiratory systems to supply fuel during sustained physical activity and to eliminate fatigue products after supplying fuel' (Caspersen et al., 1985). In addition to the role of cardiorespiratory fitness in physical functioning there is strong evidence that cardiorespiratory fitness reduces the risk of all-cause and CVD mortality in men and women (Blair et al., 1989, Mitchell et al., 2010, Lee et al., 2011, Lyerly et al., 2009, Church et al., 2005).

The relative risk of CVD mortality attributable to low cardiorespiratory fitness is greater than that for, smoking, hypertension, obesity, high cholesterol and T2DM (Figure 1.1) (Blair, 2009). Despite this, unlike these other risk factors, cardiorespiratory fitness is rarely screened for in a clinical setting. A meta-analysis on the association of cardiorespiratory fitness with all-cause mortality and CVD events in healthy individuals, including 33 studies of 102,980 participants, revealed that individuals with a low cardiorespiratory fitness had a substantially higher risk of all-cause mortality and CVD events compared with individuals with moderate and high cardiorespiratory fitness (Kodama et al., 2009). Although few studies have investigated the long-term effect of improving cardiorespiratory fitness on health, those that have, have indicated that

maintaining or improving cardiorespiratory fitness over time is associated with a reduced risk of all-cause and CVD mortality regardless of weight gain (Blair et al., 1995, Erikssen et al., 1998, Lee et al., 2011). It is therefore important to prevent loss of cardiorespiratory fitness with age to reduce mortality risk.

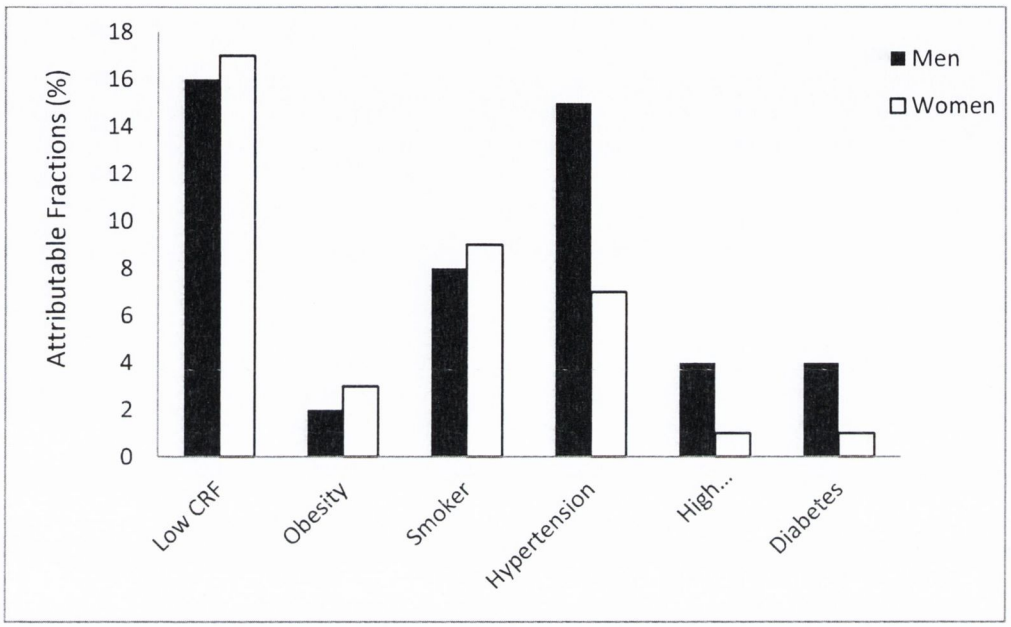

Figure 1.1 Attributable fractions (%) for all cause deaths in 40 842 (3333 deaths) men and 12 943 (491 deaths) women in the Aerobics Center Longitudinal Study. The attributable fractions are adjusted for ages and each other item in the figure. (Taken from Blair, 2009)

The protective effect of cardiorespiratory fitness on mortality is independent of a number of other risk factors including age, ethnicity, smoking status, alcohol intake, and other health conditions (Lee et al., 2010). Importantly the health benefits of being fit are independent of body composition. Men and women who are overweight or obese, but who are at least moderately fit have lower CVD mortality risk then people who are normal weight but unfit (Ortega et al., 2013, Lyerly et al., 2009, Church et al., 2005). Cardiorespiratory fitness also provides an explanation for what is sometimes known as the 'metabolically healthy but obese phenotype', i.e. obese men and women who are obese but metabolically healthy (Ortega and Andres, 1998).

Like physical activity cardiorespiratory fitness is also associated with cardiometabolic risk factors. Grundy et al. (2012) reported that triglycerides and non-HDL-C levels increase with decreasing cardiorespiratory fitness. HDL-C levels decreased with

increasing fitness. The lowest quintile of cardiorespiratory fitness had the highest SBP and the highest frequency of T2DM. There was also a strong negative association between the metabolic syndrome and fitness. Although this is likely to be due to physical activity the increase in self-reported activity across cardiorespiratory fitness quintiles was insufficient to account for this strong relationship. Although people in the highest quintile of cardiorespiratory fitness reported the highest levels of moderate and high intensity physical activity, there was not a significant difference in activity levels across the lowest three quintiles (Grundy et al., 2012).

A strong relationship between cardiorespiratory fitness and the metabolic syndrome (both present risk and future risk) has also been reported for adolescents (Janssen and Cramp, 2008). As well as being predictive of the metabolic syndrome, cardiorespiratory fitness in childhood and adolescence is a predictor of abnormal blood lipids, high blood pressure and excess of overall and central adiposity in later life (Ruiz et al., 2009). Clustering of risk factors for CVD have been shown to be strongly related to low fitness in children as young as 6 years, and low fitness at 6 years is strongly related to risk factors at 9 years (Andersen et al., 2011a). As with adults, overweight children with a high level of cardiorespiratory fitness have similar risk of developing the metabolic syndrome as normal weight children with a low fitness level (Brambilla et al., 2011).

The association between physical activity and cardiorespiratory fitness however, is more complex than might be expected. Both physical activity and cardiorespiratory fitness are inversely associated with fatal and non-fatal health outcomes. The dose-response gradient for various health outcomes is stronger across cardiorespiratory fitness categories than across physical activity categories in adults and children (Blair et al., 2001b, Berman et al., 2012). This does not necessarily mean that fitness is more important than physical activity in relation to health outcomes. Physical activity is the main determinant of cardiorespiratory fitness. The weaker relationship between physical activity and health outcomes is likely to be due to the wide use of self-reported measures of physical activity. As discussed previously, self-reported physical activity is often grossly overestimated (Atienza et al., 2011), whereas cardiorespiratory fitness can be measured objectively with a criterion method.

The question over how much physical activity is required to improve cardiorespiratory fitness is also still being investigated. To date the majority of studies have been limited

by the use of self-report measures of physical activity. It would appear that there is large variation in the amount of activity required to improve cardiorespiratory fitness and it may be unique to each individual. The current physical activity guidelines of 150 min of moderate activity per week are thought to be sufficient to improve cardiorespiratory fitness in people with low cardiorespiratory fitness to a moderate level (Garber et al., 2011). However one half of this level of activity may improve cardiorespiratory fitness in sedentary individuals (Church et al., 2007). In inactive children increases in spontaneous physical activity, rather than bouts of exercise training, may achieve improvements in fitness (Kristensen et al., 2010). A number of studies have reported that there is a stronger association between vigorous or hard activity and cardiorespiratory fitness compared to moderate activity (Gutin et al., 2005, Dencker et al., 2008, Denton et al., 2013). Ruiz et al. (2006) reported that children who achieved >26 min of vigorous physical activity per day had a higher cardiorespiratory fitness than those who achieved 10-18 min.

1.6.1 Cardiorespiratory fitness in adults and children with cerebral palsy

Few studies have investigated cardiorespiratory fitness in adults with CP. Three studies reported that young men with CP were less fit than able-bodied men (Lundberg, 1978, Fernandez, 1990, Nieuwenhuijsen et al., 2011). One study found no difference in the level of cardiorespiratory fitness between men with CP and men without CP (Tobimatsu et al., 1998). Participants reached peak heart rates of 110-198 bpm, however, indicating that not all participants were maximally exerted. The discrepancy between studies may be a result of the protocols employed to assess cardiorespiratory fitness. The limitations of using protocols developed for able-bodied people in people with CP will be discussed in the next chapter. Only one study has investigated the relationship between physical activity and cardiorespiratory fitness in adults with CP and found no association between objectively measured physical activity and cardiorespiratory fitness (Nieuwenhuijsen et al., 2011). This may be due to the low intensity at which adults with CP perform physical activity. As physical activity intensity was not assessed in this study this theory cannot be supported. Although a cross-sectional study was unable to find an association between cardiorespiratory fitness and physical activity a prospective study did report an improvement in cardiorespiratory fitness following an 8-week exercise programme (Pitetti, 1991). With appropriate exercise prescription it is therefore possible to improve cardiorespiratory fitness in this population.

There is consistent evidence to suggest that children with CP have lower cardiorespiratory fitness than their TD peers (Unnithan et al., 1998, Verschuren and Takken, 2010, Hoofwijk, 1995, Lundberg, 1978, Lundberg, 1984, van den Berg-Emons et al., 1996b). This reduced aerobic capacity is apparent even in children classified as level I and II on the GMFCS (Hoofwijk, 1995, Verschuren and Takken, 2010). Although one might expect fitness to vary with gross motor function, one study found no difference in the fitness level of children classified as level I and level II on the GMFCS (Verschuren and Takken, 2010). Similarly Parker (1993) only found moderate correlations between cardiorespiratory fitness and the sitting score and total score of the Gross Motor Function Measure (GMFM), a clinical measure designed to evaluate change in gross motor function. Verschuren et al. (2009) also found no relation between cardiorespiratory fitness, body composition and dimensions D and E of the GMFM, which measure activities in standing, and walking, running and jumping, respectively. Therefore, although decreased cardiorespiratory fitness results in a greater physical strain on the body during walking, the expected relationship between cardiorespiratory fitness and function has yet to be found. Although a number of studies have shown that aerobic exercise programmes result in improvements in cardiorespiratory fitness in both ambulatory and non-ambulatory children (Verschuren et al., 2007, Bilde et al., 2011, Van den Berg-Emons et al., 1998a) no study has investigated the association between cardiorespiratory fitness and habitual physical activity levels in children with CP.

1.7 Cerebral palsy and Cardiometabolic Risk Factors

In the preceding sections the association between reduced physical activity and cardiometabolic risk factors, obesity and cardiorespiratory fitness was discussed. In addition to reductions in physical activity (see section 1.3) and cardiorespiratory fitness (see section 1.6.1), the sarcopoenia and muscle wasting experienced by people with CP, beyond that which is associated with ageing may also contribute to metabolic dysregulation (Peterson et al., 2012a). Sarcopoenia is paralleled with significant increases in adiposity, both intra- and extra-muscular (Peterson et al., 2012a). Increased adiposity is associated with cardiovascular risk and a reduction in muscle strength and quality. This excess mass increases the demand on the body and simultaneously

decreases the ability of the musculature to react to external forces associated with everyday activity, leading to further inactivity (Peterson et al., 2012a).

It may therefore be expected that adults and children with CP are at greater risk of cardiometabolic disease. CVD, T2DM, and hypertension are not, however, predominant health complaints among adults with CP (Turk et al., 2001, Turk, 1997). The most commonly reported health conditions among adults with CP include musculoskeletal problems, bladder and bowel problems, gastroesophageal problems, and dental problems (Turk, 1997, Turk et al., 2001, Turk et al., 1997, Murphy et al., 1995). Adults with CP perceived themselves as being generally healthy and their main concerns included musculoskeletal problems, weight control, or medication use (Turk, 1997). Self-perceived health ratings and life satisfaction are related to the presence of pain or functional changes over time, but not to the severity of impairment (Sandstrom, 2007, Jahnsen et al., 2004). The severity of functional impairment however, and not a diagnosis of CP alone, was found to be associated with the presence of a number of health disorders in older adults (Henderson 2009). A study of adults with intellectual disability (including adults with CP) reported that the health conditions associated with increasing age were similar to that of the general population and included cardiovascular disease, respiratory problems, and hearing/vision problems (Janicki et al., 2002).

Despite CVD not being a primary concern amongst adults with CP Strauss et al. (1999) reported a two-three fold greater death rate from coronary heart disease among adults with CP as compared to the general population. Preventive medicine services and participation in health promotion activities are also severely underutilised by adults with CP (Murphy et al., 1995, Turk, 1997, Turk et al., 2001). Adults with CP participate to a limited extent in health screening activities and have less knowledge about cardiovascular risk factors (Capriotti, 2006). Despite the potential metabolic consequences of having CP (Bauman, 2009) few studies have investigated cardiometabolic risk factors in this population. One study reported that total cholesterol, LDL-C, HDL-C, triglycerides and blood pressure did not differ between a group of 100 children with CP (mean age 6.2 ± 2.1 yr) and 35 age- and sex-matched control children (Cece et al., 2012). Carotid intima-media thickness and CRP levels were greater in children with CP however, possibly indicating increased risk of atherosclerosis and coronary heart disease. More extensive prospective studies are required to support

this hypothesis. Although it may be expected that reduced physical activity levels from birth are responsible for endothelial dysfunction in this population this was not supported by a small study of children with CP (n=11) (Martin et al., 2012). These children had similar arterial health, including carotid intima-media thickness to youth without CP, despite lower levels of vigorous physical activity. Further investigation into the association between habitual physical activity, cardiorespiratory fitness, body composition and cardiometabolic disease risk among adults and children with CP is required.

1.8 Objectives of this Thesis

This thesis aims to investigate the effect of physical activity on body composition, cardiometabolic risk factors and cardiorespiratory fitness in adults and children with CP. Firstly the methods used to quantify physical activity intensity in adults and children with CP will be examined.

Measures of the variables investigated are presented in Chapter 2 and 3. Study 1 (Chapter 4) investigates the validity of advanced accelerometry-based devices at estimating energy expenditure in able-bodied adults and children. Study 2 (Chapter 5) investigates the validity of these devices in adults and children with CP. Study 3 (Chapter 6) cross-validates count cut-off points to quantify physical activity intensity using a triaxial accelerometer in adults and children with CP. Study 4 (Chapter 7) compares levels of habitual physical activity between adults with and without CP, and investigates the factors associated with habitual physical activity levels adults with CP. It also investigates the association between cardiometabolic risk factors, body composition and physical activity in adults with CP. Study 5 (Chapter 8) investigates the ability of anthropometric measures to indicate cardiometabolic risk factors in adults with CP. Study 6 (Chapter 9) investigates the association between physical activity, body composition and blood pressure in children with CP. The association between physical activity intensity and cardiorespiratory fitness is examined in study 7 (Chapter 10). In the discussion (Chapter 11) the results of the studies are considered together in the context of previous research in this area and suggestions for future research are highlighted.

Chapter 2 Methods

This chapter will describe the main outcome measures used in this thesis and provide an evaluation of their psychometric properties. The assessment of habitual physical activity in people with cerebral palsy (CP) is the primary theme running throughout this thesis. Objective and subjective measures of physical activity will be discussed in this chapter. The other main outcome measures discussed in this chapter are cardiorespiratory fitness, body composition and physiological markers of cardiometabolic risk. Each outcome will be discussed in relation to their accuracy and feasibility in the CP population.

2.1 Validity and Reliability

A number of factors were taken into consideration when choosing the most suitable measurement tools to investigate the outcomes of this thesis. These included the validity and reliability of the measure, and the feasibility of the measure with particular consideration to its clinical utility in the CP population.

The validity of an instrument is the degree to which it measures what it is intended to measure. Objective measures require demonstration of criterion validity, ideally against a gold standard measure. Criterion validity is the most powerful type of validity. It is an umbrella term that encompasses predictive, concurrent, convergent and discriminant validity (Ajetunmobi, 2002). To establish criterion validity a gold standard instrument, which measures what the new instrument purports to measure, must exist (Aaronson, 2002). Validity is established by examining the extent to which the new instrument provides the same results as the gold standard (de Vet et al., 2003). This thesis will investigate the concurrent validity of objective measures of physical activity in adults and children with CP. Concurrent validity can be established by collecting data from the new measurement instrument and the reference standard simultaneously (Ajetunmobi, 2002).

Although it is common to report correlations between measures when assessing the level of agreement between two measures, this should be avoided; at least not as the only reported evaluation statistic (Staudenmayer et al., 2012). Limits of agreement (Bland and Altman, 1986) should be reported when evaluating the level of agreement between two measures (Innes and Straker, 1999b, de Vries et al., 2006). When assessing the validity of an instrument it is also vital that the sample population used to validate the instrument is described in detail to clarify the population to which the validity of the instrument applies (de Vet et al., 2003, Aaronson, 2002).

The reliability of an instrument is the degree to which it is free from random error. Reliability must exist over time (test-retest reliability or intra-instrument reliability) and between measures (inter-instrument reliability) (Aaronson, 2002). As reliability is the extent to which repeated measures yield the same outcome it is inextricably linked to validity. If one or both methods have poor reliability the agreement between measures will undoubtedly be poor (de Vet et al., 2003, Bland and Altman, 1986). The intra-class correlation coefficient (ICC) is considered an adequate measure of intra-instrument and inter-instrument reliability. A value of >0.70 is rated as good (Bland and Altman, 1996, Innes and Straker, 1999a, Aaronson, 2002). Other adequate measures of reliability are the kappa coefficient, the standard error of measurement, and the coefficient of variation (CV) (Innes and Straker, 1999a, Bland and Altman, 1986, de Vries et al., 2006).

2.2 Measurement of Cardiorespiratory Fitness

Physical fitness is defined as 'a set of attributes that people have or achieve that relates to the ability to perform physical activity' (Caspersen et al., 1985). The components of physical fitness can be categorised into two groups: health-related physical fitness components and skill-related physical fitness components. Health-related components, which encompass cardiorespiratory fitness, body composition, and muscular fitness, is one of the strongest predictors of individual future health status (Thompson, 2010). The focus of the following section will be on cardiorespiratory fitness. The measurement of body composition will be discussed in section 2.3.

Cardiorespiratory fitness is related to 'the ability of the circulatory and respiratory systems to supply fuel during sustained physical activity and to eliminate fatigue

products after supplying fuel' (Caspersen et al., 1985). It can be measured in the laboratory or in the field depending on the equipment available, the patient population, and the experience of the tester.

2.2.1 Graded exercise testing

The direct measurement of maximal oxygen uptake (VO_2max) during a maximal graded exercise test is considered the criterion measure of cardiorespiratory fitness (Thompson, 2010, Heyward, 2010). Submaximal graded exercise tests can be used to predict VO_2max, however, if it is not feasible to perform a maximal test. VO_2max during a graded exercise test reflects the ability of the heart, lungs and blood to deliver oxygen to the working muscles. As VO_2max is the product of the maximal cardiac output and arterial-venous oxygen difference, it varies considerably across populations, primarily from differences in maximal cardiac output. VO_2max can be expressed in absolute ($ml.min^{-1}$) or relative terms ($ml.kg^{-1}.min^{-1}$). As VO_2 is directly related to body size VO_2 it is typically expressed in relative terms. The measurement of relative VO_2max is therefore used to classify cardiorespiratory fitness using standard references (The Cooper Institute for Aerobics Research, 2005).

Historically true VO_2max is determined by a plateau in VO_2 despite an increase in workload. Research, however, suggests that the incidence of a VO_2 plateau is highly variable (Heyward, 2010). A plateau in VO_2 is therefore no longer a requirement to indicate true VO_2max. Peak oxygen consumption (VO_2peak) attained during a graded test, i.e. the highest rate of VO_2 measured during an exercise test, is considered a valid index of VO_2max (Heyward, 2010).

If the direct measurement of VO_2 is not feasible, physiological measures [e.g. heart-rate (HR)] or test performance data (e.g. time to volitional fatigue) collected during graded maximal and submaximal tests can be used to predict VO_2max (Thompson, 2010). As many individuals may not attain a VO_2 plateau a number of other criteria should be used to indicate that VO_2max has been reached. These include: 1) failure of HR to increase with increased intensity; 2) venous lactate concentration exceeding $8mmol.L^{-1}$; 3) a respiratory exchange ratio (RER) of >1.15; 4) rating of perceived exertion greater than 17 on the original Borg scale (Heyward, 2010). Subjective signs of exhaustion may also be used to indicate that an individual has reached VO_2peak. These include inability to keep

up with the treadmill speed or maintain pedal frequency, hyperventilation or refusal to continue the test.

Graded tests, both maximal and submaximal, can be conducted using a variety of modes of exercise and protocols. Some commonly used modes of exercise are treadmill walking or running and stationary cycling. The Bruce Protocol (Bruce et al., 1973) is a commonly used example of a continuous maximal treadmill exercise test. Both the treadmill speed and gradient increase across workloads in this protocol until the participant reaches volitional fatigue or meets the criteria for the attainment of VO_2max described above.

The decision to conduct a maximal or a submaximal exercise test depends largely on the reason for the test, the profile of the participant, and the equipment and personnel available. Although a maximal test provides a more accurate assessment of VO_2max, particularly if a direct measurement of VO_2max and anaerobic threshold is obtained, medical supervision may be required to conduct such as test. Submaximal tests usually ask participants to exercise until they reach 80% of predicted maximal HR. The maximal work rate is predicted by extrapolating HR out to the predicted maximal HR and the associated maximal work rate. As such, these tests assume that a steady-state HR is achieved for each workload and that there is a constant HR-workload relationship. Although HR is the main index required to predict VO_2max other measures such as blood pressure, rate of perceived exertion and lactate may provide the researcher with valuable information about the person's functional response to exercise. Submaximal tests work on the assumption that mechanical efficiency during treadmill walking or cycling is constant for all individuals. Maximal oxygen consumption for a participant with impaired mechanical efficiency, as a result of disability, inactivity or age, will therefore be underestimated. Calculation of maximal HR with the use of prediction equations can also introduce considerable variability into the accuracy of the estimated VO_2max.

Cardiorespiratory fitness can be assessed in children using the same methods described for adults. In the laboratory a treadmill may be the better mode of exercise as children can lose concentration when asked to maintain a constant pedalling rate during a cycle ergometer test. The modified Bruce protocol is appropriate for use in children aged 4-18 years with age and sex endurance time reference values available (Wessel, 2001).

2.2.2 Field tests

Field tests are more practical, less expensive and less time consuming than a treadmill or cycle ergometer test. Walking and running tests are the most commonly used field tests to assess cardiorespiratory fitness. Examples of these tests are the 9 and 12min run tests, the 1.5 mile walk/run test and the Rockport One-Mile Fitness Walking Test. The multistage 20 m shuttle run test is a commonly used field test to estimate cardiorespiratory fitness in children (age 8-19 years) (Leger et al., 1988). It involves running between two points, 20 m apart, to the sound of a pre-recorded signal from a CD. The time between two consecutive signals shortens throughout the test until the participant can no longer keep up with the pace set by the CD. The maximal aerobic speed at the stage the participant finishes on is then used in combination with age to estimate VO_2max. Although many of these tests allow VO_2max to be predicted, the correlation between the two tends to vary considerably (Heyward, 2010). The influence of several factors, besides the capacity of the cardiorespiratory system, on endurance running performance such as motivation, running efficiency and lactate threshold (Costill et al., 1973), should be taken into consideration.

2.2.3 The assessment of cardiorespiratory fitness in children with cerebral palsy

Although the relationship between cardiorespiratory fitness and cardiovascular disease has long been established, few studies have assessed cardiorespiratory fitness in adults and children with CP. As a result of this the clinimetric properties, i.e. the validity, reliability and feasibility, of tests of cardiorespiratory fitness in this population have been under-evaluated. This section will identify tests that have been used to measure cardiorespiratory fitness in children with CP and a discussion of their clinimetric properties will be provided.

If a graded exercise test is to be used to measure VO_2max in children with CP the mode of exercise and protocol used must be carefully considered. People with CP have a musculoskeletal system with different biomechanic and energetic properties compared with their typically developing peers (Rosenbaum et al., 2007). Measurement of true cardiorespiratory fitness may therefore be masked by non-cardiorespiratory factors. Additional factors that can impact the results of exercise tests include the motor control of the person, their task understanding and sufficient familiarisation. It is vital that the

validity and reliability of graded exercise test protocols developed in the general population are established in people with CP before they are used.

Eight studies measured cardiorespiratory fitness in ambulatory children with CP using a graded treadmill test. See Table 2.1 for information on the exercise modes and test protocols that have been used to assess cardiorespiratory fitness in children with CP. Two studies used a 'half bruce' protocol (Bruce et al., 1973) and the remaining six used a self-developed treadmill procotol. Only two studies defined the criteria of attainment of VO_2max prior to the completion of the test (Verschuren et al., 2010a, Verschuren et al., 2006). Indicators of attainment of VO_2max were a HR >180 bpm and RER >0.99. Age was not found to predictive of maximum HR in children with CP (Verschuren et al., 2011) and the formula 220-age was therefore inappropriate to use to predict maximum HR. All subjects met at least one criteria of attainment of VO_2max during the graded treadmill test. Hoofwijk (1995) reported that 4/9 participants reached VO_2 plateau during the exercise test. Mean peak HR was 189 ± 17 bpm. This is similar to the peak HR reported by (Maltais et al., 2005a) (189 ± 12 bpm). Neither study however reported the number of participants who reached a HR >180bpm and therefore the number of valid tests is unknown.

Five studies used a cycle ergometer test to assess cardiorespiratory fitness in children with CP. The level of disability among children ranged from slight (no aids) to fairly severe (wheelchair users). Parker (1993) observed peak HR of 195 ± 11 bpm and 196 ± 5 bpm and an RER of 0.87 ± 0.04 and 0.90 ± 0.09, in girls and boys respectively, using a self-developed protocol. He reported similar values for HR and RER in a second study (Lundberg, 1984). When a protocol based on the McMaster protocol (Bar-Or, 2004) was employed much lower peak heart-rates were observed (176 ± 11 bpm and 168 ± 15 bpm) (van den Berg-Emons et al., 1996b, Van den Berg-Emons et al., 1998a).

Two studies used an arm ergometer test to assess cardiorespiratory fitness in non-ambulatory children with CP. One study did not report any indicator of attainment of VO_2max (Parker, 1993). Van den Berg-Emons et al. (1998a), however, reported that mean peak HR was 125 ± 9 bpm. This increased to 143 ± 18 bpm following a 9 month upper limb exercise programme suggesting that improved muscle performance contributed to any observed improvement in cardiorespiratory fitness. However, even after training participants were unable to reach maximal exertion using this protocol.

In 2006, Verschuren et al. developed two 10m shuttle run tests (SRT) to measure cardiorespiratory fitness in children and adolescents (6 to 20 yr) classified as levels I and II in the GMFCS. The SRT demonstrated excellent validity compared to a graded treadmill test, with similar VO_2peak values reported for both tests (1.7 ± 0.5 L.min^{-1} vs 1.7 ± 0.05 L.min^{-1} and 1.7 ± 0.6 L.min^{-1} vs 1.6 ± 0.6 L.min^{-1}, for children classified as GMFCS level I and II respectively). All participants reached HR >180 bpm and RER>1.0 during the SRT. In fact participants attained a higher peak HR during the SRT compared to the treadmill test (200.6±6.7 bpm vs 192.9±6.2 bpm and 199.4±6.8 bpm vs 193.1±6.1 bpm, for children classified as GMFCS level I and II respectively). As well as being a valid measure of cardiorespiratory fitness the SRT demonstrated good test-rest reliability with intraclass correlation coefficients of 0.87 or greater for HR and exercise time for both tests. Twenty-three out of 25 participants preferred the SRT over the treadmill test as they could try harder because they felt they were in control of the test and that they could stop at any time. It was not possible however to predict VO_2peak from SRT running speed. Therefore, although the SRTs demonstrate excellent validity, reliability and appear feasible it is not possible to obtain a measure of cardiorespiratory fitness that allows for comparison with TD children and adolescents. In 2010 however, SRT data was obtained on 306 children, adolescents and young adults with CP (6 to 20 yr) classified as GMFCS levels I and II (Verschuren et al., 2010a). This allowed reference values for cardiorespiratory fitness to be developed for children, adolescents and young adults with CP in order to classify them according to fitness. A 7.5 m SRT has been developed to assess cardiorespiratory fitness in children in level III of the GMFCS (Verschuren et al., 2011). Although this test is reliable it has not yet been validated. Reference data is also not available for this test and it is therefore impossible to classify children's cardiorespiratory fitness with the results from this test.

Table 2.1 Methods used to assess cardiorespiratory fitness, and indicators of attainment of maximal aerobic capacity, in children with cerebral palsy

Study	n	Age	GMFCS Level	Protocol	Criteria for attainment of VO_2max	Meet criteria
Treadmill						
(Gorter et al., 2009)	13	8-13 yr;	I and II	'half Bruce'	none	NR
(Bilde et al., 2011)	9	6-13 yr	I and II	Bruce	none	NR
(Maltais et al., 2005a)	11	10-16 yr	I and II	self-developed protocol	none	HR: 189 ± 12 bpm
(Unnithan et al., 1996)	9	12.7 ± 2.8 yr	not specified; ambulatory	self-developed protocol	none	NR
(Massin and Allington, 1999)	15	4-13 yr	not specified; ambulatory	self-developed protocol	none	NR
(Verschuren et al., 2006)	25	7-17 yr	I and II	self-developed protocol	HR >180bpm RER >1.0	All participants met criteria HR: 192.9 ± 6.2 bpm (level I) 193.1 ± 6.1 bpm (level II)

(Verschuren and Takken, 2010)	24	7-17 yr	I and II	self-developed protocol	one of: HR >180 RER >0.99 and: one subjective indicator	All participants met criteria
(Hoofwijk, 1995)	9	10-16 yr	not specified; ambulatory without aids	self-developed protocol	none	4/9 participants reached a VO_2 plateau HR: 189 ± 17 bpm RER: 1.14 ± 0.06
Bicycle ergometer						
(Lundberg, 1984)	26	Di: 11.5 ± 1.9 yr Hemi: 12.0 ± 0.3 yr Dys: 11.2 ± 2.2 yr	not specified; Slight (no aids) to fairly severe (non-ambulatory)	protocol not reported	none	RER: 0.90 ± 0.04 (diplegia) 0.96 ± 0.03 (hemiplegia) 0.99 ± 0.00

						(dyskinesia)
(Lundberg, 1978)	9	11-12 yr	not specified; Slight (no aids) to fairly severe (non-ambulatory)	protocol not reported	HR levelling	HR: 192-199 bpm HR: 195 ± 11 bpm (girls) 196 ± 5 bpm (boys) RER: 0.87 ± 0.04 (girls) 0.90 ± 0.09 (boys)
(Van den Berg-Emons et al., 1998a)	20	7-13 yr	not specified; 10 ambulant,10 non-ambulant	Mc Master protocol-based	none	HR: 175 ± 13 bpm
(van den Berg-Emons et al., 1996b)	12	7-12 yr	not specified; 8 ambulant, 4 non-ambulant	McMaster protocol-based	none	HR: 168 ± 15 bpm
(Nsenga Leunkeu et al., 2012)	24	10-16 yr	I and II	self-developed protocol	none	HR: 148.4 ± 25.1 bpm Borg scale: 12.4 ± 1.0

Arm ergometry						
(Van den Berg-Emons et al., 1998a)	20	7-13 yr	not specified; 10 ambulant, 10 non-ambulant	McMaster protocol	none	HR: 125 ± 9 bpm
(Parker, 1993)	23	9.3 ± 2.0 yr Mobile independently or with aids (including WC)	not specified; slight (no aids) to severe (wheelchair users)	protocol of Bar-Or and Zwiren	none	not reported
Field tests						
(Verschuren et al., 2007)	68	12.1 ± 2.8 yr	I and II	10m SRT	HR >180, RER >1.0	NR
(Verschuren et al., 2009)	68	12.1 ± 2.8 yr	I and II	10m SRT	HR >180 RER >1.0	NR
(Dallmeijer and Brehm, 2011)	8	6-16 yr	I and II	10m SRT	HR >190bpm RER >1.0	All participants met HR criterion

						4/7 met RER criterion
(Verschuren et al., 2011)	13	12 ± 3 yr	III	7.5m SRT	HR >180	13/15 participants met criterion
(Verschuren et al., 2006)	25	7-17 yr	I and II	10m SRT	HR >180bpm RER >1.0	All participants met criteria HR: 200.6 bpm (level I) 199.4 bpm (level II)
(Verschuren et al., 2010b)	306	6-20 yr	I and II	10m SRT	HR >180 and subjective criteria	HR: 194 ±10 bpm

HR, heart rate; RER, respiratory exchange ratio; di, diplegia; hemi, hemiplegia; dys, dyskinesia; SRT, shuttle run test

2.3 Measurement of Body Composition

2.3.1 Defining overweight and obesity in adults and children

BMI is commonly used to classify underweight, overweight and obesity in adults and children. BMI is calculated as weight (kg) divided by height squared (cm^2). The Centre for Disease Control and Prevention (CDC), International Obesity Task Force (IOTF), and World Health Organisation (WHO) define overweight as ≥25 $kg.m^{-2}$, and obesity as ≥30 $kg.m^{-2}$ in adults. To date there is no gold standard for defining overweight and obesity in children and adolescents. Although not ideal, the use of BMI has significant practical advantages: it is based on common anthropometric measures of weight and height, and it is familiar to many practitioners. BMI has been increasingly acknowledged as an acceptable indirect measure of overweight and obesity in young people (Lobstein and Frelut, 2003). Sex and age have a significant effect on body composition in children however (Rolland-Cachera et al., 1982). BMI cut-off points for adults are therefore not appropriate for use in children.

Growth reference charts were published by the CDC (Kuczmarski et al., 2000), IOTF (Cole et al., 2000), and WHO (de Onis et al., 2007). The CDC and WHO curves were developed from data on children in the United States. The IOTF charts, for use in children and adolescents 2–18 years old, were developed from a database of 97,876 boys and 94,851 girls from birth to 25 years from six countries (Brazil, Great Britain, Hong Kong, the Netherlands, Singapore and the USA). Centile curves were constructed using the LMS method, and BMI values of 25 and 30 at 18 years of age for boys and girls were tracked back to define BMI values for overweight and obesity at younger ages. Prior to the development of the IOTF charts growth reference charts for British children were developed using data for weight, height, BMI and head circumference from 37 000 children from surveys representative of England, Scotland and Wales (Cole et al., 1998). There are no generally agreed BMI criteria for classifying overweight/obesity in children of European origin. There is an emerging consensus however in favour of adopting criteria proposed by the IOTF. Overweight and obesity in children in this thesis is therefore defined by the IOTF criteria.

It has been suggested that BMI may not be a sensitive enough measure of the excess body fat associated with cardiometabolic dysregulation. Although BMI has many advantages as a measure of excess body fat, such as simplicity and reproducibility, a

significant limitation of BMI is its inability to differentiate between an elevated body fat content or increased lean mass (Franzosi, 2006, Romero-Corral et al., 2006). Romero-Corral et al. (2010) demonstrated that normal-weight obesity (i.e. people who have a normal weight based on BMI and a high body fat content) is strongly associated with cardiometabolic dysregulation, a high prevalence of the metabolic syndrome, and an increased risk of CVD mortality.

Many devices for measuring body fat percentage are not however widely available in clinical practice. There are also currently no recommended cut-off values to define high body fat percentage. This limits its use in health promotion campaigns. As a result of the limitations of measuring body fat content in a clinical setting, simple anthropometric measures of abdominal fat have been suggested as methods of indicating obesity. Waist circumference is a useful indicator of abdominal adiposity, which is strongly associated with cardiometabolic risk factors, T2DM and CVD (Nesto et al., 2009). Abdominal adiposity has a particularly strong association with cardiometabolic risk, compared to BMI, because it is indicative of increased visceral adipose tissue. The endocrine actions of visceral fat cells have a direct impact on components of cardiometabolic risk i.e. promotion of insulin resistance, dyslipidaemia, and hypertension (Despres et al., 1990, Pouliot et al., 1992, Tchernof et al., 1996).

A meta-analysis of 15 articles indicated that the risk of incident CVD increases with elevations in both waist circumference (WC) and the ratio of waist and hip circumference (WHR) (de Koning et al., 2007). This relationship was not attenuated by the inclusion of confounders such as smoking or blood lipids, suggesting that abdominal obesity is an independent risk factor for CVD over and above other abdominal obesity correlates. It has been suggested that WHR may be a superior predictor of CVD risk because hip circumference is inversely associated with dysglycaemia, dyslipidaemia, T2DM, hypertension, CVD and death (Seidell et al., 2001, Seidell et al., 1997, Lissner et al., 2001, Okura et al., 2004, Heitmann et al., 2004). This is possibly due to its correlation with other anthropometric features such as increased hip subcutaneous fat, gluteal muscle and total leg muscle mass. Researchers conducting the meta-analysis found that the relative risk for WHR was greater than WC, although not statistically significantly.

In 2008 the WHO convened an expert consultation to develop recommendations for diagnostic criteria or classifications for abdominal obesity (WHO, 2008). The expert

consultation agreed that WC, WHR and BMI are predictive of the risk of chronic disease and therefore cut-off points for WC and WHR can be used alone or in conjunction with BMI to screen for disease risk. A number of steps were required to take before arriving at appropriate WHO recommendations however. As such current recommendations do not currently exist. Based on a previous report from the WHO Expert Consultation on Obesity (WHO, 2000), the recommendations often attributed to WHO are shown in Table 2.2. The sex-specific cut-off points cited in this report are only an example and not WHO recommendations.

Table 2.2 World Health Organisation cut-off points and risk of metabolic complications

Indicator	Cut-off points	Risk of metabolic complications
Waist circumference	>94 cm (M); >80 cm (W)	Increased
Waist circumference	>102 cm (M); >88 cm (W)	Substantially increased
Waist-hip ratio	≥0.90 (M); ≥0.85 (W)	Substantially increased

M, men; W, women

Waist-height ratio (WHtR) has been proposed as another simple anthropometric measure of cardiovascular risk in adults and children. A recent meta-analysis of 31 studies reported that WHtR provides a superior tool for discriminating obesity-related cardiometabolic risk in adults, compared with BMI and WC (Ashwell et al., 2012). Analysis of suggested cut-off values from 34 analyses in 16 different papers showed the mean of proposed boundary values for WHtR, in men and women, respectively was 0.52 and 0.53 for T2DM, 0.53 and 0.50 for CVD, 0.50 and 0.50 for hypertension outcomes, 0.49 and 0.49 for lipid outcomes, and 0.50 and 0.49 for metabolic syndrome outcomes. The authors suggested the mean proposed boundary value (the first cut-off level indicating risk) for WHtR of 0.50 should be used as a public health tool for increased risk.

WC has also been shown to be a highly sensitive and specific marker of upper body fat accumulation in children (Taylor et al., 2000). Cardiometabolic risk factors associated with upper body fat accumulation correlate with WC in children and adolescents, independent of BMI (Taylor and Hergenroeder, 2011, Flodmark et al., 1994, Freedman et al., 1999). As with BMI, children's WC is age and sex specific and therefore one cut-off point cannot be applied to all data. In 2001 McCarthy et al. developed WC percentiles in British children aged 5 to 16.9 yrs. Although these curves provide a relative indication of

WC in children, cut-off points have not been developed to classify children as overweight or obese according to WC.

The utility of WHtR at predicting cardiometabolic risk has also been reported in children and adolescents (McCarthy and Ashwell, 2006, Hara et al., 2002, Savva et al., 2000, Mokha et al., 2010). WHtR is a superior method of predicting cardiovascular risk factors in children, including triglycerides, LDL-C, artherogenic index, and clustered cardiometabolic risk, compared to BMI, percentage body fat, WC and WHR (Savva et al., 2000, Hara et al., 2002, Mokha et al., 2010). In addition, WHtR not only detects central obesity and related adverse cardiometabolic risk among normal weight children, but a cut-off value of 0.50 also identifies those without such conditions among children classified as overweight/obese according to BMI (Mokha et al., 2010).

2.3.2 Defining overweight and obesity in adults and children with cerebral palsy

There has been some debate regarding the use of BMI as a predictor of CVD risk in adults and children with CP (Peterson et al., 2013, Rimmer et al., 2010). People with CP are known to have significant muscle atrophy (Lampe et al., 2006, Riad et al., 2012) and intramuscular adipose tissue infiltration (Johnson et al., 2009), which may result in adults with excess body fat being classified as normal weight according to BMI cut-off points. Despite this, the only studies to report the prevalence of obesity among children with CP used BMI to define overweight and obesity (Rogozinski et al., 2007, Hurvitz et al., 2008).

One study has investigated the ability of WC, WHR and BMI to indicate cardiometabolic risk in adults with CP. Peterson et al. (2012b) reported that WHR rather than BMI was associated with TC/HDL-C ratio, HDL-C, and triglycerides. BMI was influenced by gross motor function, with adults classified as GMFCS level IV-V having a lower BMI than adults in levels I-III (24.2 ± 6.2 $kg.m^{-2}$ vs 30.1 ± 7.6 $kg.m^{-2}$). The association between simple anthropometric measures and other cardiometabolic risk factors such as insulin resistance has not been investigated. The ability of these measures to predict cardiometabolic risk in children has not been investigated either.

2.4 Measurement of Physical Activity

There are many methods available to measure physical activity in the general population. Careful consideration should be given to several factors before choosing the most appropriate measure to address the research hypothesis. Physical activity is one of three components that contribute to total energy expenditure (EE) in humans. Basal metabolic rate (BMR) and thermogenesis provide the other two components of total EE. BMR is defined as 'the energy expended when an individual is lying at complete rest, in the morning after sleep in the post-absorptive state'. Although the contribution of BMR to total EE is variable across individuals it is thought to account for up to 60% of total EE (Levine, 2005). Many factors can influence an individual's BMR including age, sex, lean body mass, race, climate and diabetic status (Morrison et al., 1996, Froehle, 2008, Martin et al., 2004). Impaired cardiorespiratory fitness may also result in a reduced BMR (Miller et al., 2012). Thermogenesis is 'the energy expenditure above the metabolic rate in the resting state' (Jequier, 1983) and accounts for approximately 10% of total EE (Levine, 2005). Two main factors contribute to thermogenesis: food intake and cold exposure. The remainder of total EE is related to the energy expended during physical activity.

The magnitude of the energy expended during physical activity depends on the amount of muscle mass producing bodily movements and the intensity, duration and frequency of muscle contractions. These factors are often referred to as the four dimensions of physical activity i.e. frequency, intensity, duration and mode (Howley, 2001). When choosing a measure of physical activity it is important to consider whether it is the behaviour of physical activity that is being measured or the resulting energy cost of physical activity. Some measures of physical activity can only provide a description of the behaviour of physical activity such as 'occasional' or time spent in different activities. This provides inadequate information to form recommendations on how much physical activity is needed to produce health benefits. It also does not allow for cross-study comparison. All measures of physical activity should therefore yield units of energy expenditure (EE) or should allow for easy conversion of physical activity dimensions to units of EE (Lamonte and Ainsworth, 2001). It is also important to consider the interval over which measurements are recorded by an instrument. Children in particular perform physical activity in short, sporadic bursts (Bailey et al., 1995). The

measurement instrument must be sensitive enough to capture the intensity of activity over a short period of time.

EE can be expressed as kilojoules (kJ) or kilocalories (kcal), where 4.184kJ is equal to 1kcal (Davidson, 1979). Although the kJ is technically the measure of EE, the kcal (a measure of heat) is historically used to report EE. Oxygen uptake (VO_2), relative to body mass (ml oxygen.kg body size^{-1}.min^{-1}), is also used to estimate the energy cost of activities. The metabolic equivalent (MET) classification system allows activities to be assigned a unit of physical activity intensity based on the required VO_2 of an activity. One MET is considered to be resting VO_2 of an individual. The standard resting VO_2 of 3.5ml.kg^{-1}.min^{-1} is often used to calculate the MET value of an activity by expressing their rate of VO_2 as multiples of 1 MET.

Several methods of measuring physical activity and EE exist. These measures lie along a continuum of accuracy and feasibility, each with its strengths and weaknesses. A description of these methods and their limitations is provided below. As well as considering the construct to be measured it is important to find an appropriate balance between accuracy and feasibility when selecting a measurement tool.

2.4.1 Criterion measures of physical activity

EE can be measured using one of three criterion methods: indirect calorimetry, direct calorimetry and doubly labeled water (DLW). Indirect calorimetry involves measuring VO_2 and converting it to EE using formulae. VO_2 can be measured using one of several systems. The principal approaches to the measurement of EE using indirect calorimetry are total collection systems, open-circuit indirect calorimeter systems, respiratory chambers and closed-circuit systems. Most of these require only moderate expertise and training to use. The Douglas Bag is an example of a flexible total collection system where a subject breathes through a mouthpiece and the expired air is collected in a bag. After a timed collection period the volume of expired air in the bag is measured and a sample is analysed to determine oxygen and/or carbon dioxide concentrations. In an open-circuit system a participant inspires air and the expired gases are analysed. EE can be recorded for several hours or days using an open-circuit indirect calorimeter system. Expiratory collection open-circuit systems can be designed as portable devices giving them an advantage over other units of lending themselves to use in free-living conditions (Levine, 2005). The high cost of them, expertise needed to use them, and

often their bulkiness and requirement to wear a face mask make them unsuitability for use over a long period of time and limit their use in epidemiological studies. Respiratory chambers involve participants remaining inside a gas-tight sealed container of known volume for a measured period of time. Measuring changes in oxygen and carbon dioxide concentrations in the chamber over this time allows oxygen consumption and carbon dioxide production to be calculated. Direct calorimetry measures the rate of heat loss from the subject to the calorimeter. Direct calorimeters are extremely expensive to build and require expertise to establish and maintain, yet offer little beyond less expensive indirect calorimeters (Levine, 2005). For these reasons they are not often used.

The DLW method is considered a criterion method of measuring the total EE of humans in free-living conditions. This technique is based on the theory that the rate of carbon dioxide production by the body is related to the rate of oxygen and hydrogen elimination in body water. In practice subjects consume water labelled with non-radioactive isotopes (D_2O) after baseline samples of blood, urine or saliva are taken. H_2 and O in body water are tagged with D_2 and O_2 respectively. Samples of blood, urine or saliva are then collected over 7-21days. Oxygen is eliminated from the body in both body water and through carbon dioxide production. The flow of hydrogen through the body however occurs only in body water. D_2 and O concentrations in the samples of body water collected over the measurement period allow for calculation of CO_2 production and EE (Speakman, 1998, Levine, 2005). While the DLW method allows for accurate measurement of total EE in free-living conditions over a period of weeks it does not give detailed information about the intensity and time of activities.

Direct observation is considered a criterion measure of physical activity. The type, duration and frequency of physical activity can be measured, as well as an estimation of intensity using a coding system, without imposing any environmental restrictions on the individual. This method also provides information on the social and physical context of activity. It can occur in a variety of field settings however the need for an observer to be present often restricts measurements to the classroom or occupational setting. Many classification systems have been developed to accurately capture either physical activity behaviour or EE (Bailey et al., 1995, DuRant et al., 1993, MCKenzie, 1991, Sharma et al., 2011). These systems require extreme diligence from observers who code activity

performed during, often very short, periods of time. Direct observation can therefore often be expensive as it is labor intensive, time consuming and requires expertise.

2.4.2 Subjective measures of physical activity

Subjective measures of physical activity such as questionnaires, diaries/log books and interviews are often used to collect physical activity data in studies of populations because of their ease of use (Ainsworth, 2009, Lamonte and Ainsworth, 2001). Intensity can be calculated from data collected by self-report measures by assigning a MET value for an activity using the compendium of physical activities (Ainsworth et al., 2011). The subjective nature of these measures can result in overestimation of moderate-to-vigorous activity (Rutten et al., 2003, Atienza et al., 2011) and underestimation of habitual daily activity (Bassett et al., 2000). As information about the duration and intensity of physical activity is often overestimated when self-report measures are used a stronger association exists between objectively-measured physical activity and cardiometabolic risk factors (Atienza et al., 2011). The sporadic nature of children's activity can also make it difficult to categorise and quantify physical activity using a subjective measure. It is therefore advisable to use objective measures of physical activity to reduce the impact of recall bias on a study.

2.4.3 Objective measures of physical activity

The criterion measures of physical activity discussed in section 2.4.1 are considered objective measures of physical activity. For the reasons discussed above, including cost and expertise required, they are often not feasible for use in large studies of free-living physical activity. A number of methods have therefore been devised to indirectly estimate EE and physical activity from physiological measurements and other observations.

The potential of using heart-rate (HR) to predict EE has long been recognised by researchers. This potential is based on the fact that HR is linearly related to EE (or oxygen consumption) over a large range of activities (Christensen et al., 1983). The ability of HR to predict EE, however, is limited by two critical issues. Firstly the linear relationship between HR and EE breaks down at resting levels and near maximal VO_2. Secondly, the relationship between HR and EE varies considerably between individuals (Leonard, 2003). The 'flex-HR'method was developed to address these problems by

establishing the point of differentiation between resting and active levels of EE for each individual. EE is then determined by using one of two methods, depending on whether the HR lies above or below the flex point. This method requires the calibratation of HR against EE for each participant, which makes it a less suitable method to estimate EE in studies of populations. Additional factors may also affect HR, such as stress, body composition and medication (Lamonte and Ainsworth, 2001). Alone, HR may not be an accurate enough or feasible method of measuring EE in population-based studies. Some researchers, however, have attempted to combine HR into a multi-sensor system in order to improve the estimation of EE (Brage et al., 2005).

Motion sensors are mechanical devices that detect the body's movement. They can roughly be categorised as pedometers and accelerometers. Pedometers provide an objective measure of step-count and distance covered by individuals. While they are useful motivational tools they are inaccurate at predicting exercise volume or EE (Kumahara et al., 2009, Garber et al., 2011, Ainsworth, 2009). Accelerometers measure the speed and magnitude of the body's movement. Unlike pedometers many accelerometers provide information about the intensity of physical activity as well as the duration, frequency and type of activity. They are usually small unobtrusive devices making them feasible for use in free-living conditions. The ability of accelerometers to provide objective physical activity data, often in small intervals, has led to the recommendation that they be used in all population-based studies of physical activity (Colbert and Schoeller, 2011). Their superior accuracy and precision over other measures of physical activity means that they can address current questions in the field of physical activity research, relating to the dose-response effect of physical activity and the effect of different patterns of activity on health.

2.4.4 Measurement of physical activity in people with cerebral palsy

This section will now examine the objective methods used to measure physical activity in people with CP. The first step involved the identification of instruments that have been used to measure physical activity in children and adults with CP. The validity, reliability and feasibility of the included instruments in this specific population were also evaluated.

2.4.4.1 Inclusion criteria and search strategy

To be included in this review instruments had to: 1) objectively measure physical activity as defined as 'any bodily movement produced by skeletal muscles that results in energy expenditure' (Caspersen et al., 1985); 2) report physical activity in terms of frequency, duration, mode and intensity. Articles reporting on measures of physical fitness, functional ability or gait parameters were not included. Only full written reports in English were included.

A search of the electronic databases Pubmed, Embase and Cinahl was carried out in December 2009. A further search was conducted in May 2013. The aim of the search was to identify measures of physical activity whose clinimetric properties had been evaluated in people with CP. The following keywords and MESH terms, and combinations of these, were used in the search: 'habitual physical activity', 'physical activity', 'cerebral palsy', 'performance', 'psychometrics', 'clinimetrics', 'accelerometers', 'accelerometry', 'activity monitors', 'monitoring', (monitoring, ambulatory/instrumentation), (monitoring, ambulatory/methods), (monitoring, physiologic/instrumentation), ('ambulatory monitoring'/exp OR 'accelerometer'/exp OR 'accelerometry'/exp), (MH "accelerometers") OR (MH "motion analysis systems")' OR '(MH "accelerometers").

Titles and abstracts of all retrieved articles were screened and articles were excluded as appropriate. Following this, full reports were obtained to evaluate if the measurement instruments used met the inclusion criteria. The title of possible measurement instruments were then used in a secondary search to identify articles that evaluated the clinimetric properties of these instruments in people with CP.

2.4.4.2 Results

The search resulted in 13 full reports on the evaluation of 10 objective measures of activity in children with CP. No evaluations of objective measures of physical activity in adults with CP were identified. The measures identified were the Actigraph, RT3, Biotrainer, Caltrac and IDEEA accelerometers; the Uptimer; the Stepwatch, AMP and Dynaport Minimod pedometers; and the HR-flex method measured using a polar HR monitor.

Validity

The validity of 10 objective measures of physical activity has been evaluated in children with CP. Of these measures none were specifically designed to measure activity in this population. The validity of the included measures is presented in Table 2.3. The validity of these measures was investigated against a criterion method in children with CP.

The Actigraph is the most widely used accelerometer for the assessment of physical activity in children without CP due to the large volume of validation research conducted on it (McClain and Tudor-Locke, 2009). Two studies have examined the validity of the Actigaph in children with CP. The Actigraph correctly identified the time children with CP spent in moderate-to-vigorous physical activity when compared to direct observation (Capio et al., 2010) and indirect calorimetry (Clanchy et al., 2011a). The Actigraph's agreement with direct observation was less accurate during free-play ($r = 0.68$; $p < 0.01$) than during structured activities ($r = 0.72$; $p < 0.001$) (Capio et al., 2010). Although it may be able to identify time spent in activity the count output from the Actigraph remains meaningless unless converted into a more interpretable unit such as physical activity intensity or EE. Rather than developing new CP specific count thresholds, or 'cut-points', to identify time spent in sedentary activity, light physical activity and moderate-to-vigorous activity Clanchy et al., (2011a) validated published cut-points for TD children in children and adolescents with CP. The cut-points published by Evenson et al. (2008) were found to accurately identify the time children with CP spend in light activity and moderate-to-vigorous activity.

Four accelerometers that provide a direct output of EE were evaluated in children with CP. Good correlations were reported for EE from the IDEEA and EE from an indirect calorimeter ($r_p = 0.70$-0.88; $p < 0.001$) during several activities (Aviram et al., 2011). It overestimated the energy cost of a series of free-living activities, however, as well as overestimating the energy cost of treadmill walking at a comfortable speed ($p < 0.001$). In contrast, estimated EE did not differ between indirect calorimetry and the Caltrac and Biotrainer accelerometers ($p = 0.62$) (Norman, 2006). This study was limited by its small number of participants, however ($n = 5$). The lack of appropriate statistical analysis employed by both of these studies also makes it difficult to comment on the accuracy of these monitors. Neither study calculated the limits of agreement between the

accelerometer and the criterion measure (Bland and Altman, 1986) making it impossible to conclude if the level of disagreement between the measures is clinically relevant.

Although the RT3 accelerometer has been used to measure physical activity in children with CP its validity has not yet been established in this population (Maltais et al., 2005b). A pilot study was conducted to determine the relationship between RT3 measured physical activity and physical activity measured from HR monitoring. Although a good correlation was reported between the two methods ($r = 0.88$) only 11 participants were included in the study and little information was provided about the protocol or data analysis methods used. As a triaxial accelerometer, which measures accelerations in three directions, the RT3 offers a potential method of improving the accuracy of physical activity monitoring in people with a movement disorder. Criterion validity of the RT3 has yet to be established, however, in people with CP.

The validity of three pedometers (Stepwatch, AMP, Minimod) was evaluated in children with CP. The Stepwatch pedometer was excellent at detecting steps (99.7 ± 2.9% accuracy) in 81 children with CP (Bjornson et al., 2007). The Dynaport Minimod pedometer was accurate at measuring distance walked and step count during continuous walking but was inaccurate at measuring these parameters during structured activity (Kuo et al., 2009). The AMP provided a better estimate of step count and distance during structured activity but compared less favourably to the Minimod during continuous walking. Despite this a major limitation of the Minimod, which should be considered if using it to measure PA, was its failure to record 63% of data during stair ascent and 81% of data during stair descent. The Uptimer activity monitor was also validated as a measure of activity in children with CP. Although it was excellent at detecting time in the upright position (CCC = 0.98) (Pirpiris and Graham, 2004) it has similar limitations to pedometers, notably its inability to capture the energy cost of activity.

The psychometric properties of DLW have not been evaluated in adults and children with CP. It has, however, been used to assess total EE in this population (van den Berg-Emons et al., 1995, Stallings et al., 1996, Bandini et al., 1991, Johnson et al., 1997, Bell and Davies, 2010, Rieken et al., 2011). Van den Berg Emons (1996a) used DLW as a reference method to validate the HR-flex method as a measure of EE in children with CP. Although a good correlation ($r_s = 0.88$; $p < 0.001$) was found between HR monitoring and

DLW limits of agreement were approximately ± 500 kcal/day and individual variation between the two methods ranged from -16.9% to 20.0%. Only nine children, six of whom were non-ambulant, participated in this study. Data from the full measurement period (3 d) was obtained from only four participants. It is difficult, therefore, to comment on the validity of this method when such a small and diverse sample was used.

Table 2.3 Validity of objective measures of physical activity in children with cerebral palsy

Instrument	Sample	Reference Method	Validity	Study
IDEEA	n = 21; 4-10 yr GMFCS Level I: 38% Level II: 29% Level III: 33%	IC	<u>Free living activities</u> r_p=0.72** IDEEA vs IC (kcal): 11.93 ± 5.27 vs 7.15 ± 3.25** <u>Treadmill walking</u> r_p=0.70-0.88** IDEEA vs IC (kcal): 2.25 ± 0.51 vs 1.71 ± 0.79** at a comfortable speed 2.47 ± 0.64 vs 2.43 ± 1.14 at 20-30% higher than comfortable speed. <u>Stepping</u> r_p= 0.75** IDEEA vs IC (kcal): 2.05 ± 0.50 vs 1.81 ± 0.97	Aviram et al., 2011

Actigraph	n = 29; 8-16 yr GMFCS Level I: 38% Level II: 52% Level III: 10%	IC	<u>Validity of Evenson et al., (2008) cut-points for MVPA</u> Sensitivity: 81.8% Specificity: 100% Classification accuracy: 90.9%	Clanchy et al., 2011
Actigraph	n = 31; 6-14 yr GMFCS Level I: 45% Level II: 29% Level III: 26%	direct observation	<u>Structured activity (12 min)</u> $R^2 = 0.63$** $r_p = 0.79$** LOA: -1.08 min to 1.15 min of MVPA <u>Free play (10min)</u> $R^2 = 0.47$** $r_p = 0.68$* LOA: -7.6 min to 2.2 min of MVPA	Capio et al., 2010

AMP	n = 20; 10.5 ± 3 yr GMFCS Level I: 25% Level II: 60% Level III: 15%	measuring wheel and manual step-count	Structured activity LOA: -19.2 m to 12 m LOA: -40 steps to 17.7 steps Continuous walking LOA: -20.1 m to 10.5 m LOA: -16.9 steps to 10 steps	Kuo et al., 2009
Minimod	N = 20; 10.5 ± 3 yr GMFCS Level I: 25% Level II: 60% Level III: 15%	measuring wheel (m); manual step count	Structured activity LOA: -27.9 m to 23.3 m LOA: -87.8 steps to 10.4 steps Continuous walking LOA: -4.7 m to 4 m LOA: -4.1 steps to 3.3 steps	Kuo et al., 2009
Stepwatch (pilot study)	n = 81; 10-13 yr GMFCS Level I: 38% Level II: 37%	Manual step count	Accuracy 99.7 ± 2.9%	Bjornson et al., 2007

	Level III: 25%			
Caltrac and Biotrainer accelerometers	N = 5; 7-18 yr GMFCS Level I-III	IC	ANOVA: p = 0.62	Norman, 2006
RT3 (pilot study)	n= 11; 10.6 to 16.3 yr GMFCS Level I and II	HR	r = 0.88	Maltais et al., 2005
Uptimer	N = 50	direct observation	CCC = 0.98 Mean difference: 5 ± 42 s LOA: -35 s to 45 s†	Pirpiris and Graham, 2004
HR-flex	n=9; 8-13 yr 3 ambulant; 6 non-ambulant	DLW	r_s = 0.88** Individual variation (HR-DLW) -16.9% to 20% LOA: -2.3 $mJ.d^{-1}$ to 2.1 $mJ.d^{-1}$	Van den Berg-Emons et al., 1996

	(549.4 kcal.d^{-1} to 501.6 kcal.d^{-1})

*p<0.01; **p<0.001.

† approximation due to unclear graphs.

r_p= Pearson correlation coefficient; r_s = Spearman's rho correlation coefficient.

GMFCS, Gross Motor Function Classification System; CCC, Concordance correlation coefficient; IC, indirect calorimeter; HR, heart-rate; DLW, doubly-labelled water; MVPA, moderate-vigorous physical activity; LOA, limits of agreement; ANOVA, analysis of variance.

Reliability

Reliability was only reported for three measures: the IDEEA, the Uptimer, and the HR-flex method. Excellent test-retest reliability was reported for the IDEEA across two tests (r_p= 0.985 to 0.998) (Aviram et al., 2011). The two tests, however, were only separated by a ten minute interval during which time the IDEEA was not removed. This is not comparable to the test-retest reliability of the monitor over a number of days when the monitor would have to be removed and reattached for showering, water activities and possibly sleeping. Good inter-monitor agreement between the same lower limb and between two lower limbs was found for the Uptimer (ICC = 0.99) (Pirpiris and Graham, 2004). It also has good test-retest reliability between two weekend days and two weekdays (ICC = 0.88) (Pirpiris and Graham, 2004). Limits of agreement between two monitors were -120 s to 131 s (-0.1% to 0.2% of mean time). This was better than the agreement between two days (limits of agreement -1031 s to 1210 s). Aggregating days, however, improved comparisons. Particularly aggregated weekdays had better agreement with aggregated weekend days (limits of agreement: -620 s to 635 s) (Pirpiris and Graham, 2004). Intra-individual variability for the HR-flex method was found to be better in children with three sampling days as opposed to two days (5.9 ± 5.8% and 13.5 ± 6.3% , respectively; $p < 0.01$) (Van den Berg-Emons et al., 1996a).

Feasibility

Only one study has examined the feasibility of using any of these measures in children with CP. The Actigraph was tolerated well by ambulant and non-ambulant children with CP over a wear period of seven days (Gorter et al., 2012).

2.4.4.3 Conclusion and implications for future research

There is a lack of good quality research into valid and reliable objective measures of habitual physical activity in people with CP. In particular there is little published on measures that can provide information on the frequency, intensity and duration of activity in this population. These dimensions of physical activity need to be assessed to allow for meaningful comparison with physical activity guidelines and to investigate dose-response relationships between activity and health. There is an apparent scarcity of research into physical activity measures in adults with CP. Results obtained from

these studies of children and adolescents should not be extrapolated to adults because of differences in body size, movement patterns and biomechanical efficiency.

The additional factors that should be considered when selecting a measurement instrument, including price, size, comfort, monitor malfunction and ease of use (Murphy, 2009, Trost et al., 2005), were underreported in these studies. It is of particular importance that the feasibility of measures of PA is reported on when they are used in a clinical population. A greater burden may be placed on people with CP to attach activity monitors or HR monitors than that which is placed on their TD peers. The discomfort associated with wearing an activity monitor may be heightened in individuals who already experience pain high levels of pain and increased touch sensitivity (Riquelme et al., 2011). An unobtrusive activity monitor can, however, place less of a burden on a participant than a lengthy questionnaire.

From this review the Actigraph appears to be a valid and feasible measure of activity duration and intensity in children with CP (Clanchy et al., 2011a, Capio et al., 2010, Gorter et al., 2012). The Actigraph is a traditional accelerometer, in that it measures the magnitude of the body's acceleration to provide an output in terms of accelerometer counts. Recent advances in technology and modelling techniques have led to the development of new pattern recognition devices that provide alternative ways of measuring and evaluating physical activity. These advanced accelerometry-based devices use different inputs and may yield different outputs to traditional accelerometers. They may therefore improve on the assessment of physical activity, particularly in people with CP, whose biomechanical efficiency is different to that of able-bodied people. The IDEEA is one such device that demonstrated fair association with indirect calorimetry in children with CP (Aviram et al., 2011). Conclusions about the level of agreement between EE output from the IDEEA and EE from an indirect calorimeter cannot be drawn from this study, however, because of the statistical methods used. The IDEEA has also not been directly compared to a traditional accelerometer and therefore the benefit of using this device cannot be assumed. Because advanced accelerometry-based devices use principles and assumptions that are different to those of traditional accelerometers, it is difficult to directly compare them. It is important that newly developed monitors demonstrate how they improve upon other currently available techniques however. A major challenge for the field of physical

activity research is to establish procedures that allow these new devices to be directly compared to devices currently on the market.

The next chapter will identify advanced accelerometry-based devices that may potentially improve the assessment of physical activity in people with CP.

Chapter 3 Estimation of energy expenditure by accelerometry-based devices.

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3.1 Introduction

A review of the literature in the area of physical activity measurement in adults and children with cerebral palsy (CP), discussed in Chapter 2, revealed that accelerometers appear to be a feasible method of measuring activity in this population. The Actigraph, a traditional accelerometer, provided an accurate estimation of physical activity intensity in children with CP (Clanchy et al., 2011a). Recently advanced accelerometry-based devices have been developed that integrate physiological data from multiple sources to provide an estimation of energy expenditure (EE). These devices may improve the estimation of the energy cost of activities, particularly in people with movement disorders, as they don't just rely on movement data. To evaluate the advantage of using these monitors over traditional accelerometers the monitors must be validated simultaneously against a criterion measure and against devices already available.

This introduces the immediate matter of deciding what outcome measure should be used to compare monitors. The output of traditional accelerometers is generically referred to as 'counts'. Counts cannot be directly compared across different accelerometers because of differences in how the raw data is collected, processed, filtered, and scaled (Chen and Bassett, 2005). The most appropriate outcome measure to compare monitors across is EE (Welk et al., 2012). EE provides an indication of the intensity of physical activity, which allows for comparison with physical activity guidelines. There are also methods available to provide appropriate criterion data, such as indirect calorimetry or doubly-labelled water. This comparison is complicated, however, by the influence of both the raw signals and the prediction equations used to

convert raw data into EE, on the final EE output. That been said, the output of many monitoring devices is influenced by multiple factors. For example the accuracy of the outcome from an automated sphygmomanometer (i.e. mmHg) varies on the basis of the quality of the blood pressure cuff as well as the precision of the gauge. The outcome is standardised however and comparable across all blood pressure monitors. Similarly the direct outcome of EE from accelerometry-based devices provides a method of directly comparing devices regardless of the methods used to produce this outcome.

The aim of this chapter was firstly to identify accelerometry-based devices that provide direct outputs of EE in epochs of one minute or less. It was deemed important to include monitors with the ability to provide data in small epochs as current guidelines suggest that physical activity can be accumulated in 10 min bouts throughout the day. Children perform activity in even shorter bursts (Bailey et al., 1995) and therefore a monitor should also be able to detect this. The second purpose of this chapter was to examine the validity, reliability and feasibility of the selected monitors in apparently healthy adults and children.

3.2 Method

3.2.1 Inclusion criteria and search strategy

A comprehensive search of three electronic databases (Pubmed, Embase and Cinahl) was completed in April 2010 to identify activity monitors that met the above criteria. A further search was conducted in April 2012 to identify studies published in the interim. An initial search of commercially available activity monitors was conducted. The following Mesh terms and text words, and combinations of these, were used in the search: 'accelerometer', 'activity monitor', '(monitoring, ambulatory/instrumentation)', '(monitoring, ambulatory/methods)', '(monitoring, physiologic/instrumentation)', '('ambulatory monitoring'/exp OR 'accelerometer'/exp OR 'accelerometry'/exp)', '((MH "accelerometers") OR (MH "motion analysis systems")' OR '(MH "accelerometers")'. References were also searched for appropriate articles.

Twenty five activity monitors were identified in this search: the RT3 accelerometer (formerly R3D), Personal Activity Monitor (PAM), Caltrac, Actiwatch, Actigraph, Biotrainer, Activtracer, Actitrac, Actical, Kenz Lifecorder EX, Actiheart, Actimarker,

IDEEA, SWA, Actipal, Dynaport, GENEA, Mini-Motionlogger, Actitrainer, Mini-Logger Series 3000, Actillume, Z80/32KV1 activity monitor, Tracmor, ADXL202, LSI.

A further search was conducted to identify studies which had validated these monitors. To be considered for inclusion validation studies had to be conducted on healthy adults and children in the last ten years and the monitor had to be evaluated against a criterion measure of EE. This search revealed 66 validation studies on 13 monitors. Closer examination of the studies revealed that seven monitors did not provide a direct output of EE. Two monitors gave estimates of EE over total wear time only. One monitor had not been validated in children. This resulted in three monitors with the ability to provide direct outputs of EE in epochs of 1 min or less: the RT3 accelerometer, the Sensewear Pro Armband (SWA) and the Intelligent Device for Energy Expenditure and Activity (IDEEA).

Twenty-five studies examined the validity of the RT3, the SWA, and the IDEEA. A further search produced eight published studies reporting on the reliability of these monitors (see Table 3.1). Articles reporting on the validity and reliability of the IDEEA as a measure of physical activity (Zhang et al., 2003) and a gait analysis device (Gorelick et al., 2009; Maffiuletti et al., 2008; Gardner et al., 2007) were not included. Five studies validating the vector count output of the RT3, but not EE, were also not included (Vanhelst et al., 2010a; Chu et al., 2007; Rowlands et al., 2004; Arvidsson et al., 2011b; Adolph et al., 2011).

Table 3.1 Studies reporting the validity and reliability of the RT3, SWA and IDEEA.

	RT3	IDEEA	SWA
Validity	8	4	17
Reliability	5	0	3

3.3 Results

3.3.1 Properties of the selected monitors

3.3.1.1 RT3 accelerometer

The RT3 (Stayhealthy Inc.) is a small (7.1 x 5.6 x 2.8 cm), lightweight (65.2 g), unobtrusive device (Figure 3.1). The device consists of a piezoelectric element and a seismic mass which generate a variable output voltage signal when the participant

moves. The size of the voltage is proportional to the applied acceleration. The voltage is filtered, amplified and sampled at a rate of 1Hz to convert the voltage signal to a series of numbers called counts. The piezoelectric element is sensitive to accelerations in three dimensions i.e. the vertical plane (x), the antero-posterior plane (y) and the medio-lateral plane (z). A resulting vector magnitude (VM) is calculated as the square root of the sum of squared activity counts for each dimension. The RT3 can provide count data for each plane or for VM in 1-min or 1-s epochs. Inbuilt proprietary algorithms convert count data into total EE and activity EE based on age, sex, height and weight. Data can be recorded for up to 21 days.

Figure 3.1 RT3 accelerometer

3.3.1.2 Sensewear Pro Armband

The SWA (Bodymedia, Inc.) is a lightweight (83 g) activity monitor that combines accelerometry data, heat loss data, skin temperature and galvanic skin response data to provide information on body position, step count and EE (Figure 3.2). Previous versions of the armband (Pro 2) obtain accelerometry data from a biaxial accelerometer. The newer Pro3 and mini version contain a triaxial accelerometer. Physiological data is incorporated with information about participants' sex, age, height and weight to predict EE with the use of inbuilt algorithms. The manufacturers of the SWA periodically release software upgrades with new algorithms which they claim improve the estimation of EE. Continuous data can be collected for 28 days. The manufacturers suggest that the armband is worn on the right arm over the triceps muscle at the midpoint between the acromion and the olecranon.

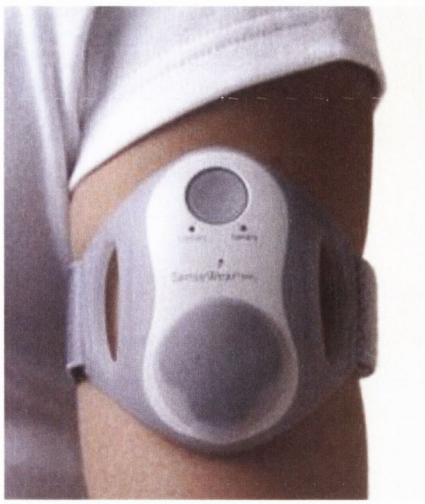


Figure 3.2 Sensewear Pro Armband

3.3.1.3 Intelligent Device for Energy Expenditure and Activity

The IDEEA (Minisun, LLC) consists of five sensors that are attached to the chest, anterior aspects of both thighs and soles of the feet, and a data collection device (59 g) that is clipped to the user's belt (Figure 3.3). The sensors contain biaxial accelerometers which collect data and transmit it through thin, flexible wires to the recorder. Before each test the device is calibrated to ensure correct placement of the sensors. The IDEEA provides information regarding the type, duration, and estimated intensity of each activity carried out by the user while wearing the device. The IDEEA can store data 32 times per second for approximately 7 days. Information about age, sex, weight, height and a subjective estimation of fitness level (1-10) is incorporated with activity monitor data to provide estimations of EE with the use of inbuilt algorithms. For further information on each monitor consult Table 3.2.

Figure 3.3 Intelligent Device for Energy Expenditure and Activity

Table 3.2 Overview of RT3, SWA and IDEEA specifications

Monitor	Type	Outcome measure	Data storage (d)	Placement	Weight (g)	Size (cm)	Price (approximation)
RT3	Triaxial accelerometer	Vector magnitude (counts), EE (kcal)	7 (kcal/min) 21 (counts)	Right hip	65.2	7.1 x 5.6 x 2.8	Monitor: €476 Monitor + docking station: €628
IDEEA	Biaxial accelerometer	EE(kcal), Power (W), Work (KJ), Time spent in different activities (min), Gait Parameters	7	5 sensors attached to anterior aspects of thighs, soles of feet and sternum. Storage unit attached to waist.	59	7.0 x 5.4 x 1.7	Monitor: €4,046 The price for second system will be €2,426 within the same order. Each additional monitor will be significantly lower.
SWA	Pro2: biaxial accelerometer Pro 3 : triaxial accelerometer	EE (kcal, METs), sleep time (min), steps, Activity duration (min)	28	Right arm over the triceps muscle	83	7.2 x 9.0 x 1.0	Armband: €324 Professional software: €1,925.00

3.3.2 Study characteristics

The RT3, the IDEEA and the SWA have been validated in both adults and children. The age of the sample population varied across studies. The monitor that was evaluated, the software version (if applicable), the age of the sample population (mean ± sd or range) and the criterion measure of EE used in the study are reported for adults and children in Tables 3.3 and 3.4, respectively. Studies that assessed the validity or reliability of the monitor in overweight or obese individuals (as defined by BMI ≥25kg.m^{-2}) exclusively were not included in this review as they were deemed to be a clinical population. Such studies have limited utility because they provide no insight into how the monitors would perform in a diverse population that is more representative of the general population. Studies that included both normal weight and overweight individuals, however, were included in the review. The activities used to evaluate the monitors varied between studies. They could however be loosely categorised as the measurement of resting EE, EE during treadmill locomotion, EE during free-living activities, and total EE/activity EE over a day or a continuous period during which numerous activities were performed.

Table 3.3 Previous literature investigating the validity of the SWA, the IDEEA and the RT3 in adults

Study	Monitor	n	Age (yr)	Reference Method
(Johannsen et al., 2010)	SWA_m (v7.1) and SWA_3 v6.1)	30	24-60	DLW
(Drenowatz and Eisenmann, 2011)	SWA (v6.1)	20	24.3±2.8	IC
(Koehler et al., 2011)	SWA_3 (v6.1)	14	30.4±6.2	DLW and IC
(Mackey et al., 2011)	SWA (v6.1) and SWA (v5.1)	19	78-89	DLW
(Berntsen et al., 2010)	SWA (v5.1)	20	19-56	IC
(Heiermann et al., 2011)	SWA_2 (v5.0)	49	60-87	IC

(Bertoli et al., 2008)	SWA (v4.0)	169	44±12	IC
(Malavolti et al., 2007)	SWA (v4.0)	99	38 ± 14	IC
(Jakicic et al., 2004)	SWA (v3.2)	40	18 - 35	IC
(Fruin and Rankin, 2004)	SWA (v1.0)	13	19 - 22	IC
(King et al., 2004)	SWA (v not specified)	21	24.7 ± 5.4	IC
(Whybrow et al., 2012)	IDEEA	14	20 - 55	DLW and IC
(Zhang et al., 2004)*	IDEEA	27	15 - 61	IC
(Lyden et al., 2011)	RT3	274	38.3 ± 12.4	IC
(Maddison et al., 2009)	RT3	36	39 ± 10	IC
(Howe et al., 2009)	RT3	212	20 - 60	IC
(Jacobi et al., 2007)	RT3	10	29.3 ± 5.2	IC
(King et al., 2004)	RT3	21	24.7 ± 5.4	IC

*includes adults and children.

SWA_m, Sensewear mini Armband; SWA_3, Sensewear Pro3 Armband; SWA_2, Sensewear Pro 2 Armband; v, version of SWA software; DLW, doubly labeled water; IC, indirect calorimetry.

Table 3.4 Previous literature investigating the validity of the SWA, the IDEEA and the RT3 in children

Study	Monitor	N	Age (yr)	Reference Method
(Arvidsson et al., 2011a)	SWA_2 (v6.1)	26	8 - 12	IC
(Calabro et al., 2009)	SWA (v6.1) and SWA (v4.2)	22	9.4 ± 1.2	IC
(Arvidsson et al., 2009a)	SWA (v6.1) and SWA (v5.1)	20	14 - 15	DLW
(Arvidsson et al., 2009b)	SWA_2 (v5.1)	12	11 - 13	IC
(Arvidsson et al., 2007)	SWA_2 (v5.1)	20	11 - 13	IC
(Dorminy et al., 2008)	SWA (v4.1)	21	10 - 14	IC
(Arvidsson et al., 2011a)	IDEEA	26	8 - 12	IC
(Arvidsson et al., 2009b)	IDEEA	12	11 - 13	IC
(Hussey et al., 2009)	RT3	20	7 - 12	IC
(Sun et al., 2008)	RT3	27	12 - 14	IC
(Kavouras et al., 2008)	RT3	42	12.2 ± 1.1	IC

SWA_2, Sensewear Pro 2 Armband; v, version of SWA software; DLW, doubly labelled water;

IC, indirect calorimetry.

3.3.3 Validity

A summary of the validity of these monitors during rest, treadmill locomotion, free-living activities and for total EE or activity EE can be seen in Appendix II.

3.3.3.1 Sensewear Pro Armband

Nine versions of the SWA software have been evaluated. Note that some studies simultaneously examined the validity of two versions of the SWA software (Arvidsson et al., 2009a, Calabro et al., 2009, Johannsen et al., 2010). Six studies looked at the validity of the SWA in children aged nine to fifteen years against indirect calorimetry (Calabro et al., 2009, Arvidsson et al., 2009b, Dorminy et al., 2008, Arvidsson et al., 2007, Arvidsson et al., 2011a) and against doubly-labelled water (DLW) (Arvidsson et al., 2009a). Twelve studies validated the SWA in adults (Mackey et al., 2011, Heiermann et al., 2011, Fruin and Rankin, 2004, Malavolti et al., 2007, Bertoli et al., 2008, Johannsen et al., 2010, Jakicic et al., 2004, Drenowatz and Eisenmann, 2011, Koehler et al., 2011, Soric and Misigoj-Durakovic, 2010, Berntsen et al., 2010, King et al., 2004).

The SWA has been proposed as a novel device for measuring resting EE without the need for expensive, often cumbersome, equipment (Bertoli et al., 2008). The disagreement between the SWA and a criterion measure, however, is too large for the SWA to credibly replace the current method of measuring resting EE in adults. Overestimations of resting EE by the SWA of 4% and 12% ($p < 0.001$) (version 5.0 [v5.0] and version 4.0 [v4.0], respectively) were reported (Heiermann et al., 2011, Bertoli et al., 2008). Although Malavolti et al. (2007) found that the SWA (v4.0) underestimated REE and Fruin and Rankin (2004) found no difference between indirect calorimetry and the SWA (v1.0), all studies reported similarly large limits of agreement (LOA). LOA ranged from -13% to 15% of total EE (Fruin and Rankin, 2004) to -18% to 31% of total EE (Bertoli et al., 2008).

There is little evidence available on the ability of the SWA to measure resting EE in children. One study evaluating the ability of the SWA to predict resting EE in children found that the SWA (v4.2) overestimated resting EE by 22%. (Dorminy et al., 2008). Three studies reported that resting EE was underestimated by the SWA by 0.2% to 32% (Arvidsson et al., 2007, Calabro et al., 2009, Arvidsson et al., 2009b). LOA were not

reported in any study (Bland and Altman, 1986). Although it may be likely that similar results will be found to those reported in adults this should be investigated further.

Three studies reported that the SWA overestimated the energy cost of treadmill walking in adults (Jakicic et al., 2004, King et al., 2004, Fruin and Rankin, 2004). As well as overestimating the energy cost of walking by 38%, LOA for the SWA (v1.0) were -7% to 81% of the mean EE. Although Jakicic et al. (2004) calculated limit of agreement plots for treadmill walking, the upper and lower LOA are not labelled, and therefore values cannot be reported. They do, however, display the increased variation between measures as intensity increases suggesting that the SWA becomes less accurate as intensity increases. An increased underestimation of EE by the SWA with increasing intensity was also found by Koehler et al. (2011) and Drenowatz and Eisenmann (2011) in endurance trained athletes. The SWA (v6.1) did not differ significantly from indirect calorimetry when athletes ran at speeds of up to 8.6 $km.h^{-1}$ during a maximal treadmill test (Koehler et al., 2011). However, it underestimated the energy cost of running at speeds of greater than 8.6 $km.h^{-1}$ ($p < 0.001$). It was reported that the SWA's (v6.1) estimation of EE plateaus at an intensity of 10 METs (Drenowatz and Eisenmann, 2011). Walking on an incline resulted in an underestimation of EE by the SWA and a large disagreement between measures (LOA: -73% to 30%) (Jakicic et al., 2004, Fruin and Rankin, 2004).

Four studies assessed the ability of the SWA to estimate EE during treadmill locomotion in children. Despite conflicting results it would appear that the SWA (v5.1) is accurate at estimating EE during slow walking speeds but, similar to adults, the SWA can underestimate EE by 9% to 43% as the intensity increases (Arvidsson et al., 2007). One study reported that the SWA (v6.1) accurately assessed EE for walking speeds of 3.2 $km.h^{-1}$, 4 $km.h^{-1}$ and 4.8 $km.h^{-1}$ (Calabro et al., 2009). Another study, however, reported that the same version of the SWA underestimated the energy cost of walking by 10% to 19% and that its accuracy was not associated with the speed of walking (Arvidsson et al., 2011a). This contradiction may be attributed to the fact that the energy cost of walking will vary between individuals for a given speed. To account for this Dorminy et al. (2008) evaluated the SWA (v4.1) while running at 60% of maximal oxygen consumption (VO_2max). The SWA overestimated EE by 43% at this intensity with LOA of -1.02 $kcal.min^{-1}$ to 2.57 $kcal.min^{-1}$ (-19% to 47%).

The SWA generally underestimates the energy cost of free-living activities. Four studies reported on the ability of the SWA to measure EE in children during free-living activities (Arvidsson et al., 2007, Calabro et al., 2009, Arvidsson et al., 2009b, Dorminy et al., 2008). Disappointingly the use of an upper limb monitor did not improve the estimation of the EE during upper limb activities. In contrast to hip worn accelerometers the SWA overestimated the energy cost of upper limb activity. The SWA was unable to accurately estimate the EE of stationary bicycling in children ($p < 0.01$) (Calabro et al., 2009, Arvidsson et al., 2009b, Arvidsson et al., 2007) with the relative mean difference between measures ranging from -25% (Calabro et al., 2009) to -51% (Arvidsson et al., 2009b). LOA were not reported.

Sedentary activities such as playing computer games, watching TV, reading and writing were overestimated by version 4.1 of the SWA (21.1%) (v4.1) ($p<0.001$) (Dorminy et al., 2008). Version 5.1 of the SWA underestimated the energy cost of sitting quietly ($p<0.01$) (Arvidsson et al., 2009b, Arvidsson et al., 2007). Similar sedentary activities were accurately assessed by version 6.1 however (Calabro et al., 2009), suggesting that the software upgrades may improve the SWA's estimation of EE.

The SWA (v5.1) accurately measured the EE of children track walking at a slow and normal speed (Arvidsson et al., 2007). Similar to treadmill locomotion, however, the SWA increasingly underestimated EE as the intensity of the exercise increased ($p<0.01$) (Arvidsson et al., 2007). The energy cost of stair walking and playing basketball in children was also underestimated by the SWA (v5.1) ($p < 0.01$) (Arvidsson et al., 2009b, Arvidsson et al., 2007).

Of the free-living activities assessed in adults, arm ergometry was the only activity to be overestimated by the SWA (29%) ($p < 0.001$) (Jakicic et al., 2004). The difference between measures increased as the magnitude of EE increased in adults (Fruin and Rankin, 2004, Jakicic et al., 2004, Koehler et al., 2011, Berntsen et al., 2010). The SWA underestimated the EE of a 30 min outdoor run by -3.5 METs with wide LOA reported (1.1 METs to 5.9 METs; mean EE not reported) (Drenowatz and Eisenmann, 2011). Energy expenditure during stationary cycling was also underestimated in adults by 8.8% to 28.9% during submaximal speeds and by 6.6 $kcal.min^{-1}$ during a maximal cycle test (Fruin and Rankin, 2004, Jakicic et al., 2004, Koehler et al., 2011). Limits of agreement were wide during both submaximal speeds (-35% to 27%) (Fruin and Rankin, 2004) and

during the maximal cycle test (-14.8 kcal.min^{-1} to 1.6 kcal.min^{-1}; mean EE not reported) (Koehler et al., 2011).

Total EE was overestimated by the SWA in children (5% to 20%) (Dorminy et al., 2008; Arvidsson et al., 2009a). Limits of agreement were similar for v6.1 and v5.1 (-10% to 31% of mean EE and -26% to 15% of mean EE, respectively) (Arvidsson et al., 2009a). Conversely, total EE was underestimated by the SWA (v6.1) in adults with wide LOA reported in all studies (Koehler et al., 2011, Mackey et al., 2011, Johannsen et al., 2010). Using v7.0 of the SWA software reduced the mean difference between EE from the SWA and EE from DLW by 3.9% (from 4.0% to <0.1%) (Johannsen et al., 2010). Limits of agreement were similar for v7.0 and v6.1 of the SWA (-27% to 19% and -23% to 21%, respectively) (Johannsen et al., 2010). The SWA also significantly underestimated activity EE ($p<0.05$) (Johannsen et al., 2010, Mackey et al., 2011). Limits of agreement for activity EE in older adults were considerably wider than those for total EE (-23% to 21% vs -95% to 41%) (Mackey et al., 2011). Although LOA for total EE were similar in older adults and young adults, LOA for activity EE were not reported in young adults making it impossible to compare cohorts.

3.3.3.2 RT3

Three studies evaluated the ability of the RT3 to measure EE in children (Hussey et al., 2009, Sun et al., 2008, Kavouras et al., 2008). Five studies examined the validity of the RT3 in adults (Maddison et al., 2009, Howe et al., 2009, King et al., 2004, Jacobi et al., 2007, Lyden et al., 2011). The RT3 has not been validated as a measure of resting EE in children or adults. In general it appears that the RT3 overestimates the energy cost of treadmill activity or activities that involve lower limb activities. In contrast, the hip mounted accelerometer underestimates the EE of free-living activities, particularly activities of daily living, which involve large upper limb movements.

The RT3 overestimated the energy cost of children walking slowly on a treadmill by 54% (Sun et al., 2008). This overestimation increased with increasing speed. Although , Kavouras et al. (2008) also reported an overestimation of EE during treadmill running (7.8%) an underestimation of EE was reported during walking (-20.7%). Hussey et al. (2009) reported a difference between the RT3 and indirect calorimetry for treadmill walking at 6km.h^{-1} ($p<0.05$). Mean EE and mean bias between measures were not, however, clearly reported. While LOA were plotted in both these studies the upper and

lower limits were unclearly labelled (Hussey et al., 2009, Kavouras et al., 2008). Similar to the SWA, the RT3 is unable to detect the energy cost of a person traversing a slope (Sun et al., 2008, Kavouras et al., 2008).

The RT3 overestimated treadmill locomotion in adults (Lyden et al., 2011, Howe et al., 2009, King et al., 2004, Jacobi et al., 2007). It appears that, although the RT3 is unable to detect a slope, the magnitude of the overestimation of EE during walking on level ground was so large that, in some cases, walking on a slope resulted in a smaller overestimation of EE rather than an underestimation of EE (Lyden et al., 2011, Jacobi et al., 2007). Contrary to reports in children, Howe et al. (2009) did not find a relationship between the accuracy of the RT3 and activity intensity.

Hussey et al. (2009) found no difference between the RT3 and indirect calorimetry when children were sitting ($p < 0.05$) but did not report the mean bias. Sun et al. (2008), however, reported underestimations of EE by the RT3 in children of 55% to 87% during activities such as sitting, standing and writing. The energy cost of children performing outdoor activities, most involving lower limb movement, was overestimated by the RT3 by 25% to 214% (Sun et al., 2008). Overestimation of EE by the RT3 increased with increasing intensity. Only catching and throwing was underestimated by the RT3 (13%). Cycling at 25 W and 50 W was underestimated by 8% and 60%, respectively (Sun et al., 2008). LOA for free-living activities were not reported.

The RT3 underestimated the energy cost of activities of daily living (Lyden et al., 2011, Howe et al., 2009). Activities with greater upper limb movement underestimated activity EE by 24.4% to 64.5% (Howe et al., 2009). No study plotted LOA for the agreement between RT3 predicted EE and criterion measured EE for treadmill or free-living activities.

The RT3 underestimated the total EE and activity EE of adults by 4% and 14%, respectively (Maddison et al., 2009). LOA for total EE were approximately -39% to 30% of mean EE (value of upper and lower limits not clearly labelled) (Maddison et al., 2009). LOA were very wide for activity EE (-131% to 102%) (Maddison et al., 2009).

3.3.3.3 IDEEA

The validity of the IDEEA was examined against indirect calorimetry in two studies of children (Arvidsson et al., 2011a, Arvidsson et al., 2009b), one study of adults

(Whybrow et al., 2012) and one study of children and adults aged 15 to 61 years (Zhang et al., 2004). Only one study reported on the ability of the IDEEA to predict resting EE.

Although a non-significant overestimation of resting EE (0.01 $kJ.kg^{-1}.min^{-1}$; 10%) was reported in children (Arvidsson et al., 2009b) LOA were not reported. The IDEEA underestimated EE by 4.2% during treadmill walking (Arvidsson et al., 2011a). The IDEEA proved more accurate than the SWA, which underestimated EE by 26.8% when the two monitors were evaluated simultaneously (Arvidsson et al., 2011a). The IDEEA was also more accurate than the SWA at higher speeds of track walking and running (Arvidsson et al., 2009b). Unlike the SWA, however, the IDEEA was unable to accurately predict the energy cost of slow or normal speeds of walking. Despite this the IDEEA had closer agreement to indirect calorimetry than the SWA for total walk/run time (+3% vs. -12%). The IDEEA was accurate at predicting the energy cost of sitting and stair walking but underestimated EE during playing basketball and jumping on a trampoline ($p < 0.001$) (Arvidsson et al., 2009b). Cycling was also underestimated by the IDEEA ($p < 0.01$) (Whybrow et al., 2012, Arvidsson et al., 2009b). The IDEEA underestimated a combination of sedentary, free-living and locomotor activities in children by 12% ($p < 0.01$) (Arvidsson et al., 2009b). Although this underestimation was smaller than the SWA's underestimation of EE for the same activities (-18%) LOA were not reported making it difficult to comment on the level of agreement between the monitors and indirect calorimetry.

Two studies reported that the IDEEA's prediction of total EE did not differ from total EE measured with whole room calorimetry (Whybrow et al., 2012, Zhang et al., 2004). The studies reported LOA of -0.233 $kcal.min^{-1}$ to 0.118 $kcal.min^{-1}$ (mean EE not reported) (Zhang et al., 2004) and -7.9 $kJ.kg^{-1}.22\ hr^{-1}$ to 32.0 $kJ.kg^{-1}.22\ hr^{-1}$ (-7% to 28%) (Whybrow et al., 2012). Doubly-labelled water measured total EE and activity EE were overestimated by the IDEEA by 27% and 74% ($p<0.001$) with LOA of -6% to 49% and -22% to 165%, respectively (Whybrow et al., 2012).

3.3.4 Reliability

Only eight studies looked at the reliability of the RT3 and SWA. No study examined the reliability of the IDEEA. Six studies looked at intra-instrument reliability and four studies looked at inter-instrument reliability. A summary of the results is presented in Appendix III.

3.3.4.1 Sensewear Pro Armband

Fruin and Rankin (2004), and Heiermann et al. (2011) found excellent intra-instrument reliability for the SWA when predicting resting EE (r=0.93-0.98; p≤0.01). A low measurement error (1.9%; 30.8 kcal.d^{-1}) (Fruin and Rankin, 2004) and narrow LOA (-0.07 kcal.min^{-1} to 0.10 kcal.min^{-1}) (Heiermann et al., 2011) were reported between resting EE measurements over two days. Intra-instrument reliability of the SWA (v6.1) between two 13 hr periods of rest, sedentary activities and exercise was high (ICC = 0.97) (Brazeau et al., 2011). The correlation between two periods of sedentary activity was low (ICC = 0.62) compared to walking (ICC = 0.95), playing basketball (ICC = 0.85) and lying (ICC = 0.98) (p ≤0.01 for all) (Brazeau et al., 2011).

3.3.4.2 RT3

The intra-instrument reliability of the RT3 was assessed in adults (Powell and Rowlands, 2004) and children (Vanhelst et al., 2010a). No difference was found in the energy cost of everyday activities between two consecutive days (Powell and Rowlands, 2004). In children, aged 10-16 yr, the coefficient of variation (CV) decreased from 17.3% ± 2.3 during sedentary activity to 6.6% ± 0.1 during vigorous activities (Vanhelst et al., 2010b).

Two studies examining the intra-instrument reliability of the RT3 by simulating human movement with mechanically powered vibrations found contradictory results (Krasnoff et al., 2008, Powell et al., 2003). Krasnoff et al. (Krasnoff et al., 2008) reported excellent CVs (0.29% - 1.81%) across VM counts of 22 RT3s . Larger CVs were reported in a study where 23 RT3s were individually vibrated at three frequencies (2.1 Hz, 5.1 Hz, 10.2 Hz) along the three axes (x, y and z) (0.00 - 67.8%) (Powell et al., 2003). Vibrations at lower frequencies (2.1 Hz), simulating sedentary activities, resulted in much greater CVs compared to vibrations at higher frequencies (0%-67.8% vs 0.3%-8.7% vs 0.2%-3.7%).

Contradictory results were also reported for the inter-instrument reliability of the RT3. Krasnoff et al. (Krasnoff et al., 2008) calculated CVs of 9.5% - 34.7% across VM counts and ICCs of 0.000 to 0.042. Coefficients of variation across all three axes (x, y, z) were 13% - 139%. Compared to this Powell et al. (Powell et al., 2003) found smaller CVs across all axes (4.2% - 38.5%) and larger ICCs (0.99; p ≤0.01).

Reneman and Helmus (2010) were the only authors to report on the inter-instrument reliability of the RT3 in vivo. In a sample of six people each carrying six monitors the inter-instrument reliability ICC was 0.80 ($p \leq 0.01$) (95% confidence interval = 0.52 - 0.95). Although the CIs were wide the lower limit was above 0.50 indicating moderate reliability. This result was obtained after one accelerometer was excluded for providing abnormal outputs. As was reported in this and other studies, inaccurate data may be collected because of unusual outputs from a small number of monitors (Reneman and Helmus, 2010, Powell et al., 2003, Chu et al., 2007).

3.3.5 Feasibility

Only 15 articles gave feedback on the feasibility of the three monitors. High compliance rates (>95%) were reported for the SWA (Brazeau et al., 2011, Johannsen et al., 2010, Koehler et al., 2011, Fruin and Rankin, 2004). Over a 14 day period 85% of participants wore the SWA for greater than 90% of the time (Arvidsson et al., 2009a). Jakicic et al. Jakicic et al. (2004) reported 17% missing data and King et al. (King et al., 2004) reported 14% missing data. In the same study King et al. (2004) reported 5% missing data for the RT3. This was lower than the 13% reported by Maddison et al. (2009) and Lyden et al. (2011). Only one study reported on compliance with the RT3 which was 12.3±2.1 out of 14 days (88%) (Maddison et al., 2009). Whybrow et al. (2012) reported that the IDEEA failed to record data for one person (6.7%). In the same study a compliance rate of 63% ± 5.3 was reported over a fourteen day period. Zhang et al. (2004) noted that participants gave positive feedback about the IDEEA. In a study comparing the IDEEA and the SWA, however, the authors commented that the SWA was more feasible than the IDEEA (Arvidsson et al., 2009b).

3.3.6 Conclusion and implications for future research

The large number of activity monitors commercially available is evident from the literature search conducted in this chapter. As well as the regular release of new monitors onto the market some manufacturers release multiple monitor models or upgraded versions of previously released models. While the influx of commercially available accelerometers may improve the quality of physical activity research it can also make monitor selection an intimidating task for researchers and clinicians. A systematic approach should therefore be employed to demonstrate that newly released monitors provide an advantage in terms of accuracy or feasibility over already available devices.

As no study has simultaneously compared the monitors included in this review caution must be taken when recommending one monitor over another. Comment can be made, however, on the respective strengths and weaknesses of each monitor.

If a monitor is being used to predict EE it is imperative that it can accurately measure the underlying resting EE. Resting EE usually lies within 10% of an individual's basal metabolic rate, which can account for up to 60% of total daily EE (Levine, 2005). No study has evaluated the ability of the RT3 to measure resting EE. One study reported on the ability of the IDEEA to measure resting EE and although it appears accurate, LOA weren't reported. The SWA has been proposed as a novel device for measuring resting EE without the need for expensive, often cumbersome, equipment (Bertoli et al., 2008). There is little evidence available on the ability of the SWA to measure resting EE in children, however, and the disagreement between the SWA and a criterion measure is too large for the SWA to be considered an accurate measure of adults' resting EE. A possible explanation for this is the small number of variables included in the monitors' prediction equations. Although information about the wearer's age, sex, weight and height are included in proprietary algorithms there is evidence to suggest that variables such as race, climate and diabetic status are significant predictors of basal metabolic rate (Morrison et al., 1996, Froehle, 2008, Martin et al., 2004). Impaired cardiorespiratory fitness may also result in a reduced resting EE (Miller et al., 2012). The inclusion of objective measures of these variables in future prediction equations should be considered.

An essential problem with accelerometers is that there are unique relationships between movement and EE for different activities. Equations based on locomotion tend to underestimate the EE of lifestyle activities (Welk, 2005). The validity of a monitor therefore depends on what activities are included in the validation protocol. While variation in study protocols helps to build evidence of validity and reliability, variation across studies can also hamper comparison between them. A major difficulty encountered when compiling this review was the lack of similarities between validation protocols. Further disparity arose between data processing methods used by authors.

Despite conflicting results between studies it appears that the SWA is generally accurate or overestimates EE at lower speeds. As the speed, and therefore intensity increases, it underestimates the EE of the activity. In fact it was unable to detect any

increase in EE above an intensity of 10 MET (Drenowatz and Eisenmann, 2011). The difficulty with any monitor accurately estimating EE for running speeds is compounded by the large variation in oxygen uptake amongst individuals. Oxygen uptake is not a direct product of speed, and the variation amongst individuals is a result of biomechanical, physiological and other factors. During walking and running at a self-selected comfortable speed individuals select the stride length and stride frequency combination that minimises energetic cost (Holt et al., 1991). Increasing stride length to adapt to an imposed speed results in a greater metabolic cost than adapting a high frequency/short stride length combination (Holt et al., 1991). The impact of stride frequency on accelerometer output has only been investigated in the RT3. The vector output from the RT3 increases linearly with both speed and stride frequency (Rowlands et al., 2007). It may not, however, detect the increased energetic cost of a long stride length/low frequency gait for a given speed.

The SWA generally underestimates free-living activity, although version 6.1 appears to be accurate at measuring sedentary activity (Calabro et al., 2009). Similarly, the RT3 overestimates the EE of treadmill activity but underestimates the EE of activities of daily living (Lyden et al., 2011, Howe et al., 2009). This may be because monitors worn on the hip or lower limbs underestimate the EE of upper limb activities. Disappointingly, use of the SWA, an upper limb monitor, did not improve detection of upper limb activity. The inability of these monitors to detect upper limb movement may also impact on the monitors' ability to estimate running EE, as the presence of arm-swing reduces the metabolic cost of running (Arellano and Kram, 2011).

Only two studies provided a comparative evaluation of the SWA and the IDEEA (Arvidsson et al., 2011a; Arvidsson et al., 2009b). Although the IDEEA overestimated treadmill locomotion it was more accurate than the SWA. It was also more accurate than the SWA at measuring track locomotion and free-living activities in children. There is, however, generally a lack of published evidence on the IDEEA. In particular no study investigated the IDEEA's ability to assess treadmill locomotion in adults.

All monitors were limited by their inability to detect the energy cost of cycling and of traversing a slope. It is possible that other environmental factors, which affect the energy cost of locomotion such as walking surface, weather conditions and footwear (Maffiuletti et al., 2012) may also not be measured by the monitors. These monitors are

also not waterproof and therefore cannot capture the EE of water activities. These limitations, however, are inherent in the majority of accelerometers.

A criticism of many studies included in this review was the lack of appropriate statistical analysis used to report results. LOA plots should be reported in all studies where the agreement between two methods of measurement is being assessed (Bland and Altman, 1986). Many studies in this review did not report LOA (Calabro et al., 2009; Arvidsson et al., 2009b; Arvidsson et al., 2011a; Sun et al., 2008; King et al., 2004; Jacobi et al., 2007). While some plotted LOA they did not report the value of the limits, the mean bias, or the mean EE for the measurement period (Hussey et al., 2009; Malavolti et al., 2007; Jakicic et al., 2004; Kavouras et al., 2008). This makes it impossible to comment on the acceptability of the agreement between measures. The importance of using LOA to assess agreement between measures is highlighted in studies that reported on total EE and activity EE. All studies reported unacceptably wide LOA for all monitors (Johannsen et al., 2010; Koehler et al., 2011; Mackey et al., 2011; Arvidsson et al., 2009a; Whybrow et al., 2012; Maddison et al., 2009). The disagreement between monitors and criterion measures was larger for activity EE than total EE (as large as -22% to 165% of mean EE) (Johannsen et al., 2010; Mackey et al., 2011; Whybrow et al., 2012).

Research is needed into the inter-monitor reliability of all monitors. This is of particular importance in epidemiological studies that may use multiple monitors to measure physical activity in specific populations. As reported in some studies inaccurate data may be collected because of unusual outputs from a small number of monitors (Reneman and Helmus, 2010; Powell et al., 2003; Chu et al., 2007). Ideally one monitor should be used on all subjects for validation studies. Where multiple monitors are being used, monitors should be calibrated prior to use. The feasibility of these monitors was also underreported. Anecdotally monitor malfunction is common and information on this should be included in all studies. Information on the acceptability of the instrument including level of comfort and tolerance, refusal rate and level of missing data, and reasons for both should be given in all accelerometer studies as this will strongly influence a researchers or clinicians choice of monitor (Aaronson, 2002).

When selecting a monitor for use clinically or in research the characteristics of the target population should be considered. Commercially available EE equations assume

that mechanical efficiency for performing a task is similar across populations. Characteristics such as age, body mass, disease status or mobility limitations may result in different physiological demands being placed on an individual for a given task, however, resulting in an inaccurate prediction of EE. The inclusion of body mass in EE equations should account for the higher metabolic rate in obese individuals for all activities (Lafortuna et al., 2008). The relationship between EE and body mass varies in relation to the type of activity performed however, e.g. weightbearing vs. non-weightbearing activities (Lafortuna et al., 2010). Similarly the proprietary algorithms included in commercially available monitors may not be able to measure the increased energetic cost of ambulation in populations with gait abnormalities. It is recommended that accelerometers are specifically validated in these populations and that results from the healthy population are not be extrapolated to other populations.

In conclusion, a lack of consistency in protocols across studies means that, like other reviews of accelerometers (De Vries et al., 2009; Trost et al., 2005), this review did not find compelling or consistent enough evidence to support the use of one monitor over another. The next section of this thesis proposes to provide a comparative evaluation of the estimation of EE by accelerometry-based devices in apparently healthy individuals without CP. The most objective method of establishing criterion and concurrent validity will be employed by simultaneously comparing the activity monitors' estimation of EE to a criterion measure.

Chapter 4 Study 1: An evaluation of energy expenditure estimation by three activity monitors

This study has been published in the European Journal of Sport Science.

Ryan, J. and Gormley, J. (2013). An evaluation of energy expenditure estimation by three activity monitors. European Journal of Sport Science. doi:10.1080/17461391.2013.776639

4.1 Objective

The aim of this study was to provide a comparative evaluation of three accelerometry-based devices at estimating energy expenditure (EE) in apparently healthy adults and children.

4.2 Methodology

4.2.1 Participants

Twenty-six adults (11 males, 15 females) and 22 children (11 males, 11 females) aged 6 to 36 years were recruited through the Faculty of Health Sciences and local schools. Ethical approval for this study was granted by the Faculty Ethics Committee. The procedures and risks involved in the study were fully explained to participants and their guardians, where appropriate, before written informed consent was obtained. The sample size required for this study was generated from data collected on 32 adults in our laboratory. Based on a mean difference of 0.15 $kcal.min^{-1}$ and a standard deviation of 0.216 $kcal.min^{-1}$, between EE from the RT3 and indirect calorimeter at rest, 21 participants in each group provided 80% power at the 0.05 α-level.

4.2.2 Instrumentation

The RT3 accelerometer, Sensewear Pro Armband (SWA) and Intelligent Device for Energy Expenditure and Activity (IDEEA) have been described in sections 3.3.1.1, 3.3.1.2,

and 3.3.1.3, respectively. Resting EE and EE during the treadmill protocol were measured using the Cosmed Quark CPET (Rome, Italy) indirect calorimeter. The Quark CPET is a standard metabolic cart that measures ventilation and gas concentrations in expired air, using a flowmeter and gas analyser. The flowmeter consists of a bidirectional turbine and optoelectronic reader. The turbines were calibrated prior to each test session using a 3L syringe to ensure accurate volume measurements. Gas calibration, including room air calibration (assuming room air is 20.93% O_2 and 0.03% CO_2) and reference gas calibration (16% O_2, 5% CO_2), was conducted prior to each test.

A pilot study was conducted on 13 participants to assess the validity of the Cosmed. Participants lay supine while oxygen consumption (VO_2) was measured with the Cosmed and a douglas bag, for 10mins each, in a random order. The mean difference between the two methods was 0.21 $ml.kg^{-1}.min^{-1}$. A paired t-test indicated that there was no difference in VO_2 between methods ($p = 0.08$). The 95% confidence intervals and Bland and Altman limits of agreement lay within ±2 $ml.kg^{-1}.min^{-1}$ (-0.03 $ml.kg^{-1}.min^{-1}$ to 0.45 $ml.kg^{-1}.min^{-1}$ and -0.57 $ml.kg^{-1}.min^{-1}$ to 0.99 $ml.kg^{-1}.min^{-1}$, respectively) indicating an acceptable level of agreement between the two methods (Atkinson et al., 2005).

4.2.3 Protocol

Participants attended the laboratory in the morning, at least 12 hr post-prandial, and having refrained from caffeine, alcohol and vigorous exercise for 12 hr prior to the test. They were also asked to refrain from nicotine and moderate exercise for 2 hr prior to the test. A note was made of any recently taken medications (Compher et al., 2006). Height was measured using standard guidelines to the nearest 0.5 cm with a calibrated stadiometer (SECA). Weight (to the nearest 0.1 kg), BMI and body fat percentage were measured in bare feet and light clothing using the Multi-Frequency Body Composition Analyser MC-180MA (Tanita Corp, Tokyo).

Participants rested in a supine position for a minimum of 7 min while the activity monitors were initiated to record EE data every minute according to the manufacturer's specifications. The three activity monitors were attached to the participants as per manufacturer's instructions. Resting EE was measured for a minimum of 15 min using a ventilated hood in a thermoneutral environment (20-25 °C) and in the absence of external stimuli (Compher et al., 2006).

Following the measurement of resting EE participants were given a 5 min familiarisation period with the treadmill (Viasys LE 300 CE). They were then fitted with a soft flexible facemask that held the flowmeter. Each time the facemask was applied it was checked to ensure there was an effective seal around the mouth. Each participant performed four activities of 5 min duration in a randomised order: 1. walking at 3 $km.h^{-1}$; 2. walking at 6 $km.h^{-1}$; 3. walking at 6 $km.h^{-1}$ on a 10% incline; 4. running at 9 $km.h^{-1}$. Each activity was separated by a 5 min rest period in a seated position during which they were allowed to breathe without the facemask and drink water only. Participants were instructed not to hold onto the safety rail during treadmill locomotion.

4.2.4 Data analysis

Data from the three monitors and the indirect calorimeter were downloaded following completion of the experimental protocol. Innerview Research Software version 6.1 was used to estimate EE from the SWA. Weir's equation was used to calculate EE from oxygen uptake (Weir, 1949). Data from the monitors were time synchronised with that from the indirect calorimeter. The final 2 min of EE data ($kcal.min^{-1}$) from supine lying and each treadmill activity was used to validate the activity monitors. Data were examined visually to check for malfunctioning units, time synchronisation and abnormal outputs before statistical analysis.

Data are reported as mean ± standard deviation. The assumptions of normal distribution and equal variance were assessed using histogram plots and the Shapiro-Wilk test. Limit of agreement (LOA) plots were calculated to assess agreement between EE from each monitor ($EE_{MONITOR}$) and EE from the indirect calorimeter (EE_{IC}) (Bland and Altman, 1986). Bias was defined as the difference between $EE_{MONITOR}$ and EE_{IC}. Pearson's product moment correlations or Spearman's rank correlations were performed between $EE_{MONITOR}$ AND EE_{IC} for each activity. Statistical significance was considered at a two-sided $p < 0.05$. All analyses were conducted using Analyse-It for Microsoft Excel, version 2.26.

4.3 Results

Steady state resting EE data was not obtained on two adults and four children. Furthermore resting EE tests were not performed on three children as they refused to fast prior to the test or were unable to tolerate the ventilated hood. RT3 malfunction

resulted in data from 5 adults being discarded. The IDEEA failed to record data on 3 participants. Five children were unable to complete 5 min running at 9 $km.h^{-1}$. Listwise deletion procedures were therefore employed to maximise sample sizes resulting in sample sizes ranging from n = 13 to n = 26.

Descriptive statistics for adults and children are provided in Table 4.1. Adults were relatively young and lean with only four males and one female classified as overweight. Two children were considered overweight and two were considered obese according to the 2007 WHO BMI z-score for children (Butte et al., 2007).

Table 4.1 Descriptive statistics for physical characteristics of adults and children

	Adults (n = 26; 11 men)	Children (n = 22; 11 boys)
Age (yr)	24.7 ± 4.4	11.5 ± 3.0
Weight (kg)	69.5 ± 12.0	44.9 ± 13.9
Height (cm)	174.3 ± 8.5	153.9 ± 16.4
BMI ($kg.m^{-2}$)	22.8 ± 2.9	18.4 ± 3.0
Body Fat (%)	22.0 ± 6.3	22.0 ± 6.3
REE ($kcal.d^{-1}$)	1397.2 ± 283.6	1308.6 ± 194.6

REE, resting energy expenditure.

Mean EE recorded by indirect calorimetry and the monitors are reported in Tables 4.2 and 4.3. All monitors overestimated the energy cost of inactivity in adults. Although the RT3 overestimated resting EE in children by 0.14 $kcal.min^{-1}$ (15%) it displayed the narrowest LOA of the three monitors. In children, the IDEEA displayed a large overestimation of REE (70%), wide LOA (-116% to 256% of mean EE), and a poor correlation with the indirect calorimeter (-0.52).

The IDEEA showed the smallest mean bias at 3 $km.h^{-1}$ (+0.8%), 6 $km.h^{-1}$ (-0.3%) and 9 $km.h^{-1}$ (+3%) in adults. The large standard deviation of the bias at 6 km. h^{-1} and 9 $km.h^{-1}$, (±1.29 $kcal.min^{-1}$ and ±2.24 $kcal.min^{-1}$, respectively), however, resulted in wide LOA. The SWA, in fact, showed closest agreement with indirect calorimetry at 6 $km.h^{-1}$, 6 $km.h^{-1}$ on an incline and 9 $km.h^{-1}$. The RT3 overestimated the energy cost of all activities except walking on an incline. This overestimation of EE appeared to decrease with increasing speed, from +84% at 3 $km.h^{-1}$ to +38% at 9 kmh^{-1}.

Table 4.2 Mean energy cost of rest and treadmill activities in adults as measured by the indirect calorimeter, SWA, RT3 and IDEEA

Activity	Indirect Calorimeter ($kcal.min^{-1}$) (n = 24 to 26)	SWA ($kcal.min^{-1}$) (n = 26)	RT3 ($kcal.min^{-1}$) (n = 21)	IDEEA ($kcal.min^{-1}$) (n = 25)
Rest	0.97 ± 0.22	1.11 ± 0.18	1.26 ± 0.19	1.28 ± 0.18
3 $km.h^{-1}$	3.91 ± 0.62	4.48 ± 0.94	4.36 ± 1.03	3.94 ± 0.67
6 km/h^{-1}	6.28 ± 0.93	6.19 ± 1.18	8.99 ± 2.20	6.26 ± 1.51
6 $km.h^{-1}$@10% incline	11.47 ± 2.12	6.86 ± 1.41	8.87 ± 2.27	6.07 ± 1.50
9 $km.h^{-1}$	11.41 ± 2.31	10.54 ± 2.07	15.94 ± 3.41	11.71 ± 2.63

Table 4.3 Mean energy cost of rest and treadmill activities in children as measured by the indirect calorimeter, SWA, RT3 and IDEEA

Activity	Indirect Calorimeter ($kcal.min^{-1}$) (n = 15 to 22)	SWA ($kcal.min^{-1}$) (n = 17 to 22)	RT3 ($kcal.min^{-1}$) (n = 17 to 22)	IDEEA ($kcal.min^{-1}$) (n = 15 to 20)
Rest	0.91 ± 0.14	0.79 ± 0.23	1.01 ± 0.17	1.60 ± 0.71
3 $km.h^{-1}$	3.22 ± 0.67	3.21 ± 1.59	3.30 ± 0.93	3.22 ± 0.45
6 km/h^{-1}	5.37 ± 1.28	4.73 ± 1.69	6.49 ± 2.11	5.14 ± 1.41
6 $km.h^{-1}$@10% incline	7.91 ± 2.56	5.00 ± 1.72	6.44 ± 1.95	4.73 ± 1.06
9 $km.h^{-1}$	9.36 ± 2.48	8.46 ± 2.83	11.55 ± 4.10	8.98 ± 1.15

Similar results emerged for children. Although the IDEEA showed the smallest mean bias at 3 $km.h^{-1}$ (+0.3%), 6 $km.h^{-1}$ (-5%) and 9 $km.h^{-1}$ (-5%), a large standard deviation of the mean bias resulted in wide LOA. Limits were narrowest for the SWA at 6 $km.h^{-1}$ and 9 $km.h^{-1}$. The RT3 also overestimated the energy cost of walking at 3 $km.h^{-1}$ (2%), 6 $km.h^{-1}$ (21%) and running at 9 $km.h^{-1}$ (23%) in children. In contrast to adults the magnitude of the overestimation of EE increased as speed increased.

All monitors were unable to detect the energy cost of traversing a slope. The RT3, however, displayed the smallest bias for this activity. This may be due to its large overestimation of the energy cost of walking on level ground. Apart from the IDEEA at rest and at 6 $km.h^{-1}$ on an incline, correlation coefficients between the three monitors and IC were moderate to good ($r = 0.63$ to $r = 0.91$; $p < 0.01$). The lower limit of the 95% confidence interval was as low as 0.27, for the RT3 at 3 $km.h^{-1}$, however, indicating a poor association between the monitor and indirect calorimeter. See Table 4.4 for more information.

Table 4.4 Limits of agreement and correlations between indirect calorimetry, the SWA, the RT3, and the IDEEA for the assessment of rest and treadmill activities (bias and LOA reported in $kcal.min^{-1}$)

		Adults			Children		
		Bias	LOA	CC [95% CI]	Bias	LOA	CC [95% CI]
Rest	SWA	0.14	-0.07 to 0.35	0.86* [0.71 to 0.94]	-0.07	-0.34 to 0.21	0.71* [0.32 to 0.90]
	RT3	0.28	0.08 to 0.48	0.87* [0.68 to 0.95]	0.14	-0.07 to 0.34	0.78* [0.45 to 0.92]
	IDEEA	0.31	0.11 to 0.51	0.91* [0.79 to 0.96]	0.64	-1.06 to 2.33	-0.52 [-0.83 to 0.04]
3$km.h^{-1}$	SWA	0.56	-0.68 to 1.81	0.72* [0.46 to 0.86]	-0.01	-2.32 to 2.29	0.75* [0.47 to 0.89]
	RT3	3.30	1.39 to 5.22	0.63* [0.27 to 0.84]	0.07	-0.91 to 1.06	0.85* [0.68 to 0.94]
	IDEEA	0.03	-0.82 to 0.88	0.74* [0.48 to 0.88]	0.01	-0.88 to 0.89	0.78* [0.52 to 0.91]
6$km.h^{-1}$	SWA	-0.10	-1.62 to 1.43	0.78* [0.57 to 0.91]	-0.64	-2.41 to 1.13	0.82* [0.62 to 0.92]
	RT3	2.66	-1.06 to 6.39	0.69* [0.37 to 0.87]	1.12	-1.56 to 3.81	0.67* {0.34 to 0.84]
	IDEEA	-0.02	-2.56 to 2.51	0.64* [0.33 to 0.83]	-0.28	-2.15 to 1.59	0.75* [0.46 to 0.90]
6$km.h^{-1}$ @ 10%	SWA	-4.60	-7.36 to -1.84	0.79* [0.58 to 0.90]	-2.91	-6.18 to 0.37	0.71* [0.42 to 0.87]

	RT3	-2.74	-6.57 to 1.09	0.66* [0.33 to 0.85]	-1.48	-5.13 to 2.18	0.67* [0.35 to 0.85]
	IDEEA	-5.29	-8.65 to -1.94	0.74* [0.49 to 0.88]	-3.16	-7.29 to 0.98	0.56 [0.16 to 0.80]
9km.h^{-1}	SWA	-0.87	-3.27 to 1.54	0.87* [0.73 to 0.94]	-0.91	-3.62 to 1.80	0.80* [0.53 to 0.93]
	RT3	4.35	-1.02 to 9.72	0.68* [0.36 to 0.86]	2.18	-2.33 to 6.70	0.83* [0.59 to 0.94]
	IDEEA	0.33	-4.06 to 4.71	0.67* [0.37 to 0.84]	-0.48	-4.64 to 3.69	0.69* [0.27 to 0.89]

*p<0.01. Sample sizes range from n = 13 to n = 26 for all activities.

LOA, limits of agreement; CC, correlation coefficient; CI, confidence intervals.

4.4 Discussion

This study provides a comparative evaluation of three monitors that provide direct outputs of EE in small epochs. Results indicate that the SWA provides the best estimate of EE in both adults and children. The SWA demonstrated the closest agreement with a criterion measure of EE for four out of five activities in adults and three out of five activities in children.

The field of accelerometer research focuses, to a large extent, on the use of counts to record physical activity data. Variation in methods of data collection, processing, filtering and scaling, however, means that counts cannot be compared across different models of accelerometers (Chen and Bassett, 2005). Counts are also a meaningless value unless converted into a more interpretable unit. Recent research indicates that EE, as opposed to time spent in activity, predicts health related outcomes (Garber et al., 2011). Reporting exercise volume in terms of EE may therefore provide data regarding the dose-response relationship between activity and health as well as providing a common unit against which both traditional accelerometers and newer accelerometry-based devices can be compared.

As reported in previous studies (Arvidsson et al., 2011a, Arvidsson et al., 2007), the SWA underestimated the energy cost of treadmill activities in children. Although the

magnitude of the underestimation was not the same across speeds, results from a previous study (Arvidsson et al., 2011a) and the current study agreed that the magnitude of the bias was independent of speed. Critically, the non-systematic effect of speed on the bias between methods indicates that the bias cannot be easily corrected for by applying a correction factor. Activities were performed in a random order to reduce any sources of unknown bias on results. It is not known, however, if this randomisation impacted the association between speed and bias.

Comparisons of the IDEEA and the SWA in children have revealed the IDEEA to provide a better estimation of EE, in terms of mean bias, during track and treadmill locomotion (Arvidsson et al., 2011a, Arvidsson et al., 2009b). These studies did not report LOA, however. If conclusions from the current study were based on the mean bias alone, the IDEEA would be considered most accurate at 3 $km.h^{-1}$, 6 $km.h^{-1}$ and 9 $km.h^{-1}$. The LOA clearly show, however, that there was closer agreement between the SWA and indirect calorimetry at 6 $km.h^{-1}$ and 9 $km.h^{-1}$, demonstrating that bias alone does not accurately portray the level of agreement between measures. Sun et al. (2008) reported that the RT3 overestimated the energy cost of children walking at 3 $km.h^{-1}$ and 6 $km.h^{-1}$ by 54% and 96%, respectively. Although the RT3 also overestimated EE at these speeds in the current study, a smaller mean bias was found: +2% and +21%, respectively. Kavouras et al. (2008) and Hussey et al. (2009), however, reported that the RT3 underestimated EE at 6 $km.h^{-1}$. As LOA were not reported by any of these studies it is difficult to comment on their findings in relation to the results of this study.

Variations in statistical analysis aside, contradictory results between studies may be due to differences in the age range of participants. Although the SWA appeared the most accurate measure in both adults and children, LOA calculated in this study were wider for children than adults for all activities. The accuracy of proprietary equations depends on the sample population in which they are developed. Not only may equations developed on adults not be applicable to children, changes in children's walking patterns with age (Bjornson et al., 2011) may reduce the accuracy of the monitors across childhood and adolescence. The RT3, IDEEA and SWA have been validated in children aged 7-14 yr, 8-17 yr, and 8-15 yr, respectively (Hussey et al., 2009, Sun et al., 2008, Zhang et al., 2004, Kavouras et al., 2008, Arvidsson et al., 2011a, Arvidsson et al., 2009b, Arvidsson et al., 2007, Arvidsson et al., 2009a, Calabro et al., 2009, Dorminy et

al., 2008). This study provides a unique evaluation of these monitors in children aged 6 to 17 years.

To date validation of the SWA (v6.1) during locomotion has only been conducted on endurance athletes (Drenowatz and Eisenmann, 2011, Koehler et al., 2011). Although the participants in the current study may be more representative of the general population, the results of the current study indicate that, as reported for endurance athletes, the SWA underestimates the energy cost of running. It has been suggested that the SWA's estimation of EE plateaus at an intensity equivalent of 10 MET (Drenowatz and Eisenmann, 2011). When adults in the current study were running at 9km.h^{-1} they were exercising at a mean intensity of 11.68 MET. Despite this, of all the activities, the SWA agreed best with IC at 9km.h^{-1} (LOA: -29% to 13%), suggesting that exercising above 10 MET did not decrease the accuracy of the SWA in this study. Although a newer version of the SWA software (v7.0) has been released since this study was conducted the manufacturers indicate that the algorithms included in v7.0 do not differ from those in v6.1 (written communication).

The three monitors assessed in this study provide an estimation of total EE which includes a resting EE component. As resting EE can account for up to 60% of total EE (Levine, 2005), if a monitor is unable to accurately predict resting EE it is likely that its measure of total EE will also be inaccurate. This is the first study to report on the ability of the RT3 to measure resting EE in adults and children. Only one study has evaluated the IDEEA as a measure of resting EE and although only a small overestimation of EE by the IDEEA was reported (10%) LOA were not calculated (Arvidsson et al., 2009b). The RT3 was the most accurate at measuring resting EE in adults and children in the current study. Despite this, EE was overestimated by 29% and 15% with LOA of 8% to 49% and -8% to 37% in adults and children, respectively. The large overestimation of resting EE, wide LOA (-116% to 256% of mean EE), and poor correlation (-0.52) observed for IDEEA data on children may have been caused by three extreme recordings for resting EE (0 kcal.min^{-1}, 2.33 kcal.min^{-1} and 3.59 kcal.min^{-1}). As there was no explanation for these values and data recorded from the same children for the remaining activities was not extreme, the removal of these children from data analysis was not justified. The decision not to remove this data from analyses was supported by Arvidsson et al. (2009a) who also reported that the IDEEA gave extreme values for resting EE in children. Despite the small bias between the IDEEA and indirect calorimetry for many activities, the IDEEA

needs to be consistently accurate for it to be considered an acceptable method of measuring EE. Monitor malfunction and non-compliance, although anecdotally common, are often underreported in studies. It is vital that information on the feasibility of monitors is included in reports as it is an important consideration in monitor selection (Trost et al., 2005).

Of the three monitors the IDEEA took the longest time to initiate because of the calibration required. Some participants, particularly children, experienced discomfort from the foot sensors of the IDEEA. The IDEEA is also the most difficult of the monitors to attach. The difficulty involved in reattaching the monitor following washing may reduce compliance with it. There was no data missing for the analysis of the SWA. The armband occasionally became loose, however, and had to be refitted. Participants generally remarked that the SWA and the RT3 were comfortable and discrete.

4.4.1 Limitations

This study is limited by the lack of free-living activities in the protocol. Locomotor activity, however, is the predominant activity in a person's day. Therefore the validation of accelerometers during this activity is of primary importance (Welk, 2005). The accuracy of a monitor should also be assessed across a range of physical activity intensities, including inactivity (Matthew, 2005), all of which were captured in this study. Future studies should comparatively evaluate these monitors during free-living activities.

A further limitation of this study was the comparison of EE during steady-state exercise. Adults and children require 3-6 min to reach a steady-state work rate (Turley and Wilmore, 1997). Habitual physical activity is usually accrued in a sporadic manner, however, particularly by children (Mark and Janssen, 2009). Reliance on steady-state data means that the ability of activity monitors to accurately record the energy cost of non-steady-state exercise during short bursts of activity was not tested. Also, as heart-rate was not monitored during the 5 min rest periods it is not known if participants fully recovered between activities. Research suggests that adults and children recover from submaximal exercise in 3-5 min, however (Turley and Wilmore, 1997).

4.5 Conclusion

In conclusion, many factors are involved in selecting an activity monitor including the research hypothesis, feasibility, validity and the burden on participants and researchers (Welk, 2005). This comparative evaluation reveals that the SWA appears to provide the most accurate estimation of EE in adults and children. It also appears to be a feasible method of measuring habitual physical activity with little or no monitor malfunction or participant discomfort reported.

These results should not be extrapolated to people with cerebral palsy however. Not only may accelerometry-based devices be unable to detect the abnormal movement patterns associated with cerebral palsy the inbuilt proprietary algorithms may not be appropriate to estimate the energy cost of locomotion for people with cerebral palsy. The next chapter will examine the criterion and concurrent validity of the SWA, the RT3 and the IDEEA at estimating energy expenditure in adults and children with cerebral palsy.

Chapter 5 Study 2: Estimation of energy expenditure by accelerometry-based devices in adults and children with cerebral palsy

5.1 Introduction

Children with cerebral palsy (CP) have an increased energy cost of locomotion compared to typically developing (TD) children (Brehm et al., 2007, Dallmeijer and Brehm, 2011). This increased energy cost of walking is associated with difficulties in performing everyday tasks (Kerr et al., 2008) and low levels of habitual physical activity (Maltais et al., 2005a). Physical activity is not only important for the prevention of chronic disease (Strong et al., 2005, Garber et al., 2011), it may stem the premature decline in function and loss of mobility experienced by many adults with CP (Damiano, 2006, Fowler et al., 2007, Opheim et al., 2009, Bottos et al., 2001). Interventions such as surgery improve the energy efficiency of gait and gross motor function (Kerr et al., 2011). Further investigation is required however, into the effectiveness of interventions at increasing everyday physical activity. To accurately assess habitual physical activity valid and feasible tools are necessary to estimate energy expenditure (EE) in people with CP. Few validated methods currently exist (Clanchy et al., 2011b).

Previous methods used to measure physical activity in people with CP include subjective questionnaires (Maher et al., 2007, Zwier et al., 2010, Martin et al., 2012), doubly-labelled water (DLW) (Bell and Davies, 2010, van den Berg-Emons et al., 1995), heart-rate (HR) monitoring (Maltais et al., 2005a, Van den Berg-Emons et al., 1998a), and pedometers (Bjornson et al., 2007, Stevens et al., 2010). Each of these has inherent limitations. Subjective measures are subject to recall bias (Bringolf-Isler et al., 2012) resulting in significant overestimation of daily moderate-to-vigorous activity (Atienza et al., 2011). They also may not capture the short, sporadic bursts of activity that children typically perform (Bailey et al., 1995). Although an objective measure of EE, DLW is an expensive technique and is often unfeasible to use in studies with large numbers of participants. In addition it does not provide information about patterns of physical activity. HR is influenced by factors other than participation in physical activity, such as

medication, environmental factors and emotional state, thereby reducing the accuracy of EE estimation from HR monitoring. There is also considerable inter-individual variation in the relationship between HR and EE. While individual calibration of HR against oxygen consumption [e.g. HR-flex method] can improve the accuracy of HR monitoring at measuring EE (Van Den Berg-Emons et al., 1996c) it reduces its feasibility in large, community-based studies. Pedometers are useful as motivational tools to monitor or promote activity but they provide little information about the intensity or energy cost of activity.

Accelerometry-based devices have been used to measure habitual physical activity in large population-based studies (Atienza et al., 2011, Luke et al., 2011). Although they have been validated for use in different segments of the population little has been done to test their use in adults and children with CP. Traditional accelerometers are worn on the hip and measure the magnitude of the body's acceleration. Raw data are provided in terms of accelerometer 'counts'. Calibration is required to convert counts into a meaningful estimate of EE or to identify count cut-off points that allow categorisation of activity into light, moderate and vigorous intensity. Advances in technology and modelling techniques have led to the development of new pattern recognition devices that provide alternative ways of measuring and evaluating physical activity. These advanced accelerometry-based devices use different inputs to assess physical activity. They may therefore improve the assessment of physical activity, particularly in people with CP, whose biomechanical efficiency is different to that of able-bodied people.

The Sensewear Pro Armband (SWA) (Bodymedia, Inc.) and the Intelligent Device for Energy Expenditure and Activity (IDEEA) (Minisun, LLC) are two such devices. The SWA is a multisensor device, worn on the upper arm that combines accelerometry data with information from several heat-related channels. Recent studies have demonstrated that it provides more accurate estimates of EE than traditional accelerometers in adults and children (Ryan and Gormley, 2013, Welk, 2007). The inclusion of heat-related variables may also improve the estimation of the energy cost of locomotion associated with CP. The IDEEA collects data from five accelerometer sensors, which are attached to the chest, anterior aspects of both thighs and soles of the feet. The ability of the IDEEA to detect 35 postures and define temporal-spatial gait parameters sets it apart from other accelerometers.

Two recent studies have evaluated the validity of the IDEEA and a traditional accelerometer at assessing physical activity in children with CP (Aviram et al., 2011, Clanchy et al., 2011a). With so many accelerometry-based devices on the market, however, it is no longer sufficient to simply validate a monitor. It is important to demonstrate that newly released models improve upon established devices.

5.2 Objective

The present study aims to evaluate the validity of advanced accelerometry-based devices at estimating EE in adults and children with CP, compared to a traditional accelerometer. It is hypothesised that the advanced, multisensor devices will more accurately assess EE compared to a traditional accelerometer.

5.3 Methodology

5.3.1 Sampling and participants

Ambulant children (≥6 years) and adults (≥18 years) with a medically confirmed diagnosis of CP were recruited for this study through the Central Remedial Clinic (CRC); a national centre that provides services for adults and children with disabilities. Individuals with a severe cognitive impairment, uncontrolled epilepsy or seizure activity, or an acute lower limb injury were excluded from participating. Physiotherapists provided seventy-nine eligible participants with information about the study over a period of nine months. Thirty-six people agreed to participate in the study.

Participants were classified as level I, II or III on the Gross Motor Function Classification System (GMFCS) by their physiotherapist. All participants completed the Physical Activity Readiness Questionnaire to screen for conditions contraindicating participation in exercise (Shephard, 1988). The procedures and risks involved in the study were fully explained to participants and their guardians, if the participant was under 18 years of age or had an intellectual disability. Written informed consent was provided before testing proceeded. Ethical approval for this study was granted by the Faculty of Health Sciences and the CRC's ethics committee.

5.3.2 Instrumentation

The RT3, SWA and IDEEA have been described in sections 3.3.1.1, 3.3.1.2, and 3.3.1.3, respectively. Oxygen uptake, measured by the Oxycon Mobile portable indirect calorimeter (Carefusion Germany 234 GmBh, Hoechberg, Germany) (Figure 5.1), was converted into EE using Weir's equation (Weir et al., 2010). The Oxycon has been shown to be an accurate measure of oxygen uptake (Rosdahl et al., 2010) and has been used previously as a criterion measure of EE in children and adults (Drenowatz and Eisenmann, 2011). It consists of a soft, flexible facemask and an analyser unit (950g) that is attached to a chest harness worn by the participant (Figure 5.1). Expired air is channeled through a bidirectional digital volume sensor. Gas concentrations are collected with a Nafion sampling tube. Participants also wore a Polar heart-rate monitor throughout the test. Gas, flow and heart-rate data were sent telemetrically to the calibration and receiver unit which is connected to a personal computer before being processed in the PC-software (JLAB, Carefusion Germany 234 GmbH, Hoechberg, Germany). Volume calibration, ambient gas calibration and reference gas calibration (reference gas tank: 16% O_2, 5% CO_2) were performed immediately prior to each test using the built-in automated procedures.

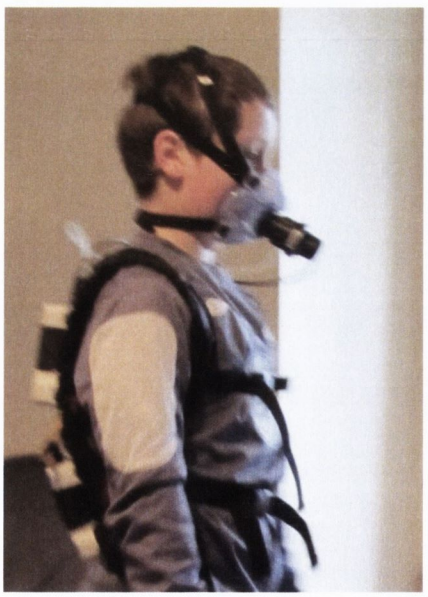


Figure 5.1 Oxycon Mobile portable indirect calorimeter

5.3.3 Protocol

Participants attended a physiotherapy gym on one occasion where their height, to the nearest 0.5 cm, and weight, to the nearest 0.1 kg, (SECA, digital scales) were measured. The activity monitors and the Oxycon were configured for each participant using their anthropometric and demographic details, and attached to each participant. In the case of significant asymmetry the RT3 and SWA were attached to the least affected side. Participants rested for 10 min before completing a series of activities. Activities were selected following pilot testing to represent locomotor activity that covered a variety of intensities while still being safe for participants to complete. Activities included walking on a 70 m corridor at maximal effort for 6 min, and walking on a calibrated treadmill at treadmill speeds of 1.0 $km.h^{-1}$, 2.0 $km.h^{-1}$, and 4.0 $km.h^{-1}$ at a 0% incline, and 1.0 $km.h^{-1}$ at a 5% incline. Children did not complete treadmill walking at 4.0 $km.h^{-1}$. All participants were given a 5 min familiarisation period with the treadmill before completing the treadmill activities. Participants rested in a seated position between each activity until their heart-rate and oxygen consumption returned to baseline values.

5.3.4 Data processing

EE from the Oxycon was observed in 30-s epochs. Data from the SWA and RT3 were recorded in 1-min epochs. Data from the IDEEA were observed in 1-s epochs. The Oxycon and each activity monitor was synchronised with a single laptop clock and exact start and stop times of each activity were recorded from this clock. Following completion of the protocol data were downloaded from the three monitors. Data were examined visually to check for malfunctioning units, time synchronisation and abnormal outputs. One's child over-ground walking data and one adult's treadmill walking data at 1.0 $km.h^{-1}$ at 5% incline were removed because of a problem with the Oxycon during these activities. RT3 data were not obtained from one adult and IDEEA data were not obtained from two adults because of equipment malfunction. One child's SWA data for treadmill walking at 2 $km.h^{-1}$ and one adult's SWA data for treadmill walking at 1 $km.h^{-1}$ and 1 $km.h^{-1}$ at 5% incline were removed because of abnormal data obtained during these activities. Final sample sizes ranged from n=8 to n=18 for adults and n=10 to n=18 for children. The final 2 min of EE data ($kcal.min^{-1}$) from each activity were extracted and averaged over the 2 min period. Mean EE, in $kcal.min^{-1}$, from each activity was used in data analysis.

5.3.5 Statistical Analysis

Descriptive variables are presented as mean ± standard deviation. A one-way repeated measures ANOVA was used to detect differences in EE between methods (statistical significance was set at $p < 0.05$). *Post-hoc* analyses using paired t-tests with the Bonferroni correction were conducted to examine specific differences in EE between each monitor and the Oxycon. The mean absolute percentage error was calculated for individual activities based on the absolute value of the individual errors. This method reflects the true error in estimation and provides the most appropriate indicator of overall error.

Further analyses were conducted to examine the level of agreement between measures. Pearson product moment correlation coefficients were calculated to evaluate the association between EE from each monitor and the Oxycon. EE for each participant was averaged across each activity to provide three correlation coefficients for the RT3, SWA and IDEEA, respectively, for adults and children. Bland-Altman plots (Bland and Altman, 1986) were also calculated to examine the level of agreement between each monitor and the Oxycon across the range of activities. Limits of agreement were calculated as 1.96 SD from the overall mean bias between the Oxycon and each monitor. Statistical analysis was performed using Analyse-It for Microsoft Excel, version 2.26.

5.4 Results

Descriptive characteristics for adults and children across GMFCS level are presented in Table 5.1. Participants were predominantly male (10 men and 10 boys). Fifteen adults (83%) and 13 children (72%) used no ambulatory aid. One adult walked with a 3-wheeled rollator, one adult walked with a stick, one adult and two children walked with 2 elbow crutches and three children walked with the aid of a K-walker. Seven children (39%) and ten adults (56%) had bilateral spastic CP; the remaining participants had unilateral spastic CP. Approximately 39% (n = 7) of adults were overweight or obese (BMI >25kg.m^{-2}) and approximately 33% of children (n = 6) were classified as overweight or obese according to the IOTF criteria Due to the variation in gross motor function between participants not all participants completed all treadmill activities: 14 adults completed treadmill walking at 1.0 km.h^{-1}, 1.0 km.h^{-1} at 5% incline, and 2.0 km.h^{-1},

respectively; 9 adults completed treadmill walking at 4.0 $km.h^{-1}$; 15, 13 and 11 children, respectively, completed treadmill walking at 1.0 $km.h^{-1}$, 1.0 $km.h^{-1}$ at a 5% incline, and 2.0 $km.h^{-1}$.

Repeated measures ANOVA revealed a significant monitor effect on EE for all activities except for over-ground walking in children. Post-hoc analyses for adults revealed that the SWA significantly underestimated resting EE and overestimated EE during treadmill walking at 1.0 $km.h^{-1}$ at 0% and 5% incline; the RT3 underestimated EE during treadmill walking at 1.0 $km.h^{-1}$ at 0% and at 5% incline; the IDEEA underestimated EE during over-ground walking (all $p < 0.01$) (Table 5.2). In children, the SWA underestimated resting EE and the RT3 underestimated EE for all treadmill activities (all $p < 0.01$).

Table 5.1 Characteristics of adults and children across levels of Gross Motor Function Classification System (GMFCS)

	Adults				Children			
	All	GMFCS I	GMFCS II	GMFCS III	All	GMFCS I	GMFCS II	GMFCS III
n	18	9	7	2	18	10	4	4
Age (yr)	31.9 ± 9.5	28.1 ± 7.8	34.9 ± 10.7	39.0 ± 8.5	11.4 ± 3.2	11.5 ± 3.8	10.0 ± 2.2	12.5 ± 1.9
Weight (kg)	68.2 ± 13.5	69.0 ± 13.3	67.8 ± 16.2	65.8 ± 10.2	44.6 ± 16.9	46.5 ± 20.9	37.0 ± 12.0	47.3 ± 8.2
Height (cm)	163.9 ± 10.3	166.6 ± 9.3	162.0 ± 12.2	158.5 ± 9.2	147.0 ± 18.5	149.5 ± 21.1	140.0 ± 20.1	147.6 ± 10.3
BMI ($kg.m^{-2}$)	25.3 ± 4.8	24.6 ± 3.8	25.9 ± 5.9	26.6 ± 7.1	20.0 ± 4.5	20.0 ± 5.2	18.5 ± 1.8	21.9 ± 4.7

Table 5.2 Mean energy expenditure (kcal.min-1) for each activity and differences (kcal.min-1) between methods. All reported as mean ± SD

	IC	SWA	IC-SWA	RT3	IC-RT3	IDEEA	IC-IDEEA
Adults							
n	9 to 18	8 to 18	8 to 18	9 to 17	9 to 17	9 to 16	9 to 16
Rest	1.27 ± 0.28	1.09 ± 0.15	0.19 ± 0.27*	1.21 ± 0.16	0.04 ± 0.24	1.07 ± 0.45	0.22 ± 0.42
Walk (overground)	6.69 ± 2.04	6.88 ± 1.60	-0.85 ± 2.32	7.52 ± 2.25	-0.85 ± 2.32	5.04 ± 1.14	1.78 ± 2.22*
Walk (1.0 $km.h^{-1}$, 0%)	3.14 ± 0.84	5.32 ± 2.48	-2.13 ± 1.97*	2.14 ± 0.54	0.99 ± 0.48*	2.72 ± 1.17	0.40 ± 1.05
Walk (1.0 $km.h^{-1}$, 5%)	3.45 ± 0.85	6.09 ± 2.72	-2.64 ± 2.19*	2.08 ± 0.43	1.38 ± 0.67*	2.59 ± 1.09	0.91 ± 1.06
Walk (2.0 $km.h^{-1}$, 0%)	3.90 ± 0.93	5.28 ± 2.89	-1.38 ± 2.64	3.13 ± 0.96	0.77 ± 1.18	3.22 ± 0.80	0.78 ± 1.07
Walk (4.0 $km.h^{-1}$, 0%)	5.10 ± 1.21	6.07 ± 1.97	-0.89 ± 2.09	4.98 ± 0.93	0.12 ± 0.83	4.48 ± 1.48	0.62 ± 1.90
Children							
n	11 to 18	10 to 18	10 to 18	11 to 18	11 to 18	11 to 18	11 to 18
Rest	1.06 ± 0.33	0.79 ± 0.28	0.28 ± 0.30*	1.03 ± 0.19	0.04 ± 0.25	1.49 ± 0.81	-0.43 ± 0.76
Walk (overground)	4.56 ± 1.47	4.39 ± 1.89	0.17 ± 1.54	4.33 ± 1.64	0.23 ± 0.92	3.92 ± 1.46	0.64 ± 1.74

Walk (1.0 km.h^{-1}, 0%)	2.52 ± 0.82	2.67 ± 1.00	-0.03 ± 0.71	1.79 ± 0.46	0.73 ± 0.47*	2.50 ± 0.58	0.02 ± 0.78
Walk (1.0 km.h^{-1}, 5%)	2.73 ± 1.08	3.50 ± 2.04	-0.63 ± 1.43	1.86 ± 0.52	0.87 ± 0.61*	2.32 ± 0.91	0.41 ± 1.25
Walk (2.0 km.h^{-1}, 0%)	3.11 ± 1.29	3.57 ± 1.56	-0.28 ± 1.31	2.20 ± 0.71	0.91 ± 0.70*	2.83 ± 0.69	0.28 ± 1.10

IC, Oxycon indirect calorimeter

In adults, the mean absolute percentage error for individual activities ranged from 8.2% to 74.9% for the SWA (mean 35.5%), from 0.4% to 37.9% for the RT3 (mean 17.2%), and from 8.4% to 24.5% for the IDEEA (mean 16.3%). The errors in EE for the SWA and the RT3 were largest for treadmill walking at 1.0 $km.h^{-1}$ at 0% incline and at 5% incline. Errors in EE estimates from the IDEEA did not vary considerably across activities (Figure 5.2). In children, the mean absolute percentage error for individual activities ranged from 0.9% to 23.0% for the SWA (mean 12.4%), from 2.5% to 26.9% for the RT3 (mean 17.0%), and from 1.0% to 46.5% for the IDEEA (mean 12.5%) (Figure 5.3). The error in EE estimation from the IDEEA was much larger for rest compared to treadmill activities. This may be attributed to an extreme value of 4.41 $kcal.min^{-1}$ recorded by the IDEEA for one child. When this was removed the mean absolute percentage error reduced from 46.5% to 36.2% for rest, and from 12.5% to 10.5% for all activities combined.

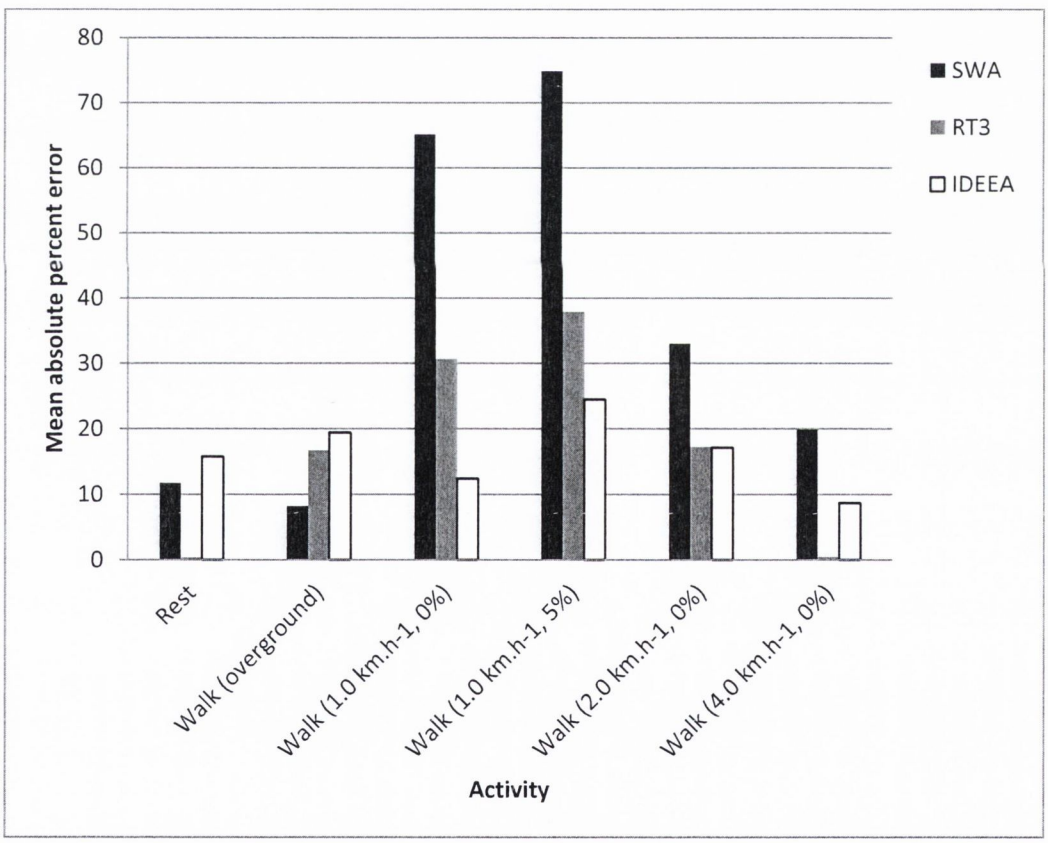


Figure 5.2 Mean absolute percentage error of the SWA, RT3 and IDEEA for adults

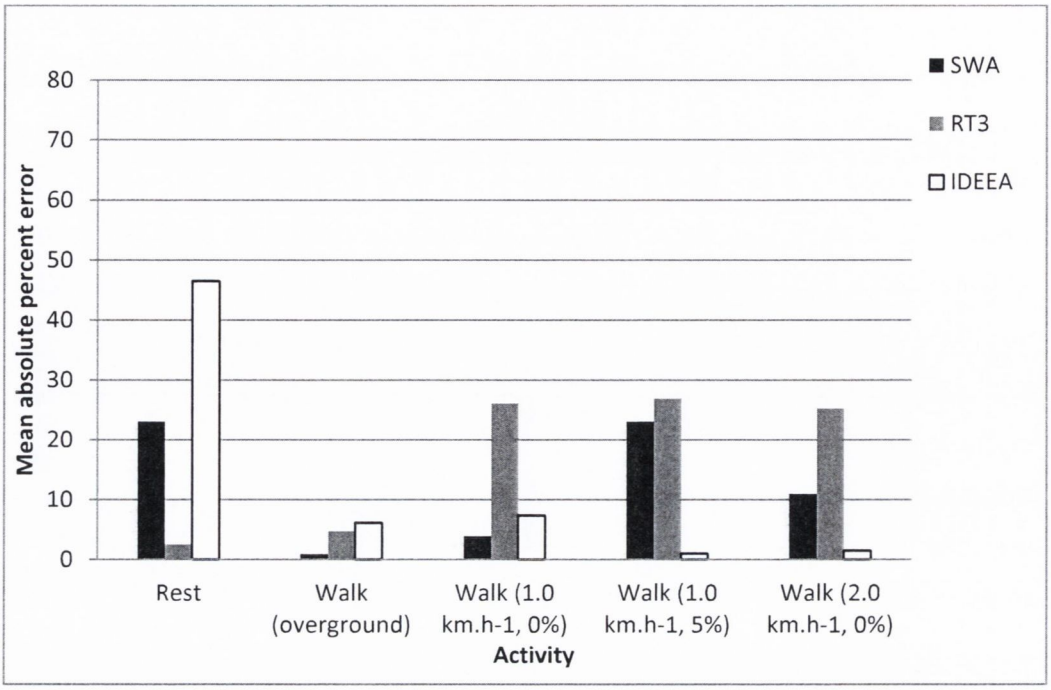
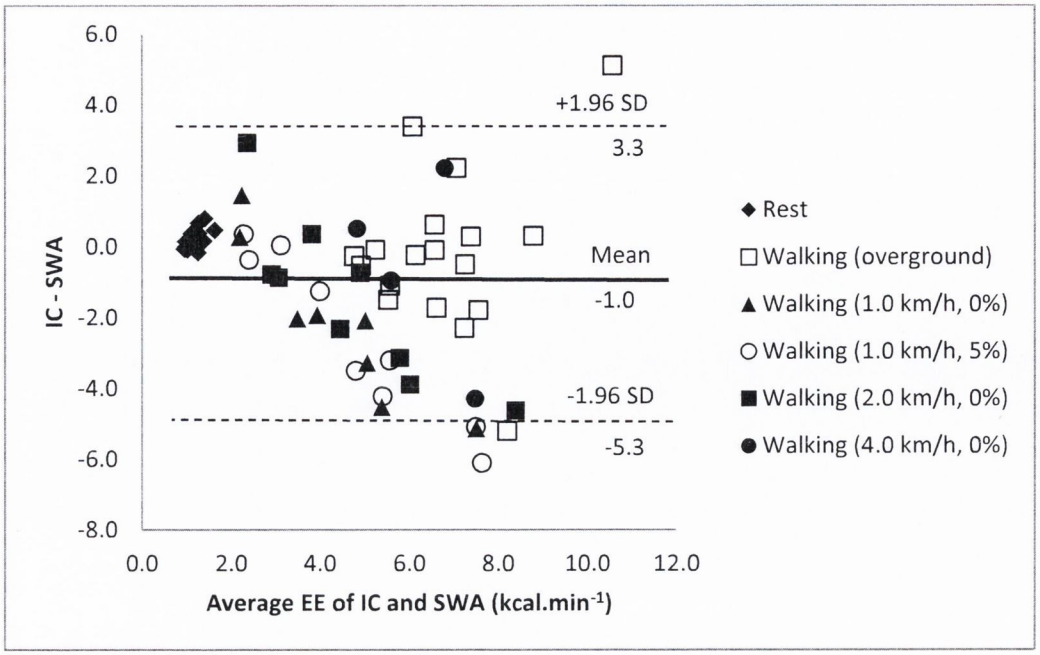
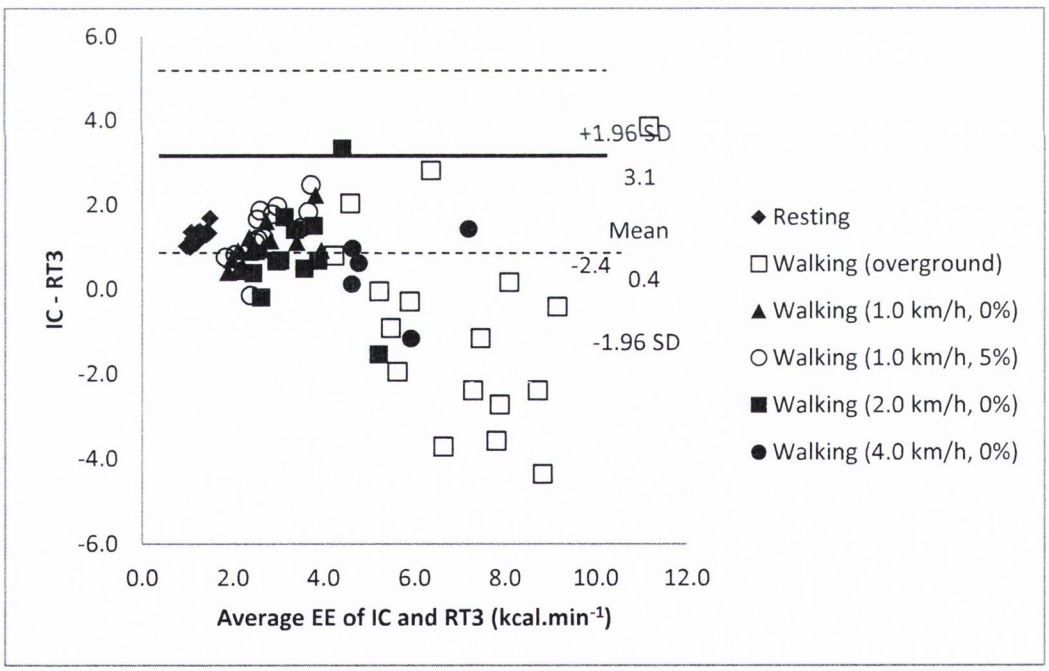


Figure 5.3 Mean absolute percentage error of the SWA, RT3 and IDEEA for children

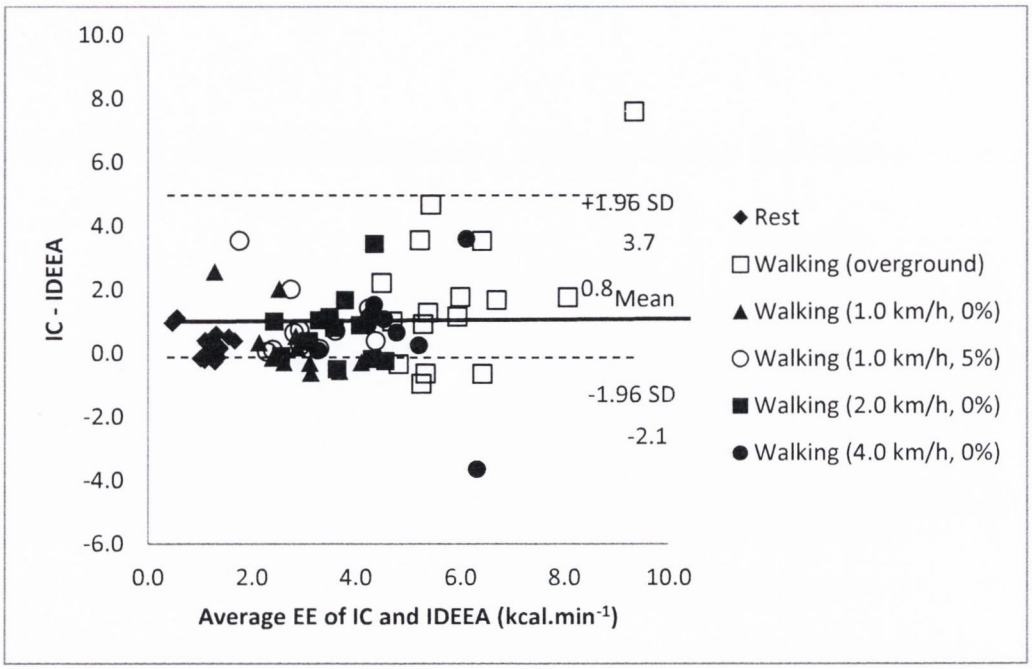
Correlation coefficients between each monitor and the IC for adults were 0.27 (95% CI: -0.23 to 0.65), 0.60 (95% CI: 0.16 to 0.84) and 0.22 (95% CI: -0.31 to 0.65) for the SWA, RT3 and IDEEA, respectively. For children correlation coefficients were 0.79 (95% CI: 0.52 to 0.92), 0.93 (95% CI: 0.82 to 0.97) and 0.28 (-0.22 to 0.66) for the SWA, RT3 and IDEEA, respectively. In adults, the overall mean bias and the limits of agreement were smallest for the RT3 (0.4 $kcal.min^{-1}$ and -2.4 $kcal.min^{-1}$ to 3.1 $kcal.min^{-1}$, respectively) (Figure 4.4 B). In children, EE from the SWA demonstrated the smallest mean bias against EE from IC (-0.05 $kcal.min^{-1}$) (Figure 4.5 A). The limits of agreement were narrowest for the RT3, however (-0.9 to 1.9 $kcal.min^{-1}$) (Figure 4.5 B).


6.0
4.0
2.0
0.0
-2.0
-4.0
-6.0
-8.0
IC - SWA
+1.96 SD
3.3
Mean
-1.0
-1.96 SD
-5.3
0.0
2.0
4.0
6.0
8.0
10.0
12.0
Average EE of IC and SWA (kcal.min-1)
Rest
Walking (overground)
Walking (1.0 km/h, 0%)
Walking (1.0 km/h, 5%)
Walking (2.0 km/h, 0%)
Walking (4.0 km/h, 0%)

A

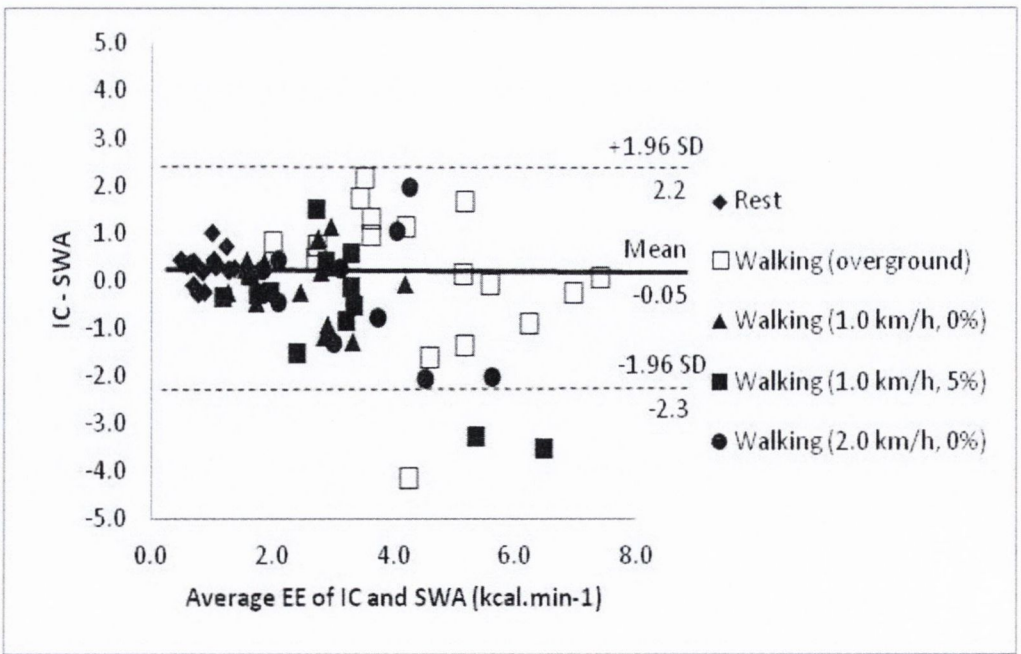

6.0
4.0
2.0
0.0
-2.0
-4.0
-6.0
IC - RT3
+1.96 SD
3.1
Mean
-2.4
0.4
-1.96 SD
0.0
2.0
4.0
6.0
8.0
10.0
12.0
Average EE of IC and RT3 (kcal.min-1)
Resting
Walking (overground)
Walking (1.0 km/h, 0%)
Walking (1.0 km/h, 5%)
Walking (2.0 km/h, 0%)
Walking (4.0 km/h, 0%)

B

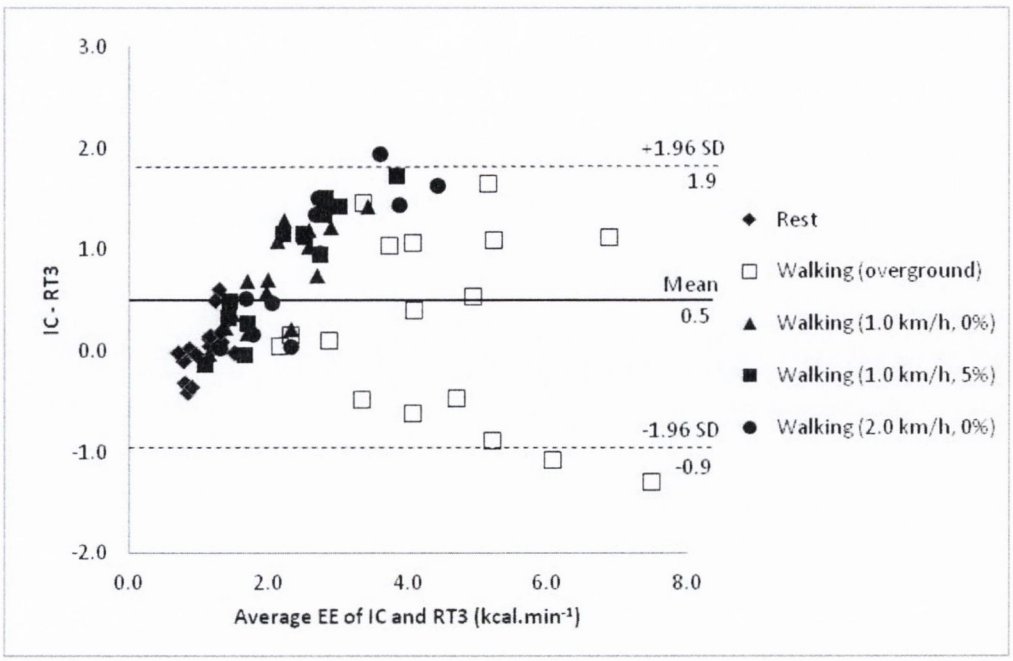


C

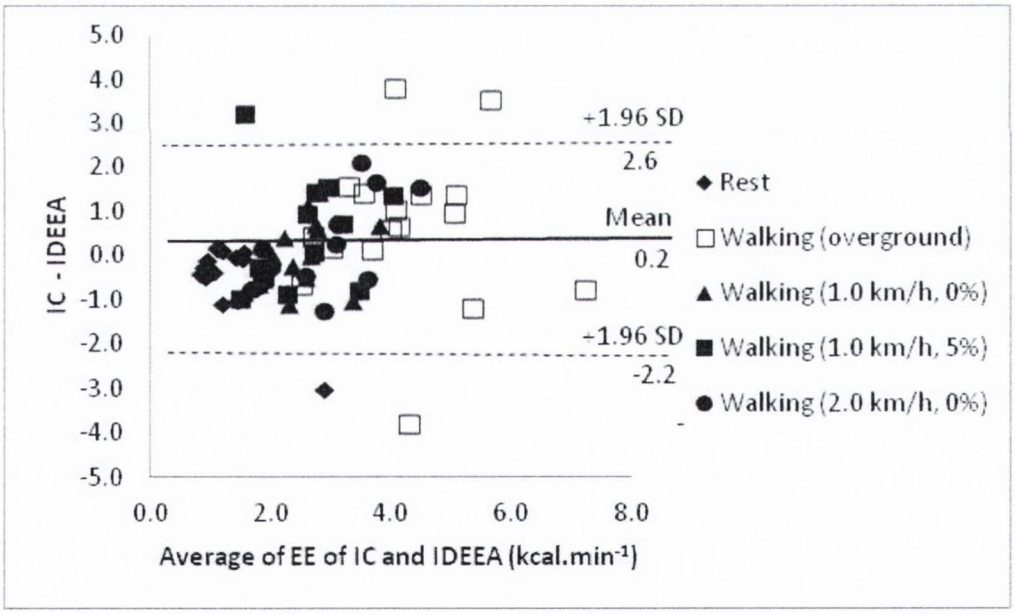
Figure 5.4 Bland–Altman plots between indirect calorimeter (IC) and SWA estimates of energy expenditure (EE), IC and RT3 estimates of EE, and IC and IDEEA estimates of EE for adults. The middle solid lines represent the mean difference between the methods: -1.0 kcal.min^{-1}, 0.4 kcal.min^{-1} and 0.8 kcal.min^{-1} for parts (A) (IC vs. SWA), (B) (IC vs. RT3), and (C) (IC vs. IDEEA), respectively.



A



B



C

Figure 5.5 Bland–Altman plots between IC and SWA estimates of EE, IC and RT3 estimates of EE, and IC and IDEEA estimates of EE for children. The middle solid lines represent the mean difference between the methods: -0.05 kcal.min-1, 0.5 kcal.min-1 and 0.2 kcal.min-1 for parts (A) (IC vs. SWA), (B) (IC vs. RT3), and (C) (IC vs. IDEEA), respectively.

5.5 Discussion

The purpose of this study was to evaluate the validity of accelerometry-based devices at estimating EE in adults and children with CP. Although advanced accelerometry-based devices were hypothesised to be more accurate at estimating EE than a traditional accelerometer, the RT3 accelerometer demonstrated better agreement with the criterion measure, with mean correlation coefficients of 0.60 and 0.93 for adults and children, respectively. The narrowest limits of agreement, for all activities combined, were also calculated for the RT3, for adults and children. Despite this the RT3 significantly underestimated EE for both adults and children (mean difference = 0.35 ± 1.42 kcal.min^{-1}, and 0.50 ± 0.71 kcal.min^{-1}, respectively, $p < 0.05$). There was also large inter-individual variation in estimates of EE, with limits of agreement ranging from -60% to 77%, of total EE, for adults and from -33% to 71%, of total EE, for children.

The RT3 underestimated EE for two out of six activities for adults and three out of five activities for children. The error in EE estimation from the RT3 ranged from -37.9% to +16.7% for adults, and from -26.9% to -2.5% for children, implying that caution must be taken when using the RT3 to estimate EE. Validation studies of the RT3 in able-bodied adults have reported that the RT3 overestimated EE by 21% to 25% during ambulatory activities on level ground (Howe et al., 2009). Overestimations of up to 108% have been observed for typically developing (TD) children walking on level ground (Sun et al., 2008, Ryan and Gormley, 2013); no study reported the mean absolute percentage error however. It is possible that the increased energy cost of locomotion associated with CP (Brehm et al., 2007, Dallmeijer and Brehm, 2011) counteracted the tendency for the RT3 to overestimate the EE of locomotion in able-bodied people, reducing the magnitude of the error in overestimation or resulting in an underestimation for some activities. As expected, and in agreement with research in able-bodied adults and children (Lyden et al., 2011, Sun et al., 2008, Ryan and Gormley, 2013, Jakicic et al., 2004), the RT3 was unable to detect the increased energy requirement of walking on a slope.

In contrast to the results of the current study, the SWA provided the best estimation of EE in adults and children without CP (Ryan and Gormley, 2013). Unlike the RT3, the SWA overestimated EE for three out of five activities for children with CP and five out of six activities for adults with CP. Although an overestimation of EE may be counterintuitive, considering the higher EE of walking that's associated with CP, it is likely a result of the

adaptations made to armswing in order to compensate for paresis. In children with unilateral CP, armswing on the least affected side is over 50% larger than the armswing of TD children (Meyns et al,. 2011). Children with bilateral CP also increase their armswing length when attempting to increase walking speed to compensate for the inability to increase leg swing length (Meyns et al., 2011). Validation studies of the SWA in adults with multiple sclerosis and in adults with chronic stroke reported similar overestimations of EE during ambulation (Coote and O'Dwyer, 2012, Manns and Haennel, 2012), with larger overestimations reported for adults with multiple sclerosis who had minimal impairments compared to those who required a mobility aid (Coote and O'Dwyer, 2012).

To date no study has validated accelerometers in adults with CP and only two have evaluated their validity in children. Clanchy et al. (2011a) validated count cut-off points for a hip-worn, traditional accelerometer for estimating activity intensity in children with CP. Differences in how raw data are collected, processed, filtered, and scaled means that counts cannot be directly compared across accelerometers (Chen and Bassett, 2005), and it is unknown how this monitor performs in comparison to other accelerometers in children with CP. Aviram et al. (2011) reported significantly better correlation coefficients for the association between EE from the IDEEA and EE from indirect calorimetry (0.70-0.88; $p<0.001$), than those calculated in the current study. The children in the study by Aviram et al. (2011) were significantly younger than the children in the current study (mean 6.41 ± 1.90 yr; range 4-10 yr), which may have contributed to the discrepancy in the results between studies. Other possible reasons for the contradictory results include differences in the level of motor impairment in the samples, differences in the intensities of the activities included in the protocol, and differences in the methods used to extract data. The inaccuracy of the IDEEA in the current study may also be due to values of 0 $kcal.min^{-1}$ been recorded for two people at rest and for one person for walking at 1.0 $km.h^{-1}$ at 0% and at 5% incline. No explanation could be provided for these abnormal values, and normal values were recorded for these participants during the remaining activities. These values were therefore included in the analysis. If these values were removed from analysis the mean absolute percentage error for the IDEEA reduced from 16.3% to 11.9%, the mean bias reduced from 0.8 $kcal.min^{-1}$ to -0.7 $kcal.min^{-1}$, but the correlation coefficient improved only marginally to 0.26, and the upper and lower limits of agreement remained the same.

Previous studies have reported obtaining extreme values from the IDEEA, with no explanation for them (Arvidsson et al., 2009a, Ryan and Gormley, 2013). Although removing these values may improve the validity of the IDEEA, validity is inextricably linked to reliability. The IDEEA needs to be consistently accurate if it is to be considered an acceptable measure of EE.

A strength of this study was the use of a standardised protocol of locomotor activities. This protocol facilitated comparison with a number of validation studies of the RT3, SWA and IDEEA in able-bodied adults and children who used track and treadmill walking protocols. Locomotor activities are also the primary activities performed in everyday life, particularly of the activities that are performed at a moderate-to-vigorous intensity. Validation of activity monitors against these activities is therefore of primary importance. The use of a reference method of oxygen uptake was also a strength of this study, as it allowed the criterion validity as well as the concurrent validity of the monitors to be evaluated.

5.5.1 Limitations

Although this study provides a comprehensive evaluation of the validity of these monitors during locomotor activity, caution should be used if drawing conclusions about the performance of these monitors during free-living activity. Also as the sample in the current study included individuals with a range of functional ability it was necessary to include a range of intensity levels in order to comprehensively evaluate these monitors in all participants. This resulted in a reduction in the number of participants completing certain activities and the small sample size did not allow for subgroup analysis across levels of functional ability.

5.6 Conclusion

Movement abnormalities associated with CP may diminish the ability of accelerometry-based devices to estimate EE in this population. Although multi-sensor, accelerometry-based devices have the potential to improve the estimation of EE in people with movement disorders, the results of the current study indicate that a traditional accelerometer provides a more accurate estimate of EE in adults and children with CP. All three monitors show large errors for estimating EE and wide limits of agreement however, and should therefore be used with caution, particularly when used at an

individual level. The authors hypothesise that a large degree of the error is a result of the inaccuracy of inbuilt algorithms that were calibrated against data collected in people without CP. With calibration of CP-specific equations, these monitors may still have the potential to accurately estimate EE in adults and children with CP.

Chapter 6 Study 3: Ability of cut-points for the RT3 accelerometer to detect moderate-to-vigorous physical activity in ambulatory children and adults with cerebral palsy

6.1 Introduction

Research into habitual levels of moderate-to-vigorous activity (MVPA), and the effects of interventions on levels of MVPA in adults and children with cerebral palsy (CP), is currently limited by the lack of valid and feasible measurement tools (Clanchy et al., 2011b). Accelerometry has gained recognition as a potentially valid and objective method of measuring physical activity without imposing a large burden on participants. Despite the large number of accelerometers commercially available only one accelerometer has been validated as a measure of physical activity in children with CP to date (Clanchy et al., 2011a). As a result, researchers and clinicians wishing to measure physical activity in this population are unable to consider other important factors, such as price and ease of use, when choosing a monitor. In Chapter 4 we reported that accelerometry-based devices provide an inaccurate estimate of energy expenditure (EE) in adults and children with CP. This is likely due to the use of proprietary algorithms that have been calibrated on data collected in able-bodied adults and children. Calibrating prediction equations on data collected from adults and children with CP may improve the ability of accelerometers to detect the intensity of activity in this population.

The RT3 accelerometer is a traditional accelerometer that was shown in Chapter 4 to provide the best agreement with EE from a criterion method in adults and children with CP. Although the RT3 provides a direct output of EE, as a traditional accelerometer it also provides raw data in counts per unit time. This is a meaningless value unless converted into an interpretable unit. It is the convention to apply count thresholds or 'cut-points' to accelerometer counts in order to express raw data as minutes spent in varying intensities of physical activity. The RT3 has previously been used in this way to measure MVPA in typically developing (TD) children and adults (Hussey et al., 2007,

Feeney et al., 2011). Two cut-points for MVPA have been derived in TD children (Vanhelst et al., 2010a, Rowlands et al., 2004) and one cut-point for MVPA has been derived in able-bodied adults (Rowlands et al., 2004). The altered relationship between energy expenditure and locomotion observed in children with CP may affect the relationship between RT3 counts and physical activity intensity however (Dallmeijer and Brehm, 2011). Without validation these cut-points cannot be applied to people with CP.

6.2 Objective

The current study was conducted to assess the ability of published RT3 cut-points to detect MVPA in ambulatory children and adults with CP. This study also aimed to determine if detection of MVPA could be improved by developing a new cut-point for this population.

6.3 Method

6.3.1 Participants

Children (≥6 years) and adults (≥18 years) with a medically confirmed diagnosis of CP, and classified as level I-III on the GMFCS were recruited for this study through the Central Remedial Clinic (CRC). Individuals with a severe cognitive impairment, uncontrolled epilepsy or seizure activity, or an acute lower limb injury were excluded from participating. Physiotherapists provided seventy-nine eligible participants with information about the study over a period of nine months. Thirty-six people agreed to participate in the study.

Participants completed the Physical Activity Readiness Questionnaire to screen for conditions contraindicating participation in exercise (Shephard, 1988). The procedures and risks involved in the study were fully explained to participants and their guardians, if the participant was under 18 years of age or had a cognitive deficit. Written informed consent was provided before testing proceeded. Ethical approval for this study was granted by the Faculty of Health Sciences and the CRC's ethics committee.

6.3.2 Instruments

The RT3 has been described in section 3.3.1.1. In the current study VM data, in counts.min^{-1}, collected throughout the protocol were used in data analysis. Oxygen consumption (VO_2), measured with the Oxycon Mobile portable indirect calorimeter (IC) was used as the criterion measure of physical activity intensity. For more information on the Oxycon see Chapter 5, section 5.3.2. The RT3 and the Oxycon were initiated using software uploaded on the same laptop. Exact start and stop times of each activity were noted from the laptop clock.

6.3.3 Procedures

Participants' height, to the nearest 0.5 cm, and weight, to the nearest 0.1 kg, (SECA, digital scales) were measured. The RT3 and IC were configured for each participant using their height, weight, sex and age, and attached to each participant. The RT3 was attached to the right hip, or the least affected side of the body in the case of participants with significant asymmetry, in the mid-axillary line. Participants then completed a series of activities. The activities included a 10 min rest period, a 6 min over-ground walking trial, and four, 5 min, treadmill activities at 1.0 km.h^{-1}, 2.0 km.h^{-1}, 4.0 km.h^{-1} and 6.0 km.h^{-1}. As it is known that accelerometers do not detect the increased energy cost of walking on an incline, data collected during treadmill walking at 1.0 km.h^{-1} at 5% incline in study 2, were not included in data analysis. The over-ground walking trial was completed on a 70 m corridor. Participants were instructed to "walk as far as possible for 6 min" in order to maximally exert themselves. A researcher walked behind the participant during the trial to monitor comfort and give standardised verbal encouragement. All participants were given a 5 min familiarisation period with the treadmill before completing the treadmill activities. Participants rested in a seated position between each activity until their heart-rate and VO_2 returned to baseline values.

6.3.4 Data Processing

On completion of the protocol, data were downloaded from the RT3. VM data from the RT3 and VO_2 data from the Oxycon were examined visually to check for any indication of equipment malfunction. The final 2 min of VO_2 and VM data for each activity were extracted and used in data analysis. Data are expressed as the mean VO_2 and mean VM per minute (ml.kg.min^{-1} and counts.min^{-1}, respectively). Metabolic equivalent (MET)

values were calculated for each activity by dividing VO_2 by resting metabolic rate (RMR). RMR was predicted for each participant from their sex, age and weight using the Oxford equations (Henry, 2005). METs and corresponding VM (counts.min^{-1}) were then categorised as light physical activity (LPA) and MVPA using age-specific MET thresholds. For children LPA was defined as 2.0-2.9 MET; MVPA was defined as ≥ 3.0 MET. For adults aged 18-39 years LPA was 2.4-4.7 MET; MVPA was ≥ 4.8 MET. For adults aged 40-64 years LPA was 2.0-3.9 MET; MVPA was ≥ 4.0 MET (Garber et al., 2011). Mean VM counts.min^{-1} were also classified as light or moderate-to-vigorous according to the cut-points identified in Table 6.1, for children and adults respectively. Average velocity of each participant during the over-ground walking trial was calculated by dividing the total distance completed by 6 min.

6.3.5 Data Analysis

Mean ± standard deviations are reported for all values. The ability of published cut-points to detect MVPA in children and adults with CP was assessed using a classification analysis whereby the sensitivity and specificity of the cut-points were determined. False positives were defined as minutes in LPA incorrectly classified as MVPA. False negatives were defined as time in MVPA incorrectly classified as LPA. In addition Cohen's kappa coefficient was used to assess the degree to which the published cut-points applied to the sample of children and adolescents with CP. Good agreement was considered as κ >0.70.

A receiver operating characteristic (ROC) curve analysis was conducted to derive a new RT3 cut-point that could accurately detect MVPA in children and adults with CP. A curve was calculated by assigning an indicator variable to counts according to their corresponding MET intensity classification (i.e. 1 = MVPA, 0 = LPA). Sensitivity, specificity and area under the ROC curve (AUC) values were also calculated for the ROC curve-derived cut-point to determine classification accuracy. Sensitivity, specificity, and AUC values of ≥ 0.90 (90%) were considered excellent, 0.80-0.89 (80-89%) good, and 0.70-0.79 (70-79%) fair. A detailed explanation of ROC curve analysis, in relation to accelerometer calibration, is provided elsewhere (Jago et al., 2007, Welk, 2005). Analyses were conducted using MedCalc for Windows, version 12.2.1.0 (MedCalc Software, Mariakerke, Belgium) and Analyse-*It* for Microsoft Excel, version 2.26. Statistical significance was set at an alpha level of <0.05.

Table 6.1 Moderate-to-vigorous physical activity cut-points for the RT3 accelerometer derived in able-bodied children and adults

Author	Sample	Criterion measure	Activities	Analysis	Cut-point
(Rowlands et al., 2004)	n = 19 19 boys, 0 girls Mean age: 9.5 ± 0.8 yr	IC	Sitting quietly, hopscotch, kicking a ball, four treadmill activities at 4, 6, 8, and 10 $km.h^{-1}$	Multiple regression Analysis	> 970 $counts.min^{-1}$
(Vanhelst et al., 2010a)	n = 40 20 boys, 20 girls Age range: 10-16 yr	None	Resting, playing a parlour game, kicking a ball, four treadmill activities at 1.5, 3, 4, and 6 $km.h^{-1}$	Receiver operating characteristic curve analysis	> 950 $counts.min^{-1}$
Rowlands et al., 2004)	n = 15 15 men, 0 girls Mean age: 20.7 ± 1.4 yr	IC	Sitting quietly, hopscotch, kicking a ball, four treadmill activities at 4, 6, 8, and 10 $km.h^{-1}$	Multiple regression Analysis	> 984 $counts.min^{-1}$

IC, indirect calorimeter

6.4 Results

Thirty-six adults and forty-three children were identified as eligible to participate in the study, 18 adults and 18 children agreed to participate. RT3 data were not obtained from one adult because of equipment malfunction. Due to the range of motor impairment in the sample not all participants completed every activity. In addition the Oxycon Mobile

failed to record data for one participant during the over-ground walking trial. At least one bout of MVPA was recorded in all participants however, resulting in 49 bouts of MVPA for adults and 30 bouts of MVPA for children.

Participants' (9 men and 10 boys) age, height, weight and BMI across GMFCS level are presented in Table 6.2. Fifteen adults (88%) and 13 (72%) children used no ambulatory aid. One adult walked with a 3-wheeled rollator, 1 adult walked with a stick, two children walked with 2 elbow crutches and three children walked with the aid of a K-walker. Seven children (39%) and 9 adults (53%) had bilateral spastic CP; the remaining participants had unilateral spastic CP. Approximately 41% (n = 7) of adults were overweight or obese (BMI >25kg.m^{-2}) and approximately 33% of children (n = 6) were classified as overweight or obese according to the IOTF criteria (Cole et al., 2000). VO_2 in ml.kg.min^{-1} and METs, and VM recorded for all activities are presented in Table 6.3. Increases in MET values coincided with an increase in VM counts across activities. The two cut-points for children detected 21 out of 30 bouts (70.0%) of MVPA in children and adolescents with CP (see Table 6.4). A kappa coefficient of 0.55 (95% CI: 0.32 - 0.77; p <0.0001) was calculated for the Vanhelst cut-point. The kappa coefficient for the Rowlands cut-point was 0.59 (95% CI: 0.38 - 0.80; p <0.0001). The ROC curve analysis identified an optimal cut-point of 689 counts.min^{-1} for discriminating between MVPA and LPA. This threshold resulted in a sensitivity of 83.3%, a specificity of 86.7% and an AUC value of 89.6% (95% CI = 77.4 - 96.6%).

The cut-point for adults detected 83.9% of MVPA in adults with CP (Table 6.4), resulting in a kappa coefficient of 0.73 (95% CI: 0.57 - 0.88; p <0.0001). ROC curve analysis derived a cut-point of 1100.5 counts.min^{-1} (Table 6.4), which resulted in an AUC of 91.8% (95% CI: 81.5 - 97.4%).

Table 6.2 Descriptive characteristics for participants across Gross Motor Function Classification Scale (GMFCS) level

	Total	GMFCS Level I	GMFCS Level II	GMFCS Level III
Children				
n	18	10	4	4
Age (yr)	11.4 ± 3.2	11.5 ± 3.8	10.0 ± 2.2	12.5 ± 1.9
Height (cm)	147.0 ± 18.5	149.5 ± 21.1	140.0 ± 20.1	147.6 ± 10.3
Body mass (kg)	44.6 ± 16.9	46.5 ± 20.9	37.0 ± 12.0	47.3 ± 8.2
BMI ($kg.m^{-2}$)	20.0 ± 4.5	19.8 ± 5.2	18.5 ± 1.8	21.9 ± 4.7
Adults				
n	17	9	7	1
Age (yr)	31.9 ± 9.8	28.1 ± 7.8	34.9 ± 10.7	45*
Height (cm)	68.7 ± 13.7	166.± 6 9.3	162.0 ± 12.2	152*
Body mass (kg)	163.9 ± 10.7	69.0 ± 13.3	67.8 ± 16.2	73*
BMI ($kg.m^{-2}$)	25.6 ± 4.8	24.6 ± 3.8	25.9 ± 5.9	31.6*

*unable to calculate mean ± standard deviation as there was only one person in this group

Table 6.3 Mean walking speed, oxygen consumption, and VM counts for rest, the over-ground walking trial, and treadmill activities

	Speed $km.h^{-1}$	n (GMFCS level [I/II/III])	VO_2 $ml.kg.min^{-1}$	VO_2 METs	VM $counts.min^{-1}$
Children					
Activity					
Rest	-	18 (10/4/4)	5.4 ± 1.6	1.2 ± 0.3	9.3 ± 15.4
Over-ground walking	3.6 ± 1.3	17 (9/4/4)	22.4 ± 6.0	5.0 ± 1.1	2027.7 ± 724.0
Treadmill walking	1.0	15 (9/3/3)	11.7 ± 2.5	2.6 ± 0.5	464. 7 ± 166.1
Treadmill walking	2.0	11 (7/3/2)	13.7 ± 2.5	3.1 ± 0.8	678.3 ± 201.8
Treadmill walking/jogging	4.0	5 (5/0/0)	15.9 ± 5.7	3.5 ± 1.1	1402.4 ± 352.9
Treadmill walking/jogging	6.0	2 (2/0/0)	-	-	-
Adults					
Activity					
Rest	-	17 (9/7/1)	3.8 ± 1.0	1.2 ± 0.3	13.6 ± 27.2
Over-ground walking	4.2 ± 1.2	17 (9/7/1)	20.3 ± 7.4	6.4 ± 1.9	2515.7 ± 858.8
Treadmill walking	1.0	15 (9/6/0)	10.4 ± 3.5	3.3 ± 1.1	448.0 ± 292.3
Treadmill walking	2.0	14 (9/5/0)	12.7 ± 4.5	4.0 ± 1.3	894.5 ± 467.5
Treadmill walking/jogging	4.0	9 (8/1/0)	17.1 ± 3.6	5.5 ± 1.1	1575.8 ± 269.4
Treadmill walking/jogging	6.0	5 (5/0/0)	25.7 ± 5.3	8.1 ± 1.7	3493.7 ± 2032.2

Note: unable to calculate mean and standard deviation for children during treadmill walking/jogging at 6.0 $km.h^{-1}$ due to the small number of participants who completed this activity

Table 6.4 Sensitivity and specificity for the cut-points developed in the current study and for published cut-points calibrated on able-bodied children and adults

Study	Cut-point (counts.min^{-1})	Sensitivity (%)	Specificity (%)
Children			
Current study	>689	83.3	86.7
Rowlands et al. (2004)	>970	70.0	94.4
Vanhelst et al. (2010)	>950	70.0	88.9
Adults			
Current Study	>1100.5	83.9	88.9
Rowlands et al. (2004)	>984	83.9	88.6

6.5 Discussion

The aim of the present study was firstly to evaluate the ability of RT3 cut-points, calibrated in able-bodied children and adults, to detect MVPA in children and adults with CP. As expected, increasing MET values corresponded with increasing VM counts across all activities. Only 70% of MVPA was detected when published cut-points were applied to RT3 data recorded in children with CP however. The health benefits associated with MVPA are not associated with light physical activity or total physical activity (Janssen and Leblanc, 2010). It is therefore important that a measure of physical activity can discriminate between light and moderate-to-vigorous physical activity. If a published RT3 cut-point is used to measure activity in children and adolescents with CP, incorrect classification of MVPA may moderate the association between activity and health in this population. However, when a published cut-point was applied to RT3 data recorded in adults with CP 83.9% of MVPA was detected. An equally high level of specificity was observed suggesting that this cut-point is appropriate for use in adults with CP.

The second aim of the study was to determine if the development of a new cut-point could improve detection of MVPA in children and adults with CP. ROC curve analysis demonstrated that the RT3 could successfully distinguish between LPA and MVPA in children with CP. The cut-point of 689 counts.min^{-1} resulted in an AUC of 89.6% (95% CI: 77.4-96.6%) indicating excellent classification accuracy. The cut-point yielded by ROC curve analysis was lower than the published cut-points resulting in a higher sensitivity

(83%) but lower specificity (87%). It is up to the researcher when choosing a cut-point to determine if a lower sensitivity or a lower specificity is more acceptable. In this case the authors believe that it is important that a cut-point can correctly identify MVPA and therefore a lower cut-point is more appropriate.

Three factors may have contributed to the discrepancy between the ROC curve-derived cut-point and the published cut-points. Firstly, the Rowlands cut-point for children was originally identified using multiple linear regression analysis. Cut-points derived from regression analysis are generally higher than those derived from ROC curve analysis (Welk, 2005). It has been illustrated that regression analysis results in accelerometer cut-points that exhibit high specificity values but relatively low sensitivity values when cross-validated in an independent sample (Welk, 2005). This is apparent in the current study in which the Rowlands cut-point exhibited excellent specificity (94%) but only fair sensitivity (70%), indicating poor discriminative ability of the cut-point. As the Rowlands cut-point has not been cross-validated in a group of TD children as part of the original study or in subsequent studies, its rate of misclassification in the current sample cannot be compared to that in a sample of TD children and adolescents.

Unlike the Rowlands cut-point the Vanhelst cut-point was derived using an ROC curve and therefore the discrepancy between cut-points cannot be attributed to differences in analysis. The discrepancy, however, may have resulted from the different methods used to classify physical activity intensity. In the current study indirect calorimetry was used as the criterion measure of EE in order to capture individual variation in metabolic cost. A criterion measure of EE was not used to classify physical activity intensity when calibrating the Vanhelst cut-point; instead activities were classified as light, moderate and vigorous according to the expected MET value of the activity. This method may have resulted in misclassification of some activity intensities. Cross-validation of the Vanhelst cut-point in an independent sample of TD children, however, resulted in excellent sensitivity (98%), good specificity (84%), and excellent agreement between the calibration and validation groups ($\kappa = 0.91$) (Vanhelst et al., 2010a). This suggests that a cut-point of 950 counts.min^{-1} is appropriate to discriminate between LPA and MVPA in TD children but does not appear sensitive enough to differentiate between LPA and MVPA in children and adolescents with CP.

The more liberal cut-point for MVPA yielded in the current study may be explained by the altered relationship between energy expenditure and ambulation in children and adolescents with CP. Children with CP have a slower maximal walking speed than their TD peers (Dallmeijer and Brehm, 2011). The energy cost of locomotion is also approximately 40% higher in children with CP (Brehm et al., 2007). As a result it is likely that children with CP will reach a moderate-to-vigorous level of intensity at a slower walking speed. This slower walking speed results in the RT3 undergoing a smaller acceleration, leading to a proportionally lower RT3 count output. Published cut-points may therefore be too high to detect MVPA in children with CP and a lower cut-point may be necessary to avoid misclassifying MVPA in this population.

The energy cost of walking, however, increases with severity of functional impairment (Kerr et al., 2008). The higher functional ability of the adults with CP, compared to children in the current study, may explain why a cut-point developed in able-bodied adults was able to accurately identify MVPA in adults with CP, but not children. However the acceptable agreement observed between the published cut-point and data collected in adults with CP should be interpreted with caution. The lower confidence interval of the kappa coefficient was 0.57, indicating poor agreement.

The ability of a published cut-point to detect MVPA in adults with CP may also be explained by the use of age-specific MET thresholds to classify activity intensity. These thresholds classify the relative intensity of an activity, which is known to vary with age (Knaggs et al., 2011), therefore improving the precision of individual estimates of activity intensity. Age-specific MET thresholds are not available for children. It must also be noted that MET thresholds used to define physical activity intensity in an able-bodied population may not be appropriate to use in people with CP because of the increased metabolic cost of activity (Bell and Davies, 2010). As a MET threshold to identify MVPA in adults and children with CP has not been defined the thresholds used in the current study were deemed the most appropriate method of classifying activity intensity.

The ROC curve-derived cut-point for adults with CP was approximately 100 counts.min^{-1} higher than the published cut-point. Despite this the two cut-points had a similar level of sensitivity and specificity. This difference in the cut-points may be a result of the activities included in the protocol. Accelerometers are known to overestimate the energy cost of locomotor activities, and hence yield higher accelerometer cut-points

(Welk, 2005). They are also known to underestimate the energy cost of free-living activities (Welk, 2005). When calibrating a cut-point in able-bodied adults, Rowlands included two free-living activities (hopscotch and kicking a football) which probably countered the high count output from the RT3 during locomotor activities and reduced the final cut-point. The appropriateness of using these free-living activities to calibrate an accelerometer cut-point is questionable given the small likelihood of adults performing these activities in everyday life. Aside from this, 100 counts.min^{-1} is approximately equivalent to a resting value of VO_2, and therefore did not result in a significant difference between the sensitivity or specificity values of cut-points.

The Actigraph accelerometer is the only accelerometer that has been validated as a measure of physical activity intensity in children and adolescents with CP to date (Clanchy et al., 2011a). A published cut-point for the Actigraph (Evenson et al., 2008) exhibited good sensitivity (81.8%) and excellent specificity (100.0%) for detecting MVPA in a sample of children and adolescents with CP. The sample of children used to validate the Actigraph was more able than that in the current study, however, with only 10% (vs. 22%) of participants classified as GMFCS level III, and only 14% (vs. 28%) requiring a mobility aid. This variation in the energy cost of locomotion amongst children with CP is captured by the current study.

6.5.1 Limitations

The present study has some limitations that should be addressed. The use of locomotor activities, both standardised and self-selected, allowed all participants to reach a level of MVPA, regardless of their degree of motor impairment. Only three participants, however, reached a vigorous intensity level (≥ 6.0 MET). Moderate and vigorous MET thresholds were therefore combined and compared to a single cut-point for MVPA. Although this allows for comparison to the current physical activity guidelines for children and adults (US Department of Health and Human Services, 2008) future studies should investigate the ability of the RT3 to detect vigorous physical activity in children and adults with CP. In addition, although age, sex and weight specific RMR values were used to calculate MET values, individual measurement of RMR may have improved the estimation of activity intensity. Equipment and time limitations prevented RMR measurements from being performed. Finally, while the sample size is similar to that of other validation and calibration studies (Rowlands et al., 2004, Hussey et al., 2009,

Clanchy et al., 2011a) it is acknowledged to be small. As a result we were unable to perform subgroup analysis according to GMFCS level. The demographic characteristics of the participants indicate that the sample of children was diverse enough to capture the natural variability within the target population of ambulatory children with CP, however, particularly the different levels of functional ability. On the other hand the sample of adults included a high proportion of people with minimal impairments and therefore the results of this study should not be extrapolated to a more severely disabled population of adults with CP.

6.6 Conclusion

In conclusion, the RT3 presents as an objective and feasible method of measuring physical activity in ambulatory children and adults with CP. RT3 counts increased in line with increasing physical activity intensity. Participants were also compliant with the device and no monitor malfunction was observed. Using published cut-points to classify physical activity intensity may result in an underestimation of MVPA in children with CP. A cut-point of 689 counts.min^{-1} is presented to potentially improve the detection of MVPA in ambulatory children and adolescents with CP and allow the RT3 to be used in future studies of habitual levels of MVPA. Cross-validation of this cut-point is however, required in an independent sample of ambulatory children with CP. A published cut-point developed in able-bodied adults demonstrated an acceptable level of agreement with data collected on adults with CP and presents as a potential method of classifying MVPA in this population.

Chapter 7 Study 4: Physical activity and cardiometabolic risk factors in adults with cerebral palsy

7.1 Introduction

Although cerebral palsy (CP) is a non-progressive disorder, it is well reported that adults with CP experience a number of secondary conditions with age. These include pain, fatigue, stiffness, and poor balance (Opheim et al., 2009, Van Der Slot et al., 2012, Sandstrom et al., 2004), and can lead to a decline in physical functioning and loss of mobility from early adulthood. Between 30% and 52% of adults with CP reported experiencing deterioration in walking function (Bottos et al., 2001, Opheim et al., 2009). Loss of mobility is most commonly observed between the age of 20 and 40 years (Bottos et al., 2001). Deterioration in physical functioning over time may lead to difficulties performing everyday activities and potentially an inactive lifestyle.

Only two studies have objectively measured physical activity in adults with CP to date and have reported conflicting results (Nieuwenhuijsen et al., 2009, van der Slot et al., 2007). Van der Slot et al. (2007) reported that ambulatory adults with unilateral spastic CP were as active as their able-bodied peers. Nieuwenhuijsen et al. (2009) found that ambulatory and non-ambulatory adults with bilateral spastic CP were less active than their able-bodied peers. Gross motor function was a significant predictor of physical activity in both studies, and adults with minimal impairments achieved similar levels of physical activity to adults without CP. Although these studies provided information about total physical activity in adults with CP, time spent in individual domains of activity such as sedentary behavior, light activity and moderate-to-vigorous activity was not investigated.

Decreased levels of moderate-to-vigorous physical activity and increased sedentary behaviour are both independently associated with risk factors for cardiovascular disease (CVD) and type II diabetes mellitus (T2DM) including obesity, dyslipidemia, hypertension, insulin resistance, hyperglycemia, and increased inflammatory markers (i.e. C-reactive protein) (Loprinzi et al., 2013, Luke et al., 2011, Camhi et al., 2011, Healy

et al., 2011). The current American College of Sports Medicine (ACSM) guidelines recommend that adults accumulate 150 minutes of moderate activity or 75 minutes of vigorous activity per week to reduce their risk of cardiovascular disease and premature mortality (Garber et al., 2011). The potentially increased risk of adults with CP developing CVD or T2DM as a result of reduced activity levels has led to a comparison been made to spinal cord injury – a population known to have insulin resistance, dyslipidemia, and an elevated presence of T2DM (Bauman, 2009). Despite this no study has investigated levels of moderate-to-vigorous activity and their association with cardiometabolic risk factors in adults with CP.

7.2 Objective

The purpose of this study was two-fold. Firstly the aim was to assess everyday levels of physical activity, and sedentary behaviour among adults with CP, compared to adults without CP, and the factors associated with physical activity. The second aim of this study was to examine the relationship between physical activity and cardiometabolic risk factors in adults with CP. The objectives of the study were as follow:

1) To compare everyday levels of sedentary behaviour, light, moderate and vigorous physical activity in adults with CP to age- and sex-matched adults without CP.
2) To determine the factors that influence everyday levels of sedentary, moderate and vigorous activity in adults with CP.
3) To investigate the association between physical activity and body composition, systolic blood pressure (SBP), diastolic blood pressure (DBP), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), TC/HDL-C ratio, low-density lipoprotein cholesterol (LDL-C), triglycerides, glucose, insulin, insulin resistance, glycated haemoglobin (HbA_{1c}), C-reactive protein (CRP), and 25-hydroxyvitamin D levels (25OHD).

7.3 Method

7.3.1 Participants

Adults (≥18 years) with a medically confirmed diagnosis of CP, classified as level I-V in the Gross Motor Function Classification System (GMFCS) (see section 1.1.1.1) were recruited for this study. Adults with a severe cognitive impairment and pregnant women were excluded from participating in this study. Study 4 will only include data collected from ambulatory adults with CP (i.e. GMFCS levels I-III). A nationwide strategy was employed to recruit adults with CP into this study. A list of registered General Practitioners (GPs) in the Republic of Ireland was obtained from the Irish College of General Practitioners website. Letters were sent to 1367 GPs providing them with information about the study and the inclusion/exclusion criteria. GPs were requested to identify suitable candidates and provide them with Participant Information Leaflets (PILs).

Managers of community-based physiotherapy services in 10 Health Service Executive (HSE) areas (Meath, Wicklow, Kildare/West Wicklow, Dublin North Central, North West Dublin, Dun Laoghaire, Dublin South City, Dublin South East, Dublin West, Dublin South West) were contacted regarding the study and asked to provide contact details for all physiotherapists working in these HSE areas. Four managers responded to the request and physiotherapists working in these areas were informed about the study and requested to give suitable candidates PILs. Permission was obtained from the Irish Society of Chartered Physiotherapists to email members who belonged to the Chartered Physiotherapists in Community Care and Charted Physiotherapists in Private Practice employment groups, and the Chartered Physiotherapists in Intellectual Disability interest group, who were provided with information about the study and requested to give suitable candidates PILs. A letter with information about the study, flyers and PILs were sent to disability officers in nine Institutes of Technology and six Universities in Ireland with the request to supply information to suitable candidates. Physiotherapy managers in 14 acute hospitals in Ireland were informed about the study and asked to provide colleagues with information about the study and identify potential participants.

Services that provided assistance to people with disabilities were informed about the study by post, telephone and email and asked to give potential participants PILs. A page providing information about the study was established on Facebook. Facebook groups

associated with physical activity, public health and CP were asked to share a link to the page with their members. An ad was also placed on Facebook, which targeted adults (≥18 years) with a disability who lived in Ireland. A separate webpage was created on the Trinity College website to provide potential participants with more information about the study and allow them to conveniently contact the researcher. Finally, letters and PILs were sent to 263 adults with CP who were on the database of the Central Remedial Clinic (CRC). Ethical approval for this study was granted by the Faculty of Health Sciences and the CRC's ethics committee.

7.3.2 Measurements

7.3.2.1 Body composition

Standing height (i.e. stature) was measured using a portable stadiometer (Invicta Plastics Ltd., Leicester, England). Participants were asked to stand as upright as possible without shoes, with their heels together and their head in the Frankfurt Plane (i.e. an imaginary horizontal line running between the ear hole and the lower border of the eye). Height was read at the end of a gentle inspiration to the nearest mm. Body mass was measured to the nearest 0.1 kg in bare feet and light clothing using an electronic platform scale (SECA 635). BMI was calculated as $kg.m^{-2}$. Overweight and obesity were identified as a BMI ≥25 $kg.m^{-2}$ and ≥30 $kg.m^{-2}$ respectively.

Waist circumference (WC) was measured, on bare skin, to the nearest 0.1 cm midway between the lower rib margin and the iliac crest at the end of gentle expiration. Hip circumference (HC) was measured to the nearest 0.1 cm at the end of gentle expiration around the maximum circumference of the buttocks. For females this is usually at groin level. For males it is normally about 2-4 inches below the navel. Participants wore minimal clothing. Both WC and HC measurements were taken with the subject standing erect with arms hanging loosely from the body. The mean of two measurements was used for both WC and HC. Waist-hip ratio (WHR) was calculated by dividing WC by HC. Waist-height ratio (WHtR) was calculated by dividing WC by height.

7.3.2.2 Cardiometabolic risk factors

Blood pressure was measured from the right arm or the least affected side, in the case of significant asymmetry, using the Omron 705 IT BP monitor. The Omron 705 IT has demonstrated excellent validity in adults under the British Hypertension Society criteria

(El Assaad et al., 2003; Coleman et al., 2006). Participants rested in a seated position with their back supported for at least five minutes prior to the measurement been taken, as recommended by the 2012 Canadian Hypertension Education Program (Daskalopoulou et al., 2012). The appropriate cuff size was selected for the participant based on their arm circumference. The cuff was placed so that the lower edge was 3cm above the elbow crease and the bladder was centred over the brachial artery. The measurement was taken with the participant's legs uncrossed and their arm bare and supported with the cuff at heart level. Participants were asked not to talk while the measurement was being taken. Three measurements were taken at a 1-2 min interval. The average of the last two measurements was used in data analysis.

Blood was drawn following an overnight fast and processed according to standard procedures in the Central Pathology Laboratory at St. James's Hospital. Insulin was measured by electrochemiluminescence immunoassay (Elecsys Insulin Assay, Roche Diagnostics GMBH). Enzymatic, colorimetric assays (Roche/Hitachi **cobas c** systems) were used to measure fasting glucose, TC, HDL-C and triglycerides. LDL-C was calculated using the Friedewald equation. High performance liquid chromatography (Arkray/Adams A1c HA-8160 Analyser System) was used to measure HbA_{1c} and CRP was measured by particle enhanced immunoturbidimetric assay (Roche/Hitachi **cobas c** systems). 25OHD was measured on the API 4000 LC/MS/MS system (Norwolk, Connecticut).

The metabolic syndrome, a term used to describe the presence of multiple cardiometabolic risk factors, was defined according the Joint Interim Statement of the IDF Task Force on Epidemiology and Prevention, National Heart, Lung and Blood Institute, American Heart Association, World Heart Federation, International Atherosclerosis Society and International Association for the Study of Obesity (Alberti et al., 2009). The criterion for the clinical diagnosis of the metabolic syndrome requires the presence of any three of the following: 1) central obesity (WC ≥94 cm for men and ≥80 cm for women, IDF cut points for people of European origin); 2) increased triglycerides ≥150 mg/dL, use of lipid medications or self-reported diagnosis of hypertriglyceridemia; 3) low HDL-C (<40 mg/dL for men and <50 mg/dL for women), or drug treatment for reduced HDL-C; 4) increased blood pressure (systolic pressure ≥130 mmHg and/or diastolic pressure ≥85 mmHg), or current usage of hypertensive drug treatment in a patient with a history of hypertension; and 5) high fasting blood glucose (≥100 mg/dL), current use of anti-diabetic medication or previously diagnosed diabetes.

The Homeostasis Model Assessment index (Matthews et al., 1985) was used to evaluate insulin resistance. The model describes the interactions between glucose and insulin dynamics using the following formula: [fasting insulin ($mU.L^{-1}$) x fasting glucose ($mmol.L^{-1}$)]/22.5. It is suitable for use in people with glucose intolerance, mild to moderate diabetes and other insulin resistant conditions.

7.3.2.3 Physical activity

Physical activity was measured in ambulatory participants with the RT3 accelerometer (Stayhealthy Inc). The RT3 has been described in detail in section 3.3.1.1. Physical activity data for age- and sex-matched control participants without CP (age-matched to within 5 years) were also obtained from a database collected between 2009 and 2013. All participants were asked to wear the RT3 for 7 days on their right hip (or least affected side in the case of significant asymmetry) in the midaxillary line. Participants were told to wear the RT3 for waking hours and only to remove it for bathing and swimming. Participants were asked to record the times that they removed the monitor and the activities they completed while not wearing the monitor. Vector magnitude count data were collected in 1-min epochs.

Valid activity data were defined as having at least four days data, of at least 10 hours wear time per day (Ward et al., 2005). Sedentary activity was defined as <100 $counts.min^{-1}$, light activity (LPA) was defined as 100-984 $counts.min^{-1}$, moderate activity (MPA) was defined as 984-2341 $counts.min^{-1}$, vigorous activity (VPA) was defined as >2341 $counts.min^{-1}$ (Rowlands et al., 2004). Data are presented as time spent in light, moderate and vigorous activity accumulated in 1-min intervals. Time spent in moderate-to-vigorous activity accumulated in 10-min intervals (MVPA) is also presented as the current ACSM guidelines indicate that moderate-to-vigorous activity should be accumulated in bouts of at least 10 minutes (Garber et al., 2011). We allowed for one minute of activity below the moderate activity count threshold before the bout was considered to be ended. Percentage time spent in sedentary activity (i.e. minutes spent in sedentary activity/total wear time) and mean activity counts per minute ($counts.min^{-1}$) are also presented. Finally the percentage of adults with and without CP meeting the ACSM recommendation for physical activity was calculated.

7.3.2.4 Procedure

The procedure involved participants presenting to the exercise laboratory in the Trinity Centre of Health Sciences on one morning following a 12 hour overnight fast. Participants were allowed to drink water during the fast and medications for cardiovascular stability were permitted (i.e. anti-hypertensive medications). Participants were informed of the testing procedures before written informed consent was obtained. In the case of participants with a mild to moderate cognitive impairment their guardians also provided written informed consent. Participants were classified according to the GMFCS and according to the classification system from the Surveillance of Cerebral Palsy in Europe (see section 1.1.1.1) (Rosenbaum et al., 2007), in which the dominant type of tone or movement abnormality associated with CP is categorised as spastic, dystonic, choreoathetoid, or ataxic; spastic CP is further classified as unilateral or bilateral. This information was confirmed with their physiotherapist when in doubt and where available. Information was also obtained from participants about their current employment status, history of cardiovascular disease and T2DM, and current use of medication. Employment status was subdivided into i) in full-time employment/full-time student, ii) in part-time employment/part-time student, iii) unemployed. Part-time employment was defined as working three days or less per week.

Following a period of rest in a seated position participants' blood pressure was measured. Secondly, anthropometric data including body mass, stature, WC and HC were measured. Following this a fasting venous blood sample was obtained by a researcher trained in venepuncture. Participants were then provided with water and a snack before being given the RT3 with written and verbal instructions on how to use it. Participants were also provided with a stamped addressed envelope to return the monitor to the researcher.

7.3.3 Data Analysis

Statistical analysis was performed using Analyse-it for Microsoft Excel (version 2.20) and IBM SPSS Statistics (version 19). The distribution of the data was checked for normality by the Kolmogorov-Smirnov test. The logarithm function was applied to TC/HDL-C ratio, insulin, HOMA-IR and 25OHD to transform this data to a normal distribution. Means and standard deviations were computed for each of the normally distributed continuous variables. Means and standard deviations of TC/HDL-C ratio, insulin, HOMA-IR and

25OHD are presented in the original scale. Medians and interquartile ranges were computed for skewed data. Prevalence data is presented as percentages. The following three cut-offs were applied to CRP to categorise risk of developing CVD: 1. <0.1 $mg.dL^{-1}$ (low risk); 2. 0.1-0.3 $mg.dL^{-1}$ (average risk); 3. >0.3 $mg.dL^{-1}$ (high risk) (Loprinzi et al., 2013). Hypertension was defined as systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥90 mmHg, as per the 2013 ESH/ESC Guidelines for the Management of Arterial Hypertension (Mancia, 2013). People who reported taking any hypertension lowering medication were automatically classified as hypertensive. The presence or absence of cardiometabolic risk factors was defined according to laboratory reference values. People who reported taking any cholesterol medication were automatically classified as having abnormal TC, TC/HDL-C ratio, HDL-C and LDL-C. Insufficient 25OHD was defined as ≤50nmol/L (Nowson and Margerison, 2002; van der Mei et al., 2007).

Differences between continuous variables with a normal distribution were determined by independent t-tests and one-way analysis of variance (ANOVA). Differences between continuous variables with a skewed distribution were determined by Mann-Whitney U tests and Kruskal-Wallis one-way analysis of variance. Pearson's χ^2 test was used for comparison of independent groups of categorical data.

Two primary multiple regression analyses were performed. The first analysis was used to determine the factors that were associated with time spent in moderate-to-vigorous physical activity (accumulated in bouts of ≥10 min), in adults with CP. Each of the independent variables (age, sex, BMI, employment status, GMFCS classification, diagnostic classification, intellectual status) were entered into a separate regression model. Dummy indicator variables were created for categorical variables with more than two categories. These dummy variables were treated as one variable, where all or none of the dummy variables pertaining to an independent variable were entered into the model at one time. Dummy indicator variables for GMFCS were defined as: 1. 1 if GMFCS level I, 0 otherwise; 2. 1 if GMFCS level III, 0 if otherwise. Dummy indicator variables for employment status were defined as: 1. 1 if in full-time employment, 0 otherwise; 2. 1 if unemployed, 0 otherwise. Dummy indicator variables for diagnostic classification were defined as: 1. 1 if unilateral spastic CP, 0 otherwise; 2. 1 if 'other' (i.e. dystonic, choreoathetoid, or ataxic), 0 otherwise. Significant variables were entered into the final model.

The second analysis was performed to determine the association between each cardiometabolic outcome (i.e. BMI, WC, WHtR, WHR, SBP, DBP, TC, HDL-C, TC/HDL-C ratio, LDL-C, triglycerides, insulin, plasma glucose, HbA_{1c}, HOMA-IR, CRP, 25OHD) and physical activity outcome. The independent variables (i.e. physical activity outcome) included in the analyses were percentage time in sedentary behaviour, LPA, MPA, VPA, MVPA, and mean counts.min^{-1}. Separate regression analyses were conducted for each dependent variable (i.e. cardiometabolic outcome) using the following model: block 1: age, sex, GMFCS; block 2: independent variable. GMFCS was entered as two dummy indicator variables as defined above. When SBP or DBP was the dependent variable of interest the model included drug therapy (i.e. self-report of taking any hypertension lowering medication coded as 1 if yes or 0 if no) in block 1. When TC, HDL-C, LDL-C, or TC/HDL-C ratio was the dependent variable, drug therapy (i.e. self-report of taking any cholesterol medication coded as 1 if yes or 0 if no) was included in block 1.

These analyses were repeated firstly without adjusting for GMFCS level. They were then repeated without controlling for GMFCS level and additionally controlling for total physical activity (mean counts.min^{-1}). Variance inflation factors <5 suggested that multicollinearity was not an issue.

Logistic regression analyses were conducted to investigate the association between the metabolic syndrome, high risk CRP (dependent variables) and each physical activity component (independent variables). Analyses were initially controlled for age and sex before additionally controlling for total activity. Statistical significance was set at $p < 0.05$. The R square, F value, and where appropriate, the R square change and F change, of the final model are presented. Statistical significance was set at $p<0.05$. The significance level was adjusted using the Bonferroni correction for multiple comparisons.

7.4 Results

Fifty-five adults were recruited for this study. Forty-three participants responded to letters sent via the CRC (16% response rate). Seven participants received information about the study from their GP. Five participants were recruited by word-of-mouth. The

number of adults with CP living in the Republic of Ireland is unknown and therefore we were unable to calculate the proportion of adults who participated in this study. Information was also not available on the non-responders and therefore we cannot compare characteristics between responders and non-responders.

Physical activity data were collected on forty-one ambulatory participants and forty-one age- and sex-matched adults without CP. Two adults (5%) were taking antihypertensive medication. Three adults (7.3%) were taking cholesterol medication. A value for plasma glucose was missing for one person and the HbA_{1c} assay was missing for one person due to processing errors. One person reported a pre-diagnosis of type I diabetes mellitus. This person was removed from all analyses of blood biomarkers of glucose metabolism (i.e. plasma glucose, insulin, HOMA-IR, HbA_{1c}) and the metabolic syndrome. Participant characteristics are presented by GMFCS level in Table 7.1. There was no significant difference in sex across GMFCS level. Adults in GMFCS level I were younger than adults in level II ($p < 0.001$); there was no difference in age between adults in levels I and III or in levels II and III. There was also no difference in BMI across GMFCS level.

Table 7.1 Participants' physical and demographic characteristics by Gross Motor Classification System level

	Total (n = 41)	GMFCS level I (n = 13)	GMFCS level II (n = 18)	GMFCS level III (n = 10)
Male, female	19, 22	9, 4	7, 11	3, 7
Age, mean (SD), yr	36.5 (12.5)	27.6 (10.8)	43.4 (11.0)	35.6 (10.0)
Age, range, yr	18-62	18-53	25-62	18-54
Height, mean (SD), cm	163.85 (10.9)	170.8 (11.9)	163.7 (7.3)	155.0 (9.1)
Body mass, mean (SD), kg	65.9 (13.1)	72.6 (15.3)	65.3 (8.6)	58.4 (13.3)
Diagnostic Classification, n (%)				
Spastic	37 (90.2)	13 (100.0)	14 (77.8)	10 (100.0)
Unilateral	15 (40.5)	10 (76.9)	4 (22.2)	1 (10.0)
Bilateral	22 (59.5)	3 (23.1)	10 (55.6)	9 (90.0)
Other	4 (9.8)	0 (0.0)	4 (22.2)	0 (0.0)
Employment status, n (%)				
Full-time	22 (53.7%)	10 (76.9)	9 (50.0)	3 (30.0)
Part-time	8 (19.5%)	0 (0.0)	4 (22.2)	4 (40.0)
Unemployed	11 (26.8%)	3 (23.1)	5 (27.8)	3 (30.0)

[a]Data from non-spastic forms of CP were combined to form one group due to the small number of participants with ataxic, dystonic, or choreoathetoid CP.

All participants wore the RT3 for a median (IQR) of 7.0 (1.0) days. Adults with CP wore the RT3 for a median (IQR) time of 840.5 (88.5) min per day; adults without CP wore the RT3 for a mean time of 841.2 (59.3) min per day. There was no significant difference in wear time between groups ($p = 0.53$). A summary of physical activity outcomes across GMFCS are presented in (Table 7.2).

Adults with CP spent more time in sedentary behaviour and less time in LPA, MPA, VPA, and MVPA than adults without CP. They also participated in significantly less total activity (mean counts.min^{-1}). MPA, VPA, MVPA and counts.min^{-1} declined across GMFCS levels I, II and III, respectively. Post-hoc analysis revealed that adults in level I spent

significantly more time in MPA, MVPA and had higher counts.min^{-1} than adults in level III ($p < 0.01$ for all). There were no significant differences between any adjacent GMFCS level for MPA, VPA, MVPA or counts.min^{-1} after the significance level was adjusted for multiple comparisons. There was no difference in time in any physical activity outcome between adults with CP in level I and age- and sex-matched control participants. A trend towards a significant difference for VPA was observed however ($p = 0.57$). Adults in level II spent more time in sedentary behaviour ($p < 0.001$) and less time in LPA than control participants ($p < 0.01$). They also had lower mean counts.min^{-1} than adults without CP ($p < 0.01$). There was no difference in MPA, VPA or MVPA between adults in GMFCS level II and control participants however. Adults in level III spent significantly more time in sedentary activity, less time in LPA, MPA, VPA, MVPA, and had lower mean counts.min^{-1} than control participants ($p < 0.01$ for all).

Adults with unilateral spastic CP spent less time in sedentary behaviour and more time in MPA, VPA and MVPA than adults with bilateral CP. They also had significantly higher mean counts.min^{-1}. Data from adults with non-spastic forms of CP were excluded from the analysis due to the small numbers of adults in this group ($n = 4$).

Twenty-two adults without CP (53.7%) and ten adults with CP (24.4 %) met the ACSM guideline for physical activity ($\chi^2 = 7.38$, $p < 0.01$). The number of adults meeting the guideline declined across GMFCS level I, II and III [$n = 7$ (53.8%), $n = 3$ (16.7%), $n = 0$ (0.0%), respectively; $\chi^2 = 9.92$, $p = 0.007$]. Adherence to vigorous activity guidelines was not calculated due to the small quantity of vigorous activity achieved by adults with CP. Multiple regression analysis of each potential explanatory variable revealed that sex, GMFCS level, and diagnostic classification were significantly associated with MVPA (Table 7.3). When these three variables were included in the final model only GMFCS (1) (i.e. dummy variable defined as 1. if GMFCS level I or 0. if other) was significantly associated with MVPA accounting for 29% of the variance (Table 7.4).

Cardiometabolic risk factors are summarised across GMFCS level in Table 7.5. The prevalence of the metabolic syndrome was 20.5%, overweight/obesity according to BMI was 41.5%, central obesity was 36.6%, hypertension was 17.1%, high TC was 29.3%, low HDL-C was 9.8%, high LDL-C was 26.8%, high CRP was 14.6%, high fasting glucose was 7.3%, high triglycerides was 14.6%, high insulin was 4.9%, low 25OHD was 58.5%. There was no difference in any risk factor across GMFCS levels. Regression analyses revealed

that when age, sex and GMFCS level were adjusted for there was a trend towards a significant association between MPA and WC and WHtR (Table 7.6).When age and sex only were adjusted for MPA was significantly associated with WHtR (Table 7.7). When total activity was additionally controlled for MPA remained associated with WHtR (Table 7.8). Significant associations were also observed between MPA and WC, systolic blood pressure and diastolic blood pressure when the analysis was adjusted for age, sex and total activity (Table 7.8). Logistic regression analysis revealed that neither physical activity nor sedentary behavior was associated with the metabolic syndrome or high risk CRP.

Table 7.2 Physical Activity Measures for adults without CP and for adults with CP by Sex, Age, GMFCS, Diagnostic Classification, Weight Status, and Employment Status. Data presented as mean (SD) unless stated otherwise

	Sedentary behaviour (%)	Light activity (min.d^{-1})	Moderate activity (min.d^{-1})	Vigorous activity (min.d^{-1})	Mod and Vig in 10-min bouts (min.d^{-1})	Mean counts per min
Adults without CP	49.9 (9.5)	337.26 (94.0)	50.8 (38.8)†	18.3 (22.8)†	24.9 (27.6)†	315.6 (135.8)†
Adults with CP	63.3 (10.3)	260.7 (72.0)	33.3 (36.4)†	5.2 (7.4)†	6.1 (23.4)†	218.3 (105.4)
p value	<0.0001	<0.0001	0.0007	0.0004	0.0021	<0.0001
Sex						
Men (n = 19)	62.3 (11.3)	260.2 (73.0)	41.5 (26.9)	5.6 (12.3)†	12.6 (32.3)†	241.6 (120.4)
Women (n = 22)	64.1 (9.5)	261.2 (72.9)	29.2 (21.0)	2.7 (6.7)†	0.0 (16.8)†	198.1 (88.4)
p value	0.5687	0.9654	0.1072	0.3077	0.0271	0.1910
Age						
18-35 yr (n = 19)	63.1 (9.4)	232.3 (112.4)†	39.1 (20.3)	6.7 (15.3)†	12.6 (24.3)†	243.1 (112.4)
36-62 yr (n = 22)	63.4 (11.2)	266.2 (76.9)	21.5 (39.2)†	2.6 (5.9)†	0.0 (17.0)†	196.9 (96.4)
p value	0.9092	0.4967	0.1781	0.0120	0.0592	0.1636
GMFCS						
Level I (n = 13)	62.0 (9.9)	246.8 (66.8)	45.5 (17.5)	14.7 (27.4)†	27.4 (21.6)	278.7 (122.6)
Level II (n = 18)	61.0 (9.8)	282.2 (70.1)	37.7 (28.0)	4.3 (3.1)	6.5 (17.0)†	214.3 (82.5)
Level III (n = 10)	69.2 (10.3)	240.2 (78.4)	16.2 (14.0)	1.2 (5.6)†	0.0 (0.5)†	147.0 (74.3)

p value	0.1082	0.2411	0.0105	0.0280	0.0009	0.0085
Diagnostic Classification						
Spastic (n = 37)	64.2 (10.1)	255.5 (71.4)	29.3 (36.4)†	5.0 (7.5)†	6.0 (23.5)†	206.1 (142.6)†
Unilateral (n = 15)	60.0 (7.0)	265.6 (61.0)	42.4 (18.7)	8.6 (19.3)†	24.0 (21.9)	273.2 (107.5)
Bilateral (n = 22)	67.0 (11.0)	248.6 (78.3)	17.6 (27.9)†	2.0 (5.3)†	0.0 (7.1)	171.2 (87.6)
p value	0.0347	0.4855	0.0085	0.0133	0.0037	0.0032
Other (n = 4)[a]	54.9 (9.4)	208.6 (68.0)	55.8 (25.3)	4.8 (3.5)	12.8 (9.6)	271.4 (72.8)
Weight Status						
Normal (n = 24)	61.9 (10.2)	289.3 (136.1)†	38.9 (26.2)	5.7 (6.5)†	8.2 (23.7)†	229.7 (91.8)
Overweight/obese (n = 17)	65.2 (10.4)	240.2 (64.0)	29.2 (21.0)	1.1 (7.7)†	1.4 (20.3)†	171.8 (151.3)†
p value	0.3110	0.1530	0.2137	0.0980	0.3826	0.1947
Employment status						
Full-time (n = 22)	62.3 (9.4)	271.5 (68.4)	41.3 (24.7)	5.2 (10.2)†	16.5 (27.2)†	228.9 (89.9)
Part-time (n = 8)	68.8 (11.6)	232.6 (69.7)	17.7 (17.7)	3.0 (3.2)	1.3 (9.9)†	156.4 (92.2)
Unemployed (n = 11)	61.3 (10.6)	259.4 (81.4)	34.7 (23.5)	5.8 (6.7)†	7.0 (9.9)†	242.1 (132.5)
p value	0.2327	0.4344	0.0609	0.3733	0.3233	0.1718

†variable not normally distributed; data presented as median (IQR). [a]Data from non-spastic forms of CP excluded from the analysis due to the small numbers in this group.

Table 7.3 Multiple regression analyses for each potential explanatory variable on moderate-to-vigorous activity (10-min bouts)

Explanatory variable	B(SE)[a]	B	p value
Age	-0.217 (0.226)	-0.152	0.342
Sex	11.430 (5.346)	0.324	0.039
GMFCS level			
GMFCS (1)	17.173 (5.450)	0.454	0.003
GMFCS (2)	-8.851 (5.905)	-0.216	0.142
Diagnostic Classification			
Diagnostic Classification (1)	17.360 (5.433)	0.475	0.003
Diagnostic Classification (2)	6.221 (8.819)	0.105	0.485
Employment status			
Employment status (1)	4.161 (6.504)	0.118	0.526
Employment status (2)	-8.218 (8.184)	-0.185	0.322
BMI	0.042 (0.797)	0.008	0.958

[a]Unstandardised coefficients. [b]standardised coefficients.

B, beta coefficient; SE, standard error.

Table 7.4 Results obtained from linear regression analysis assessing the association between physical activity parameters and personal and cerebral palsy-related factors

	Unstandardised Coefficients B(SE)	Standardised Coefficients B	*T*	p value
GMFCS (1)	14.286 (6.503)	0.378	2.197	0.035
GMFCS (2)	-6.734 (6.331)	-0.164	-1.064	0.295
Diagnostic Classification (1)	7.478 (6.108)	0.205	1.224	0.229
Diagnostic Classification (2)	5.414 (8.705)	0.091	0.622	0.538

R square=0.358; F=5.024, p <0.01; n=41. B, beta coefficient; SE, standard error.

Table 7.5 Cardiometabolic risk factors among participants with cerebral palsy presented across Gross Motor Function Classification System levels I, II and III

	Total	Level I	Level II	Level III
BMI, mean (SD), $kg.m^{-2}$	24.5 (3.6)	24.7 (3.8)	24.4 (3.0)	24.2 (4.5)
BMI ≥25 $kg.m^{-2}$, n (%)	17 (41.5)	7 (53.8)	5 (27.8)	5 (50.0)
Central obesity[a], n (%)	15 (36.6)	4 (30.8)	7 (38.9)	4 (40.0)
WC, mean (SD), cm	82.9 (11.5)	83.3 (13.5)	83.6 (10.1)	80.9 (12.1)
WHR, mean (SD)	0.85 (0.09)	0.85 (0.10)	0.85 (0.09)	0.86 (0.08)
WHtR, mean (SD)	0.51 (0.07)	0.49 (0.07)	0.51 (0.06)	0.52 (0.07)
Systolic BP, mean (SD), mmHg	126.6 (13.9)	127.2 (17.2)	127.1 (14.6)	125.0 (7.6)
Diastolic BP, mean (SD), mmHg	75.7 (9.2)	72.2 (12.0)	78.4 (8.3)	75.4 (4.5)
Total Cholesterol, mean (SD), $mmol.L^{-1}$	4.63 (0.88)	4.38 (0.92)	4.89 (0.93)	4.49 (0.68)
HDL-Cholesterol mean (SD), $mmol.L^{-1}$	1.57 (0.38)	1.41 (0.36)	1.66 (0.36)	1.64 (0.38)
TC/HDL-C ratio, mean (SD)	2.95 (1.29)	3.32 (1.17)	2.95 (1.17)	2.75 (1.35)
LDL-cholesterol, mean (SD), $mmol.L^{-1}$	2.66 (0.76)	2.54 (0.84)	2.84 (0.71)	2.50 (0.74)
Triglyceride†, median (IQR), $mmol.L^{-1}$	0.8 (0.4)	0.95 (0.51)	0.81 (0.25)	0.75 (0.29)
Plasma Glucose†, median (IQR), $mg.dL^{-1}$	84.6 (10.8)	84.6 (9.6)	85.5 (9.6)	81.9 (9.6)
Insulin, mean (SD), $mU.L^{-1}$	8.5 (1.7)	8.1 (1.7)	8.5 (1.8)	9.1 (1.5)
HOMA-IR, mean (SD)	1.86 (1.78)	1.70 (1.74)	1.91 (1.95)	2.04 (1.48)
HbA_{1c}, mean (SD), $mmol.mol^{-1}$	26.5 (2.8)	31.2 (1.8)	32.1 (3.5)	32.9 (2.6)
C-reactive Protein				
<0.1 $mg.dL^{-1}$, n (%)	25 (61.0)	8 (61.5)	10 (55.6)	7 (70.0)
0.1-0.3 $mg.dL^{-1}$, n (%)	10 (24.4)	4 (30.8)	3 (16.7)	3 (30.0)
>0.3 $mg.dL^{-1}$, n (%)	6 (14.6)	1 (7.7)	5 (27.8)	0 (0.0)
25OH vitamin D, mean (SD), $nmol.L^{-1}$	42.7 (1.7)	39.8 (1.5)	42.7 (2.0)	47.5 (1.5)

[a]Defined as waist circumference ≥80 cm for women or ≥94 cm for men; †variables with a skewed distribution.

Table 7.6 Results obtained from the linear regression assessing the association between physical activity parameters and waist-to-height ratio (Model 1) and waist circumference (Model 2) adjusting for age, sex and GMFCS level.

	Unstandardised Coefficients B(SE)	Standardised Coefficients B	p value
Model 1			
Age	0.003 (0.001)	0.578	0.001
Sex	0.047 (0.018)	0.367	0.013
GMFCS (1)	0.019 (0.025)	0.135	0.458
GMFCS (2)	0.024 (0.023)	0.158	0.319
MPA	-0.001 (0.000)	-0.288	0.068
Model 2			
Age	0.440 (0.130)	0.478	0.002
Sex	14.686 (2.798)	0.645	0.000
GMFCS (1)	3.092 (3.840)	0.127	0.426
GMFCS (2)	-0.438 (3.616)	-0.17	0.904
MPA	-0.114 (0.063)	-0.241	0.081

Model 1: R square = 0.397; R square change = 0.061; F = 4.618, p = 0.002; n = 41. Model 2: R square = 0.539; R square change = 0.043; F = 8.177, p <0.001; n = 41.

B, beta coefficient; SE, standard error.

Table 7.7 Results obtained from the linear regression assessing the association between physical activity parameters and waist-to-height ratio (Model 1) adjusting for age and sex.

	Unstandardised Coefficients B(SE)	Standardised Coefficients B	p value
Model 1			
Age	0.003 (0.001)	0.509	0.000
Sex	0.049 (0.017)	0.381	0.008
MPA	-0.001 (0.000)	-0.314	0.026

Model 1: R square = 0.377; R square change = 0.091; F = 7.455, p = 0.001; n = 41.

B, beta coefficient; SE, standard error.

Table 7.8 Results obtained from the linear regression assessing the association between physical activity parameters and waist-to-height ratio (Model 1), waist circumference (Model 2), systolic blood pressure (Model 3), diastolic blood pressure (Model 4), adjusting for age, sex and total activity (mean counts.min^{-1}).

	Unstandardised Coefficients B(SE)	Standardised Coefficients B	p value
Model 1			
Age	0.003 (0.001)	0.538	0.000
Sex	0.050 (0.017)	0.384	0.007
Mean counts.min^{-1}	0.000 (0.000)	0.269	0.250
MPA	-0.001 (0.001)	-0.538	0.028
Model 2			
Age	0.419 (0.103)	0.455	0.000
Sex	15.393 (2.577)	0.676	0.000
Mean counts.min^{-1}	0.042 (0.021)	0.386	0.054
MPA	-0.244 (0.093)	-0.518	0.012
Model 3[a]			
Age	0.357 (0.162)	0.308	0.047
Sex	10.978 (4.329)	0.375	0.023
Antihypertensive Medication	4.659 (9.821)	0.073	0.638
Mean counts.min^{-1}	0.069 (0.034)	0.523	0.048
MPA	-0.337 (0.150)	-0.592	0.031
Model 4[a]			
Age	0.314 (0.109)	0.427	0.007
Sex	0.810 (2.839)	0.045	0.777
Antihypertensive Medication	6.465 (6.439)	0.154	0.322
Mean counts.min^{-1}	0.046 (0.022)	0.530	0.044
MPA	-0.239 (0.098)	-0.636	0.020

[a]additionally adjusted for antihypertensive medication

Model 1: R square = 0.397; R square change = 0.061; F = 4.618, p = 0.002; n = 41. Model 2: R square = 0.575; R square change = 0.082; F = 12.171, p = 0.000; n = 41. Model 3: R square = 0.283; R square change = 0.104; F = 2.756, p = 0.033; n = 41. Model 4: R square = 0.293; R square change = 0.120; F = 0.2897, p = 0.027; n = 41.

B, beta coefficient; SE, standard error.

7.5 Discussion

The results of the current study indicate that adults with CP spend more time in sedentary activity and less time in physical activity than adults without CP. These findings are in agreement with previous studies of adults and children with CP (Nieuwenhuijsen et al., 2009; Maher et al., 2007; Zwier et al., 2010). This is the first study however, to quantify the time that adults with CP spend in light, moderate and vigorous intensity activity. When taken as a group, adults with CP spend less time in all intensities of physical activity compared to age- and sex-matched able-bodied mates. In addition, a significantly smaller proportion of adults with CP meet physical activity guidelines compared to adults without CP. The quantity and intensity of physical activity achieved by adults with CP was strongly associated with gross motor function. MPA was negatively associated with a number of cardiometabolic risk factors suggesting that this population is at increased risk of developing chronic disease as a result of reduced levels of activity.

The current guidelines recommend that adults achieve 150 minutes of moderate activity per week, or approximately 21 minutes per day, accumulated in bouts of at least 10 min (Garber et al., 2011). Adults with CP in the current study only achieved 6.1 minutes of MVPA per day. It is not possible to compare this to the level of physical activity reported in other studies of adults with CP because of differences in how activity was measured and defined. The use of an accelerometer in the current study provides empirically relevant data that allows for comparison with data collected by large research groups (such as the National Health and Nutrition Examination Survey). As a group, adults with CP accumulated significantly less MVPA than adults without CP. Adults in GMFCS level I, however, accumulated 27.4 min per day, resulting in more than half of these adults meeting the guideline. Previous studies have also reported that adults and children in level I achieved similar levels of physical activity as able-bodied peers (Nieuwenhuijsen et al., 2009; Maher et al., 2007; Bjornson et al., 2007).

Adults in level II of the GMFCS spent more time in sedentary activity, and less time in light activity and total activity (as indicated by mean counts.min^{-1}) than adults without CP. Interestingly they accumulated similar levels of MPA and VPA as control participants. It may be possible that adults with mild-to-moderate impairments try to keep up with

their able-bodied peers and participate in everyday life. In fact 50% of adults in level II were in full-time employment. Trying to balance the workload of daily life with the greater energetic cost of locomotion associated with CP (Kerr et al., 2008) may result in an energy imbalance. Chronic fatigue is a primary complaint amongst adults with CP, and it is particularly prevalent among those with moderate motor impairments (Jahnsen et al., 2003; van Der Slot et al., 2012). Adults classified in level II may reduce their light activity and increase sedentary activity in an attempt to preserve energy. These results should be interpreted with caution however, as despite achieving similar levels of MPA and VPA as able-bodied participants only 16.7% of adults classified in level II met the recommendation for physical activity. It is well reported that adults with CP have low levels of cardiorespiratory fitness (Fernandez, 1990). This may prevent them from accumulating MVPA in bouts of 10 minutes or more. An exercise intervention may be required to improve cardiorespiratory fitness in deconditioned adults with CP in order to increase everyday levels of MVPA.

As expected, adults in GMFCS level III participated in the least amount of physical activity; no adults in this group met the physical activity guideline. As well as accumulating little or no MVPA they spent a large proportion of the day in sedentary behaviour. There is evidence in the general adult population that sedentary behaviour is strongly associated with T2DM and cardiometabolic risk factors, independent of time in MVPA (Stamatakis et al., 2012; Healy et al., 2011). In the current study however, sedentary behaviour was not associated with any cardiometabolic risk factor. This may be because the relationship between objectively measured sedentary behaviour and cardiometabolic risk factors is less consistent than that between self-reported sedentary behaviour and risk factors (Stamatakis et al., 2012). Some research suggests that the type of sedentary behaviour, in particular TV-viewing, rather than the volume of sedentary behavior is associated with cardiometabolic risk factors (Stamatakis et al., 2012; Carson & Janssen, 2011). This information was not captured by accelerometry in the current study.

Although no association was observed between sedentary behavior and cardiometabolic risk factors, MPA was negatively associated with a number of risk factors. This is in contrast to a recent study in Dutch adults with CP that was unable to find an association between physical activity and cardiovascular risk factors (van der Slot

et al., 2013). This is likely because the association between each component of physical activity and risk factors was not investigated by van der Slot et al. (2013).

The association between physical activity and risk factors may be mediated through the effect of excess adiposity on cardiometabolic disease. In the current study MPA was associated with measures of central adiposity but not BMI. Similarly, anthropometric measures of central obesity, but not BMI, are associated with cardiometabolic risk factors in adults with CP (Peterson et al., 2012), possibly because BMI is unable to identify excess adiposity in adults with reduced muscle mass. Future studies investigating the effect of exercise interventions in adults with CP should evaluate changes in abdominal adiposity and subsequent changes in cardiometabolic risk.

An unexpected finding of this study was the high prevalence of insufficient serum 25OHD among adults with CP. The prevalence of insufficient 25OHD, defined as ≤50nmol/L (Nowson and Margerison, 2002, van der Mei et al., 2007), was 58.5%. This was considerably higher than levels of 25OHD insufficiency reported in the general Irish population (Hill et al., 2006). Maintaining adequate levels of 25OHD may be particularly important for adults with CP as low 25OHD is associated with inferior balance, gait speed, muscle mass, muscle function, and risk of fractures in older adults (Scott et al., 2010; Gerdhem et al., 2005). Although the current study found no association between physical activity and 25OHD, a prospective study of older adults found that baseline physical activity levels are predictive of future 25OHD (Scott et al., 2010). Adults with CP may therefore be at greater risk of 25OHD insufficiency. This is an area that requires further research.

7.5.1 Limitations

There are a number of limitations to this study that warrant discussion. Although everyday physical activity was strongly associated with GMFCS and cardiometabolic risk factors the direction of causality cannot be assumed given the cross-sectional design of this study. Deterioration in gross motor function may be accelerated by reduced participation in physical activity. There is currently no information about the effect of physical activity on physical functioning in adults with CP. As the secondary conditions experienced by adults with CP, such as pain, stiffness and loss of mobility, are often likened to premature aging however, inferences may be made from research on older

adults. Physical activity prevents or mitigates functional limitations in older adults (Nelson et al., 2004; Keysor, 2003; Pahor et al., 2006). It also reduces risk of falls and injuries from falls (Panel on Prevention of Falls in Older Persons, American Geriatrics Society and British Geriatrics Society, 2011). Regular physical activity may therefore delay the deterioration in walking function experienced by many adults with CP, particularly the significant proportion who report declining from level I to level II on the GMFCS (Sandstrom et al., 2004; McCormick et al., 2007; Opheim et al., 2009).

Another limitation of this study was that cardiometabolic risk factors were not measured in adults without CP and could therefore not be compared across populations. There was also no assessment of dietary intake so this potential confounder could not be controlled for.

. The small sample size limits the ability to extrapolate these results to a wider population of adults with CP. The sample size may also have been insufficient to detect significant associations. Despite every effort being made to trace and recruit adults with CP into this study there was low participation. Similar issues with recruitment have been identified in other studies of adults with CP (Van Der Slot et al., 2012, Nieuwenhuijsen et al., 2009). Reasons for non-participation were not reported. There could be a number of reasons that contributed to the low participation such as lack of transport, not having a family member or friend to accompany them and not being able to take time off work. Some of these issues were raised by participants who contacted the researcher for further information about the study. Although these issues could be overcome it is likely that some people who received the study invite did not contact the researcher for further information. In addition, many people who participated in the study were currently availing of services in the Central Remedial Clinic and had a good relationship with the members of staff who sent them the study invite. A large proportion of adults with CP do not receive rehabilitative services. International research reported that less than one-third of adults with CP are under the regular control of a rehabilitation physician (Hilberink et al., 2007). These people who received the study invite may not have participated because they had no relationship with staff in the Central Remedial Clinic or felt aggrieved by the lack of services available for them. As a result of the low participation there may have been some selection bias in the sample. In particular adults with an interest in preventive health and being physically active may have been more likely to participate.

The use of an accelerometer to measure physical activity in this study resulted in data being captured from one point in time. This may not have been a true representation of participants' habitual activity and wearing the monitor may have motivated them to exercise. Participants were however, unable to see the volume of activity they were completing while wearing the monitor.

The use of an accelerometer may be viewed as a strength of this study as research in the general population suggests that there is a stronger association between accelerometer-measured physical activity data and cardiometabolic risk factors in comparison to self-report measures (Atienza et al., 2011). This however could not be verified in the current study as self-reported physical activity was not recorded.

7.6 Conclusion

The results of this study suggest that a large proportion of adults with CP do not meet physical activity guidelines. As well as spending less time in total physical activity, adults with CP spent less time in MPA and VPA, and more time in sedentary behaviour than their able-bodied peers. The negative association between MPA and cardiometabolic risk factors suggests that policy and intervention should be implemented to increase MPA in adults with CP in order to reduce cardiometabolic disease risk in this population.

Chapter 8 Study 5: A comparison of body mass index, waist circumference, waist-hip ratio and waist-height ratio as predictors of cardiometabolic risk factors in adults with cerebral palsy

8.1 Introduction

The results of Chapter 7 indicate that ambulatory adults with CP do not meet physical activity guidelines. It is likely that even less non-ambulatory adults meet these guidelines. Reduced participation was negatively associated with a number of risk factors for cardiovascular disease (CVD) and type II diabetes mellitus (T2DM). This supports the hypothesis that the two- to three-fold greater mortality rate as a result of coronary heart disease reported among adults with cerebral palsy (CP) compared to adults without CP (Strauss et al., 1999), is a result of reduced physical activity. Despite this increased risk there are currently no national screening programmes that monitor cardiometabolic risk in this population. Indeed little is known about the prevalence of cardiometabolic risk factors in this population. Preventive programmes are a vital component of reducing the prevalence of CVD and T2DM worldwide (Federation, 2006). As atherosclerosis is a progressive process, however, it has usually progressed to an advanced stage before the symptoms of CVD become apparent, and preventive programmes are implemented.

Obesity is an independent risk factor for CVD mortality (Romero-Corral et al., 2010, Dudina et al., 2011, Faeh et al., 2011). The relationship between obesity and CVD is mediated through the negative effect of excess adiposity on cardiometabolic risk factors including blood pressure, blood lipids, insulin resistance (IR), plasma glucose, and C-reactive protein (CRP) (Dattilo and Kris-Etherton, 1992, Flechtner-Mors et al., 2000, Heilbronn et al., 2001). Recognising obesity in adults with CP is an important step to identifying those with increased risk of CVD. Although body mass index (BMI) is historically used to classify obesity, a significant limitation of BMI is its inability to differentiate between an elevated body fat content and increased muscle mass

(Franzosi, 2006, Romero-Corral et al., 2006). Normal weight obesity (i.e. people who have a normal weight based on BMI cut-off points and a high body fat content) is strongly associated with cardiometabolic dysregulation, a high prevalence of the metabolic syndrome, and an increased risk of CVD mortality (Romero-Corral et al., 2010). The ability of BMI cut-off points to identify cardiometabolic risk may be further compromised in adults with CP, a population known to have reduced muscle volumes (Riad et al., 2012, Lampe et al., 2006). Accurately measuring body fat content in a clinical setting is not always feasible. Simple anthropometric measures such as waist circumference (WC), waist-hip ratio (WHR), and waist-height ratio (WHtR) have therefore been adopted as quick indicators of abdominal obesity in the general population. Not only are these measures quick and easy to use, research suggests they are superior tools, in comparison to BMI, for identifying cardiometabolic risk (Ashwell et al., 2012, de Koning et al., 2007).

To date, only one study has investigated the ability of simple anthropometric measures to predict cardiometabolic risk among adults with CP (Peterson et al., 2012b). WHR was found to be a significant predictor of high-density lipoprotein cholesterol (HDL-C), total cholesterol/high-density lipoprotein cholesterol (TC/HDL-C) ratio, and triglycerides. The association between anthropometric measures and other cardiometabolic risk factors, in particular blood pressure, insulin resistance, glucose, and inflammatory markers, has not been investigated in adults with CP.

8.2 Objective

The first aim of this study was to investigate the prevalence of cardiometabolic risk factors in a sample of adults with CP. The second aim was to investigate associations between simple indicators of adiposity and cardiometabolic risk factors in this population.

8.3 Method

8.3.1 Participants

Recruitment for Study 5 was described in Chapter 7 section 7.4.1.

8.3.2 Measurements

8.3.2.1 Body Composition

Stature, body mass, WC, WHR and WHtR were measured in participants as described in Chapter 7 section 7.4.2.1. In the case of non-ambulatory participants stature was predicted from knee height using equations developed by Chumlea et al. (1994). Knee height was measured with the knee and ankle held at 90°, from the posterior surface of the thigh, just proximal to the patella, to the sole of the foot, using a calipers. To measure body mass in non-ambulatory participants, participants sat on a chair placed on the scale, which did not influence weight due to the pre-TARE function. BMI was calculated as $kg.m^{-2}$. Overweight and obesity were identified as a BMI ≥25 $kg.m^{-2}$ and ≥30 $kg.m^{-2}$, respectively.

8.3.2.2 Cardiometabolic risk factors

Blood pressure, total cholesterol (TC), HDL-C, triglycerides, low density lipoprotein cholesterol (LDL-C), CRP, glucose, and insulin were measured as described in section 7.4.2.2. The metabolic syndrome and HOMA-IR were also calculated as described in section 7.4.2.2.

Hypertension was defined as systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥90 mmHg, as per the 2013 ESH/ESC Guidelines for the Management of Arterial Hypertension (Mancia, 2013). People who reported taking any hypertension lowering medication were automatically classified as hypertensive. The presence or absence of TC, HDL-C, LDL-C, triglycerides, glucose, and insulin was defined according to laboratory reference values. High risk CRP was defined as >0.3 $mg.dL^{-1}$ (Loprinzi et al., 2013). Insulin resistance was defined by the 75^{th} percentile of HOMA-IR of the participants being studied (HOMA-IR = 2.51) (Balkau and Charles, 1999). People who reported taking any cholesterol medication were automatically classified as having abnormal TC, TC/HDL-C ratio, HDL-C and LDL-C.

Smoking behavior was assessed in a face-to-face interview. Smoking was recorded as yes/no and classified as heavy (≥20 cigarettes/day) or not.

8.3.2.3 Procedure

The procedure used in study 4b is outlined in section 7.4.2.3.

8.3.3 Data Analysis

The distribution of the data was checked for normality by the Kolmogorov-Smirnov test. The logarithm function was applied to TC/HDL-C ratio, insulin, and HOMA-IR to transform this data to a normal distribution. Means and standard deviations were computed for each of the normally distributed continuous variables. Means and standard deviations of TC/HDL-C ratio, insulin, and HOMA-IR are presented in the original scale. Medians and interquartile ranges were computed for skewed data. Prevalence data are presented as percentages. The following three cut-offs were applied to CRP to categorise risk of developing CVD: 1, <0.1 $mg.dL^{-1}$ (low risk); 2, 0.1-0.3 $mg.dL^{-1}$ (average risk); 3, >0.3 $mg.dL^{-1}$ (high risk) (Loprinzi et al., 2013). Differences between continuous variables with a normal distribution were determined by independent t-tests. Differences between continuous variables with a skewed distribution were determined by Mann-Whitney U tests. Pearson's χ^2 test was used for comparison of independent groups of categorical data. Pearson's partial correlation test (controlled for sex) was used to examine correlations between gross motor functioning and each anthropometric measure.

Linear regression analyses was performed to determine the association between each cardiometabolic outcome (i.e. SBP, DBP, TC, HDL-C, TC/HDL-C ratio, LDL-C, triglycerides, insulin, plasma glucose, HOMA-IR, CRP) and anthropometric measures (BMI, WC, WHR, WHtR). Separate regression analyses were conducted for each dependent variable (i.e cardiometabolic outcome) using the following model: block 1: age, sex, ambulatory status; block 2: independent variable (i.e. anthropometric measure). When SBP or DBP was the dependent variable of interest the model included drug therapy (i.e. self-report of taking any hypertension lowering medication coded as 1 if yes or 0 if no) in block 1. When TC, HDL-C, LDL-C, or TC/HDL-C ratio was the dependent variable, drug therapy (i.e. self-report of taking any cholesterol medication coded as 1 if yes or 0 if no) was included in block 1. The R-square value, R square change, and F value were calculated. Coefficients and standard errors in the final models are presented.

A receiver operating characteristic (ROC) curve analysis was conducted to compare the anthropometric measures at predicting the presence of cardiometabolic risk factors. An area under the ROC curve (AUC) of >0.90 is considered excellent; 0.80 - 0.90 is considered good; 0.70 - 0.80 is considered fair. All analyses were performed using

Analyse-it for Microsoft Excel (version 2.20) and IBM SPSS Statistics (version 19). Statistical significance was set at $p < 0.05$.

8.4 Results

Fifty-five adults were recruited for this study. Forty-three participants responded to letters sent via the CRC (16% response rate). Seven participants received information about the study from their GP. Five participants were recruited by word-of-mouth. Eleven adults (20%) were on antihypertensive drug treatment and five adults (9%) were taking cholesterol medication. There was no significant difference in the proportion of people taking antihypertensive medication or cholesterol medication between ambulatory and non-ambulatory groups. Only one person reported smoking (less than 20 cigarettes per day). A value for CRP and insulin was missing for one non-ambulatory person and a value for plasma glucose was missing for one ambulatory person, as a result of processing errors. One person reported a pre-diagnosis of type I diabetes mellitus. This person was removed from all analyses of blood biomarkers of glucose metabolism (i.e. plasma glucose, insulin, HOMA-IR) and the metabolic syndrome. Hip circumference was not obtained from two non-ambulatory adults because of significant contractures.

The demographic and diagnostic distribution of participants is presented in Table 8.1. There was significantly less females in the non-ambulatory group compared to the ambulatory group ($p < 0.05$). There was no difference in age between the two groups. The prevalence of the metabolic syndrome in the total cohort was 22.6% (Table 8.2). The prevalence of the metabolic syndrome was higher in non-ambulatory people compared to ambulatory people (not statistically significant). The prevalence of hypertension, hypertriglyceridemia and low HDL-C was also higher in non-ambulatory participants (Table 8.2). Only the prevalence of low HDL-C was significantly different between groups ($p < 0.05$).

Table 8.1 Demographic and diagnostic distribution of participants by ambulatory status

	Total (n = 55)	Ambulatory (n = 41)	Non-Ambulatory (n = 14)
Males, females	31, 24	19, 22	12, 2
Age, mean (SD), yr	37.5 (13.3)	36.5 (12.5)	40.3 (15.7)
Age, range, yr	18-65	18-62	18-65
Diagnostic Classification, n (%)			
Spastic CP	49 (89.1)	37 (90.2)	12 (85.7)
Unilateral	15 (30.6)	15 (40.5)	-
Bilateral	34 (69.4)	22 (59.5)	12 (100.0)
Other[a]	6 (10.9)	4 (9.8)	2 (14.3)
GMFCS, n (%)			
I	13 (23.6)	13 (31.7)	-
II	18 (32.7)	18 (43.9)	-
III	10 (18.2)	10 (24.4)	-
IV	8 (14.5)	-	8 (57.1)
V	6 (10.9)	-	6 (42.9)
Employment status, n (%)			
Full-time	25 (45.5)	22 (53.7)	3 (21.4)
Part-time	8 (14.5)	8 (19.5)	-
Unemployed	22 (40.0)	11 (26.8)	11 (78.6)

[a]Dyskinetic and ataxic CP were combined to form one group due to the small numbers of participants with these diagnoses.

Table 8.2 Participants' anthropometric measures and cardiometabolic outcomes by ambulatory status

	Total	Ambulatory	Non-Ambulatory
Height, mean (SD), cm	163.3 (10.0)	163.9 (10.9)	161.7 (7.0)
Weight, mean (SD), kg	64.9 (14.0)	65.9 (13.1)	61.9 (16.5)
BMI, mean (SD), $kg.m^{-2}$	24.2 (4.4)	24.5 (3.6)	23.6 (6.2)
BMI ≥25 $kg.m^{-2}$, n (%)	18 (32.7)	14 (34.1)	4 (28.6)
BMI ≥30 $kg.m^{-2}$, n (%)	4 (7.3)	3 (7.3)	1 (7.1)
Central obesity[a], n (%)	20 (36.4)	15 (36.6)	5 (35.7)
WHR, mean (SD)	0.87 (0.09)	0.85 (0.09)	0.92 (0.10)
WHtR, mean (SD)	0.51 (0.08)	0.51 (0.07)	0.53 (0.11)
Systolic BP, mean (SD), mmHg	126.2 (14.3)	126.6 (13.9)	125.1 (15.8)
Diastolic BP, mean (SD), mmHg	76.0 (9.8)	75.7 (9.2)	76.6 (11.9)
Hypertension (%)[b]	11 (20.0)	7 (17.1)	4 (28.6)
Total Cholesterol, mean (SD), $mmol.L^{-1}$	4.5 (0.9)	4.6 (0.9)	4.2 (0.9)
Hypercholesterolaemia, n (%)	16 (29.1)	12 (29.3)	4 (28.6)
HDL-Cholesterol, mean (SD), $mmol.L^{-1}$	1.48 (0.39)	1.57 (0.38)	1.21 (0.29)
Low HDL-Cholesterol, n (%)	9 (16.4)	4 (9.8)	5 (35.7)

TC/HDL-C, mean (SD)	3.1 (1.3)	3.0 (1.3)	3.5 (1.3)
LDL-cholesterol, mean (SD), $mmol.L^{-1}$	2.64 (0.77)	2.66 (0.76)	2.56 (0.82)
High LDL-C, n (%)	15 (27.3)	11 (26.8)	4 (28.6)
Triglyceride†, median (IQR), $mmol.L^{-1}$	0.8 (0.5)	0.8 (0.4)	0.8 (1.1)
Hypertriglyceridemia, n (%)	9 (16.4)	6 (14.6)	3 (21.4)
Plasma Glucose†, median (IQR), $mg.dL^{-1}$	84.6 (10.8)	84.6 (10.8)	84.6 (10.8)
Hyperglycaemia, n (%)	3 (5.7)	3 (7.7)	0 (0.0)
Insulin, mean (SD), $mU.L^{-1}$	8.1 (1.7)	8.5 (1.7)	7.7 (3.9)
HOMA-IR, mean (SD)	1.74 (1.74)	1.86 (1.78)	1.45 (1.62)
High C-reactive Protein	9 (16.4)	6 (14.6)	3 (21.4)
Metabolic syndrome, n (%)	12 (22.6)	8 (20.5)	4 (28.6)

[a]Defined as waist circumference ≥80 cm for women or ≥94 cm for men; [b]including participants on anti-hypertensive medication; †variables with a skewed distribution.

Only 4 participants (7.3%) were obese according to BMI cut-offs. The prevalence of elevated waist circumference, however, was 36.4%. BMI ranged from 12.3 $kg.m^{-2}$ to 36.8 $kg.m^{-2}$; WC ranged from 64 cm to 126.5 cm; WHR ranged from 0.68 to 1.11; WHtR ranged from 0.36 to 0.81. BMI, WHtR, the prevalence of overweight/obesity (defined by BMI ≥25 $kg.m^{-2}$), and the prevalence of central obesity (defined by WC ≥80/94 cm for women and men, respectively) did not differ between ambulatory and non-ambulatory participants. Non-ambulatory participants had a higher WHR ($p < 0.05$) than ambulatory participants. Pearson's partial correlations revealed GMFCS was associated with HC ($r = -0.356$; $p < 0.05$) and WHR ($r = 0.287$; $p < 0.05$), when adjusted for sex.

The significant associations found between anthropometric measures and cardiometabolic outcomes are presented in Tables 8.3, 8.4 and 8.5. WC was associated with HOMA-IR, triglycerides, and SBP. WHR and WHtR were associated with HOMA-IR and triglycerides. BMI was associated with HOMA-IR only.

Table 8.3 Results obtained from the linear regression assessing the association between anthropometric measures and HOMA-IR

	Unstandardised Coefficients B(SE)	Standardised Coefficients B	*P*-value
Model 1			
Waist circumference	0.009 (0.003)	0.480	0.001
Model 2			
BMI	0.025 (0.007)	0.451	0.001
Model 3			
Waist-hip ratio	1.018 (0.438)	0.405	0.024
Model 4			
Waist-height ratio	1.340 (0.394)	0.446	0.001

Model 1: R square = 0.294; R square change = 0.160; F = 5.216, $p < 0.01$. Model 2: R square = 0.311; R square change = 0.176; F = 5.642, $p < 0.01$. Model 3: R square = 0.231; R square change = 0.086; F = 3.596, $p < 0.05$. Model 4: R square = 0.297; R square change = 0.163; F = 5.292, $p < 0.01$. B, beta coefficient; SE, standard error.

Table 8.4 Results obtained from the linear regression assessing the association between anthropometric measures and triglycerides

	Unstandardised Coefficients B(SE)	Standardised Coefficients B	*P*-value
Model 1			
Waist circumference	0.020 (0.006)	0.450	0.003
Model 2			
Waist-height ratio	3.033 (0.993)	0.407	0.004
Model 3			
Waist-hip ratio	2.741 (1.033)	0.452	0.011

Model 1: R square = 0.142; R square change = 0.140; F = 4.913, p <0.01. Model 2: R square = 0.277; R square change = 0.135; F = 4.784, p <0.01. Model 3: R square = 0.266; R square change = 0.108; F = 4.353, p <0.01 B, beta coefficient; SE, standard error.

Table 8.5 Results obtained from the linear regression assessing the association between anthropometric measures and systolic blood pressure

	Unstandardised Coefficients B(SE)	Standardised Coefficients B	*P*-value
Model 1			
Waist circumference	0.376 (0.151)	0.352	0.016

Model 1: R square = 0.337; R square change = 0.084; F = 4.992, p <0.01. B, beta coefficient; SE, standard error.

The AUC for BMI, WC, WHR and WHtR at predicting the presence of cardiovascular risk factors are shown in Table 8.7. ROC curve analysis was not performed on insulin and glucose due to the small number of people defined as having abnormal levels of these risk factors (n = 2 and n = 3, respectively). The AUC for hypertension, high TC, high HOMA-IR, high LDL-C, and for the presence of two or more risk factors were highest for WC (0.681-0.763). The AUC for low HDL-C and high triglycerides were highest for WHtR (0.711 and 0.816, respectively).

Table 8.6 Area under curves (95% CI) for anthropometric measurements

	BMI	WC	WHR	WHtR
Hypertension	0.693*	0.747*	0.726*	0.694*
AUC (95% CI)	(0.505 - 0.881)	(0.541 - 0.952)	(0.530 - 0.922)	(0.491 - 0.898)
High TC	0.627	0.681*	0.634	0.641
AUC (95% CI)	(0.462 - 0.791)	(0.525 - 0.837)	(0.465 - 0.804)	(0.479 - 0.804)
Low HDL-C	0.624	0.692	0.708	0.711*
AUC (95% CI)	(0.416 - 0.833)	(0.527 - 0.857)	(0.531 - 0.886)	(0.522 - 0.901)
High LDL-C	0.652	0.713*	0.688*	0.667
AUC (95% CI)	(0.481 - 0.822)	(0.545 - 0.882)	(0.518 - 0.857)	(0.495 - 0.839)
High triglycerides AUC (95% CI)	0.681 (0.482 - 0.880)	0.791** (0.643 - 0.940)	0.731* (0.558 - 0.903)	0.816** (0.657 - 0.975)
High HOMA-IR	0.599	0.725*	0.715*	0.599
AUC (95% CI)	(0.425 - 0.774)	(0.553 - 0.897)	(0.530 - 0.900)	(0.425 - 0.774)
High CRP	0.587	0.587	0.605	0.580
AUC (95% CI)	(0.386 - 0.787)	(0.403 - 0.770)	(0.402 - 0.808)	(0.392 - 0.768)
2+ risk factors	0.750**	0.763**	0.681	0.737*
AUC (95% CI)	(0.613 - 0.887)	(0.618 - 0.909)	(0.518 - 0.844)	(0.594 - 0.881)

*p <0.05; **p <0.01

8.5 Discussion

The prevalence of the metabolic syndrome in this relatively young cohort of adults with CP was 22.6%. The prevalence of the metabolic syndrome in ambulatory adults with CP was similar to that reported in a population of Irish adults aged 50-69 years (21%)

(Villegas et al., 2004) and an American population age >20 years (21.8%) (Beltran-Sanchez et al., 2013). The prevalence of 28.6% reported in non-ambulatory adults with CP was significantly higher than prevalence reported in Irish and white American adults (Beltran-Sanchez et al., 2013; Villegas et al., 2004). As well as having higher clustered cardiometabolic risk, non-ambulatory adults had a higher prevalence of a number of individual risk factors compared to ambulatory adults. Worryingly, although 16 participants (29.1%) had elevated levels of total cholesterol, only 5 participants were on medication for dyslipidaemia. This highlights the need for screening programmes to monitor cardiometabolic risk among adults with CP.

A recent study investigated the prevalence of cardiovascular disease risk factors in a Dutch population of adults with CP (age 25-45 yr; mean age 36.6 yr) (Slot et al., 2013). Although the prevalence of hypertension in the Dutch cohort was higher than that in the current study (25.6%) the prevalence of elevated TC, hyperglycaemia, and low HDL-C was lower (7.0%, 0.0% and 11.6%, respectively). This is likely because the Dutch cohort was mildly affected compared to the current sample, with only two adults classified as non-ambulatory.

The prevalence of obesity, defined by BMI, was higher in both Dutch adults with CP (18.5%) and the general Irish adult population (25%) (Morgan et al., 2008) compared to the current sample. Despite a relatively low prevalence of obesity, the prevalence of elevated waist circumference in the current study was 36.4%. The relationship between obesity and CVD mortality is well-established (Poirier et al., 2006; Katzmarzyk et al., 2012; Dudina et al., 2011). The association between obesity and mortality is mediated through the effect of excess adiposity on blood pressure, blood lipids, insulin sensitivity, plasma glucose, and inflammatory markers (Dattilo and Kris-Etherton, 1992; Flechtner-Mors et al., 2000; Heilbronn et al., 2001). The findings of this study indicate that BMI, WC, WHR and WHtR are associated with cardiometabolic risk factors in adults with CP. This is in agreement with previous studies of the general population (Schneider et al., 2007; Can et al., 2009; Aekplakorn et al., 2006). Of the anthropometric measures examined in this study WC is the best relative predictor of cardiometabolic risk factors in adults with CP as indicated by ROC curve analysis. The finding that WC is a better predictor of cardiometabolic risk is supported by the finding that more than a fifth of the current sample had clustered cardiometabolic risk, despite a relatively low prevalence of obesity.

Although BMI has traditionally been used to define overweight/obesity, indicators of abdominal obesity (i.e. WC, WHtR and WHR) have been shown to be superior indicators of cardiometabolic risk factors in the general population (Wang et al., 2005; Despres and Lemieux, 2006; Ashwell et al., 2012; Snijder et al., 2003). It is likely that this is because central adiposity provides an indication of visceral adipose tissue (VAT). It is well recognised that CVD has an inflammatory component (Libby, 2002; Willerson and Ridker, 2004). The secretion of proinflammatory cytokines and adipokines from VAT contribute to insulin resistance, hypertension and dyslipidaemia (Despres et al., 2008), and may provide the link between central obesity and CVD. Imaging techniques such as magnetic resonance imaging, abdominal computed tomography, and dual energy x-ray absorptiometry provide accurate measurements of VAT but are expensive and often unfeasible to use in the clinical setting. The consistent association between WC and cardiometabolic risk factors in this study suggests that WC provides a proxy measure of VAT among adults with CP and can be used to identify those at risk of CVD and T2DM.

There has been some debate regarding the use of BMI as a predictor of CVD risk in adults with CP (Peterson et al., 2013, Rimmer et al., 2010). A previous study reported that BMI was not associated with cardiometabolic risk factors in adults with CP (Peterson et al., 2012); however insulin resistance was not one of the risk factors investigated. People with CP are known to have significant muscle atrophy (Lampe et al., 2006, Riad et al., 2012) and intramuscular adipose tissue infiltration (Johnson et al., 2009), which may result in adults with excess body fat being classified as normal weight according to BMI cut-off points. Despite this, BMI cut-off points are still used to report the prevalence of obesity among adults and children with CP (Slot et al., 2013, Rogozinski et al., 2007, Hurvitz et al., 2008). Although these studies highlight the significant problem of obesity among people with CP the extent of the problem may in fact be underestimated. The results of this study indicate that WC is a better predictor of hypertension, dyslipidaemia, and insulin resistance in adults with CP than BMI. Defining obesity according to WC may therefore provide a more accurate depiction of obesity-related cardiometabolic risk in adults with CP. Thresholds of 80 cm for women and 94 cm for men have been proposed for classifying abdominal obesity in able-bodied adults of European origin (Alberti et al., 2009). Further research is required to determine if these thresholds are appropriate for classifying abdominal obesity in adults with CP.

In agreement with previous research (Peterson et al., 2012b) WHR was associated with a number of cardiometabolic risk factors; however the relative predictive power of WHR was not as high as WC. It has been suggested that, compared to WC, WHR is a superior predictor of CVD risk in the general population because it includes a measure of HC. HC is inversely associated with hyperglycaemia, dyslipidaemia, diabetes, hypertension, CVD and death (Seidell et al., 2001, Seidell et al., 1997, Lissner et al., 2001, Okura et al., 2004, Heitmann et al., 2004). In this study the predictive power of WHR may have been influenced by the its association with gross motor function. This association was a result of the inverse relationship between HC and GMFCS - a not unexpected relationship considering the correlation of HC with gluteal muscle and total leg muscle mass (Seidell et al., 1989, Seidell et al., 1997), which atrophy in non-ambulatory adults (Wu and Bogie, 2013). As well as being influenced by gross motor function, WHR is more difficult to perform and a less reliable measure than WC in the general population (Kushi et al., 1988, Rimm et al., 1990). Difficulty with obtaining HC measurements from non-ambulatory participants or participants with significant contractures may increase the potential for error when measuring WHR in adults with CP. In contrast WC is a simple and feasible measure to take on ambulatory and non-ambulatory adults in a clinical setting.

8.5.1 Limitations

There are several limitations to this study. The number of adults with CP living in the Republic of Ireland is unknown and therefore it was not possible to calculate the proportion of adults who participated in the current study. It was also not possible to obtain information about the non-responders to this study and therefore not possible to compare characteristics between responders and non-responders. Limitations associated with sample size and sample characteristics are discussed in Chapter 7 section 7.5.1. As a result of the small sample size we were unable to adjust for sex when conducting ROC curve analysis. However, only WC and WHR are known to be associated with sex. Adjusting for sex would therefore likely improve the predictive power of these measures. It is unlikely that the order of outcomes would be any different.

8.6 Conclusions

The results of this study indicate that the prevalence of the metabolic syndrome in this relatively young cohort of adults with CP was similar to that in a population of older, able-bodied, adults. This has significant implications for their long-term health, and highlights the need for risk factor screening and preventive strategies from young adulthood.

WC provides an indicator of hypertension, dyslipidaemia and insulin resistance in adults with CP regardless of age, sex or gross motor functioning, above the information that is obtained from BMI. It therefore presents as a quick and easy clinical measure of cardiometabolic disease risk, which should be used instead of or in conjunction with BMI, when identifying adults with CP at risk of CVD and T2DM.

Chapter 9 Study 6: The relationship between physical activity, body composition and blood pressure in children with cerebral palsy

9.1 Introduction

Children with cerebral palsy (CP) participate in low levels of everyday physical activity compared to their typically developing (TD) peers (Carlon et al., 2012). In particular they accumulate less moderate and vigorous activity and spend more time in sedentary activities like sitting and lying (Capio et al., 2012, Martin et al., 2012). Physical inactivity is contributing to the growing epidemic of childhood obesity. Although children with CP were historically thought of as short and light for their age, the prevalence of obesity in this population has significantly increased in recent years. In 2003-2004 the prevalence of obesity was 16.5%, an increase of 7.7% over the previous decade (Rogozinski et al., 2007). In 2007 a prevalence of 18.2% was reported (Hurvitz et al., 2008). Perhaps counter intuitively the prevalence of obesity was highest among ambulatory children with minimal impairments (22.7%) who would be expected to be more active than non-ambulatory children (Hurvitz et al., 2008). Moderate-to-vigorous physical activity (MVPA), particularly sustained bouts of MVPA, are required to prevent weight gain in children (Dorsey et al., 2011, Trost et al., 2001, Ness et al., 2007). The motor impairments associated with CP, including muscle weakness, poor selective motor control, spasticity and decreased balance (Rose and McGill, 2005, Stackhouse et al., 2005, Ostensjo et al., 2004), may prevent children from accumulating habitual physical activity of this intensity.

The epidemic of overweight and obesity in TD children is contributing to the increased number of children with high blood pressure values (Thompson et al., 2007). The prevalence of hypertension in children and adolescents ranges from 2% to 5% (Shay et al., 2013, McNiece et al., 2007, Acosta et al., 2012), and increases progressively with body mass index (BMI) (Sorof et al., 2004). The prevalence of 'pre-hypertension', a classification created to identify those at greater risk of developing hypertension, ranges from 12% to 20% (McNiece et al., 2007, Shay et al., 2013, Zhu et al., 2007). Elevated

blood pressure in childhood is associated with the development of atherosclerosis (Berenson et al., 1998, Mahoney et al., 1996), particularly when combined with childhood obesity (Raitakari et al., 2003). Children who retain high blood pressure from childhood to adulthood are also more likely to have adult type II diabetes mellitus (T2DM) (Morrison et al., 2012). Physical activity is a primary therapeutic intervention for the prevention and treatment of obesity and hypertension in childhood (National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents, 2004).

9.2 Objective

The aim of this study was three-fold. Firstly the aim was to investigate the prevalence of obesity and hypertension among a cohort of ambulatory children with CP. The second aim was to investigate the number of children meeting current physical activity guidelines of 60 min of moderate-to-vigorous activity per day. The third aim of this study was to investigate the association between physical activity, obesity and blood pressure in children with CP.

9.3 Methods

9.3.1 Participants

Ambulatory children with CP were recruited for this study from eight centres throughout the Republic of Ireland that provide services for adults and children with disabilities. The centres were as follows: the Central Remedial Clinic (CRC), Clontarf; CRC, Scoil Mochua; Enable Ireland, Cork; Enable Ireland, Kerry; Enable Ireland, Bray; Enable Ireland, Sandymount; Enable Ireland, Kildare; Enable Ireland, Tallaght.

Children were age 6 to 17 years and classified as level I, II or III on the Gross Motor Function Classification System (GMFCS) [6] (see section 1.1.1.1). Children were also classified according to the classification system from the Surveillance of Cerebral Palsy in Europe (see section 1.1.1.1) (Rosenbaum et al., 2007), in which the dominant type of tone or movement abnormality associated with CP is categorised as spastic, dystonic,

choreoathetoid, or ataxic; spastic CP is further classified as unilateral or bilateral. Exclusion criteria for this study were pregnancy, a severe intellectual disability, or having undergone surgery in the previous six months. Physiotherapists in Enable Ireland centres provided suitable children and their guardians with participant information leaflets (PILs). The database of the CRC, Clontarf and Scoil Mochua, was searched to identify children who met the inclusion/exclusion criteria. This resulted in 227 children; letters and PILs were sent to these children and their guardians. Ethical approval for this study was granted by the Faculty of Health Sciences' ethics committee, the CRC's ethics committee, and the Enable Ireland Research Ethics and Quality Committee.

9.3.2 Measurements

9.3.2.1 Body composition

Standing height was measured using a portable stadiometer (Invicta Plastics Ltd., Leicester, England). Participants were asked to stand upright without shoes, with their heels together and their head in the Frankfurt Plane (i.e. an imaginary horizontal line running between the ear hole and the lower border of the eye). Height was read at the end of a gentle inspiration to the nearest 0.1 cm. Body mass was measured to the nearest 0.1 kg in bare feet and light clothing using an electronic platform scale (SECA 635). BMI was calculated as $kg.m^{-2}$. Height was expressed as standard deviation scores (zHeight) using the 1990 British Growth References (Cole et al., 1998). BMI was expressed as standard deviation scores using the IOTF growth charts (Cole et al., 2000). Overweight and obesity were defined according to IOTF criteria.

Waist circumference (WC) was measured on bare skin, to the nearest 0.1 cm, midway between the lower rib margin and the iliac crest at the end of gentle expiration. The measurement was taken with the subject standing erect with arms hanging loosely from the body. The measurement was taken two times and the mean of the two measurements was used in data analysis. Waist-height ratio (WHtR) was calculated by dividing waist circumference by height.

9.3.2.2 Blood pressure

Blood pressure was measured from the right arm or the least affected side, in the case of significant asymmetry, using the Omron 705 IT BP monitor. The Omron 705 IT has been validated as an accurate device for blood pressure measurement in children and

adolescents (Stergiou et al., 2006). Participants rested in a seated position with their back supported for at least five minutes prior to the measurement being taken, as recommended by the 2012 Canadian Hypertension Education Program (Daskalopoulou et al., 2012). The appropriate cuff size was selected for the participant based on their arm circumference. Cuff sizes were 17-22 cm, 22-32 cm, and 32-42 cm. The cuff was placed so that the lower edge was 3cm above the elbow crease and the bladder was centred over the brachial artery. The measurement was taken with the participant's legs uncrossed, and their arm bare and supported with the cuff at heart level. Participants were asked not to talk while the measurement was being taken. Up to four attempts were made to collect three measurements at a 1-2 min interval. The average of the last two measurements was used in data analysis. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were expressed as standard deviation scores (zSBP and zDBP, respectively) developed from data collected in nearly 23, 000 British children and young people (Jackson et al., 2007). Children with SBP or DBP above the 98th centile were classified as hypertensive and children with SBP or DBP between the 91st and 98th centiles were classified as 'pre-hypertensive'.

9.3.2.3 Physical activity

Participants' everyday physical activity levels were measured with the RT3 accelerometer (Stayhealthy Inc). The RT3 has been described in detail in section 3.3.1.1. All participants were asked to wear the RT3 for 7 days on their right hip (or least affected side in the case of significant asymmetry) in the midaxillary line. Participants were told to wear the RT3 for waking hours and only to remove it for bathing and swimming. Participants were asked to record the times that they removed the monitor and the activities they completed while not wearing the monitor. Vector magnitude count data were collected in 1-min epochs.

Valid activity data were defined as having at least four days data, of at least 10 hours wear time per day (Ward et al., 2005). Sedentary activity was defined as <41 counts.min^{-1}, light activity (LPA) was defined as 41-950 counts.min^{-1}, moderate activity (MPA) was defined as 950-3410 counts.min^{-1}, vigorous activity (VPA) was defined as >3410 counts.min^{-1} (Vanhelst et al., 2010a). Data are presented as time spent in LPA, MPA, VPA, and moderate-to-vigorous activity (MVPA) accumulated in 1-min bouts. Time spent in MVPA accumulated in 10-min bouts is also presented. One minute of activity below

the moderate activity count threshold was allowed for before the bout was considered to be ended. Percentage time spent in sedentary activity (i.e. minutes spent in sedentary activity/total wear time) and mean activity counts.min^{-1} are also presented. Finally the percentage of children meeting the guideline of 60 min of MVPA activity per day was calculated (WHO, 2010).

9.3.2.4 Procedures

Testing took place at the sites named in section 9.1.1. Participants and their guardians were informed of the testing procedures before written consent was obtained from guardians and written assent was obtained from children. Following a period of rest in a seated position participants' blood pressure was measured. Body mass, height, and WC were measured. Participants were then provided with the RT3 and written and verbal instructions on how to use it. Participants were also provided with a stamped addressed envelope to return the monitor to the researcher.

9.3.3 Data Analysis

The distribution of the data was checked for normality using the Kolmogorv-Smirnov test. Age, WC, WHtR, MPA, VPA, mean counts.min^{-1}, MVPA (1-min bouts) and MVPA (10-min bouts) were non-normally distributed. MPA, VPA, counts.min^{-1}, MVPA (1-min bouts) and MVPA (10-min bouts) were subsequently square-root transformed. Means and standard deviations (SD) are presented for each continuous variable with a normal distribution. Medians and interquartile ranges (IQR) are presented for continuous variables with a skewed distribution. Prevalence data are presented as percentages. One-way analysis of variance tests, with post-hoc LSD tests, were used to determine differences in normally distributed continuous variables across GMFCS levels. Kruskal-Wallis one-way analysis of variance was used to investigate differences across GMFCS level for continuous variables with a skewed distribution. Independent t-tests were used to investigate sex differences between normally distributed continuous variables. Sex differences between continuous variables with a skewed distribution were determined by Mann-Whitney U tests. Pearson's χ^2 test was used for comparison of the prevalence rates.

Bivariate correlation coefficients (Spearman's rho) were calculated to investigate the association between age and zBMI, WC, WHtR, zSBP, zDBP, and each physical activity

component. Three primary multiple linear regression analysis were used to investigate the association between blood pressure, markers of total and central adiposity, and physical activity outcomes controlling for age, sex, and GMFCS level. The first analysis examined the association between blood pressure (zSBP and zDBP) and markers of body fat. Each marker of body fat was examined in a different regression model. The second analysis investigated the association between blood pressure and physical activity outcomes. The third analysis investigated the association between markers of body fat (zBMI, WC, WHtR) and physical activity outcomes. Each physical activity outcome was examined in a different regression model. Finally, logistic regression was used to examine the relationship between each physical activity parameter and elevated blood pressure (i.e. pre-hypertension or hypertension). Statistical significance was set at $p < 0.05$. Analyses were performed using SPSS, version 19.

9.4 Results

Blood pressure was not obtained from four children (one child in GMFCS level I and three children in GMFCS level III). WC, and hence WHtR, was not obtained from 2 children (both level III in the GMFCS). Participants' characteristics (n = 90) are presented across GMFCS level (Table 9.1). There was no difference in age across GMFCS level. Children in level I of the GMFCS were significantly taller than children in level III ($p < 0.001$). Table 9.2 presents participants' zBMI, WC, WHtR, zSBP and zDBP. In GMFCS level I, boys had a higher zSBP than girls ($p < 0.05$); there were no other sex differences within GMFCS levels. Across GMFCS level, girls in level II had a smaller WHtR and zBMI than girls in level I ($p < 0.05$ for both), and a smaller WHtR than girls in level III ($p < 0.05$). Fourteen children (15.5%) were classified as overweight. A further three children (3.3%) were classified as obese (two in GMFCS level I and one in level II). All children with obesity were male. Eleven children (19.3%), 3 children (21.4%), and 3 children (15.8%) were classified as overweight/obese in GMFCS level I, II and III, respectively; there was no significant difference in the prevalence of overweight/obesity across GMFCS level ($\chi^2 = 1.84$, $p = 0.912$). Six girls (18.2%) and 11 boys (19.3%) were classified as overweight/obese; there was no difference in overweight/obesity across sex ($\chi^2 = 0.017$, $p = 0.896$). Nine children (10.5%) were classified as hypertensive and 10 children (11.6%) were classified as pre-hypertensive. The nine children with hypertension and six

of the children with pre-hypertension were in GMFCS level I. Among children classified as overweight/obese, 6 children (35.2%) were pre-hypertensive or hypertensive.

Valid activity data were collected on 73 children. There was no difference in age, zBMI, WC, WHtR, zSBP or zDBP between children with and without activity data. Approximately 75% of children met the guideline of 60 minutes of MVPA per day. This declined across GMFCS level with 88%, 55%, and 47% of children in level I, II and III, respectively, meeting the guideline ($\chi^2 = 12.600$, $p < 0.01$). One-way analysis of variance revealed there was a significant difference in time spent in sedentary activity, MPA, VPA, MVPA, MVPA (10-min bouts) and total activity (mean counts.min^{-1}) across GMFCS level (Table 9.3). Children in level I spent more time in MPA, VPA, MVPA, MVPA (10-min bouts) total activity and less time in sedentary activity than children in level III ($p < 0.01$ for all). Children in level I also spent more time in MVPA (10-min bouts) than children in level II ($p < 0.05$).

Table 9.1 Characteristics of participants across levels of the Gross Motor Function Classification System. Data presented as mean (SD) unless otherwise stated

	All	GMFCS I	GMFCS II	GMFCS III
N	90	57	14	19
Age, yr	10.0 (6.0)†	10.0 (6.0)†	10.1 (2.9)	11.8 (4.0)
zHeight	-0.30 (1.28)	0.04 (1.10)	-0.42 (1.44)	-1.21 (1.25)
Males:females	57:33	38:19	9:5	10:9
Classification of CP, n (%)				
Spastic unilateral	48 (53.3)	42 (73.7)	5 (35.7)	1 (5.3)
Spastic bilateral	39 (43.3)	14 (24.6)	8 (57.1)	17 (89.5)
Non-spastic	3 (3.3)	1 (1.8)	1 (7.1)	1 (5.3)

†data not normally distributed, median (IQR) presented

Age was positively correlated with WC (0.625, $p < 0.01$) and zDBP ($r = 0.261$, $p < 0.05$). Age was negatively correlated with LPA ($r = -0.266$, $p < 0.05$) MPA ($r = -0.445$, $p < 0.01$), MVPA ($r = -0.398$, $p < 0.01$), counts.min^{-1} ($r = -0.422$, $p < 0.01$), and positively correlated with sedentary activity ($r = 0.532$, $p < 0.01$).

When age, sex and GMFCS were controlled for zSBP, but not zDBP, was positively associated with zBMI ($\beta = 0.249$, $p < 0.05$; R square change = 0.059) and WC ($\beta = 0.324$, $p < 0.05$; R square change = 0.062). Figure 9.1 shows the relationship between zSBP and

WC, and between zSBP and zBMI. There was no association between zSBP, zDBP and any physical activity outcome. Similarly, there was no association between any measure of body fat and any physical activity parameter. Logistic regression revealed that the likelihood of hypertension increased with decreasing time in MVPA, VPA and total activity, and increasing time in sedentary activity ($p < 0.05$ for all) (Table 9.4).

Table 9.2 Participants' physical characteristics across Gross Motor Classification System (GMFCS) level. Data presented as mean (SD) unless stated otherwise

		N	zBMI	WC	WHtR	zSBP	zDBP
GMFCS level I	Male	38[a]	0.33 (1.20)	66.8 (10.5)	0.45 (0.06)	-0.14 (1.23)	0.98 (1.40)
	Female	19	0.43 (0.95)	63.5 (10.2)	0.44 (0.05)	-0.82 (0.99)	0.40 (1.38)
	All	57	0.36 (1.11)	65.7 (10.4)	0.44 (0.07)†	-0.37 (1.19)	0.78 (1.41)
GMFCS level II	Male	9	0.54 (1.35)	61.4 (9.5)	0.44 (0.06)	-0.73 (0.82)	0.74 (0.58)
	Female	5	-0.87 (0.99)	54.5 (2.0)	0.39 (0.03)	-0.86 (1.41)	0.74 (0.51)
	All	14	0.03 (1.38)	59.0 (8.3)	0.41 (0.06)†	-0.78 (1.02)	0.74 (0.53)
GMFCS level III	Male	10[b]	0.31 (0.79)	64.9 (8.2)	0.45 (0.03)	-0.73 (0.51)	0.48 (0.57)
	Female	9[c]	0.22 (1.04)	60.6 (7.6)	0.46 (0.03)	-1.42 (0.86)	0.89 (0.88)
	All	19	0.27 (0.89)	63.1 (8.0)	0.45 (0.03)	-1.04 (0.75)	0.66 (0.73)

[a]one value missing from zSBP and zDBP; [b]one value missing from zSBP and zDBP; [c] two values missing from zSBP, zDBP, WC and WHtR.

†data not normally distributed, presented as median (IQR).

zBMI, z-scores for BMI; WC, waist circumference; WHtR, waist-height ratio; zSBP, z-scores for systolic blood pressure; zDBP, z-scores for diastolic blood pressure.

Table 9.3 Physical activity outcomes across levels of the Gross Motor Function Classification System (GMFCS). Data presented as mean (SD) unless stated otherwise

	n	Sedentary Activity (%)	Light Activity (min)	Moderate Activity (min)	Vigorous Activity (min)	Mod-to-vig Activity (min)	Mod-to-vig activity (10-min bouts) (min)	Mean Counts.min^{-1}
GMFCS level I	49	31.7 (12.2)	410.4 (69.1)	94.0 (4.8)	7.5 (2.3)	102.8 (5.8)	37.2 (6.7)	431.1 (15.7)
GMFCS level II	9	37.2 (11.9)	404.6 (69.4)	63.4 (6.9)	3.0 (4.0)	68.0 (9.1)	15.0 (10.1)	321.6 (14.8)†
GMFCS level III	15	42.3 (15.8)	390.2 (110.3)†	56.5 (9.2)	2.2 (1.4)	59.5 (9.8)	13.4 (7.3)	284.5 (24.0)
p value		0.022	0.197	0.005	0.013	0.005	0.003	0.006

†skewed distribution, data presented as median, (IQR).

Mod, moderate; Vig, vigorous

Table 9.4 Odds ratios (OR) and 95% confidence intervals (CI) for physical activity outcomes in hypertensive children

Independent variable (normotensive vs. hypertensive)	OR	95% CI	*P*-value
Sedentary activity	1.066	1.001-1.135	0.047
Light activity	0.999	0.990-1.007	0.739
Moderate activity	0.678	0.460-0.999	0.050
Vigorous activity	0.606	0.372-0.986	0.044
Moderate-to-vigorous activity	0.701	0.494-0.994	0.046
Moderate-to-vigorous activity (10-min bouts)	0.771	0.579-1.026	0.075
Mean counts.min^{-1}	0.758	0.602-0.955	0.019

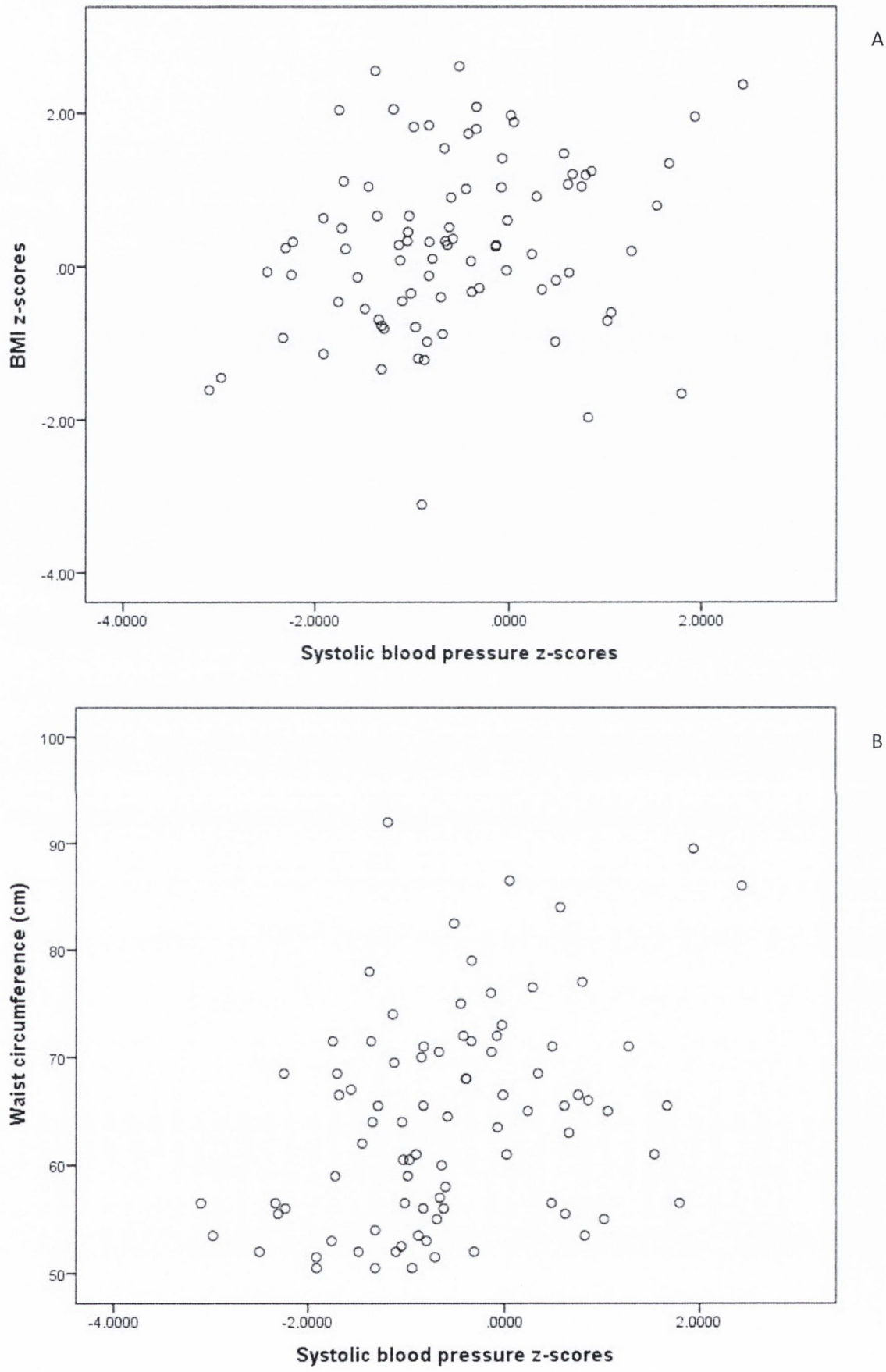


Figure 9.1 Correlation between a) BMI and systolic blood pressure, and b) waist circumference and systolic blood pressure

9.5 Discussion

This is the first study to demonstrate that anthropometric measures of total and central adiposity are positively associated with blood pressure in children and adolescents with CP. This is consistent with findings in TD children (Schiel et al., 2006; Ruiz et al., 2007; Rosner et al., 2000; Bluher et al., 2013). In addition, elevated blood pressure in children and adolescents with CP is associated with decreased time spent in MVPA, VPA, and total activity, and increased time spent in sedentary activity. Increasing physical activity and decreasing sedentary activity should therefore be a primary aim of rehabilitation in order to prevent children with CP developing elevated blood pressure.

The prevalence of overweight/obesity in the current study was 18.9%. In agreement with previous research (Rogozinski et al., 2007; Hurvitz et al., 2008) overweight/obesity was highest among children with minimal impairments (19.3% in GMFCS level I and 21.4% in GMFCS level II). This was lower, however, than the prevalence reported among a cohort of US children with CP (29.1%) (Hurvitz et al., 2008) and lower than that reported among TD children in the Republic of Ireland (23% and 28% among boys and girls, respectively) (Whelton et al., 2007). A convenience sample was recruited for this study and it is possible that participants were healthier than the general population of children with CP as they had to volunteer to have their body composition and physical activity measured.

Despite the relatively low prevalence of overweight/obesity, 10% of children had elevated blood pressure. This is higher than recent reports in TD children, with values ranging from 2.9% to 4.9% in Irish and American children and adolescents (Kilbride et al., 2013; Shay et al., 2013). A significant proportion of children with overweight/obesity had elevated blood pressure. The prevalence rate of elevated blood pressure among these children (35.2%) was similar to the prevalence of hypertension reported in TD children with obesity (25% to 51%) (Finucane et al., 2008; Genovesi et al., 2008; Sorof et al., 2002). Although this suggests that classification of weight status into normal-weight or overweight/obese may be clinically useful for identifying children at increased risk of obesity hypertension, the prevalence of hypertension is known to increase across the entire range of BMI values (Rosner et al., 2000; Sorof et al., 2002). A simple threshold may not be adequate to define risk of hypertension among children. Furthermore, the

results of this study indicate that BMI may not be the best anthropometric indicator of elevated blood pressure in children with CP.

The use of BMI cut-offs to define overweight/obesity is limited by its inability to distinguish between people with excessive adiposity and those with large muscle mass. BMI is a poor predictor of body fat in children with CP (Kuperminc et al., 2010), possibly because it does not recognise that children with CP have reduced muscle volumes compared to age-matched able-bodied peers (Lampe et al., 2006). Applying BMI cut-off points developed in the general population to children with CP may result in incorrect classification of children with excess body fat as 'normal' weight. Normal-weight obesity (i.e. a normal body weight according to BMI but a high body fat percentage) is prevalent among the general population and is associated with cardiometabolic dysregulation, a high prevalence of the metabolic syndrome, and an increased risk of CVD mortality (Romero-Corral et al., 2010).

In the current study, a stronger association was observed between systolic blood pressure and WC, compared to BMI. In Chapter 8, WC was also found to be more strongly associated with cardiometabolic risk in adults with CP. WC provides an indicator of visceral adipose tissue (Taylor et al., 2000), which is associated with increased cardiometabolic risk in children (Taylor and Hergenroeder, 2011, Lee et al., 2006). Classifying obesity among children with CP according to WC thresholds may provide a more accurate indicator of those at risk of cardiometabolic disease compared to BMI. However, the clinical utility of WC is currently limited by the lack of consensus regarding what threshold should be used to classify central obesity in children. It has been suggested that WHtR ≥0.50 is a clinically useful threshold of identifying TD children of a normal-weight who have increased cardiometabolic risk (Mokha et al., 2010). However, the results of this study and others (Sijtsma et al., 2013, Bluher et al., 2013) indicate that WHtR is not superior to WC or BMI in predicting blood pressure in TD children or children with CP.

Not unexpectedly, a linear relationship between physical activity and systolic blood pressure or diastolic blood pressure was not found in the current study. Studies investigating the association between objectively measured physical activity and blood pressure in TD children have found inconsistent results (Andersen et al., 2006, Gaya, 2009). This is likely because the relationship between blood pressure and physical

activity appears to be non-linear (Mark and Janssen, 2008). There is significant evidence that physical activity has a greater effect on blood pressure values in the high risk range (Mark and Janssen, 2008). This also appears to be the case in children and adolescents with CP. The non-linear relationship observed among children with CP may also be due to the method used to measure physical activity. As a single cut-off point was used to classify physical activity in all children the accuracy of physical activity classification may have differed across GMFCS levels. Discrepancies in the accuracy of physical activity measurement among children could explain why a linear relationship between physical activity and blood pressure was not observed.

A study of the dose-response relationship between blood pressure and physical activity in TD children reported that both total activity and MVPA were associated with elevated blood pressure values (Mark and Janssen, 2008); however considerably fewer minutes were required in MVPA than total physical activity to reduce the likelihood of hypertension. Unlike the current study, the independent association between VPA, MPA and blood pressure was not investigated. The results of the current study indicate that although total activity, moderate-to-vigorous activity, and vigorous activity alone were negatively associated with elevated blood pressure moderate activity alone was not. This finding is in agreement research in TD children that suggests that VPA, but not MPA, is associated with lower cardiometabolic risk in children (Hay et al., 2012, Ried-Larsen et al., 2013). It is possible that VPA is acting on blood pressure through its effect on body fat. Unlike the current study, studies of TD children have found an association between VPA and body fat, above that of MPA (Dencker et al., 2008, Hussey et al., 2007, Dorsey et al., 2011). It is possible that an association between physical activity and anthropometric measures was not observed in the current study because of the small number of children with overweight/obesity who had valid activity data (n=12), and the heterogeneity of the sample. Age, sex, and GMFCS level are known to affect physical activity volume and intensity (Hussey et al., 2007, Trost et al., 2002, Stevens et al., 2010, Maher et al., 2007). As a result of the relatively small sample size, these factors may have masked the association between physical activity and obesity.

A strength of this study was the use of an accelerometer to measure physical activity. This provides empirically relevant data that allows for comparison with national guidelines and with data collected in population based-studies such as the National Health and Nutrition Examination Survey. Only one study has used an accelerometer to

measure physical activity in children with CP to date however (Capio et al., 2012), which makes it difficult to directly compare these findings the results of other studies. In agreement with previous research in children and adolescents with CP, total physical activity declined with age (Maher et al., 2007, Stevens et al., 2010), and sedentary activity increased with age (Stevens et al., 2010). This is the first study however, to demonstrate that VPA was not independently associated with age. This may explain why BMI was not positively associated with age despite the negative association between total activity and age.

This is the first time information about the number of children with CP meeting the physical activity guideline of 60 minutes of MVPA daily has been provided. Although 77% of children met the guideline, this is smaller than the 90% of TD adolescents who met the guideline when physical activity was measured by the same method (Denton et al., 2013). The mean time spent in moderate activity was also less than that reported for TD children (boys 114.3 min and girls 96.6 min) when physical activity was measured by the same method. The fact that even the most sedentary children spend 30-40 min in MVPA when measured with accelerometry (Andersen et al., 2006) is accounted for in recent WHO guidelines that recommend that children obtain 60 minutes of MVPA daily on top of their activities of daily living (WHO, 2010). This recommendation has yet to be adopted as national guidelines. However it is probably a more suitable guideline given that clustered cardiovascular risk is raised in children who accumulate less than 90 minutes of MVPA per day (Andersen et al., 2006). Of concern, children in level II and III only accumulated 68 and 60 min, respectively, of MVPA per day. Despite this, the prevalence of hypertension was higher among children in level I who accumulated more MVPA. This finding is difficult to explain. It may be because the smaller proportion of participants in levels II and III, compared to level I, resulted in a biased sample. It is also possible that, as discussed in Chapter 6, using a single set of cut-off points to classify physical activity intensity among all children with CP resulted in an underestimation of physical activity intensity among children in level III, who use significantly more energy to walk at a given speed compared to children in level I and II (Kerr et al., 2008). Development of specific cut-off points according to GMFCS level may improve physical activity classification in this population.

9.5.1 Limitations

There are a number of limitations to this study that require discussion. As mentioned in section 9.5 valid activity data were obtained on a relatively small number of participants with overweight/obesity. Also, a large proportion of children were in level I of the GMFCS, compared to level II or III, which limits the ability to compare results across GMFCS level. In addition the cut-points applied to activity data to define sedentary, light, moderate and vigorous activity were calibrated on TD children. They may therefore underestimate the intensity of activity performed by children with CP, particularly children in GMFCS level III, who use greater energy during walking compared to TD children and to children in level II and III (Brehm et al., 2007).Finally, although this study found a high prevalence of children with blood pressure values in the hypertensive range it cannot be diagnosed as hypertension without elevated readings on at least three occasions. The presence of elevated blood pressure is known to decrease between the first and third readings (Sorof et al., 2004). However, when blood pressure was assessed on one occasion in TD Irish children the prevalence of elevated blood pressure was lower than that in the current study (4.9%) despite more children being classified as overweight/obese (28%).

9.5.2 Conclusion

In conclusion, total and central adiposity are associated with systolic blood pressure in children with CP. Although decreased time in total physical activity and MVPA are associated with elevated blood pressure in children with CP, the strongest association was observed for VPA alone. This has significant implications for exercise prescription in children with CP and suggests that healthcare professionals should be promoting participation in vigorous activities, such as sport, rather than participation in moderate activities, such as play, in this population.

Chapter 10 Study 7: The relationship between physical activity and cardiorespiratory fitness in children with cerebral palsy.

10.1 Introduction

It is well reported that children with cerebral palsy (CP) participate in reduced levels of everyday physical activity compared to their typically developing (TD) peers (Carlon et al., 2012; Maher et al., 2007; Zwier et al., 2010). Physical inactivity can lead to deconditioning and is likely responsible for the low levels of cardiorespiratory fitness evident in this population (Unnithan et al., 1998; Verschuren and Takken, 2010; Hoofwijk, 1995). In 2003 the American Physical Therapy Association's Section on Pediatrics and its Research committee highlighted the critical need to identify and promote effective interventions to improve cardiorespiratory fitness in children with CP (Fowler et al., 2007). Cardiorespiratory fitness plays an important role in daily physical functioning in adults and children with CP. Reduced cardiorespiratory fitness, in combination with the increased cost of locomotion associated with CP, increases the physical strain of comfortable walking in children with CP (Dallmeijer and Brehm, 2011). Adults with CP cite poor endurance as a reason for deterioration in walking function and premature loss of mobility (Opheim et al., 2009). In addition, there is substantial evidence that low cardiorespiratory fitness in childhood is associated with obesity, hypertension, dyslipidaemia, insulin resistance and the metabolic syndrome (Andersen et al., 2011a; Janssen and Cramp, 2007; Klasson-Heggebo et al., 2006; Brage et al., 2004).

Cardiorespiratory fitness has been shown to track between childhood and young adulthood (Campbell et al., 2001). It is therefore vital that intervention to improve fitness occurs in childhood. There is evidence that aerobic exercise interventions can improve cardiorespiratory fitness in children with CP (Butler et al., 2010, Verschuren et al., 2007). This does not carryover to habitual levels of physical activity however, and as a result, decreases in cardiorespiratory fitness are observed at follow-up assessment (Verschuren et al., 2007; van den Berg-Emons et al., 1998). More information is required about the association between habitual physical activity and cardiorespiratory fitness in children with CP in order to guide clinicians about the volume and intensity of physical activity that they should be promoting.

Vigorous physical activity is more strongly associated with cardiorespiratory fitness in TD children, compared to moderate activity (Denton et al., 2013; Dencker and Andersen, 2011; Hussey et al.,

2007). The motor impairments associated with CP, including muscle weakness, poor selective motor control, spasticity and decreased balance (Rose and McGill, 2005; Stackhouse et al., 2005; Ostensjo et al., 2004), may however prevent children accumulating habitual activity of an adequate intensity to improve cardiorespiratory fitness. Increased sedentary behaviour, such as time spent sitting or lying, has recently been identified as a possible contributor to low cardiorespiratory fitness in children, independent of moderate-to-vigorous physical activity (Santos et al., 2013; Sandercock and Ogunleye, 2013; Sandercock and Ogunleye, 2012). Sedentary behaviour is higher among children with CP compared to TD children (Stevens et al., 2010; Mc Manus et al., 2008) and increases with age, disproportionately to the increase observed in TD adolescents (Stevens et al., 2010). Intervention to reduce sedentary behaviour may therefore be a feasible and effective method of improving cardiorespiratory fitness in children with CP.

10.2 Objective

The first aim of this study was to investigate the association between cardiorespiratory fitness, blood pressure and body fat in children with CP. The second aim of this study was to determine the intensity of habitual physical activity (i.e sedentary, light, moderate or vigorous) that is associated with cardiorespiratory fitness in children with CP.

10.3 Methods

10.3.1 Participants

The method used to recruit for Study 6 was described in Chapter 9 section 9.3.1. Only children in level I and II of the GMFCS are included in study 7 because, at present, there is no valid field test of cardiorespiratory fitness in children classified as level III.

10.3.2 Measurements

10.3.2.1 Body composition

The methods used to measure body composition are described in Chapter 9 section 9.3.2.1.

10.3.2.2 Blood pressure

The method used to measure blood pressure is described in Chapter 9, section 9.3.2.2.

10.3.2.3 Cardiorespiratory fitness

Cardiorespiratory fitness was reflected by the level achieved on the 10 m shuttle run test (SRT) (Verschuren et al., 2006). This test is described fully in Appendix XI. A 10 m walkway was marked out in a quiet area. Children were asked to walk between the two markers at a set incremental speed determined by a signal. The test starts at a speed of 5 $km.h^{-1}$ for children classified in GMFCS level I, and at 2 $km.h^{-1}$ for children in GMFCS level II. The speed increases by 0.25 $km.h^{-1}$ every minute. Heart-rate was monitored throughout the test using a polar heart rate monitor. The criteria for a valid test were a maximal heart-rate ≥180 bpm plus a subjective indication of fatigue such as shortness of breath or unwillingness to continue. The psychometric properties of this test were presented in section 2.2.3.

10.3.2.4 Physical activity

Physical activity was measured using the RT3 accelerometer. The procedures used to collect and define activity data are described in Chapter 9 section 9.1.2.3.

10.3.2.5 Procedures

The procedure used in study 7 is outlined in Chapter 9 section 9.1.2.4. In addition, cardiorespiratory fitness was measured using the 10 m SRT.

10.3.3 Data Analysis

The distribution of the data was checked for normality by the Kolmogorov-Smirnov test. Age, waist circumference (WC), waist-height ratio (WHtR), moderate physical activity (MPA), vigorous physical activity (VPA), moderate-to-vigorous activity in 10-min bouts (MVPA), and mean $counts.min^{-1}$ were non-normally distributed. Age was log transformed. MPA, VPA, MVPA and mean $counts.min^{-1}$ were square-root transformed for the main analyses. Mean and standard deviations (SD) are presented for normally distributed continuous data. Median and interquartile ranges (IQR) are presented for non-normally distributed continuous variables. Independent t-tests were used to assess differences across sex for age, z-scores for height (zHeight), z-scores for BMI (zBMI), z-scores for systolic blood pressure (zSBP), z-scores for diastolic blood pressure (zDBP), light physical activity, MPA, MVPA VPA, $counts.min^{-1}$, percentage sedentary time and cardiorespiratory fitness. Mann-Whitney U test was used to assess sex differences for WC and WHtR. Bivariate correlation coefficients were calculated to assess correlations between cardiorespiratory fitness and age, zHeight, WC, WHtR, zBMI, zSBP and zDBP.

Multiple regression analysis was used to investigate the association between cardiorespiratory fitness and markers of total and central adiposity, when controlling for age, sex, and GMFCS level. Each marker of body fat was examined in a different regression model. Multiple regression analysis was also performed to determine the association between cardiorespiratory fitness and blood pressure (zSBP and zDBP), after controlling for age, sex and GMFCS level. Follow-up regression analyses were performed to examine whether the association was independent of body fat by additionally controlling for BMI, WC and WHtR in separate analyses. A final linear regression analysis was performed to examine the association between cardiorespiratory fitness and physical activity outcomes. Each physical activity outcome was examined in a different regression model. Children were then stratified into tertiles according to their degree of cardiorespiratory fitness using reference centile curves for the 10-m SRT based on sex, GMFCS level, and height (Verschuren et al., 2010a). A one-way analysis of variance was used to compare zBMI, WC, WHtR, zSBP, zDBP and physical activity components across tertiles, with LSD post-hoc tests as appropriate. The level of significance was set at $p < 0.05$. Analyses were performed using SPSS, version 19.

10.4 Results

Seventy-one children were recruited for this study. Four children were removed from analysis as they did not reach a maximal heart-rate ≥180 bpm during the SRT. Physical activity data were not obtained on twelve children; four children did not meet the criteria for valid wear-time; eight children returned monitors without any data because of interference with the monitor or battery malfunction. This resulted in a total sample size of $n = 55$.

Descriptive statistics are presented in Table 10.1. No significant sex differences were found for age, zHeight, zBMI, WC, WHtR, zDBP, LPA, MPA, VPA, MVPA, percentage sedentary time, counts.min^{-1} and cardiorespiratory fitness. zSBP was significantly higher in males than females ($p < 0.05$).

Table 10.1 Characteristics of participants (n=55)

Males:females	34:21
Age, y:mo, mean (SD)	11:1 (0.1)
zHeight, cm, mean (SD)	-0.01 (1.21)
zBMI, mean (SD)	0.25 (1.16)
Waist circumference, cm, median (IQR)	65.0 (15.0)
Waist-height ratio, median (IQR)	0.43 (0.07)
zSBP, mean (SD)	-0.37 (1.21)
zDBP, mean (SD)	0.84 (1.33)
GMFCS level, n (%)	
Level I	45 (81.8)
Level II	9 (16.4)
Classification of cerebral palsy, n (%)	
Spastic unilateral	38 (69.1)
Spastic bilateral	15 (27.3)
Non-spastic	2 (3.6)

zBMI, z-scores for BMI; zSBP, z-scores for systolic blood pressure; zDBP, z-scores for diastolic blood pressure; GMFCS, Gross Motor Function Classification System

The mean (SD) level achieved on the SRT test was 9.0 (4.0) min. According to reference centile curves 8 children (14.5%), 24 children (43.6%), and 23 children (41.5%) were categorized as low, middle and high fitness, respectively. Percentage time spent in sedentary behaviour, time spent in each component of physical activity, and mean counts.min^{-1}, for the total sample and across fitness tertiles are presented in Table 10.2.

Table 10.2 Percentage time spent in sedentary behavior, time spent in each component of physical activity, and mean counts.min-1 across cardiorespiratory fitness tertiles. Data presented as mean (SD).

Cardiorespiratory fitness tertile	Percentage sedentary time (%)	LPA (min)	MPA (min)	VPA (min)	MVPA (min)	Mean counts.min^{-1}
Low	29.0 (7.7)	420.2 (33.9)	88.3 (4.3)	4.2 (1.0)	24.2 (4.4)	407.9 (12.8)
Middle	33.6 (12.8)	407.2 (65.3)	83.7 (5.7)	4.9 (2.2)*	28.0 (6.7)	383.1 (16.8)
High	32.8 (12.2)	406.9 (74.0)	95.3 (6.2)	10.6 (3.5)*	44.9 (9.7)	453.7 (20.7)
All	32.6 (11.9)	409.0 (65.0)	89.1 (5.6)	6.9 (2.8)	34.0 (8.0)	415.6 (17.9)

*Significant difference between variables, $p<0.05$

LPA, light physical activity; MPA, moderate physical activity; VPA, vigorous physical activity; MVPA, moderate-to-vigorous physical activity in 10-min bouts

The level achieved on the SRT was positively associated with age ($r = 0.608$, $p < 0.01$), and negatively associated with zBMI ($r = -0.459$, $p < 0.01$) and WHtR ($r = -0.519$, $p < 0.01$). The multiple regression analysis revealed that zBMI, WC, and WHtR were negatively associated with cardiorespiratory fitness ($p < 0.01$ for all) after controlling for age, sex, and GMFCS level (Table 10.3). Regression analysis also revealed that zSBP, but not zDBP, was negatively associated with cardiorespiratory fitness ($p < 0.05$) (Table 10.3). The significant association between zSBP and cardiorespiratory fitness remained when WHtR was included in the model ($p < 0.05$), but not when WC or zBMI were added. When the association between cardiorespiratory fitness and physical activity domains was examined cardiorespiratory fitness was associated with total activity (mean counts.min^{-1}) ($p < 0.05$), MVPA ($p < 0.05$) and VPA ($p < 0.01$) (Table 10.3). Vigorous physical activity accounted for 12.5% of the variance in cardiorespiratory fitness. Cardiorespiratory fitness was not associated with time spent in sedentary, light, or moderate activity.

Table 10.3 Results from linear regression analyses showing the associations between measures of body fat, blood pressure, physical activity and cardiorespiratory fitness.

	Unstandardised Coefficients B(SE)	Standardised Coefficients B	R square change
zBMI	-1.176 (0.324)	-0.345**	0.109
Waist circumference	-0.201 (0.042)	-0.517**	0.165
Waist-height ratio	-29.846 (6.123)	-0.436**	0.168
zSBP	-826 (0.340)	-0.252*	0.055
zSBP[a]	-0.575 (0.323)	-0.176	0.025
zSBP[b]	-0.446 (0.308)	-0.136	0.015
zSBP[c]	-0.600 (0.291)	-0.183*	0.015
Mean counts.min^{-1}	0.242 (0.101)	0.259*	0.054
Mod-to-vig physical activity	0.387 (0.145)	0.276*	0.065
Vigorous physical activity	0.883 (0.223)	0.372**	0.125

*p<0.05, **p <0.01.
All analyses controlled for age, sex and GMFCS level.
[a]Analysis was additionally controlled for zBMI. [b]Analysis was additionally controlled for waist circumference. [c] Analysis was additionally controlled for waist-height ratio.
zBMI, z-scores for BMI; zSBP, z-scores for SBP; mod-to-vig, moderate-to-vigorous.

When children were stratified according to cardiorespiratory fitness there was no difference in age, zDBP, percentage sedentary time, LPA, MPA, MVPA or counts.min^{-1} across tertiles. Children in the most fit tertile spent significantly more time in VPA compared to children in the middle tertile *(*p <0.05) (Figure 10.1). Children in the least fit tertile had a significantly higher zBMI, WC and WHtR than children in the middle and high tertile (p <0.01 for all) (Figure 10.2). Children with the lowest fitness also had the highest zSBP, although this did not reach statistical significance (p = 0.09). Table 10.4 shows zBMI, WC, and WHtR by tertiles of cardiorespiratory fitness.

Table 10.4 BMI, waist circumference, and waist-height ratio across cardiorespiratory fitness tertiles. Data presented as mean (SD) unless otherwise stated

	zBMI	WC (cm)	WHtR
Low cardiorespiratory fitness	1.79 (0.49)	76.2 (8.9)	0.54 (0.04)
Middle cardiorespiratory fitness	0.24 (1.07)	63.0 (10.8)	0.44 (0.06)
High cardiorespiratory fitness	-0.06 (1.00)†	61.0 (12.5)†	0.42 (0.03)

†data not normally distributed, presented as median (IQR).

zBMI, z-scores for BMI; WC, waist circumference; WHtR, waist-height ratio.

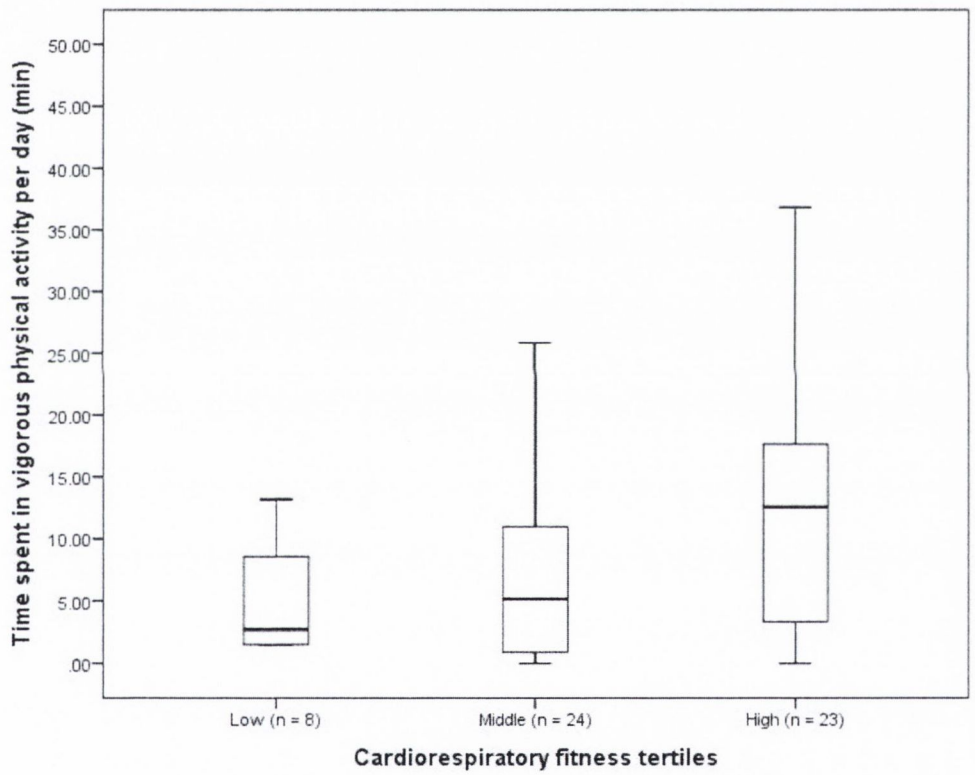
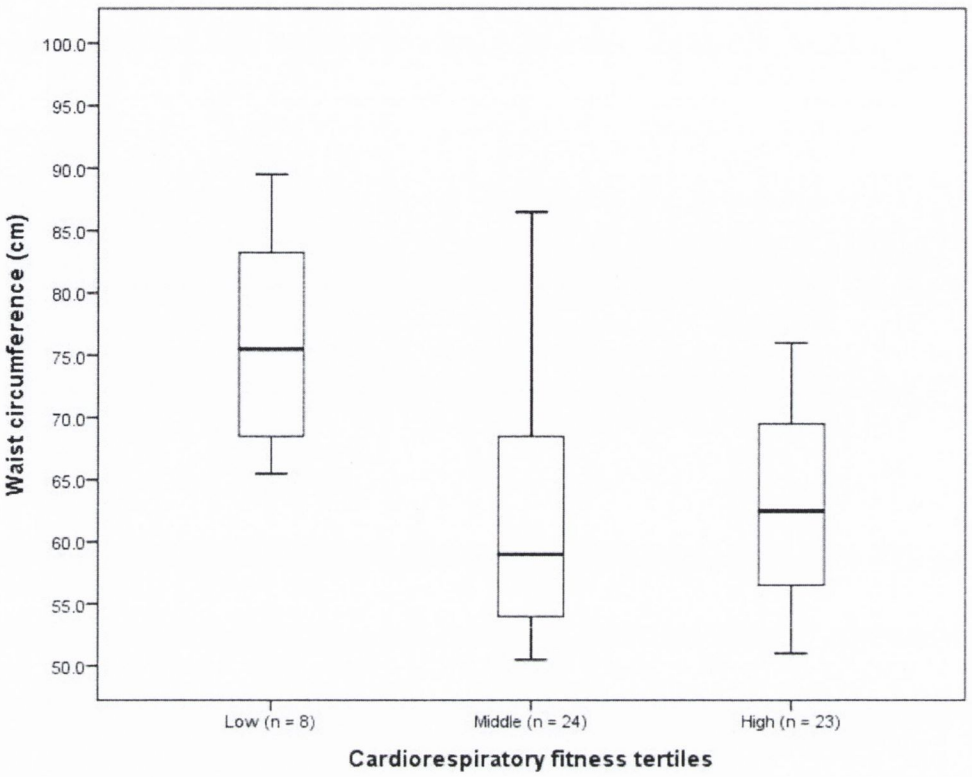


Figure 10.1 Time spent in vigorous physical activity per day across low, middle and high fitness



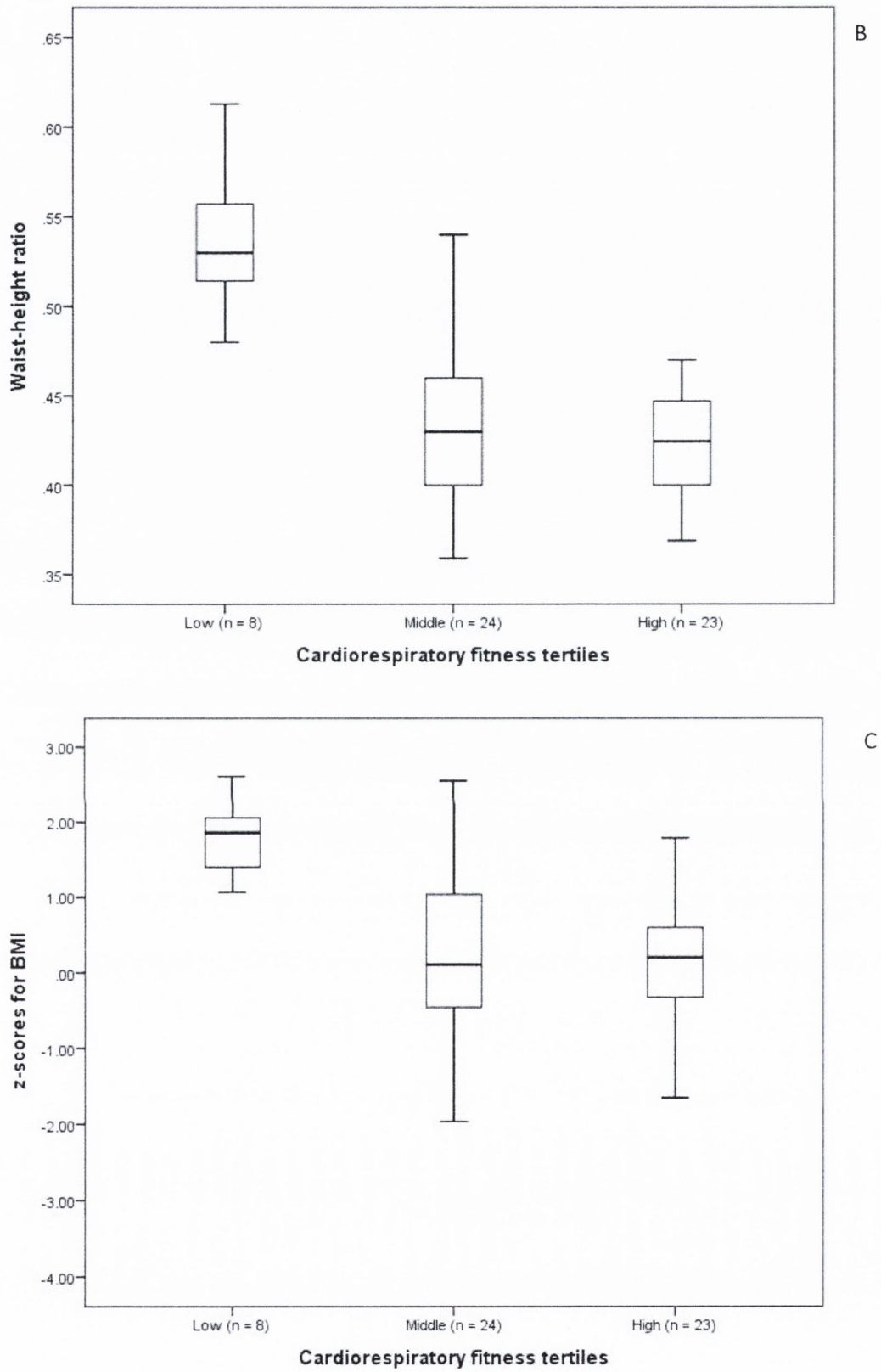


Figure 10.2 Anthropometric measures (A, waist circumference, B, waist-height ratio, C, BMI) across low, middle and high fitness

10.5 Discussion

This is the first study to examine the relationship between cardiorespiratory fitness, adiposity and blood pressure in children with CP. Central adiposity and systolic blood pressure were negatively associated with cardiorespiratory fitness. In addition, children in the lowest fitness level had the highest WC, WHtR and BMI. In agreement with research in TD children (Dencker et al., 2008, Hussey et al., 2007, Gutin et al., 2005), vigorous activity but not light or moderate activity, was positively associated with cardiorespiratory fitness in children with CP. Healthcare professionals should therefore be promoting participation in vigorous activities, like sport, rather than moderate activities, like play, in order to improve cardiorespiratory fitness, and the associated cardiometabolic risk profile of children with CP.

Children with CP are known to have low levels of cardiorespiratory fitness in comparison to their TD peers (Verschuren and Takken, 2010, van den Berg-Emons et al., 1996b). Although it has been hypothesised that this has a negative effect on their cardiometabolic health (Fowler et al., 2007) this is the first study to demonstrate the association between cardiorespiratory fitness, blood pressure and body fat in children with CP. The strongest relationship between anthropometric measures and cardiorespiratory fitness was observed for WC. This is in agreement with a study of TD children (Klasson-Heggebo et al., 2006) and is likely because WC is an indicator of visceral adipose tissue. Visceral adipose tissue is associated with a number of risk factors for cardiovascular disease, including blood pressure, triglycerides, insulin resistance, and the metabolic syndrome, in children and adolescents (Kwon et al., 2011; Kim and Park, 2008). In Chapter 9, the association between blood pressure and body fat, particularly central adiposity, was demonstrated in children with CP. In addition, exercise intervention is known to reduce visceral adipose tissue in the absence of weight loss (Kay and Fiatarone Singh, 2006). In the current study, although both central adiposity and systolic blood pressure were associated with cardiorespiratory fitness, the association between blood pressure and cardiorespiratory fitness was not independent of body fat. This indicates that improving cardiorespiratory fitness may reduce systolic blood pressure in children with CP largely through its positive effect on body fat.

Blood pressure, particularly systolic blood pressure, and obesity are known to track from childhood to adulthood (Chen and Wang, 2008; Juhola et al., 2011). Children who don't

retain childhood risk factors into adulthood however, can reduce the likelihood of developing adult type II diabetes mellitus in young adulthood (Morrison et al., 2012). Implementation of risk factor screening and preventive programmes in childhood is therefore essential to reduce the risk of adult cardiometabolic disease. Early intervention may be even more important in children with CP who are known to have low levels of cardiorespiratory fitness in childhood (Verschuren and Takken, 2010), and who report premature loss of mobility (Bottos et al., 2001) and reduced participation in habitual physical activity in adulthood (Nieuwenhuijsen et al., 2009).

Total activity, sustained bouts of moderate-to-vigorous activity and vigorous activity alone were positively associated with cardiorespiratory fitness suggesting that participation in any kind of physical activity should be encouraged among children with CP. Only vigorous physical activity however differed significantly across fitness levels when fitness was classified according to reference centile curves. This suggests that when promoting physical activity to improve cardiorespiratory fitness, and by association reduce cardiometabolic risk, in children with CP, a particular emphasis should be placed on vigorous physical activity. Children are encouraged to reduce sedentary time because of its association with cardiometabolic disease risk factors (Carson and Janssen, 2011, Chapter 9). Reducing sedentary activity may not however improve cardiorespiratory fitness in children with CP. The lack of an association between sedentary activity and fitness observed in this study is in agreement with a recent study in TD children (Denton et al., 2013). Previous studies were unable to find a relationship between physical activity and cardiorespiratory fitness in children or adults with CP (Nieuwenhuijsen et al., 2011; Maltais et al., 2005a). This is likely because the methods used to measure physical activity were unable to distinguish between different domains of physical activity. A strength of the current study was the use of an accelerometer, which allowed differentiation between light, moderate and vigorous physical activity.

The relationship between vigorous physical activity and cardiorespiratory fitness observed in this study has serious implication for the prescription of physical activity in children with CP. Although current guidelines recommend that children with a disability accumulate 60 min of moderate-to-vigorous activity daily, where possible (WHO, 2010), only vigorous activity or sustained bouts of moderate-to-vigorous activity are associated with cardiorespiratory fitness. In fact, children with the lowest fitness accumulated 88.3 minutes of moderate activity per day, which was not significantly different to that of

children with the highest fitness ($p = 0.685$). This indicates that children with CP may achieve the physical activity guideline yet have low cardiorespiratory fitness. Children in the middle and highest fitness tertile, in the current study, accumulated approximately 5 and 11 minutes of vigorous activity daily, respectively, and had a lower BMI and WC than children in the least fit tertile. Research in TD children suggests that achieving more than 7 minutes of vigorous physical activity daily is associated with a reduced likelihood of being overweight and having hypertension (Hay et al., 2012).

Vigorous activity is equivalent to ≥6 METs, and includes activities involving a hard effort like running, jumping and skipping (Ainsworth et al., 2011). It is recognised that there is heterogeneity among children with CP and not all children may be able to reach activity of a vigorous intensity. The children in this study however had very minimal impairments. The results indicate that while these children can accumulate VPA, many may not accumulate adequate levels. In children, vigorous activity is mainly accumulated through participation in sport and physical education (PE). There is consistent evidence that participation in sport is low among children with CP (Imms et al., 2008; Palisano et al., 2007; Mc Manus et al., 2008). Only 52.9% of children with a mild impairment report participating in sport a few times a week, compared to 79.3% of TD children (Mc Manus et al., 2008). Personal and environmental factors play a key role in determining the extent to which children and adolescence with CP participate in sport. Barriers that children report include feeling insecure or like an outsider, the perception that sports aren't fun, and that learning the motor skills required is too time consuming (Verschuren et al., 2012). Parents are also reluctant to let their child with CP participate in sport as they fear their child won't fit in, they have difficulty with watching their child struggle (i.e. losing) or not being picked for a team, and are aware that sports teams do not have a suitable level for children with CP (Verschuren et al., 2012). In order to improve and maintain cardiorespiratory fitness in children with CP a holistic approach is required from early childhood to overcome these barriers.

10.6 Limitations

There are a number of limitations to this study. Notably, the cross-sectional design does not allow a causal relationship to be inferred from the results. For example, although it is possible that participation in vigorous physical activity improves fitness it is also

possible that having a high fitness level enables children to participate in more vigorous physical activity. Some studies have reported a difference in the association between physical activity intensity and cardiorespiratory fitness between girls and boys (Denton et al., 2013). The relatively small sample size in the current study did not allow for separate analyses to be performed by sex. Regression analyses were however adjusted for sex. The SRT test in the current study does not allow for prediction of VO_2 from the level achieved on the test. Levels of cardiorespiratory fitness presented in the current study are therefore relative to children with CP only and do not give an indication of the absolute fitness of the cohort. In addition, a single set of cut-points, developed on TD children, was used to classify physical activity in this study. As indicated in Chapter 6, this may have resulted in the underestimation of physical activity intensity in some children, particularly those in GMFCS level II. Also the sample was limited to children in GMFCS levels I and II as there is no validated fitness test for children in GMFCS levels III, IV and V. The results of this study therefore cannot be generalised to the greater pediatric CP population. Some reports suggest however that approximately 60% of children with CP are classified in GMFCS levels I and II (Australian Cerebral Palsy Register, 2013).

10.7 Conclusions

Children with CP are known to have reduced levels of cardiorespiratory fitness relative to TD children. This study demonstrates that children with CP with low cardiorespiratory fitness have increased body fat and blood pressure. Screening for risk factors and preventive programmes should therefore be implemented in this population from an early age. When promoting physical activity in children with CP, healthcare professionals should place an emphasis on participation in vigorous activity, like sport, rather than light, or moderate activity.

Chapter 11 Discussion

11.1 Introduction and Main Findings

The association between reduced physical activity, all-cause mortality, hypertension, coronary heart disease, stroke and type II diabetes mellitus (T2DM) is well established (Chapter 1, section 1.4). Physical activity has a positive effect on a number of cardiometabolic risk factors in adults and children including systolic blood pressure (SBP), triglycerides, high density lipoprotein-cholesterol (HDL-C), plasma glucose, insulin, and insulin resistance (Chapter 1, section 1.4 and 1.4.1). It also plays an important role in preventing obesity (Chapter 1, section 1.5). In addition to the role of physical activity in reducing the risk of chronic disease, physical activity is associated with physical function (Chmelo et al., 2012). It has been established that adults and children with CP participate in less physical activity than their able-bodied peers (Chapter 1, section 1.3.1 and 1.3.2). As a result of reduced physical activity levels, the 2003 American Physical Therapy Association Section on Paediatrics and its Research Committee determined that there was a critical need to identify and promote effective physical fitness interventions for children with CP (Fowler et al., 2007). However, almost a decade on there is still little information about the association between physical activity and physical fitness in people with CP. The aim of this thesis was to investigate the association between physical activity, body composition, cardiorespiratory fitness, and cardiometabolic risk factors in adults and children with CP.

At the time that the studies presented in this thesis commenced, there were limited methods available to measure physical activity in adults and children with CP (Clanchy et al., 2011b). While studies had used self-report measures, pedometers, activity monitors, and heart-rate monitoring to measure physical activity in adults and children with CP, few of these methods had been validated in this population. Accelerometers present as objective measures of physical activity duration, frequency and intensity that are feasible to use in large samples (Chapter 2, section 1.3.4.3). The abnormal movement patterns associated with CP, as well as the increased energy expenditure during locomotion, mean that accelerometers may not be accurate at measuring physical activity in this population. New accelerometry-based devices that combine information from multiple sensors were identified as potential methods of improving the estimation

of energy expenditure (EE) in this population. The literature review presented in Chapter 3 identified three accelerometry-based devices that provide estimates of EE in intervals of 1 minute or less. These devices had not been directly compared in adults or children without CP and therefore there was no information about the concurrent validity of them in the general population.

In study 1 the criterion and concurrent validity of the RT3 accelerometer, the Sensewear Pro Armband (SWA) and the Intelligent Device for Energy Expenditure and Activity (IDEEA) was investigated in adults and children without CP. The results of this study indicated that the SWA provided the best estimate of EE in adults and children without CP. However, even when the SWA demonstrated the best agreement with a criterion measure, during running, limits of agreement ranged from -29% to 13% of the mean EE.

In study 2 the criterion and concurrent validity of the RT3, the SWA and the IDEEA was investigated in adults and children with CP. The RT3 provided the most accurate estimation of EE in comparison to the gold standard. There was significant inter-individual variation, however, and the RT3 underestimated EE by up to 37.9% in adults and up to 26.9% in children. The results of this study indicated that caution must be used when using the RT3 to estimate EE in adults and children with CP, particularly at an individual level.

The RT3 is a traditional accelerometer, which is conventionally used to indicate the quantity of time that individuals spend in sedentary, light, moderate or vigorous activity. In order to translate the count output of accelerometers into a more meaningful unit cut-points are applied to raw data. The accuracy of previously published cut-points at estimating physical activity intensity was investigated in study 3. In children, the published cut-points incorrectly classified moderate-to-vigorous activity as light activity 30% of the time. Published cut-points had a higher sensitivity value (83.9%) in adults, as a result of fewer incorrect classifications. A new moderate-to-vigorous cut-point of 689 counts.min^{-1} was identified for children with CP. The sample size was insufficient to cross-validate this cut-point however, and therefore requires cross-validated in an independent sample.

In study 4 everyday levels of physical activity were compared between adults with and without CP. Adults with CP were less active than adults without CP. Gross motor function was the main determinant of physical activity levels in people with CP, and

those with the highest gross motor function achieved similar levels of light, moderate and vigorous activity as those without CP. Moderate physical activity was negatively associated with a number of cardiometabolic risk factors.

In study 5 the prevalence of cardiometabolic risk factors in adults with CP was investigated. More than a fifth of a relatively young cohort of adults with CP had the metabolic syndrome and more than a third were centrally obese. The results of this study also indicated that waist circumference (WC) is a stronger predictor of cardiometabolic risk factors, including hypertension, dyslipidaemia, and insulin resistance in adults with CP, compared to BMI, waist-hip ratio (WHR), and waist-height ratio (WHtR).

In study 6 the association between physical activity, body composition and blood pressure was investigated in children with CP. Total and central adiposity was associated with SBP in children with CP. Total physical activity, moderate-to-vigorous physical activity, and vigorous activity were negatively associated with high risk blood pressure values. Sedentary activity was positively associated with high risk blood pressure values.

In study 7 the association between cardiorespiratory fitness, blood pressure, and body fat was investigated in children with CP. Cardiorespiratory fitness was negatively associated with systolic blood pressure and body fat, particularly central adiposity. The association between cardiorespiratory fitness and blood pressure was not independent of body fat. Total activity, sustained bouts of moderate-to-vigorous activity and vigorous activity alone, but not sedentary, light or moderate activity, were associated with cardiorespiratory fitness. Only vigorous physical activity differed across levels of fitness, classified according to reference curves.

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11.2 Analysis of Key Points

11.2.1 Measuring physical activity in people with cerebral palsy

Accelerometers provide physical activity data that allows for comparison with physical activity guidelines and are also a feasible method of quantifying physical activity in adults and children with CP (Gorter et al., 2012). In addition, they provide empirically relevant data because large-scale studies of free-living populations, including NHANES, are using them to establish the association between physical activity and health. Concurrent validation of three accelerometry-based devices revealed that the SWA was the best device at estimating EE in adults and children without CP. However, when evaluated in adults and children with CP, the SWA overestimated the cost of locomotion. Comparatively, the RT3 provided a better estimate of EE. The large variation in individual estimates however, suggests that the RT3 should be used with caution if being used to estimate EE in adults and children with CP. The literature on validation of accelerometers has typically demonstrated that monitors are valid for group level estimates but are of limited utility for individual estimation (Welk et al., 2012).

An essential problem with accelerometers is that there is a large variation in oxygen uptake among individuals for a given activity. Oxygen uptake is not a direct product of speed, and the variation among individuals is a result of biomechanical, physiological and other factors. Body mass (Peyrot et al., 2012), age (Hall et al., 2013), gait parameters (Holt et al., 1991) and environmental factors all influence oxygen uptake in the general population. There are also unique relationships between movement and EE for different activities. The activities used to calibrate the inbuilt equations of the three accelerometry-based devices in study 1 and 2 are unknown. It is reasonable to think that they were calibrated against locomotor-based activities as these are the most commonly performed activities, which exceed resting levels of EE, in daily life. Equations based on locomotion tend to underestimate the EE of lifestyle activities (Welk, 2005). Even if equations are individually calibrated for different activities, the relationship between EE and activity varies depending on body mass e.g. weightbearing versus non-weightbearing activities (Lafortuna et al., 2010). With so many variables affecting energy output it may be too much to expect accelerometers to provide accurate point estimates of EE for individuals. In addition to the limitations of accelerometry-based devices in the general population, the in-built equations used to estimate EE are unlikely

to account for the increased metabolic cost of locomotion that is evident among adults and children with CP. Study 2 demonstrated that there was a large degree of error in the EE estimates from these devices for adults and children with CP.

From the results of study 2 it was hypothesised that the inbuilt proprietary algorithms, and not the raw data, was the largest contributor to error. Using raw data to categorise activity according to intensity has the potential to provide an estimate of the range of EE that reduces the degree of error associated with point estimates of EE. Only one study has used an accelerometer (the Actigraph) to measure physical activity intensity in children with CP in this way (Capio et al., 2012). Published cut-points validated by Clanchy et al. (2011a), were used to classify activity in this study. Although published cut-points for the Actigraph were reasonably accurate at classifying physical activity intensity in children with CP (81.8% sensitivity) this was not the case in study 3. Classifying moderate-to-vigorous activity according to a published cut-point for the RT3 resulted in only 70% sensitivity. The most likely explanation for the disagreement between the two studies is the characteristics of the sample. In addition to the factors that influence oxygen uptake that are mentioned above, the variation in oxygen uptake among children with CP is influenced by the additional factors of gross motor function, type and anatomical distribution of motor abnormality (Kerr et al., 2008). A larger proportion of children in study 3, compared to the Actigraph validation study, were classified in GMFCS level III and used a mobility aid. Differences in the gross motor function of the sample would also explain why a published cut-point accurately classified moderate-to-vigorous physical activity in adults with CP in study 3, who as a group had minimal impairments.

Although published cut-points for accelerometers may accurately classify physical activity intensity in people with minimal impairments, the rate of misclassification is likely to increase among people with more severe impairments, whose oxygen uptake is greater for a given activity (Kerr et al., 2008). Ideally accelerometer cut-points should be calibrated for each individual against oxygen uptake in order to optimally measure physical activity. This reduces the feasibility of using accelerometers, however, and is quite impractical if they are to be used in population-based studies. A more feasible method of improving the ability of accelerometers to identify physical activity intensity in people with CP would be to calibrate individual cut-points for each level of the GMFCS, thereby accounting for a large part of the variation in oxygen uptake. The

sample size in study 3 did not allow this to be done. Until this is done, accelerometers should continue to be used to measure physical activity in people with CP as they offer many advantages over the other available methods. The limitations of using accelerometers to measure physical activity in people with CP should be acknowledged, however, and results should be interpreted with caution.

11.2.2 Measuring body composition in people with cerebral palsy

An aim of this thesis was to examine the association between physical activity and body composition in adults and children with CP. In order to investigate this association, accurate measures of obesity must be determined in people with CP. The term 'body composition' refers to the relative proportions of fat, bone and muscle mass in the human body. Excess body fat i.e. obesity, is strongly and positively associated with blood pressure, total blood cholesterol, type II diabetes, and all-cause and cardiovascular disease mortality (Dudina et al., 2011, Jousilahti et al., 1996, Katzmarzyk et al., 2012). As a direct method of measuring body composition (i.e. chemical analysis of a cadaver) is not possible, and indirect methods such as hydrodensiometry, MRI scans, dual-energy x-ray absorptiometry (DXA), DLW and plethysmography are often unfeasible, quick, clinical methods are required to indicate obesity-related cardiometabolic risk. Doubly indirect methods, which include skinfolds and bioelectrical impedance analysis (BIA), are sometimes used as an alternative method of measuring body composition in the field. The validity of these measurements in adults and children with CP is limited (Macedo et al., 2008, Hildreth et al., 1997, van den Berg-Emons et al., 1998b, Stallings et al., 1995, Gurka et al., 2010, Bell et al., 2012). Furthermore not all healthcare professionals are trained in these methods or have the necessary equipment available to them.

Historically BMI has been used as a quick method of defining excess body fat. Even in the general population, however, BMI is unable to identify those with excess body fat who are at risk of CVD mortality (Romero-Corral et al., 2010). This is likely because BMI is unable to differentiate between muscle mass and excess body fat. The inability to differentiate between muscle mass and fat mass may be a particular limitation to using BMI to define obesity in adults and children with CP who are known to have reduced muscle volumes (Lampe et al., 2006) and intramuscular adipose tissue (Johnson et al., 2009). Indeed BMI was a poor predictor of body fat in children with CP ($R^2 = 0.27$) and

showed poor agreement with percentage body fat by DXA (kappa value <0.7). (Kuperminc et al., 2010).

Indices of central obesity have been proposed as alternative methods of defining obesity in the general population (Ashwell et al., 2012, de Koning et al., 2007). In fact WC, rather than BMI, is included in the joint interim statement on the definition of the metabolic syndrome (Alberti et al., 2009), highlighting the importance of abdominal obesity in indicating future risk of T2DM and CVD. In study 5 WC, WHR, WHtR, and BMI were associated with cardiometabolic risk factors in adults with CP. This might be expected, as any measure of obesity will capture the increased risk of cardiometabolic disease associated with excess body fat, to some extent. This has been shown in the general population (Schneider et al., 2007, Can et al., 2009, Aekplakorn et al., 2006). Of these measures, however, WC had the best predictive ability for indicating high cholesterol, insulin resistance, and high SBP. The results of study 5 suggest that WC can be used to provide a quick and simple indicator of cardiometabolic disease risk in adults with CP, above that which would be obtained from measuring BMI. This is most likely because WC is a more sensitive indicator of visceral adipose tissue, which may be high in individuals with CP despite having muscle wasting in their extremities.

Similar results were observed in children with CP. In study 6 and 7 both WC and BMI were associated with blood pressure and low cardiorespiratory fitness in children. A stronger association, however, was observed between WC and SBP and between WC and cardiorespiratory fitness, compared to BMI. This suggests that WC may be a more clinically useful measure to obtain when assessing cardiometabolic risk in children with CP as well as adults. This may also explain why, despite the relatively low prevalence of overweight and obesity among children and adults with CP respectively, the prevalence of hypertension and the metabolic syndrome was relatively high.

The use of WC is limited however by the lack of consensus regarding what threshold should be used to classify central obesity. In adults the IDF recommend 80 cm for women and 94 cm for men. The WHO recommends 88 cm for women and 102 cm for men. Thresholds for the general population may not be applicable for adults with CP. The small sample size in study 4 did not allow for identification of an optimal threshold that would indicate abdominal obesity in adults with CP. Similarly, it was not possible to identify optimal cut-off points for WC in children with CP. WC growth percentiles

developed on American children suggest that adolescents exceed adult WC thresholds between the 75th and the 90th percentile (Fernandez et al., 2004, Cook et al., 2009). Absolute cut-offs of ≥80.5 cm for males and ≥81 cm for females have been suggested for American adolescents [28]. As the WC threshold for adult females of European origin are 80 cm, these thresholds may not be appropriate for use in Irish children and adolescents. McCarthy et al. [29] developed waist circumference percentiles in British children age 5.0 to 16.9 yr. These were developed on data collected in 1988 however and may be out of date, as 76% of Irish children had a WC greater than the 75th percentile (Hussey et al., 2007). Cut-off points for defining central obesity were also not provided with these percentiles.

Studies that previously reported the prevalence of obesity in children with CP defined obesity using BMI thresholds developed in the general population (Rogozinski et al., 2007, Hurvitz et al., 2008). Using WC thresholds developed in the general population to define central obesity in adults with CP may therefore be acceptable at present until further evidence emerges.

11.2.3 Physical activity in adults with cerebral palsy

In agreement with previous research (Nieuwenhuijsen et al., 2009) the results of study 4 indicated that adults with CP participate in less physical activity than adults without CP. This is the first study to demonstrate that not only are adults with CP less active than adults without CP, they spend less time in moderate and vigorous activity. When analysed according to GMFCS level however, adults with CP classified in GMFCS level I participated in similar levels of moderate, vigorous and total activity as adults without CP. In fact GMFCS level was the only factor significantly associated with moderate, vigorous and total activity. Although adults in GMFCS level II participated in less total activity than adults without CP they participated in similar levels of moderate and vigorous activity. This is possibly because they have minimal impairments and are trying to keep up with able-bodied persons on a daily basis. As a result, it is likely that they spend more time in sedentary behaviour than adults without CP in order to conserve energy and reduce the chronic fatigue experienced by many adults with CP (van der Slot et al., 2012). Despite accumulating similar levels of moderate and vigorous activity as adults without CP adults in level II still only accumulated 6.5 minutes of moderate-to-vigorous activity daily. This is well below the recommended 21 minutes daily (150

minutes per week). They also only achieved 4.3 minutes of vigorous activity daily. Vigorous activity is required to improve cardiorespiratory fitness in adults (Ceaser et al., 2013). Low levels of vigorous activity may therefore lead to deconditioning, which prevents adults with CP accumulating sustained bouts of moderate-to-vigorous activity.

Not unexpectedly, no adults in GMFCS level III met physical activity guidelines. This is a worrying observation, which may have a detrimental effect on their health. It may be expected that adults with poor gross motor function are unable to participate in many day-to-day activities of a moderate-to-vigorous nature because of their physical impairments. However a number of environmental factors also contribute to the inability of people with poor gross motor function participating in physical activity. Mobility preferences are linked to considerations regarding safety, practicality, or social acceptability (Palisano et al., 2009). Mobility is important for self-sufficiency and independence and therefore using assistive devices like wheeled mobility may allow individuals with CP to participate efficiently in daily life. This however, feeds into a negative cycle of reduced participation in habitual physical activity, deconditioning, deterioration in mobility and reduced activity.

As gross motor function declines and adults require the use of assistive devices, physical restrictions and transport restrictions may also impact on their access to exercise facilities (Shikako-Thomas et al., 2008). As well as problems with accessibility, adults with CP report experiencing social difficulties with attending gyms and that they 'feel out of place' there (Sandstrom et al., 2004). Not only do they feel unable to attend public gyms but many adults with CP report not having access to appropriate healthcare or rehabilitation supports (Sandstrom et al., 2009, Moll and Cott, 2012). They therefore feel like they have insufficient knowledge about the frequency, intensity and type of activities that they should perform (Sandstrom et al., 2009). Adults who reported deterioration in walking function attributed it to impaired balance, reduced muscle strength, reduced cardiorespiratory fitness and walking speed, and pain and stiffness (Opheim et al., 2009). Only a small proportion of adults attributed deterioration in walking function to reduced training. It appears that adults with CP are unaware of the positive influence of physical activity on all of these factors (Wong et al., 2003, Goodpaster et al., 2008, Panel on prevention of falls in older persons, American Geriatrics Society and British Geriatrics Society, 2011) and therefore the potential ability of physical activity to stem the decline in function. People with CP should be educated

about the role of physical activity in managing their condition throughout their lifetime. If, as is common, access to rehabilitation is no longer available to adults with CP when they reach 18 years of age, it is important that they are educated on the type, quantity and intensity of physical activity that they should perform while they are still attending rehabilitative services. The burden on these services may be significantly reduced if preventive programmes are in place and adults with CP only require minor modifications to their exercise programme over time.

Low levels of cardiorespiratory fitness among adults with CP (Fernandez, 1990, Nieuwenhuijsen et al., 2011) may be a barrier to increasing habitual levels of physical activity. The small quantity of sustained bouts moderate-to-vigorous activity recorded in adults in level II and III in study 4 suggests that the adults in this study were deconditioned. Targeted interventions may therefore be necessary to improve physical activity levels and cardiorespiratory fitness in adults with CP with poor baseline levels of fitness. Improvements in cardiorespiratory fitness following interventions do not however, necessarily translate into increased habitual physical activity (Butler et al., 2010). While exercise programmes may be initially beneficial to increase activity in sedentary adults with CP a holistic approach that tackles the personal and environmental factors associated with reduced participation in physical activity is required in conjunction with these programmes.

11.2.4 Physical activity in children with cerebral palsy

As with adults, moderate, vigorous and total activity decreased with decreases in gross motor function among children. Sedentary activity increased with decreases in gross motor function. Children who participate in low levels of moderate-to-vigorous activity are at increased risk of cardiometabolic disease (Chaput et al., 2013, Ekelund et al., 2012, Andersen et al., 2006). This relationship is independent of time spent in sedentary activity. However, sedentary activity is also associated with cardiometabolic risk factors (Stamatakis et al., 2012, Carson and Janssen, 2011, Chaput et al., 2013) and may be a more feasible method of reducing cardiometabolic risk in children with moderate impairments.

There are contradictory reports as to whether the association between sedentary activity and cardiometabolic risk factors is independent of moderate-to-vigorous activity. The discrepancy may be a result of the different methods used to measure

sedentary activity. Volume of sedentary activity, as measured by accelerometry, does not appear to be associated with risk factors, independent of physical activity [30,31]. The association between TV-viewing and risk factors is however independent of physical activity [31,32]. The same association was not found for PC time or game time (Stamatakis et al., 2012), suggesting that confounding factors, such as consumption of high energy food or the influence of TV advertisements on unhealthy behaviours, may contribute to this relationship. The specific domain of TV-viewing was not measured as part of this thesis. Little information is available regarding specifically TV-viewing in children with CP. Computer use is high among children with CP however, with 65.4% of children with a mild disability and 73.9% of children with a moderate disability using a computer a few times per week compared to only 42.8% of TD children (McManus et al., 2008). An average screen time of 28.6 h per week was reported among adolescents with CP, which although high, is similar to normative values in TD adolescents [33].

Overall, 75% of children with CP met the guideline of 60 min of moderate-to-vigorous activity daily. This declined significantly across GMFCS level resulting in only 47% of children in level III meeting the guideline. Although this might seem relatively high, 90% of TD children age 10-14 years met the guideline when activity was measured with the RT3 (Denton et al., 2013). This is similar to the rate among children in level I of the GMFCS (88%), and supports evidence that children in level I are as active as TD children (Bjornson et al., 2007), at least at a moderate-to-vigorous level.

11.2.5 Cardiometabolic risk factors in adults with cerebral palsy

It was hypothesised that adults and children with CP would have increased risk of cardiometabolic disease as a result of being inactive. The results of this thesis support this hypothesis. Moderate physical activity was negatively associated with a number of cardiometabolic risk factors. The prevalence of the metabolic syndrome in adults with CP was also higher than that in a population of older Irish adults. This suggests that young and middle-aged adults with CP have a similar level of cardiometabolic risk to that of older able-bodied adults. The prevalence of the metabolic syndrome and a number of individual cardiometabolic risk factors was higher in non-ambulatory adults compared to ambulatory adults. As physical activity was not measured in non-ambulatory adults this cannot be attributed to differences in physical activity levels, although it is a plausible explanation. Even among young ambulatory adults, the prevalence of the metabolic

syndrome was similar to that in older able-bodied adults. The prevalence of the metabolic syndrome or individual risk factors did not differ across GMFCS levels I-III, however, despite adults in level III participating in reduced levels of physical activity. This may be because the method used to measure physical activity underestimated the energy expenditure in adults in level III, who are known to expend more energy for a given activity than adults in level I and II (Kerr et al., 2008).

Although the prevalence of the metabolic syndrome was high in adults with CP, the prevalence of individual risk factors was relatively low compared to Irish and white American adults (Villegas et al., 2004, Morgan et al., 2008, Beltran-Sanchez et al., 2013). This would suggest that although, fewer adults with CP have individual risk factors, those that have risk factors have clustering of a number of factors, which is particularly detrimental for their health. It is important to identify people with the metabolic syndrome in order to aggressively intervene and prevent further adverse changes in their metabolic state. Worryingly, despite the high prevalence of the metabolic syndrome, few adults were receiving lipid lowering medication. This may be because of the relatively young age of the cohort, who wouldn't typically be screened for cardiometabolic risk factors. The results of this thesis indicate that adults with CP have increased risk for CVD and T2DM, and screening for risk factors should occur from early adulthood.

11.2.6 Cardiometabolic risk factors in children with cerebral palsy

A high prevalence of elevated blood pressure was observed among children with CP (21.1%), particularly among children in level I of the GMFCS (26.8%). This was despite a relatively low prevalence of overweight/obesity. Physical activity was not found, however, to be associated with blood pressure, throughout the range of values. There is conflicting evidence regarding the association between physical activity and blood pressure in TD children. Some studies have found a weak relationship between moderate-to-vigorous physical activity and systolic and diastolic blood pressure (Janssen et al., 2013, Andersen et al., 2006, Mark and Janssen, 2008). Others have found a weak relationship between moderate-to-vigorous activity and DBP only (Knowles et al., 2013, Chaput et al., 2013) or between moderate-to-vigorous activity and SBP only (Ekelund et al., 2012).

A stronger relationship has been observed between physical activity and blood pressure in the high risk range (Mark and Janssen, 2008, Kelley et al., 2003). This is in agreement with the findings in the current study, which demonstrated that moderate-to-vigorous activity, vigorous activity, and total activity, were negatively associated with elevated blood pressure in children with CP. The strongest relationship was found between decreased vigorous activity and elevated blood pressure and moderate activity alone was not associated with blood pressure. Few studies have examined the independent relationship of moderate and vigorous activity with cardiometabolic risk in TD children. When this was investigated in TD children similar results were found; vigorous activity but not moderate activity reduced the risk of being overweight and having elevated blood pressure (Hay et al., 2012). Mean exposure to vigorous physical activity, but not moderate-to-vigorous activity, during childhood is also associated with reduced clustered cardiometabolic risk in adolescence (Ried-Larsen et al., 2013).

Nine children in GMFCS level I (16%) had blood pressure values in the hypertensive range despite 88% meeting the physical activity guidelines. This may be because children in level I meet the guidelines by accumulating moderate physical activity rather than vigorous activity. Only one study has reported the difference in vigorous physical activity between 11 children with CP and 11 TD children, using a self-report measure (Martin et al., 2012). As expected, children with CP participated in less vigorous physical activity than TD children. Despite this no differences were seen in any measured indices of vascular health between groups. The questionnaire used to assess physical activity may not have been sensitive enough to determine absolute differences in time spent in each physical activity intensity. The small number of children in the study may also have affected the results of the study.

The hypothesis that children with CP participate in less vigorous activity, despite meeting physical activity guidelines, is supported by the fact that even children with low cardiorespiratory fitness accumulated, on average, 88 minutes of moderate activity per day; not significantly different to the time accumulated by the most fit children. They did however accumulate less vigorous physical activity. An examination of the differences in objectively measured vigorous physical activity between children with and without CP is required. The reason why the prevalence of hypertension was higher among children in

level I, despite higher activity levels, is difficult to explain. It may be that the small number of participants that were in level II and III resulted in a biased sample. A likely explanation is that using a single set of cut-off points to classify physical activity intensity resulted in intensity being underestimated in children in level II and III. Children in level III use significantly more energy to walk at a given speed compared to children in level I and II (Kerr et al., 2008). Inaccurate classification of physical activity intensity in some GMFCS levels may also explain why a linear relationship between blood pressure and physical activity was not observed. In light of this, caution must be taken when interpreting the results of Chapters 9 and 10. Although vigorous activity may be important to improve cardiorespiratory fitness and reduce cardiometabolic risk factors it is still unclear what constitutes vigorous physical activity or how to measure habitual vigorous activity in children with mild to moderate impairments.

Lifestyle factors, particularly dietary habits, may also have contributed to the high prevalence of elevated blood pressure in children in level I. Children in level I may have similar unhealthy lifestyle habits to TD children, more so than children in level III who are more severely disabled. As well as possibly having similar lifestyle habits to TD children, it is likely that children in level I also participate in less vigorous activity than TD children. This would increase their risk of cardiometabolic disease.

As well as being associated with elevated blood pressure, vigorous activity is required to improve cardiorespiratory fitness in children with CP. This adds to the large volume of evidence that indicates that children require high intensity physical activity to improve cardiorespiratory fitness (Hay et al., 2012, Denton et al., 2013, Aires et al., 2010, Parikh and Stratton, 2011). Cardiorespiratory fitness, unlike physical activity, was associated with total and central adiposity, and systolic blood pressure. Although this would indicate that fitness is more important than physical activity for health in children with CP, the two concepts cannot be separated. Physical activity is the principal determinant in cardiorespiratory fitness, albeit in combination with a genetic component. The most likely explanation as to why fitness, but not activity, was associated with cardiometabolic risk is that there is less error associated with the method used to measure fitness.

Research in the general population also indicates that there is a stronger dose-response relationship between fitness and health, because until recently, measurement of

physical activity has relied on self-report tools (Blair et al., 2001). This inevitably leads to misclassification of physical activity. Most studies investigating the relationship between cardiorespiratory fitness and health have used objective, laboratory-based methods to measure fitness, which reduce misclassification. Although an objective method was used to measure physical activity in children with CP, the significant variation in the energy cost of locomotion within this population may have resulted in a number of misclassifications.

11.2.6.1 Are the guidelines for physical activity appropriate for adults with cerebral palsy?

Only 24.4% of adults with CP met the guideline of 150 min of moderate physical activity accumulated in bouts of 10 minutes, as recommended by the ACSM. The proportion of people meeting the guideline declined significantly across GMFCS. Despite adults in GMFCS level II only spending 6.5 minutes in moderate-to-vigorous physical activity, 16.3% met the guideline. This was a result of the significant variation in time spent in moderate-to-vigorous activity within the group. No adults in level III achieved 150 minutes of moderate activity in 10 minute bouts. They did, however, accumulate 16.2 minutes of moderate activity per day in 1 minute bouts suggesting that 21 minutes of moderate activity daily (150 minutes weekly) in 1 minute bouts is not an unfeasible target. The fact that virtually no adults in level III accumulated moderate-to-vigorous activity in 10 minute bouts suggests that this group is deconditioned. The health benefits of accumulating activity in 10 minute bouts rather than 1 minute bouts are still under debate (Murphy et al., 2009). Recent studies have shown, however, that there are benefits associated with accumulating moderate-to-vigorous activity in bouts of less than 10 minutes (Loprinzi and Cardinal, 2013, Fan et al., 2013).

There are currently no physical activity guidelines for people with CP. The results of this thesis indicate that there's a high prevalence of clustered cardiometabolic risk among ambulatory adults with CP and that physical activity is negatively associated with cardiometabolic risk factors. Although physical activity differed across GMFCS levels however cardiometabolic risk factors did not. This is likely because the energy expended by adults in GMFCS level III was underestimated by the method used to measure physical activity.

The results of study 4 indicate that the guideline for apparently healthy adults of 150 min of moderate-to-vigorous activity daily, accumulated in 10-min bouts, is feasible for adults in GMFCS level I and II to achieve but not level III. Physical activity guidelines for adults aged over 65 years, and 50-64 years with clinically significant chronic conditions or functional limitations that affect movement ability, fitness or physical activity, are also 150 min of moderate activity per week. It is suggested that this should be in addition to routine light activity, or moderate intensity activities that last for less than 10 min (Nelson et al., 2007). Only 2.5% of older adults met these guidelines when physical activity was objectively measured (Harris et al., 2009). This is only slightly higher than the proportion of adults in level III who achieved this guideline. These guidelines have been developed largely from information obtained from self-report measures of physical activity. The inaccuracy of self-report measures means that, even in the general population, these recommendations may not be optimal for reducing cardiometabolic risk. With a large volume of research regarding the relationship between objectively measured physical activity and health emerging in recent years, particularly from NHANES, reevaluation of the guidelines is required.

11.2.6.2 Are the guidelines for physical activity appropriate for children with cerebral palsy?

The guidelines for children recommend achieving 60 minutes of moderate-to-vigorous physical activity daily. Results from this thesis underscore the importance of emphasising vigorous activity, rather than moderate activity, in physical activity guidelines for children with CP. Up to now most studies have only investigated levels of total physical activity, moderate activity, and inactivity in children with CP. Although total activity has some benefits and is associated with reduced metabolic cost of walking (Maltais et al., 2005) and improved biomechanical walking economy (Maltais et al., 2005b) in children with CP, the results of this thesis indicate that vigorous activity, rather than total activity, is more strongly associated with reduced cardiometabolic risk and improved cardiorespiratory fitness. Improving cardiorespiratory fitness also reduces the physical strain of walking in children with CP (Dallmeijer and Brehm, 2008), hence improving their ability to function in day-to-day life. In study 7, children in the highest fitness tertile accumulated approximately 11 minutes of vigorous activity per day. Children in the middle fitness tertile accumulated approximately 5 minutes of vigorous activity per day, and had a lower BMI and WC than children in the lowest fitness tertile.

Research in TD children that demonstrated that children require at least 7 minutes of vigorous physical activity daily to reduce their risk of being overweight and having elevated systolic blood pressure [27]. This also seems to be a reasonable guideline in children with CP.

Although the results of this thesis indicate that children with CP in level I and II of the GMFCS have the physical capability to achieve 7 minutes of vigorous activity a day, children with disabilities face unique environmental and personal barriers when trying to increase their physical activity. Long-term aerobic exercise interventions can improve cardiorespiratory fitness in children with CP (Butler et al., 2010). This does not carryover to increased habitual physical activity, however (Butler et al., 2010), and therefore improvements are likely to be transient. Indeed evaluation of fitness programmes revealed decreased levels of cardiorespiratory fitness at follow-up [25,26]. A more holistic approach is required to increase participation in physical activity, particularly vigorous activity. Children accumulate the majority of vigorous activity during participation in sport. A recent study of children with CP found that fundamental movement skills proficiency, particularly product-orientated outcomes, is associated with participation in sport (Capio et al., 2012). As this was a cross-sectional study it is difficult to determine the direction of causality. The finding would suggest however that rehabilitation should include training programs to improve fundamental movement skills. Improvements have been shown to be possible in children with disabilities (Capio et al., 2013).

Even children with the physical capability of participating in sport often chose not to. Despite many children with CP recognising the benefits of physical activity, they report a number of personal and environmental barriers that prevent them from participating (Verschuren et al., 2012). These include physical and psychological factors like feeling like an outsider, the perception that sports aren't fun, fatigue, and feeling that the time required to learn a skill is too long. Environmental factors include the lack of opportunities to participate in sport, the lack of accessibility, negative attitudes of their peers, and trainers not being properly informed about the child's condition or how to include the child in the team. Parents are also concerned about their children participating in sport because their child might not fit in or be bullied, they were hesistant to ask a trainer to support their child, and they did not like observing their child struggling with sport (i.e. losing). These factors reflect the anecdotal information from participants in the current thesis. Adults reported that not being included in sports,

not being picked for teams, and being unable to keep up with their peers when in school, resulted in them losing motivation to participate in sport and ultimately giving up. Parents struggled with encouraging their child to keep up participation in sport when they saw their child was not being accepted by their peers or was having difficulty keeping up with others. In addition, even children who enjoyed participating in sport reported not being picked for school teams and finding it difficult to find appropriate organisations where they could play with children at a similar level to them. Besides the Football Association of Ireland's CP team there are few sports teams dedicated to children with CP. Even children who were members of the football team reported wanting to participate in other sports but not having the opportunity to.

Unlike exercise programmes, there is limited evidence behind the effectiveness of traditional therapeutic approaches in children with CP [34]. Rehabilitative programmes should be modified to reflect this so that children with CP are obtaining the maximal benefit out of the limited time they have in rehabilitation. However, improvements made in rehabilitation may not carry over to increased participation in everyday activity and improved cardiorespiratory fitness. If rehabilitation is to have a long-term benefit for children with CP rehabilitative services need to expand their support to include supervised sports or training programmes in schools or in the community that allow children with CP to play with other children of a similar ability. Healthcare professionals, who are knowledgeable about the child's disability and are educated to prescribe appropriate exercise, should be leading these programmes. This will make participation in sport more enjoyable and less intimidating for children with CP and their parents.

11.3 Critical Analysis of this Work

There are a number of limitations to the work in this thesis. A convenience sample was recruited for all studies in this thesis. This method of recruitment was adopted because of the limited access to adults and children with CP. There is no current register of people with CP in the Republic of Ireland. The number of adults and children with CP in Ireland is therefore unknown. The majority of rehabilitative services are only provided up until age 18 years, which makes it particularly difficult to contact adults with CP. International research reported that less than one-third of adults with CP are under the regular control of a rehabilitation physician (Hilberink et al., 2007). Despite every effort

being made to trace and recruit adults with CP into this study participation was low. Similar issues with recruitment have been identified in other studies of adults with CP (Van Der Slot et al., 2012, Nieuwenhuijsen et al., 2009). Adults who were health aware and interested in obtaining information about their risk factors may have been more likely to participate in studies 4 and 5, which could have biased the results. Similarly, children and their parents had to volunteer to participate and as a result the cohort in studies 6 and 7 may have been relatively healthy compared to the general population of children with CP. This would, however, mean that the prevalence of cardiometabolic risk factors are in fact higher than indicated in this thesis.

This method of recruitment also resulted in a large number of children classified in level I compared to levels II and III (63% vs. 16% and 21%). There is no information about the prevalence of children with CP, in each level of the GMFCS, in Ireland to compare this to. Data obtained in Australia, pertaining to births between 1993 and 2006, show that of ambulatory children with CP 50% are in level I, 35% are in level II and 15% are in level III [35].

The criterion method of measuring cardiorespiratory fitness is the direct measurement of VO_2 during a graded maximal exercise test. Measuring VO_2 during the SRT was not feasible. The data obtained from the SRT cannot be converted to VO_2. Reference values developed on a representative sample of children with CP throughout Europe were therefore relied on to classify fitness. While these allow for classification of the relative fitness of children with CP the absolute fitness of the children is unknown. Furthermore this test is not acceptable for use in adults with CP or in children in GMFCS level III. A trial was conducted using a SRT in children in level III (Verschuren et al., 2011). The results indicated that the majority of children could not reach a HR of >180bpm and therefore results were inaccurate. This test has also not been validated in children with CP and there are no reference values available for it. Similarly a trial was conducted using the SRT to assess cardiorespiratory fitness in adults with CP. This test has been validated on adults up to the age of 20 years. The results of the trial indicated that it was a feasible method of assessing fitness in young adults with CP but that fewer middle-aged and older adults with CP were able to reach a heart-rate of >180 bpm.

The limitation of using accelerometer cut-points that have been developed in able-bodied people to estimate energy expenditure in people with CP has been discussed at

length. It should be noted, however, that this may have resulted in an underestimation of physical activity intensity in people with CP, particularly those with greater functional limitations. There are also a number of limitations to using accelerometers. A large proportion of activity data obtained from children was not valid or was missing (17%). This was despite several children wearing the monitor more than once in an attempt to obtain valid data. Reports of missing data have ranged from 8% to 32% in TD children (Dencker et al., 2008; Hussey et al. 2007; Chaput et al., 2013; Ekelund et al., 2012). Accelerometers also cannot capture swimming or water activities. Adolescents with CP report participating in swimming more than TD adolescents (Maher et al., 2007), which may have resulted in an underestimation of time in physical activity. Only 16 (21.3%) children in study 6 reported swimming for between 1 and 3 hours a week, with the majority (n = 14) only swimming for one hour. Only 6 adults (14.6%) reported swimming for between 1 and 3 hours in study 4. Accelerometers also provide information about volume of sedentary activity only and not type of activity. The limitation of this is discussed in section 11.2.4. Accelerometers also only provide an indication of habitual physical activity as they are worn for typically seven days.

Finally, all of the studies conducted in this thesis were of a cross-sectional design. Therefore a conclusion cannot be drawn regarding the direction of causality between any of the associations found in this thesis. For example overweight/obese children with CP may reduce their levels of physical activity and as a result their cardiorespiratory fitness decreases, or children with low fitness may become overweight/obese as a result of participating in low levels of physical activity.

11.4 Future Research

There is potential for future research arising from the results presented in this thesis. Further research is required to identify an association between physical activity and cardiometabolic risk factors in adults with CP. A comparison of cardiorespiratory fitness to cardiometabolic risk factors in this population may provide more conclusive results because of the error involved in measuring physical activity in adults with CP. The association between physical activity and cardiorespiratory fitness in adults has only been investigated in one study and the method used to measure activity in this study did not distinguish between different intensities of physical activity (Nieuwenhuijsen et al.,

2011). It is likely that the results found for children in chapter 10 are similar to those in adults with CP but this requires verification.

Future research should investigate if physical activity and cardiorespiratory fitness are associated with other risk factors for cardiometabolic disease in children with CP such as blood lipids or insulin resistance. In addition, this study only investigated the role of two components of physical fitness (cardiorespiratory fitness and body composition) in protecting against cardiovascular risk factors as the majority of research to date has focused on these areas. There is emerging evidence that muscular fitness protects against cardiovascular risk factors in adults and children (Artero et al., 2012). This is an area that requires investigation in people with CP. Longitudinal studies are also required to deduce the direction of causality of the associations between physical activity, body composition, and cardiorespiratory fitness. Interventional studies are required to investigate if exercise programmes can reduce cardiometabolic risk factors in adults and children with CP.

11.5 Conclusion

In summary, the findings of this thesis indicate that adults with CP, particularly adults in GMFCS levels II and III, participate in reduced levels of moderate, vigorous, and total physical activity. Reduced moderate physical activity was associated with increases in a number of cardiometabolic risk factors. There was no difference however in the levels or prevalence of cardiometabolic risk factors across GMFCS level, despite differences in habitual physical activity. The prevalence of the metabolic syndrome was relatively high, however, among this relatively young cohort of adults. The prevalence of clustered risk and individual risk factors was higher among non-ambulatory adults with CP, compared to ambulatory adults.

Of concern, although nearly 30% of adults had hypercholesterolaemia, only 30% of these adults were on cholesterol medication. This suggests that risk factors for cardiometabolic disease are not identified in this population. Preventive screening may not have occurred in this cohort because of the relatively young age of these adults or possibly because of the relatively low prevalence of obesity. The results of this thesis indicate that waist circumference, however, is a better indicator of cardiometabolic risk

in adults with CP, than BMI. All screening should therefore include measurement of waist circumference, instead of or in conjunction with BMI. This may improve early detection of those at risk of cardiometabolic disease.

Similarly, a stronger association was observed between waist circumference and elevated blood pressure in children with CP, compared to BMI. Waist circumference also increased as cardiorespiratory fitness decreased. Physical activity is a primary intervention for reducing elevated blood pressure and improving cardiorespiratory fitness in children with CP. Time spent in total activity, moderate-to-vigorous activity and vigorous activity alone was strongly, inversely associated with both elevated blood pressure and cardiorespiratory fitness in children with CP. Moderate activity alone was not. Healthcare professionals should therefore be promoting participation in vigorous physical activity, such as sport, rather than moderate activity, among children with CP from a young age.

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Appendices

Appendix I Gross Motor Function Classification System

Introduction and User Instructions:

The Gross Motor Function Classification System for Cerebral Palsy is based on self-initiated movement with particular emphasis on sitting (truncal control) and walking. When defining on a 5-level classification system, our primary criterion was that the distinctions in motor function
between levels must be clinically meaningful. Distinctions between levels of motor function are based on functional limitations, the need for assistive technology including mobility devices (such as walkers, crutches, and canes) and wheeled mobility, and, to a much lesser extent, quality of movement. Level I includes children with neuromotor impairments whose functional limitations are less than what is typically associated with cerebral palsy and children who have traditionally been
diagnosed as having "minimal brain dysfunction" or "cerebral palsy of minimal severity." The distinctions between levels I and II, therefore, are not as pronounced as the distinctions between the other levels, particularly for infants less than 2 years of age. The focus is on determining what level best represents the child's present abilities and limitations in motor function. Emphasis is on the child's usual performance in home, school, and community settings. It is therefore important to classify on ordinary performance (not best capacity), and not to include judgements about prognosis. Remember the purpose is to classify a child's present gross motor function, not to judge quality of movement or potential for improvement. The descriptions of the 5 levels are broad and are not intended to describe the function of individual children. For example, an infant with
hemiplegia who is unable to crawl on hands and knees, but otherwise fits the description of level I, would be classified in level I. The scale is ordinal, with no intent that the distance between levels be considered equal or that children with cerebral palsy are equally distributed among the 5 levels. A summary of the distinctions between each pair of levels is provided to assist in determining the level that most closely resembles a child's current gross motor function. The title for each level represents the highest level of mobility that a child will achieve between 6–12 years of age. We recognize that classification of motor function is dependent on age, especially during

infancy and early childhood. For each level, therefore, separate descriptions are provided for children in several age bands. The functional abilities and limitations for each age interval are intended to serve as guidelines, are not comprehensive, and are not norms. Children below age 2 should be considered at their correct age. An effort has been made to emphasize children's function rather than their limitations. Thus, as a general principle, the gross motor function of children who are able to perform the functions described in any particular level will probably be classified at or above that level; in contrast, the gross motor function of children who cannot perform the functions of a particular level will likely be classified below that level.

LEVEL I—Walks without restrictions; limitations in more advanced gross motor skills.

Before 2nd birthday: Infants move in and out of sitting and floor sit with both hands free to manipulate objects. Infants crawl on hands and knees, pull to stand and take steps holding onto furniture. Infants walk between 18 months and 2 years of age without the need for any assistive mobility device.

From age 2 to 4th birthday: Children floor sit with both hands free to manipulate objects. Movements in and out of floor sitting and standing are performed without adult assistance. Children walk as the preferred method of mobility without the need for any assistive mobility device.

From age 4 to 6th birthday: Children get into and out of, and sit in, a chair without the need for hand support. Children move from the floor and from chair sitting to standing without the need for objects for support. Children walk indoors and outdoors, and climb stairs. Emerging ability to run and jump.

From age 6 to 12: children walk indoors and outdoors, and climb stairs without limitations. Children perform gross motor skills including running and jumping but speed, balance, and coordination are reduced.

LEVEL II—Walks without assistive devices; limitations walking outdoors and in the community.

Before 2nd birthday: Infants maintain floor sitting but may need to use their hands for support to maintain balance. Infants creep on their stomach or crawl on hands and knees. Infants may pull to stand and take steps holding onto furniture.

From age 2 to 4th birthday: Children floor sit but may have difficulty with balance when both hands are free to manipulate objects. Movements in and out of sitting are

performed without adult assistance. Children pull to stand on a stable surface. Children crawl on hands and knees with a
reciprocal pattern, cruise holding onto furniture and walk using an assistive mobility device as preferred methods of mobility.
From age 4 to 6th birthday: Children sit in a chair with both hands free to manipulate objects. Children move from the floor to standing and from chair sitting to standing but often require a stable surface to push or pull up on with their arms. Children walk without the need for any assistive mobility device indoors and for short distances on level surfaces outdoors. Children climb stairs holding onto a railing but are unable to run or jump.
From age 6 to 12: children walk indoors and outdoors, and climb stairs holding onto a railing but experience limitations walking on uneven surfaces and inclines, and walking in crowds or confined spaces. Children have at best only minimal ability to perform gross motor skills such as running and jumping.

Distinctions between levels I and II:

Compared with children in level I, children in level II have limitations in the ease of performing movement transitions; walking outdoors and in the community; the need for assistive mobility devices when beginning to walk; quality of movement; and the ability to perform gross motor
skills such as running and jumping.

LEVEL III—Walks with assistive mobility devices;
limitations walking outdoors and in the community.

Before 2nd birthday: Infants maintain floor sitting when the low back is supported. Infants roll and creep forward on their stomachs. From age 2 to 4th birthday: Children maintain floor sitting often by
"W-sitting" (sitting between flexed and internally rotated hips and knees) and may require adult assistance to assume sitting. Children creep on their stomach or crawl on hands and knees (often without reciprocal leg movements) as their primary methods of self-mobility. Children may pull
to stand on a stable surface and cruise short distances. Children may walk short distances indoors using an assistive mobility device and adult assistance for steering and turning.

From age 4 to 6th birthday: Children sit on a regular chair but may require pelvic or trunk support to maximize hand function. Children move in and out of chair sitting using a stable surface to push on or pull up with their arms. Children walk with an assistive mobility device on level surfaces and climb stairs with assistance from an adult. Children frequently are transported when travelling for long distances or outdoors on uneven terrain.

From age 6 to 12: children walk indoors or outdoors on a level surface with an assistive mobility device. Children may climb stairs holding onto a railing. Depending on upper limb function, children propel a wheelchair manually or are transported when traveling for long distances or outdoors on uneven terrain.

Distinctions between levels II and III:

Differences are seen in the degree of achievement of functional mobility. Children in level III need assistive mobility devices and frequently orthoses to walk, while children in level II do not require assistive mobility devices after age 4.

LEVEL IV—Self-mobility with limitations; children are transported or use power mobility outdoors and in the community.

Before 2nd birthday: Infants have head control, but trunk support is required for floor sitting. Infants can roll to supine and may roll to prone.

From age 2 to 4th birthday: Children floor sit when placed, but are unable to maintain alignment and balance without use of their hands for support. Children frequently require adaptive equipment for sitting and standing. Self-mobility for short distances (within a room) is achieved through rolling, creeping on stomach, or crawling on hands and knees without reciprocal leg movement.

From age 4 to 6th birthday: Children sit on a chair but need adaptive seating for trunk control and to maximize hand function. Children move in and out of chair sitting with assistance from an adult or a stable surface to push or pull up on with their arms. Children may at best walk short distances with a walker and adult supervision but have difficulty turning and maintaining balance on uneven surfaces. Children are transported in the community. Children may achieve self-mobility using a power wheelchair.

From age 6 to 12: Children may maintain levels of function achieved before age 6 or rely more on wheeled mobility at home, school, and in the community. Children may achieve self-mobility using a power wheelchair.

Distinctions between levels III and IV:

Differences in sitting ability and mobility exist, even allowing for extensive use of assistive technology. Children in level III sit independently, have independent floor mobility, and walk with assistive mobility devices. Children in level IV function in sitting (usually supported), but independent mobility is very limited. Children in level IV are more likely to be transported or use power mobility.

LEVEL V—Self-mobility is severely limited even with the use of assistive technology.

Before 2nd birthday: Physical impairments limit voluntary control of movement. Infants are unable to maintain antigravity head and trunk postures in prone and sitting. Infants require adult assistance to roll.

From age 2 to 12: Physical impairments restrict voluntary control of movement and the ability to maintain antigravity head and trunk postures. All areas of motor function are limited. Functional limitations in sitting and standing are not fully compensated for through the use of adaptive equipment and assistive technology. At level V, children have no means of independent mobility and are transported. Some children achieve self-mobility using a power wheelchair with extensive adaptations.

Distinctions between levels IV and V:

Children in level V lack independence even in basic antigravity postural control. Self mobility is achieved only if the child can learn how to operate an electrically powered wheelchair.

Appendix II Results of 25 studies reporting on the validity of the SWA, the IDEEA and the RT3.

Monitor	Sample	Ref.	Validity				Study
			Rest	Treadmill	Free-living activities	TEE	
SWA_m (v7.1)	n=30; 24-60yrs	DLW	Not reported	Not reported	Not reported	Mean: 2774±576kcal.d^{-1} Bias: -22±310kcal.d^{-1} (-0.1%) LOA: -630 to 585kcal.d^{-1} ICC: 0.85 **AEE** Mean: 983±486kcal.d^{-1} Bias: -119±286kcal.d^{-1} (-12%)* LOA: not reported ICC: 0.63	(Johannsen et al., 2010)
SWA_3 (v6.1)	n=30;	DLW	Not reported	Not reported	Not reported	Mean: 2774±576kcal.d^{-1}	(Johannsen et al., 2010)

	24-60yrs					Bias: -112±325kcal.d^{-1} (-4%) LOA: -749 to 525kcal.d^{-1} ICC: 0.80	
						AEE Mean: 983±486kcal.d^{-1} Bias: -123±278kcal.d^{-1} (-13%)* LOA: not reported ICC: 0.63	
SWA (v6.1)	n=20; 24.3±2.8yr	IC	Not reported	65% VO2 max Mean: 10.89 METs Bias: -1.5 METs	Run (30mins) Mean: 13.23 METs Bias: -3.5 METs	Not reported	(Drenowatz and Eisenmann, 2011)

(-14%)*	(-26%)*
LOA: -1.7 to	LOA: 1.1 to 5.9 METs
4.8METs	r_p: 0.66

<u>75% VO2 max</u>

Mean: 12.48 METs

Bias: -2.9 METs

(-23%)*

LOA: -0.1 to

5.8 METs

<u>85% VO2 max</u>

Mean: 14.09 METs

Bias: -4.6 METs

(-33%)*

LOA: 1.2 to 8.0 METs

SWA_3 (v6.1)	n=14; 30.4±6.2yr	DLW	Not reported	Not reported	Not reported	Mean: 3620±900kcal.d^{-1} Bias: -65±665kcal.d^{-1} (-2%)** LOA: -1368 to 1238kcal.d^{-1} r: 0.73	(Koehler et al., 2011)
		IC	Not reported	<u>Maximal test</u> Mean: not reported Bias:-4.5kcal.min^{-1}** LOA:-11.4 to 2.4kcal.min^{-1}	<u>Maximal cycle test</u> Mean: not reported Bias: -6.6kcal.min^{-1}** LOA:-14.8 to 1.6kcal.min^{-1}	Not reported	
SWA (v6.1)	n=19; 78-89yrs	DLW	Not reported	Not reported	Not reported	Mean: 2040±472kcal.d^{-1} Bias: -28±225kcal.d^{-1}	(Mackey et al., 2011)

						(+1%) LOA: -478 to 422kcal.d^{-1} ICC: 0.896 **AEE** Mean: 583±242kcal.d^{-1} Bias: -156±198kcal.d^{-1} (-27%)* LOA: -552 to 240kcal.d^{-1} ICC: 0.645	
SWA (v5.1)	n=19; 78-89yrs	DLW	Not reported	Not reported	Not reported	Mean: 2040±472kcal.d^{-1} Bias: +25±211kcal.d^{-1} (+1%) LOA: -397 to 447kcal.d^{-1} ICC: 0.904	(Mackey et al., 2011)

						AEE Mean: 583±242kcal.d^{-1} Bias: -108±185kcal.d^{-1} (-19%)* LOA: -478 to 262kcal.d^{-1} ICC: 0.720	
SWA (v5.1)	n=20; 19-56yrs	IC	Not reported	Not reported	Lifestyle and sporting activities (120mins) Mean: not reported Bias: -43.4±261.0kcal (-9%) LOA: -304.5 to 217.6kcal ICC: 0.73	Not reported	(Berntsen et al., 2010)

SWA_2 (v5.0)	n=49; 60-87yrs	IC	Mean: 1377±228kcal.d^{-1} Bias: +167±271kcal.d^{-1} (+12%)** LOA:-438 to 105kcal.d^{-1} r_p: 0.61	Not reported	Not reported	Not reported	(Heiermann et al., 2011)
SWA (v4.0)	n=169; 44±12yrs	IC	<u>Males</u> Mean: 1784±283kcal.d^{-1} Bias:+108kcal.d^{-1} (+6%)** LOA: -330 to 545kcal.d^{-1} LCCC: 0.583	Not reported	Not reported	Not reported	(Bertoli et al., 2008)

			Females Mean: 1409±188kcal.d^{-1} Bias: +55kcal.d^{-1} (+4%)** LOA: -269 to 378kcal.d^{-1} LCCC: 0.579				
SWA (v4.0)	n=99; 38±14yrs	IC	Mean: 1700±330kcal.d^{-1} Bias: Not reported (approx. 160kcal.d^{-1} [-9%] calculated from reported	Not reported	Not reported	Not reported	(Malavolti et al., 2007)

			means) LOA: approx. -506 to 182kcal.d^{-1}† r_p: 0.86				
SWA (v3.2)	n=40; 18-35yrs	IC	Not reported	<u>Walking@ 4.82km.h^{1}</u> <u>on 0%, 5%, 10%</u> <u>incline</u> Mean: not reported Bias: -14.9±17.5kcal (-6.9±8.5%)** LOA: not reported ICC: 0.77 <u>@ 0% incline</u> Mean: not reported Bias: +1.3±0.5kcal.min	<u>Cycling</u> Mean: not reported Bias: -32.4±18.8kcal (-28.9±13.5%)** LOA: not reported ICC: 0.28 <u>Stepping</u> Mean: not reported Bias: -28.2±20.3kcal (-17.7±11.8%)** LOA: not reported	Not reported	(Jakicic et al., 2004)

[1]*	ICC: 0.63
LOA: not reported	Arm ergometry
ICC: 0.72	Mean: not reported
	Bias: +21.7±8.7kcal
@ 5% incline	(+29.3±13.8%)**
Mean: not reported	LOA: not reported
Bias:	ICC: 0.63
-0.3±0.6kcal.min^{-1}*	
LOA: not reported	
ICC: 0.76	
@ 10% incline	
Mean: not reported	
Bias: -2.4kcal.min^{-1}*	
LOA: not reported	
ICC: 0.66	

SWA (v1.0)	n=13; 19-22yrs	IC	Mean: 1.3±0.1kcal.min^{-1} Bias: not reported (approx. 0kcal.min^{-1} calculated from reported means) LOA: -0.17 to 0.20kcal.min^{-1} r_p: 0.76	<u>Walking@4.83km.h^{-1}</u> Mean: approx. 4kcal.min^{-1} Bias: +38%* LOA: -0.29 to 3.25kcal.min^{-1} r_p:0.69 <u>Walking@6.44km.h^{-1}</u> Mean: approx. 6kcal.min^{-1} Bias: +14%* LOA: -1.90 to 3.62kcal.min^{-1} r_p: 0.54	<u>Cycling (40mins)</u> <u>Early stage (1-10mins)</u> Mean: 9.4±1.5kcal.min^{-1} Bias: -8.8% LOA: not reported r_p:0.11 <u>Mid stage (21-23mins)</u> Mean: 9.3±1.4kcal.min^{-1} Bias: -4.0% LOA: -3.26 to 2.52kcal.min^{-1} r_p: 0.12	Not reported	(Fruin and Rankin, 2004)

				<u>Late stage (31-40mins)</u> Mean: 9.2±1.8kcal.min^{-1} Bias -1.3% LOA: not reported r_p: 0.03			
				<u>Walking@6.44km.h^{-1} on 5% incline</u> Mean: approx. 8.5kcal.min^{-1} Bias: -22%* LOA: -6.24 to 2.52kcal.min^{-1} r_p: 0.47			
SWA (v not specified)	n=21; 24.7±5.4yrs	IC	Not reported	<u>Walking @ 3.24 to 12.84km.h^{-1}</u> Mean: 3.31±0.33 to 14.88±1.77kcal.min^{-1} Bias: not reported Approx. +1.25 to 3.71kcal.min^{-1} (+8 to	Not reported	Not reported	(King et al., 2004)

				59%)** LOA: not reported $r_{p:}$ 0.65 to 0.85			
SWA_2 (v6.1)	n=26 (11 normal BMI); 8-12yrs	IC	Not reported	<u>Walking @ 2, 4, 5, 6km.h^{-1}</u> Mean: not reported Bias: -26.8±9.1%# Bias @ 2,4,5,6km.h^{-1}: -10±32%, -15±17%, -17±15%, -19±13% LOA: not reported	Not reported	Not reported	(Arvidsson et al., 2011a)
SWA (v6.1)	n=22; 9.4±1.2yrs	IC	<u>Rest</u> Mean: 1.18±0.31kcal.min^{-1} Bias:	<u>Walking @ 3.2km.h^{-1}</u> Mean:2.25±0.61kcal.min^{-1} Bias: -0.02±0.70kcal.min^{-1} (-	<u>Colouring</u> Mean: 1.25±0.32kcal.min^{-1} Bias:	<u>Resting, free-living and treadmill activities (41mins)</u> Mean: Not reported	(Calabro et al., 2009)

-0.25±0.26kcal.min^{-1}	0.8%)	-0.05±0.95kcal.min^{-1}	Bias: -0.13kcal.min^{-1}
(-20.7%)*	LOA: not reported	(-4.0%)	(-16.3±12.4%)
LOA: not reported		LOA: not reported	LOA: -0.78 to
	Walking @ 4km.h^{-1}		1.04kcal.min^{-1}
	Mean:	Computer games	r_p: 0.71
	2.49±0.45kcal.min^{-1}	Mean:	
	Bias: +0.02kcal.min^{-1}	1.13±0.44kcal.min^{-1}	
	(+0.8%)	Bias:	
	LOA: not reported	-0.05±0.95kcal.min^{-1}	
		(-4.9%)	
	Walking @ 4.8km.h^{-1}	LOA: not reported	
	Mean:		
	2.67±0.55kcal.min^{-1}	Cycling	
	Bias:	Mean:	
	+0.09±0.83kcal.min^{-1}	3.99±1.35kcal.min^{-1}	
	(+3%)	Bias:	
	LOA: not reported	-1.00±1.28kcal.min^{-1}	

					(-25%)* LOA: not reported		
SWA (v4.2)	n=22; 9.4±1.2yrs	IC	<u>Rest</u> Mean: 1.18±0.31kcal.min^{-1} Bias: -0.38±0.41kcal.min^{-1} (-32%)* LOA: not reported	<u>Walking @ 3.2km.h^{-1}</u> Mean:2.25±0.61kcal.min^{-1} Bias:+0.79±0.91kcal.min^{-1} (+35%)* LOA: not reported <u>Walking @ 4km.h^{-1}</u> Mean: 2.49±0.45kcal.min^{-1} Bias: +0.68±0.99kcal.min^{-1} (+27%)* LOA: not reported	<u>Colouring</u> Mean: 1.25±0.32kcal.min^{-1} Bias: +0.28±0.67kcal.min^{-1} (+22%)* LOA: not reported <u>Computer games</u> Mean: 1.13±0.44kcal.min^{-1} Bias: -0.02±0.38kcal.min^{-1} (-2%)	<u>Resting, free-living and treadmill activities (41mins)</u> Mean: Not reported Bias: +0.39kcal.min^{-1} (+32%)** LOA: -1.46 to 0.69kcal.min^{-1} r_p: 0.72	(Calabro et al., 2009)

					LOA: not reported		
				Walking @ 4.8km.h^{-1}			
				Mean:	Cycling		
				2.67±0.55kcal.min^{-1}	Mean: 3.99±1.35kcal.min^{-1}		
				Bias: +0.97±1.25kcal.min^{-1}	Bias:		
				(+36%)*	-0.10±1.64kcal.min^{-1}		
				LOA: not reported	(-3%)		
					LOA not reported		
SWA (v6.1)	n=20; 14-15yrs	DLW	Not reported	Not reported	Not reported	Mean: 194±31kJ.kg.d^{-1} Bias: -10±21kJ.kg.d^{-1} (5%)* LOA: -20 to 60kJ.kg.d^{1} r: 0.74	(Arvidsson et al., 2009a)

SWA (v5.1)	n= 20; 14-15yrs	DLW	Not reported	Not reported	Not reported	Mean: 194±31kJ.kg.d^{-1} Bias: +17±20kJ.kg.d^{-1} (+9%)* LOA:-50 to 30kJ.kg.d^{-1} r: 0.79	(Arvidsson et al., 2009a)
SWA_2 (v5.1)	n=12; 11-13yrs	IC	Mean: 0.10±0.01 kJ.kg.$^{-1}$.min^{-1} Bias: -0.01±0.01 kJ.kg^{-1}.min^{-1} (-10%)* LOA: not reported	Not reported	<u>Free-living activities</u> <u>(48mins)</u> Mean: 25±2.8kJ.kg.min^{1} Bias: -4.49±2.65kJ.kg^{-1} (-18%)* LOA: not reported <u>Track walk and run</u> Mean: 11.6±1.3kJ.kg^{-1}.min^{-1}	Not reported	(Arvidsson et al., 2009b)

Bias: -1.39±kJ.kg^{-1} (-12%)*

LOA: not reported

Sitting

Mean:

0.12±0.02kJ.kg^{-1}.min^{-1}

Bias: -0.03±0.02kJ.kg^{-1}

(-25%)*

LOA: not reported

Cycling

Mean:

0.51±0.06kJ.kg^{-1}.min^{-1}

Bias: -0.25kJ.kg^{-1}.min^{-1}

(-49%)*

LOA: not reported

SWA_2 (v5.1)	n=20; 11-13yrs	IC	Mean: 4.3±0.5kJ.min^{-1} Bias: -0.7kJ.min^{1} (0.2%)** LOA: not reported	<u>Walking @ 2 and 3km.h^{-1}</u> Mean: 11.8±2.8kJ.min^{-1} and 12.4±2.6kJ.min^{-1} Bias: +1.3±3.1kJ.min^{-1} (+11%) and +0.1±2.9kJ.min^{-1} (+0.8%) LOA: not reported <u>Walking/running @ 4km.h^{-1} to 10km.h^{-1}</u> Mean: 12.8±2.4kJ.min^{-1}	<u>Sitting</u> Mean: 5.6±0.5kJ.min^{-1} Bias: -2.0±0.9kJ.min^{-1} (-36%)** LOA: not reported <u>Cycling</u> Mean: 23.5±3.8kJ.min^{-1} Bias: -12.0±3.7kJ.min^{-1} (-51%)** LOA: not reported	Not reported	(Arvidsson et al., 2007)

				to 26.1±4.7kJ.min^{-1} Bias: -1.2±2.6kJ.min^{-1} (-9%)* to -11.1±3.5kJ.min^{-1} (-43%)** LOA: not reported			
SWA (v4.1)	n=21; 10-14yrs	IC	<u>Resting metabolic rate</u> Mean: 1.05±0.24kcal.min^{-1} Bias: +22%** LOA: not reported <u>Sleeping</u> Mean:	<u>60% VO2 max (30mins)</u> Mean: 5.49±1.92kcal.min^{-1} Bias: +0.78kcal.min^{-1} (+14%)** LOA: -1.02-2.57kcal.min^{-1}	<u>Sedentary activities</u> Mean: 1.61±0.24kcal.min^{-1} Bias: +0.34kcal.min^{-1} (+21%)** LOA:-0.25 to 0.93kcal.min^{-1}	<u>TEE (23hours)</u> Mean: 1.42±0.23kcal.min^{-1} Bias: +0.28kcal.min^{-1} (+20%)** LOA: not reported	(Dorminy et al., 2008)

			0.92±0.21kcal.min^{-1} Bias: +16%** LOA: not reported				
IDEEA	n=14; 20-55yrs	DLW	Not reported	Not reported	Not reported	<u>TEE</u> Mean: 139±20kJ.kg^{-1}.d^{-1} Bias: +38kJ.kg^{-1}.d^{-1} (+27%)** LOA: 8.4 to 67.8kJ.kg^{-1}.d^{-1} LCCC: 0.280 <u>AEE</u> Mean: 2.3±1.3MJ.d^{-1} Bias:+1.7MJ.d^{-1} (+74%)** LOA: -0.5 to 3.8MJ.d^{-1}	(Whybrow et al., 2012)

						LCCC: 0.083	
		IC			Cycling Mean: 22.8±4.61kJ.min^{-1} Bias-14.5kcal.min^{-1} (-63%)** LOA: not reported	TEE (22hours) Mean: 116±11kJ.kg^{-1} Bias: +12.1kJ.kg^{-1} (+10%)** LOA: -7.9 to 32.0kJ.kg^{-1} LCCC: 0.484	(Whybrow et al., 2012)
IDEEA	n=26 (11 normal BMI); 8-12yrs	IC	Not reported	Walking @ 2, 4, 5, 6km.h^{-1} Mean: not reported Bias: +4.2±9.6%# Bias @ 2,4,5,6km.h^{-1}: +15±19%, +1±16%, -5±13%, -10±13%, respectively	Not reported	Not reported	(Arvidsson et al., 2011a)

			LOA: not reported				
IDEEA	n=12; 11-13yrs	IC	Mean: 0.10±0.01 $kJ.kg^{-1}.min^{-1}$ Bias: +0.01±0.03 $kJ.kg^{-1}.min^{-1}$ (+10%) LOA: not reported	Not reported	<u>Free-living activities</u> <u>(48mins)</u> Mean: 25.0±2.8$kJ.kg^{-1}.min^{-1}$ Bias: -2.90$kJ.kg^{-1}$ (-12%) * LOA: not reported <u>Track walk and run</u> Mean: 11.6±1.3$kJ.kg^{-1}.min^{-1}$ Bias: 0.29±0.95$kJ.kg^{-1}$ (+3%)* LOA: not reported	Not reported	(Arvidsson et al., 2009b)

Sitting

Mean:

0.12±0.02kJ.kg^{-1}.min^{-1}

Bias: -0.02±0.03kJ.kg^{-1}

(-17%)*

LOA: not reported

Cycling

Mean:

0.51±0.06kJ.kg^{-1}.min^{-1}

Bias: approx.

-0.31kJ.kg^{-1}.min^{-1}

(-61%)*

LOA: not reported

IDEEA	n=27; 15-61yrs	IC	Not reported	Not reported	Not reported	<u>Resting, free-living and treadmill activities (50mins)</u> Mean: not reported Bias: -0.075kcal.min^{-1} LOA: -0.599 to 0.449kcal.min^{-1} Accuracy: 98.9±6.0% r: 0.973	(Zhang et al., 2004)
	Subsample of n=10; 20-53years	WR IC	Not reported	Not reported	Not reported	Mean: not reported Bias: -0.057kcal.min^{-1} LOA: -0.233 to 0.118kcal.min^{-1} Accuracy: 95.1±2.3% r: 0.959	(Zhang et al., 2004)

RT3	n=20; 7-12yrs	IC	Not reported	<u>Walking @ 3km.h^{-1}</u> Mean: approx. 2kcal.min^{-1}† Bias: approx. 0kcal.min^{-1}† LOA: approx. -2.5 to 0.75kcal.min^{-1}† r_p: 0.56 <u>Walking @ 6km.h^{-1}</u> Mean: approx. 4kcal.min^{-1}† Bias: approx. -1kcal.min^{-1}†* LOA: approx. -3 to 0.5kcal.min^{-1}†	<u>Sitting</u> Mean EE: not reported Bias: no significant difference (value not reported) LOA: not reported	Not reported	(Hussey et al., 2009)

Walking @ 6km.h^{-1} on a 10% incline

Mean: approx. 5kcal.min^{-1}†

Bias: no significant difference (value not reported)

LOA: not reported

Running @ 9km.h^{-1}

Mean: approx. 6.5kcal.min^{-1}†

Bias: no significant difference (value not reported)

LOA: not reported

				r_p: 0.84			
RT3	n=27; 12-14yrs	IC	Not reported	<u>Walking @ 3km.h^{-1} on 0, 5, 10% incline</u> Mean: 1.40±0.30kcal.min^{-1} to 2.23±0.37kcal.min^{-1} Bias: +0.76 to -0.50kcal.min^{-1} (+54% to -22%)# LOA: not reported <u>Running @ 6km.h^{-1}</u> Mean: 3.25±0.62kcal.min^{-1} Bias: +3.12kcal.min^{-1} (+96%)#	<u>Sedentary activities</u> Mean: 0.60±0.10 to 1.04±0.25kcal.min^{-1} Bias:-0.52 to -0.57kcal.min^{-1} (-55% to -87%)# LOA: not reported <u>Cycling @ 25W and 50W</u> Mean: 1.19±0.36 and 2.40±0.43kcal.min^{-1} Bias: -0.10 and -1.44kcal/min^{-1} (-8 and -60%)#	Not reported	(Sun et al., 2008)

LOA: not reported	LOA: not reported
Running @ 8km.h^{-1} Mean: 3.92±0.60kcal.min^{-1} Bias: +4.22kcal.min^{-1} (+108%)# LOA: not reported	Catch and throw Mean: 0.92±0.16kcal.min^{-1} Bias: -0.122kcal.min^{-1} (-13%)# LOA: not reported
	Lower limb outdoor activities Mean: 0.88±0.18 to 2.34±0.31kcal.min^{-1} Bias: +0.334 to +5.017kcal.min^{-1} (+33 to +214%)# LOA: not reported

RT3	n=42; 12.2±1.1yrs	Not reported	<u>Walking @4km.h^{-1}</u> Mean: 0.106±0.017 kcal.kg^{-1}.min^{-1} Bias: -0.022kcal.kg^{-1}.min^{-1} (-20.7%)* LOA: not reported <u>Walking @ 4km.h^{-1} on 6% incline</u> Mean:0.119±0.018 kcal.kg^{-1}.min^{-1} Bias: approximately -0.036kcal.kg^{-1}.min^{-1} (-30%) LOA: not reported	Not reported	Not reported	(Kavouras et al., 2008)

Walking @ 6km.h^{-1}

Mean: 0.140±0.020

kcal.kg^{-1}.min^{-1}

Bias: -0.004

kcal.kg^{-1}.min^{-1}

(-2.8%)

LOA: not reported

Walking @ 6km.h^{-1} on 6% incline

Mean:

0.156±0.22

kcal.kg^{-1}.min^{-1}

Bias: approximately

-0.019kcal.kg^{-1}.min^{-1}

(-12%)

				LOA: not reported			
				<u>Running @ 8km.h^{-1}</u> Mean: 0.217±0.028 kcal.kg^{-1}.min^{-1} Bias: 0.017kcal.kg^{-1}.min^{-1} (+7.8%)* LOA: not reported			
RT3	n=274; 38.3±12.4yrs	IC	Not reported	<u>Walking/running @ 4.82km.h^{-1}, 5.6km.h^{-1}, 8km.h^{-1}</u> Mean: not reported Bias +0.9 to	<u>Seventeen activities of daily living</u> Mean: not reported Bias: -1.6kcal LOA: not reported RMSE: 3.8	<u>Variety of treadmill and activities of daily living</u> Mean: not reported Bias: -0.5kcal LOA: not reported RMSE: 2.9	(Lyden et al., 2011)

+1.8kcal*

LOA: not reported

RMSE: 1.3 to 2.9

Walking/running @ 4.82km.h^{-1}, 5.6km.h^{-1} and 8km.h^{-1} on 3% incline

Mean: not reported

Bias: -0.4kcal* to +0.2kcal

LOA: not reported

RMSE: 1.9 to 2.4

All treadmill activity

Mean: not reported

Bias: +0.5kcal*

Washing dishes

Mean: not reported

Bias: -0.6kcal

LOA: not reported

RMSE: 1.0

Ascending stairs

Mean: not reported

Bias: -7.6kcal

LOA: not reported

RMSE: 7.9

				LOA: not reported RMSE: 1.8			
RT3	n=36; 39±10yrs	IC	Not reported	Not reported	Not reported	TEE Mean: 12809kJ.d^{-1} Bias: -539kJ.d.$^{-1}$ (-4%)# LOA: approx. -5000kJ.d^{-1} to 3900kJ.d^{-1} AEE Mean: 3448kJ.d^{-1} Bias: -485kJ.d^{-1} (-14%)# LOA: approx. -4500kJ.d^{-1} to 3500kJ.d^{-1}	(Maddison et al., 2009)
RT3	n=212; 20-60yrs	IC	Not reported	Walking/running @ 4.82km.h^{-1},	Various activities of daily living	Treadmill and activities of daily living	(Howe et al., 2009)

5.61km.h^{-1},	Mean: 5.1±0.1kcal.min^{-1}	Mean: 5.6±0.1kcal.min^{-1}
8.03km.h^{-1}	Bias: -1.75±0.11kcal.min^{-1}	Bias:
Mean: 3.5±0.1 to	(-34.3%)**	-0.47±0.06kcal.min^{-1}
9.3±0.1kcal.min^{-1}	LOA: not reported	(-8.4%)*
Bias:		LOA: not reported
+0.86±0.06kcal.min^{-1} to		
1.91±0.16kcal.min^{-1} (+21 to +25%)**		
LOA: not reported		
Walking/running @ 4.82km.h^{-1}, 5.61km.h^{-1}, 8.03km.h^{-1}; all at 3% incline		
Mean: 4.6±0.1 to		
10.8±0.2kcal.min^{-1}		
Bias: -0.38±0.08		

kcal.min^{-1}** to

+0.30±0.15

kcal.min^{-1}*

(-9%** to +3%*)

LOA: not reported

<u>All treadmill activity</u>

Mean: 6.0±0.1kcal.min^{-1}

Bias:
+0.54±0.05kcal.min^{-1}

(+9%)**

LOA: not reported

RT3	n=10; 29.3±5.2yrs	IC		Walking@ 2km.h^{-1}, 3km.h^{-1}, 4km.h^{-1} on 4% incline Mean: not reported Bias: +45.7±67.2% LOA: not reported			(Jacobi et al., 2007)
RT3	n=21; 24.7±5.4yrs	IC	Not reported	Walking/running @ 3.24 to 12.84km.h^{-1} Mean: 3.67±0.61 to 16.71±2.22kcal.min^{-1} Bias: not reported Approx. +0.94 to 3.61kcal.min^{-1} (+12 to 57%)** LOA: not reported r_p: 0.18 to 0.75	Not reported	Not reported	(King et al., 2004)

*p<0.05, **p<0.001

† approximation, axes unclearly labelled.

p value not reported.

TEE, total energy expenditure; AEE, activity energy expenditure; Bias, mean bias (±standard deviation) between methods (monitor-reference); LOA, limits of agreement; Mean, mean energy expenditure (±standard deviation) of measurement period as measured by reference method; r_p, Pearson's product-moment correlation co-efficient; LCCC, Lin's concordance correlation coefficient; ICC, intraclass correlation coefficient; RMSE, root mean square error

Appendix III Results from eight studies reporting on the reproducibility of the SWA and RT3

Motion Sensor	Sample	Reproducibility	Study
SWA_3 (v6.1)	n = 34; 18 - 45 yr	r_p = 0.82*	
		ICC_{2d} = 0.62* - 0.98*	(Brazeau et al., 2011)
SWA (v5.0)	n = 49; 60 - 87 yr	$r_{p\ 2d}$ = 0.98*	(Heiermann et al., 2011)
SWA (v1.0)	n = 13; 18 - 25 yr	$r_{p\ 2d}$ = 0.93*	
		LOA_{2d}: -0.07 $kcal.min^{-1}$ to 0.10 $kcal.min^{-1}$	(Fruin and Rankin, 2004)
RT3	n = 60; 10 - 16 yr	CV: 6.6% - 17.3%	(Vanhelst et al., 2010b)
RT3	n = 6; 36.1 ± 9.4 yr;		
	n = 6 monitors	ICC=0.80*	
		r_p = 0.78†	(Reneman and Helmus, 2010)
RT3	n = 22 monitors	Intra-instrument CV : 0.29% - 1.81%	
		Inter-instrument CV: 9.5% - 34.7%	
		Intra-instrument ICC = 0.000 - 0.042†	(Krasnoff et al., 2008)
RT3	n = 1; 24 yr;		
	n =8 monitors	Inter-instrument CV: 1.5%-14.4%	(Powell and Rowlands, 2004)

RT3	n = 23 monitors	Inter-instrument ICC = 0.99*	
		Inter-instrument CV: 4.2% - 26.7%	
		Intra-instrument CV: 0.00% - 67.8%	(Powell et al., 2003)

*p≤0.01; † p value not reported.

r_p, Pearson's product-moment correlation co-efficient; LOA, limits of agreement; SWA_3, pro3 armband; CV, coefficient of variation; d, day; s, sampling times

Appendix IV Raw energy expenditure data from adults in study 1

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U
1	ID	EErest	EE3km	EE6km	EE6km10%	EE9km	SWArest	SWA3km	SWA6km	SWA6km10%	SWA9km	RT3 rest	RT3 3km	RT3 6km	RT3 6km10%	RT3 9km	IDEEA rest	IDEEA 3km	IDEEA6km	IDEEA 6km10%	IDEEA 9km
2	A01	0.97	3.16	4.90	9.00	9.18	0.98	3.59	4.79	4.89	8.54	-	-	-	-	-	1.49	2.96	3.00	4.22	7.27
3	A02	0.75	3.87	5.51	11.88	10.50	0.96	3.68	5.31	8.04	8.60	1.07	3.41	6.80	11.62	13.36	1.07	3.20	5.19	10.70	9.58
4	A03	0.92	3.68	6.51	10.40	10.52	1.06	3.69	5.55	6.62	10.22	-	-	-	-	-	1.18	3.62	6.01	5.52	12.00
5	A04	0.69	3.34	4.88	9.95	7.99	0.93	3.97	4.59	5.62	8.70	-	-	-	-	-	1.05	3.01	4.49	4.25	8.80
6	A05	0.72	3.83	6.32	11.30	10.13	0.98	4.00	5.70	6.24	9.46	1.10	4.19	9.69	8.78	15.14	1.10	3.44	5.34	4.87	10.10
7	A06	1.29	4.25	6.11	11.84	12.19	1.34	4.00	6.25	6.43	11.15	1.44	3.84	7.34	6.96	14.48	1.57	4.52	7.71	6.79	16.50
8	A07	1.20	4.97	8.22	13.49	14.60	1.32	5.08	7.45	8.22	12.67	-	-	-	-	-	1.41	4.30	6.70	6.45	14.60
9	A08	1.11	3.12	5.88	11.41	11.01	1.00	4.07	5.86	7.01	9.89	-	-	-	-	-	1.40	3.39	5.48	8.01	9.37
10	A09	1.06	3.64	5.95	10.71	10.06	1.15	3.71	4.96	4.89	10.27	1.26	3.52	6.52	5.88	13.48	1.29	3.47	4.82	4.37	13.30
11	A10	0.88	3.62	4.92	8.98	9.24	1.00	3.40	4.54	5.06	9.60	1.10	2.58	6.51	6.69	13.18	1.18	3.46	5.10	4.74	10.60
12	A11	-	4.25	6.68	12.14	13.17	1.20	3.85	6.52	6.31	10.41	1.35	5.55	9.51	9.18	16.76	1.37	4.11	6.42	5.75	12.40
13	A12	1.39	4.96	8.41	15.44	16.98	1.48	5.91	7.62	7.73	14.53	1.63	4.81	10.42	10.15	16.54	1.52	4.99	7.30	7.34	9.65
14	A13	1.19	4.74	7.38	14.01	15.05	1.38	6.48	8.50	7.37	12.77	1.54	5.46	9.75	9.65	22.15	1.49	4.86	7.80	6.91	17.30
15	A14	1.08	4.57	7.34	14.41	14.96	1.15	4.67	6.59	8.37	12.06	1.28	4.25	9.68	10.06	16.58	1.48	4.61	6.73	6.77	13.20
16	A15	0.93	3.92	5.83	12.36	12.35	1.04	4.08	5.51	6.88	10.74	1.19	4.27	9.60	8.42	16.26	1.26	4.12	6.31	6.13	11.70
17	A16	0.61	3.34	5.80	7.19	8.63	0.96	3.71	5.57	5.93	8.44	1.07	3.60	7.85	7.02	13.91	1.07	3.44	5.79	5.11	9.66
18	A17	1.01	4.60	6.90	11.10	11.27	0.99	6.46	6.37	8.04	9.99	1.14	5.78	9.42	9.26	13.79	1.19	4.20	6.62	6.41	10.80
19	A18	1.09	4.04	6.33	14.05	11.96	1.27	4.77	6.14	9.82	10.22	1.37	4.03	10.32	12.97	16.44	-	-	-	-	-
20	A19	0.92	3.43	6.31	13.15	11.98	1.26	4.70	7.25	7.49	12.74	1.42	4.24	9.28	9.00	17.27	1.40	4.40	8.19	6.86	14.00
21	A20	1.04	4.69	6.91	13.37	12.88	1.26	5.85	7.31	8.81	13.80	1.45	6.53	14.84	13.54	25.19	1.35	4.66	7.55	6.78	14.10
22	A21	0.73	3.22	5.76	8.62	8.55	0.92	4.99	8.11	7.22	8.98	1.05	5.69	12.73	10.77	16.70	1.03	3.68	10.10	6.30	10.50
23	A22	-	4.39	6.21	11.72	12.23	1.20	5.09	6.71	7.28	12.19	1.36	4.92	9.40	8.37	17.21	1.40	4.75	6.73	6.35	14.10
24	A23	1.33	4.50	7.36	13.53	13.12	1.38	5.55	8.33	8.97	14.65	1.53	4.90	9.87	9.94	20.43	1.45	4.96	7.99	7.59	14.80
25	A24	0.85	3.45	5.39	10.03	9.95	0.96	3.80	5.25	5.03	8.54	1.09	3.52	6.99	7.12	13.13	1.10	3.45	5.19	4.64	11.20
26	A25	0.78	3.17	6.05	8.41	8.84	0.87	3.66	4.94	4.84	6.93	0.99	3.65	6.65	5.49	12.03	1.12	2.81	4.33	3.95	8.13
27	A26	0.74	3.00	5.51	9.59	9.32	0.92	3.59	5.12	5.38	8.09	1.04	2.91	5.72	5.37	10.74	1.07	4.13	5.56	4.95	9.18

Appendix V Raw energy expenditure data from children in study 1

ID	Eerest	EE3km	EE6km	EE6km10%	EE9km	SWArest	SWA3km	SWA6km	SWA6km10%	SWA9km	RT3rest	RT33km	RT36km	RT36km10%	RT39km	IDEEArest	IDEEA3km	IDEEA6km	IDEEA6km10%	IDEEA9km
C01	1.07	3.17	5.68	9.79	10.49	0.88	3.28	5.07	5.44	9.48	1.12	2.76	5.56	7.05	11.19	1.12	3.21	4.98	4.44	9.00
C02	-	3.62	5.29	8.34	8.46	-	4.20	5.01	5.48	9.13	-	3.56	6.19	5.84	10.88	-	3.71	5.56	5.41	10.80
C03	-	3.16	5.39	8.55	8.44	-	5.40	4.15	8.13	7.59	-	3.21	6.07	5.68	11.82	-	3.26	5.40	5.27	9.61
C04	-	2.19	3.53	3.59	-	0.38	0.84	1.89	1.96	-	0.69	2.06	3.82	4.06	-	1.92	2.34	3.66	3.35	-
C05	-	1.91	2.60	2.69	-	0.45	1.27	2.45	2.48	-	0.83	2.01	4.55	5.00	-	1.65	2.50	4.06	3.88	-
C06	0.67	2.51	4.99	6.58	6.25	0.56	2.04	3.11	3.29	3.96	0.82	2.24	5.34	5.76	7.29	1.74	3.14	5.12	5.24	6.87
C07	0.85	3.14	4.08	8.12	8.36	0.74	3.29	4.86	5.23	8.06	0.98	3.24	5.16	5.44	8.86	-	-	-	-	-
C08	0.85	2.40	4.32	6.25	6.22	0.59	1.93	2.87	4.27	4.86	0.86	2.47	5.63	7.03	8.44	3.59	3.12	3.97	3.96	6.13
C09	0.77	2.44	3.97	4.44	-	0.51	0.98	3.06	2.76	-	0.79	2.17	4.72	4.30	-	1.73	2.97	3.71	3.77	-
C10	-	3.21	5.17	5.67	7.21	0.76	2.59	3.45	3.67	6.19	0.99	3.37	6.20	5.28	10.59	1.45	3.01	4.62	4.35	7.72
C11	0.87	3.02	5.19	8.38	8.75	0.78	2.09	3.57	4.15	6.48	1.00	3.64	6.40	6.82	12.31	1.29	3.03	4.75	4.30	8.29
C12	1.21	3.21	5.39	8.43	9.45	0.96	4.21	5.76	6.05	10.07	1.19	3.73	7.07	6.44	11.72	1.28	3.72	5.57	4.80	11.90
C13	0.79	3.33	5.43	7.44	7.86	0.77	3.07	3.72	3.87	6.08	1.01	2.22	2.96	3.32	5.01	2.33	2.96	5.32	4.69	8.53
C14	0.89	3.76	5.68	7.54	-	0.94	3.58	5.16	4.33	-	1.02	5.45	9.94	8.04	-	1.34	3.21	4.38	4.48	-
C15	0.90	3.37	6.59	10.11	-	0.94	1.70	4.46	4.89	-	1.02	3.43	7.45	9.64	-	1.79	3.22	4.96	4.58	-
C16	0.86	3.30	5.16	8.53	8.99	0.86	1.11	4.99	5.68	8.50	1.08	3.33	6.64	5.96	10.12	0.00	3.15	4.80	4.29	8.81
C17	0.93	4.91	8.00	13.33	16.26	1.10	4.93	7.65	7.65	14.46	1.25	5.14	12.07	11.89	22.43	1.48	3.93	10.30	8.40	10.20
C18	-	3.29	5.18	8.81	8.47	0.92	3.79	5.38	4.67	9.20	1.08	3.34	6.76	6.56	10.21	1.90	3.31	4.42	4.33	7.72
C19	1.04	3.81	7.76	10.75	10.30	0.92	4.64	8.57	8.57	9.04	1.13	3.94	9.35	9.58	12.34	1.07	3.20	5.85	6.10	9.25
C20	1.10	4.25	7.26	12.21	12.31	1.28	6.54	7.05	5.72	14.50	1.43	4.57	9.35	5.90	19.62	1.47	4.36	6.43	4.41	9.92
C21	-	3.25	5.16	7.79	8.76	-	4.89	5.93	6.05	8.96	-	3.49	5.79	6.22	12.40	-	3.10	4.92	4.49	9.92
C22	0.87	3.42	5.66	8.28	9.00	0.82	4.25	5.81	5.74	7.20	1.02	3.18	5.82	5.81	11.09	-	-	-	-	-

Appendix VI Raw energy expenditure data for adults in study 2

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y
1	ID	EE_6MWT	SWA_6MWT	RT3_6MWT	IDEEA_6MWT	EE rest	SWA rest	RT3_rest	IDEEA_rest	EE_1km	SWA1km	RT3_1km	IDEEA_1km	EE_1km5%	SWA 1km5%	RT3_1km5%	DEEA_1km5%	EE_2km	SWA_2km	RT3_2km	IDEEA_2km	EE_4km	SWA_4km	RT3_4km	IDEEA_4km
2	CPA01	7.53	7.25	9.93	5.86	1.15	1.22	1.41	1.42	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3	CPA02	8.17542	5.95	8.02	4.65	1.16	1.15	1.29	1.35	2.97	1.52	2.07	2.8	-	-	-	-	4.53	5.27	3.03	3.55	7.91	5.69	6.49	4.32
4	CPA03	5.32	6.13	5.95	5.66	0.95	1	1.09	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5	CPA04	4.779	6.23	8.5	5.75	0.98	1.06	1.19	1.2	2.97	4.3	1.75	3.28	3.37	4.63	1.72	3.23	3.99	3.64	2.29	3.19	5.08	4.57	4.47	4
6	CPA05	6.036	8.4	8.5	6.75	1.29	1.23	1.42	1.41	3.41	6.69	2.26	3.97	3.96	7.17	2	3.26	4.44	3.45	5.99	4.59	-	-	-	-
7	CPA06	8.96	8.65	9.38	7.19	1.37	1.4	1.5	1.48	3.97	6.05	2.86	4.26	4.58	10.69	2.75	4.19	4.22	7.36	3.55	4.4	5.34	9.63	6.51	5.09
8	CPA07	5.2	5.29	5.26	4.2	1.31	0.94	1.09	1.01	3.12	7.65	2.18	2.58	3.29	7.52	2.08	2.56	4.07	7.96	2.67	2.93	5.12	6.07	4.15	3.59
9	CPA08	7	7.51	-	3.46	1.31	1.02	-	1.29	-	-	-		-	-	-		-	-	-		-	-	-	
10	CPA09	5.6	10.81	3.57	3.39	1.46	1.08	1.22	1.32	4.94	10.03	2.71	3.56	4.36	10.05	2.49	3.55	6.08	10.71	2.74	2.54	-	-	-	-
11	CPA10	4.55	5.19	5.61	5	0.93	0.99	1.06	1.09	2.48	4.51	1.93	2.77	3.05	6.55	1.95	2.82	3.29	5.61	2.63	2.91	4.68	8.12	4.56	3.78
12	CPA11	6.38	6.25	8.05	5.11	1.29	1.03	1.12	0.98	2.33	2.03	1.63	2.47	2.46	2.11	1.65	2.35	2.52	3.3	2.72	2.51	3.32	3.39	4.13	3.23
13	CPA12	6.32	6.25	9.61	4.75	1.12	1	1.09	0	2.56	-	1.66	0	3.53	-	1.67	0	3.82	0.9	3.34	2.78	4.83	5.33	5.25	3.68
14	CPA13	13.13	8.02	9.28	5.55	1.3	1.01	1.22	1.3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
15	CPA14	4.53	4.9	3.84	-	1.06	0.91	0.98	-	2.09	2.93	1.69	-	2.22	2.59	1.47	-	2.64	3.51	2.26	-	-	-	-	-
16	CPA15	5.75	7.43	6.05	4.84	1.47	1.3	1.27	1.27	2.83	2.81	1.95	3.45	3.14	3.1	1.97	2.49	3.39	5.43	2.71	3.39	5.11	5.75	4.82	4.45
17	CPA16	6.52	6.62	9.25	5.37	1	0.99	1.09	1.1	2.31	6.63	1.89	1.97	2.32	7.22	2.47	2.27	2.93	7.81	3.06	1.93	4.49	-	4.4	8.14
18	CPA17	6.96	8.45	11.03	-	1.18	1.34	1.47	-	4.41	6.9	3.49	-	4.24	5.24	2.79	-	4.02	1.75	4.14	-	-	-	-	-
19	CPA18	7.77	4.39	4.96	3.11	1.3	0.93	1	0.9	3.64	6.32	1.93	1.52	3.76	6.21	1.99	1.75	4.63	2.2	2.65	2.36	-	-	-	-

Appendix VII Raw energy expenditure data for children in study 2

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U
1	ID	EE_6MWT	SWA_6MWT	RT3_6MWT	DEEA_6MWT	EE rest	SWA_rest	RT3_rest	IDEEA_rest	EE_1km	SWA_1km	RT3_1km	IDEEA_1km	EE_1km5%	SWA_1km5%	RT3_1km5%	DEEA_1km5%	EE_2km	SWA_2km	RT3_2km	IDEEA_2km
2	CPC02	4.29	2.55	3.89	3.69	0.64	0.76	0.95	1.75	2.35	2.59	1.64	2.84	-	-	-	-	3.23	2.98	2.27	2.99
3	CPC03	2.91	2.47	2.81	2.47	1.60	0.89	0.99	1.54	-	-	-	-	-	-	-	-	-	-	-	-
4	CPC04	4.26	2.95	3.21	2.82	1.22	0.81	1.10	1.06	-	4.46	-	-	-	5.28	-	-	-	-	-	-
5	CPC05	4.47	5.81	4.93	3.79	0.63	0.92	1.04	1.07	2.26	3.43	1.68	2.5	1.64	3.17	1.68	2.15	2.36	3.67	2.31	2.82
6	CPC06	3.10	2.36	3.57	2.91	0.80	0.45	0.81	1.03	1.68	1.42	1.31	1.94	-	-	-	-	-	-	-	-
7	CPC08	2.17	6.32	2.12	2.84	0.74	0.44	0.83	1.03	1.14	1.40	1.17	1.99	1.02	1.37	1.15	2	1.32	-	1.30	2.08
8	CPC11	7.44	7.37	6.31	3.9	1.25	0.93	1.10	1.13	3.52	2.37	2.30	2.11	3.73	6.99	2.30	2.19	4.60	6.62	3.16	2.93
9	CPC12	3.76	5.37	4.37	3.61	0.89	0.62	0.88	1.03	1.50	1.97	1.27	2.14	1.60	1.90	1.27	2.14	1.86	2.31	1.70	2.15
10	CPC13	4.59	2.42	3.52	3.53	0.87	0.48	0.84	1.27	2.05	1.65	1.36	2.05	1.69	1.58	1.20	1.95	1.93	1.72	1.42	1.8
11	CPC14	5.19	5.06	4.65	3.79	1.18	0.91	1.12	1.03	2.67	3.96	1.59	2.7	2.78	3.65	1.63	2.7	3.48	5.55	1.98	2.76
12	CPC15	5.54	5.62	6.61	4.57	1.50	1.25	1.51	1.58	4.15	4.22	2.72	3.48	4.71	8.25	2.99	3.36	5.25	3.29	3.62	3.72
13	CPC16	-	-	-	-	0.94	0.75	0.97	1.99	1.78	1.35	1.61	2.87	1.84	2.11	1.57	2.73	2.29	1.88	1.81	3.54
14	CPC17	2.40	1.59	2.24	6.2	0.68	0.25	0.70	1.19	-	-	-	-	-	-	-	-	-	-	-	-
15	CPC18	5.97	4.31	4.31	2.17	1.22	0.85	1.07	1.04	3.19	2.31	2.00	2.05	3.47	1.98	2.13	2.04	-	-	-	-
16	CPC19	5.77	6.66	4.67	4.4	1.37	1.15	1.27	4.41	3.11	2.84	2.08	2.42	3.58	3.00	2.07	2.86	-	-	-	-
17	CPC20	6.84	7.08	8.13	7.59	1.40	1.18	1.21	1.44	2.87	2.71	1.58	3.89	3.08	3.60	1.96	3.89	3.36	4.13	2.01	3.9
18	CPC21	4.09	3.13	2.62	2.5	0.73	1.00	1.08	1.12	2.44	3.37	2.23	2.02	3.21	3.37	2.26	0	4.58	3.54	2.64	2.46
19	CPC22	4.76	3.63	5.64	5.93	1.48	0.50	0.98	2.19	3.09	2.73	2.34	2.49	3.09	2.69	1.93	2.15	-	-	-	-

Appendix VIII Raw oxygen uptake and vector magnitude count data for adults in study 3

	A	B	C	D	E	F	G	H	I	J	K	L	M
1	**ID**	**VO2rest**	**VO21km**	**VO22km**	**VO24km**	**VO26km**	**VO26MWT**	**Vmrest**	**VM1km**	**VM2km**	**VM4km**	**VM6km**	**VM6MWT**
2	CPA01	2.8	20.2	23.7	-	-	19.3	0.0	1407.5	2221.5	-	-	2863.5
3	CPA02	3.1	8.2	13.2	24.9	-	17.0	0.0	297.1	660.8	1970.9	-	2553.1
4	CPA03	2.7	-	-	-	-	26.7	2.5	-	-	-	-	1787.5
5	CPA04	3.7	9.7	12.2	19.0	26.9	21.2	0.0	228.9	451.2	1345.5	2488.2	2998.6
6	CPA05	3.2	8.6	11.2	-	-	38.8	0.0	278.2	1510.1	-	-	2339.2
7	CPA06	4.4	10.1	10.3	13.7	22.7	16.4	0.0	412.5	619.9	1520.1	2079.4	2387.2
8	CPA07	5.8	10.5	14.9	19.0	-	13.6	41.9	529.2	750.7	1420.3	-	1921.2
9	CPA08												
10	CPA09	3.8	13.2	-	-	-	14.6	7.8	549.0	-	-	-	862.1
11	CPA10	3.4	8.9	11.3	16.5	-	34.3	0.0	404.7	725.3	1619.4	-	2562.5
12	CPA11	5.3	9.1	10.1	14.9	22.0	23.1	46.3	309.2	869.2	1594.3	2871.4	3606.8
13	CPA12	4.0	9.1	13.7	17.3	34.4	14.1	0.0	260.4	1015.8	1878.3	7075.5	3845.9
14	CPA13	3.9	-	-	-	-	12.6	31.5	-	-	-	-	3364.4
15	CPA14	3.8	7.4	9.5	-	-	17.7	0.0	337.5	602.1	-	-	1344.2
16	CPA15	3.6	6.9	8.2	12.8	-	21.4	1.5	210.0	445.5	1100.5	-	1479.7
17	CPA16	3.6	8.1	10.1	15.9	22.3	17.8	0.0	370.0	912.6	1732.6	2954.0	3767.6
18	CPA17	2.6	9.9	9.1	-	-	-	0.0	580.9	765.8	-	-	2743.4
19	CPA18	5.9	15.9	20.8	-	-	15.5	99.9	544.1	973.2	-	-	2339.7

Appendix IX Raw oxygen uptake and vector magnitude count data for children in study 3

	A	B	C	D	E	F	G	H	I	J	K	L	M
1	**ID**	**V02rest**	**VO26MWT**	**VO21km**	**VO22km**	**VO24km**	**VO26km**	**Vmrest**	**VM6MWT**	**VM1km**	**VM2km**	**VM4km**	**VM6km**
2	CPC02	3.2	27.8	11.7	15.8	-	-	4.0	1997.0	474.9	901.5	-	-
3	CPC03	7.1	13.3	-	-	-	-	4.0	1089.7	-	-	-	-
4	CPC04	5.9	20.4	-	-	-	-	36.3	1367.9	-	-	-	-
5	CPC05	2.7	18.0	9.2	9.6	7.3	18.5	3.0	2038.0	338.3	669.4	961.7	3128.4
6	CPC06	7.2	26.8	15.1	-	-	-	0.0	3136.2	563.6	-	-	-
7	CPC08	7.4	23.2	10.6	12.0	20.5	-	16.0	1537.1	418.4	570.4	1277.1	-
8	CPC11	5.3	29.5	14.4	18.3	-	-	0.0	2773.2	636.3	1096.8	-	-
9	CPC12	5.7	24.2	10.8	12.0	-	-	4.7	3039.9	345.3	721.4	-	-
10	CPC13	7.2	36.2	16.2	15.3	-	-	0.0	2831.4	547.5	615.7	-	-
11	CPC14	4.8	21.4	10.8	14.2	21.7	-	3.8	1900.1	255.7	465.3	1928.8	-
12	CPC15	3.8	14.3	10.5	13.7	-	-	1.5	1665.1	396.3	689.4	-	-
13	CPC16	5.6	-	10.4	13.0	15.5	-	51.8	-	541.7	689.3	1350.2	-
14	CPC17	6.6	23.1	-	-	-	-	0.0	1901.7	-	-	-	-
15	CPC18	5.7	26.5	14.1	-	-	-	0.0	1877.0	538.8	-	-	-
16	CPC19	3.9	16.9	9.3	-	-	-	34.4	1314.0	339.7	-	-	-
17	CPC20	4.8	23.2	9.5	11.2	14.6	20.9	1.5	2395.2	191.6	334.6	1494.3	1833.2
18	CPC21	2.6	13.9	8.5	15.6	-	-	0.0	698.0	525.1	707.8	-	-
19	CPC22	7.2	23.0	14.8	-	-	-	6.5	2908.7	857.0	-	-	-

Appendix X Raw data for adults in study 4 and 5

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z	AA	AB	AC
1	ID Code	Sex	Age	GMFCS	SBP	DBP	Height	Weight	WC	HC	Chol	HDLC	NonHDL	LDLCALC	THR	TRIG	CRP mg/dL	GLUR	HBA1C	INSULIN	HOMA-IR	VitD	Sed PA	LPA	MPA	VPA	MVPA bouts	Mean counts	total wear
2	S1	1	53	1	146.00	96.00	169.90	94.40	101.50	103.00	5.78	1.12	4.66	3.70	5.20	2.08	2.00	5.00	35.00	10.30	2.34	85.00	408	239.43	62.14	16.71	30.86	359.02	726.29
3	S2	0	40	2	107.00	67.00	154.50	63.00	73.00	102.25	4.90	1.68	3.22	2.98	2.90	0.53	1.00	4.30	35.00	4.60	0.90	76.00	488.86	311.29	65.57	8.43	24	285.27	874.14
4	S3	1	24	1	160.00	91.00	177.50	88.70	102.30	109.50	5.20	1.14	4.06	3.50	4.60	1.21	1.00	4.80	31.00	26.10	5.69	49.00	376.9	273.6	44.86	70.57	70.86	552.43	752.14
5	S4	0	37	3	119.00	85.00	153.50	43.70	68.00	84.00	3.43	1.48	1.95	1.62	2.30	0.72	1.00	-	32.00	4.80	-	55.00	584.71	298.71	11.71	1.43	0	147.86	896.57
6	S5	0	38	3	126.00	70.00	141.50	55.30	81.25	99.00	4.73	2.02	2.71	2.41	2.30	0.66	1.00	4.60	35.00	10.10	2.11	36.00	705.86	175	1.43	0.14	0	68.86	882.57
7	S6	0	54	3	116.00	79.00	154.00	45.50	66.00	86.00	4.98	1.23	3.75	3.44	4.00	0.67	2.00	4.50	37.00	4.90	1.00	88.00	456.86	358.14	48.57	6	6.14	304.48	869.57
8	S7	1	58	5	125.00	74.00	166.00	58.90	76.00	87.00	4.02	1.35	2.67	2.33	3.00	0.75	3.00	4.30	33.00	3.30	0.65	32.00	-	-					
9	S8	1	40	3	124.00	78.00	169.00	81.20	98.00	105.00	4.85	1.26	3.59	3.16	3.80	0.93	2.00	5.00	29.00	12.80	2.91	37.00	619.4	144	1.4	0	0	64.02	764.6
10	S9	1	57	2	120.00	74.00	162.00	72.80	99.00	101.50	5.19	1.74	3.45	3.05	3.00	0.87	1.00	4.30	30.00	6.10	1.19	28.00	551.43	242	30	0	1.43	171.76	823.29
11	S10	1	38	5	124.00	72.00	168.00	49.40	88.00	-	4.62	1.29	3.33	2.94	3.60	0.85	2.00	5.00	37.00	7.60	1.73	38.00	-	-					
12	S11	1	35	2	127.00	82.00	174.00	73.30	87.00	96.00	5.74	1.70	4.04	3.75	3.40	0.62	1.00	5.00	28.00	11.30	2.57	64.00	488.33	232.33	33.33	5.83	7	221.31	759.83
13	S12	0	28	2	126.00	87.00	162.50	59.20	87.00	95.00	3.16	1.17	1.99	1.78	2.70	0.46	1.00	4.50	27.00	4.10	0.84	16.00	475.5	200.25	37.75	7.5	6	210.84	721
14	S13	1	54	2	113.00	69.00	174.50	75.60	89.00	97.50	5.76	1.85	3.91	3.54	3.10	0.80	1.00	15.80	35.00	4.10	2.94	90.00	500.71	337.57	57	5	24.14	258.03	896
15	S14	1	34	2	129.00	76.00	177.00	73.90	93.00	98.50	4.42	1.56	2.86	2.49	2.80	0.80	1.00	2.80	26.00	5.80	0.74	38.00	529	255.6	14.6	8.6	12.6	176.04	812
16	S15	0	24	4	109.00	61.00	153.10	58.00	79.00	90.00	3.62	1.36	2.26	1.99	2.70	0.59	1.00	3.70	31.00	10.20	1.72	44.00							
17	S16	0	46	2	127.00	69.00	165.00	54.90	73.00	93.00	5.32	1.84	3.48	3.20	2.90	0.60	1.00	4.60	32.00	6.80	1.42	57.00	545	323	14	1.14	0	159.2	883.71
18	S17	1	41	4	117.00	69.00	172.50	66.20	79.00	87.50	5.36	0.87	4.49	3.71	6.20	1.69	2.00	4.60	31.00	4.80	1.00	56.00				-			
19	S18	1	57	4	130.00	85.00	161.00	42.00	62.00	73.00	4.42	1.33	3.09	2.67	3.30	0.92	1.00	4.70	36.00	3.80	0.81	26.00				-			
20	S19	1	39	5	118.00	88.00	161.00	56.80	100.00	-	3.30	0.57	2.73	1.59	5.80	2.48	2.00	5.00	30.00	6.50	1.48	62.00				-			
21	S20	1	27	1	149.00	84.00	171.50	80.60	101.00	102.50	5.65	1.25	4.40	3.89	4.50	1.10	1.00	4.40	29.00	8.00	1.60	34.00	540.29	303.71	29.29	1.14	1.57	170.5	874.57
22	S21	1	44	4	159.00	105.00	170.00	60.10	71.00	91.00	4.92	1.32	3.60	3.35	3.70	0.55	1.00	5.00	35.00	6.50	1.48	62.00	-	-	-	-			
23	S22	0	44	2	139.00	85.00	167.00	68.00	83.00	103.00	5.60	1.26	4.34	3.73	4.40	1.32	3.00	4.70	37.00	9.70	2.07	35.00	372.2	279.8	41.2	5.2	16.4	280.99	698.4
24	S23	1	18	1	124.00	57.00	184.50	92.50	93.50	108.50	3.32	1.10	2.22	1.86	3.00	0.79	1.00	4.40	31.00	6.90	1.38	40.00	511.71	286.71	48.43	17.29	18.43	281.13	864.29
25	S24	1	19	4	133.00	78.00	161.00	72.50	92.00	90.00	4.51	1.24	3.27	2.94	3.60	0.72	1.00	4.40	32.00	12.20	2.44	58.00	-	-	-	-			
26	S25	0	36	3	134.00	72.00	152.00	50.50	76.50	85.00	4.65	2.10	2.55	2.19	2.20	0.78	1.00	-	-	-	-	34.00	670.50	190.50	7.67	0.50	0.00	97.92	869.17
27	S26	1	64	4	148.00	75.00	157.00	90.80	126.50	113.50	6.15	1.75	4.40	3.96		1.74	-	5.40	-	-	-	-	-	-	-	-			
28	S27	1	25	1	132.00	60.00	180.00	81.80	81.00	90.50	3.68	1.52	2.16	1.92	2.40	0.53	1.00	4.90	28.00	4.70	1.05	44.00	610.71	177.00	22.43	0.43	0.00	128.66	810.57
29	S28	0	60	2	166.00	87.00	167.50	75.20	96.00	112.50	5.70	1.87	3.83	3.32	3.00	3.00	2.00	5.50	36.00	14.20	3.55	77.00	398.40	232.00	36.40	0.80	10.00	206.07	667.40
30	S29	0	36	3	116.00	73.00	148.00	56.00	85.00	93.50	4.38	1.39	2.99	2.63	3.20	3.20	1.00	4.40	30.00	12.40	2.48	26.00	485.00	280.29	22.29	7.71	0.00	208.84	795.29
31	S30	0	30	5	109.00	61.00	152.00	53.80	80.50	92.00	4.18	1.55	2.63	2.38	2.70	0.55	1.00	4.40	28.00	9.50	1.90	40.00							
32	S31	1	41	3	137.00	74.00	158.50	80.40	103.50	101.50	4.94	1.16	3.78	3.26	4.30	1.12	1.00	5.10	35.00	13.40	3.11	36.00	472.29	362.14	20.71	6.71	8	194.12	861.86
33	S32	0	52	2	142.00	85.00	155.00	54.80	68.00	91.00	6.98	2.83	4.15	3.72	2.50	0.93	2.00	4.80	36.00	16.70	3.64	98.00	515.86	324	49.29	6.14	0	255.51	895.29
34	S33	1	65	4	137.00	88.00	165.00	75.40	101.00	95.00	3.00	0.98	2.02	1.18	3.10	1.82	3.00	4.80	35.00	17.10	3.73	39.00							
35	S34	1	33	2	112.00	68.00	166.50	66.00	82.00	92.50	4.14	1.27	2.87	2.50	3.30	0.81	3.00	4.50		4.30	0.88	75.00	381.00	401.29	86.57	5.57	9.43	346.67	874.43
36	S35	1	19	1	129.00	72.00	180.50	69.90	74.50	93.50	2.93	1.13	1.80	1.58	2.60	0.47	2.00	4.30	31.00	8.20	1.60	36.00	453.67	320.83	44.17	5.33	14.5	231.33	835.33
37	S36	1	34	4	109.00	72.00	167.00	80.40	89.00	90.50	4.58	0.97	3.61	3.12	4.70	1.07	3.00	4.70	27.00	8.60	1.84	33.00							
38	S37	1	18	3	134.00	73.00	171.00	62.70	77.50	93.50	3.46	1.96	1.50	1.20	1.80	0.65	1.00	3.60	31.00	8.50	1.39	46.00	643	189.5	6.67	0.83	0	89.92	839.83
39	S38	0	41	2	125.00	78.00	159.00	72.00	87.00	101.50	3.61	1.40	2.21	1.55	2.60	1.43	3.00	5.00	33.00	43.80	9.95	82.00	598.17	228.67	11	0	0	119.63	838.67
40	S39	0	19	1	103.00	61.00	161.50	51.00	64.00	94.00	4.77	1.88	2.89	2.56	2.50	0.71	2.00	5.00	31.00	12.00	2.73	54.00	480.29	311.14	67	11	26.57	287.26	869.43
41	S40	0	22	3	121.00	78.00	153.00	48.50	72.00	88.50	5.49	2.13	3.36	3.00	2.60	0.79	1.00	4.70	34.00	8.00	1.71	68.00	575	206.5	22.5	2.83	0	157.08	807.17
42	S41	0	33	2	114.00	74.00	156.50	55.50	73.00	94.00	5.13	1.72	3.41	3.09	3.00	0.70	1.00	4.90	32.00	9.10	2.03	13.00	443	352.57	48.29	6.71	23.14	245.92	850.71
43	S42	0	23	1	105.00	63.00	162.50	54.40	67.50	93.00	3.86	1.66	2.20	1.89	2.30	0.68	1.00	4.40	31.00	7.60	1.52	16.00	502.71	184.57	51.43	42.29	45.57	390.43	777.14
44	S43	1	33	5	129.00	79.00	161.00	74.80	97.00	102.00	3.45	1.16	2.29	1.93	3.00	0.78	1.00	4.80	25.00	6.10	1.33	78.00							
45	S44	0	25	2	130.00	88.00	158.50	46.90	67.00	86.00	4.64	1.43	3.21	2.73	3.20	1.05	3.00	4.50	35.00	10.20	2.09	14.00	625.75	193.5	11	1.25	2.5	112.67	831.5
46	S45	1	43	1	134.00	76.00	179.00	83.00	93.00	101.50	3.55	1.23	2.32	1.96	2.90	0.78	2.00	5.90	34.00	7.20	1.93	50.00	372.29	253.71	61.71	2.57	37.43	274.79	690.29
47	S46	1	62	2	138.00	74.00	167.00	67.70	95.50	93.50	4.40	1.59	2.81	2.38	2.80	0.93	3.00	5.80	32.00	11.20	2.95	51.00	369.14	356.57	106.86	8.29	48.14	407.06	840.86
48	S47	1	22	1	126.00	70.00	186.50	72.70	79.50	98.00	3.70	2.12	1.58	1.38	1.70	0.44	1.00	4.70	32.00	3.80	0.81	28.00	633.17	201.17	52.83	41.5	55.33	320.63	928.83

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z	AA	AB	AC
50	S49	1	44	2	142.00	96.00	170.00	64.70	85.50	91.00	3.78	1.63	2.15	1.79	2.30	0.79	1.00	5.20	31.00	9.30	2.20	19.00	761.57	156.86	15.86	4.14	0	105.42	938.43
51	S50	0	24	1	114.00	67.00	160.50	58.10	70.50	98.00	4.95	1.81	3.14	2.87	2.70	0.58	1.00	4.10	30.00	3.70	0.69	66.00	471.57	335.57	52.29	23.43	21.29	321.22	882.86
52	S51	0	40	1	111.00	74.00	146.70	56.90	81.50	98.50	4.89	0.92	3.97	3.14	5.30	1.81	3.00	4.50	31.00	11.80	2.41	33.00	590.5	112.25	4.25	0.25	0	67.15	707.25
53	S52	1	22	1	120.00	67.00	159.80	59.60	73.50	88.50	4.65	1.39	3.26	2.75	3.30	1.11	1.00	4.80	31.00	9.60	2.09	29.00	617	209	50.43	14.71	34.29	238.39	892.57
54	S53	1	18	5	104.00	66.00	149.00	27.40	54.00	66.00	3.24	1.20	2.04	1.80	2.70	0.52	1.00	4.40	31.00	4.10	0.82	112.00							
55	S54	0	41	2	111.00	73.00	158.50	58.90	74.00	101.00	5.22	1.49	3.73	3.35	3.50	0.82	1.00	3.80	27.00	6.50	1.12	56.00	507.67	386.17	3.67	0	0	147.4	897.5
56	S55	0	52	2	119.00	80.00	152.40	73.70	93.00	114.00	4.30	1.80	2.50	2.14	2.40	0.79	2.00	4.80	33.00	11.00	2.40	37.00	557.33	264.50	15.83	2.67	0.00	146.39	840.50
57																													

Appendix XI Instructions for Shuttle Run Test

Tests: Two shuttle run tests (SRT) for GMFCS level I (SRT-I) and level II (SRT-II)

Measurement: aerobic capacity

Population: children, adolescents, and young adults who had cerebral palsy and who were classified at Gross Motor Function Classification System (GMFCS) levels I and II
Equipment Required: flat, nonslip surface; marking cones; measuring tape; 2 shuttle run test CDs; CD player; recording sheets; heart rate monitor
Preparations and Conditions
SRT-I and SRT-II: The course is 10 m long. Mark each end of the course with the marking cones and measuring tape.
Participants should wear sports clothing and shoes, and use their own personal walker and orthoses if applicable. Each participant also should wear a heart rate monitor.
Shuttle Run Test I and II Protocol
Participants walk or run between 2 markers at a set incremental speed.
GMFCS Protocols
There are 2 CDs for the shuttle run tests. Shuttle run test I (SRT-I) is for children, adolescents, and young adults classified at GMFCS level I. The SRT-I starts at a speed of 5 km/h. Shuttle run test II (SRT-II) is for children, adolescents, and young adults classified at GMFCS level II. The SRT-II starts at 2 km/h. Speed is increased by 0.25km/h every minute in each test. Each CD begins with a brief introduction to the test. The introduction is followed by a 5-second countdown to the start of the test. Thereafter, the CD emits a single beep at regular intervals.
• The walking or running pace is determined by a series of beeps on the accompanying CD.
• The participant should walk or run to the opposite end of the course when the first beep sounds. The participant should then continue walking or running at this speed, aiming at the opposite end of the course each time there is a beep.
• The participant should always place 1 foot either on or behind the 10-m mark at the end of each shuttle. If the participant arrives at the end of the shuttle before the beep sounds, then he or she should turn around, wait for the beep, and resume an adjusted walking or running speed.
• The walking or running speeds at the start of the test are very slow. On the SRT-I and the SRT-II, the participant has 7.2 and 18 seconds, respectively, to walk or run the 10-m shuttle.
• The walking or running speed is gradually increased. After each minute, the time interval between beeps decreases. The first speed is referred to as "level 1," the second speed is referred to as "level 2," and so on.
• Each level lasts approximately 1 minute, and each CD continues up to level 23. The end of each shuttle is denoted by a single beep; the end of each half level is denoted by a double beep; and the end of each level is denoted by a double beep and by the commentator on the CD.
• The test is finished when the participant is more than approximately 1.5 m (no markers necessary) away from the marker 2 consecutive paced signals within 1 level.
• The participant is instructed to walk or run for as long as possible, until he or she can no longer keep up with the speed set by the CD, at which point he or she should voluntarily withdraw from the test. In some cases, the person conducting the test may

need to withdraw the participant when it becomes apparent that he or she is dropping behind the required pace and is unable to reach the marker on 2 consecutive shuttles.
• The test result is measured in units of a "level" (e.g., 13) and a "half level" (e.g., 14.5). The final level that a participant has completed is recorded on a recording sheet.
• The heart rate is read from the wrist monitor at the end of the test and recorded on a recording sheet. This heart rate can be used to determine whether a participant has performed maximally (a heart rate of >180 bpm).

Some participants find it difficult to coordinate their walking or running speed with the pace of the audio signal.
Therefore, it is recommended that someone assist participants during the first stages of the test. Once participants understand the instructions, they can continue the test without assistance. Participants who continue to experience difficulty pacing themselves should be accompanied throughout the test. In this situation, an additional person is required to accompany a participant to ensure the reliability and validity of the test.

Appendix XII Raw data for children in studies 6 and 7

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S
1	ID	Sex	GMFCS	Age	SBP	DBP	Height	Weight	WC	HC	SRT level	Sed PA	LPA	MPA	VPA	MVPA	bouts	mean counts	Total wear time
2	T1	1	1	8	113	63	137	34.4	65.5	74	4	208.71	423.86	92.86	3.43	96.29	39.29	405.09	728.71
3	T2	0	1	7	91	63	136	37.6	71.5	75.5	3	145.67	427.00	82.67	1.50	84.17	13.67	413.89	657.00
4	T3	1	1	10	116	70	146.5	41	66.5	82.5	5	261.14	488.00	57.86	3.71	61.57	31.14	285.07	810.57
5	T5	0	1	7	87	52	131.5	27.5	56	68	5	167.60	505.40	80.80	4.60	85.40	24.20	400.41	758.40
6	T6	0	2	16	92	64	140.5	33.2	56.5	72.5	13.5	248.50	515.50	18.75	0.00	18.75	5.00	234.62	783.00
7	T7	1	1	9	100	52	133	25	53.5	59	5	-	-			-			-
8	T8	1	1	8	87	48	125.5	25.4	55.5	62.5	10	95.50	531.67	118.50	7.17	125.67	25.00	496.85	752.83
9	T9	1	1	12	132	53	163	65	89.5	97	5	251.71	461.71	51.71	2.00	53.71	14.71	275.03	767.00
10	T10	1	1	8	100	56	132.5	27.6	56	66	5	371.17	276.83	73.00	3.17	76.17	19.83	287.59	724.17
11	T11	1	1	13	139	75	158	68.6	86	98.5	8	228.83	399.83	104.33	15.67	120.00	50.33	495.44	748.67
12	T12	1	2	10	108	68	149	44.7	63.5	80.5	16								
13	T13	1	1	14	128	75	172.5	51.4	65	85	9	400.43	342.86	29.00	0.00	29.00	15.29	171.82	772.29
14	T14	1	2	7	97	69	112	24.1	59.0	67.5	7.5	206.71	453.43	69.14	0.29	69.43	5.29	330.29	729.71
15	T15	1	1	6	100	62	120.8	24.7	58.0	64.5	5.0	76.43	446.00	155.71	11.00	166.71	55.00	671.94	689.14
16	T16	1	1	9	105	66	138.7	40.6	71.5	81	10	-	-			-			-
17	T17	1	1	11	113	89	161.6	45.6	65	81	10	319.00	316.25	74.75	1.00	75.75	33.75	289.18	711.00
18	T18	0	1	12	101	62	153.5	47.7	71.5	88.5	9								
19	T19	1	3	14	102	58	151.3	44.7	66.5	76.5	17.5	352.29	477.43	62.86	0.29	63.14	17.43	259.46	893.00
20	T20	1	2	8	92	54	126	24	53	66	12	-	-			-			-
21	T21	0	1	7	123	83	124.5	29.9	65.5	72.5	3	244.86	445.00	92.86	5.71	98.57	28.29	392.08	788.43
22	T22	1	1	15	117	55	171.6	55.1	68	86	13	337.14	474.29	72.14	4.29	76.43	28.00	298.79	887.86
23	T23	0	2	10	103	64	138.2	30.3	51.5	67	7	257.29	452.29	60.57	0.43	61.00	5.29	293.10	770.57
24	T24	0	1	9	105	66	126	24.6	52	63	4	133.43	491.57	161.00	5.86	166.86	47.14	574.15	791.86
25	T25	0	3	6	105	63	118.5	27.1	61	66	4.5	217.14	466.29	68.29	0.14	68.43	9.43	322.34	751.71
26	T29	1	1	8	98	42	128.5	25.1	56.5	61.5	6	174.17	481.5	136.67	4.67	141.33	32.83	514.99	797
27	T30	0	1	17	129	65	169.2	67.5	76.5	98.5	9.5	164.75	477.5	84.25	1.25	85.5	33.75	388.08	727.75
28	T31	1	1	14	106	51	164.5	46.6	65.5	81	4.5	98	558	69.5	2.33	71.83	6.67	404.45	727.83
29	T32	1	2	7	98	56	130.5	23.6	50.5	61	13.5								

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S
59	T62	1	3	8	100	55	137	38.8	65.5	76.5	7	305.57	392.71	47.00	0.57	47.57	9.43	238.75	745.86
60	T63	1	3	17	116	69	165.5	49.9	70	84	9.5	455.43	318.29	31.71	3.71	35.43	14.71	202.87	809.14
61	T64	1	1	10	94	59	138	36.9	68.5	78.5	5.5	273.43	324.00	102.14	16.86	119.00	75.57	527.96	716.86
62	T65	1	1	17	124	66	170	61.3	76	93	17.5	464.43	363.00	50.29	13.57	63.86	38.43	281.78	891.43
63	T66	1	1	11	109	58	152	41.5	66.5	76.5	12	285.50	344.67	87.67	13.33	101.00	41.17	440.20	731.67
64	T67	1	2	14	117	64	167	60.9	72	87	14.5	320.29	423.71	77.14	12.57	89.71	26.14	362.34	833.71
65	T68	0	3	16	-	-	154	45	-	-	-	565.71	310.43	27.57	2.14	29.71	5.71	155.12	906.29
66	T69	1	1	8	92	48	130	28.3	59	66.5	9	137.40	373.60	119.80	11.60	131.40	76.60	595.11	642.40
67	T70	0	2	12	120	66	149	31.3	53.5	70.5	10.5	444.86	276.71	45.14	0.57	45.71	12.29	201.63	758.71
68	T71	1	1	10	84	51	145	30	53.5	69.5	12	266.43	378.57	87.57	8.14	95.71	39.57	419.30	741.14
69	T72	1	3	14	116	68	157.5	48.1	70.5	79.5	19	509.50	267.25	51.75	1.75	53.50	8.25	204.78	830.25
70	T73	0	1	7	85	46	120	22	52	60.5	10	207.00	446.60	87.80	7.80	95.60	29.80	409.64	749.20
71	T74	1	1	17	114	69	162.5	56.6	74	87.5	16	153.40	405.20	230.00	40.60	270.60	178.20	927.78	829.20
72	T75	1	3	16	124	55	180	65.1	73	84	16	419.86	387.43	34.71	2.86	37.57	3.14	197.09	845.00
73	T76	0	1	15	106	57	163	52.5	67	88.5	15	401.86	358.14	74.71	14.71	89.43	36.57	372.60	849.00
74	T77	0	2	11	105	65	140	30.7	55	72.5	11	273.50	407.83	67.17	3.00	70.17	7.17	324.77	751.33
75	T78	0	3	13	109	65	152	56.2	70.5	96	4								
76	T79	0	3	15	98	66	152	45.1	68.5	86.5	5	301.50	431.75	23.50	0.75	24.25	0.00	181.51	757.50
77	T80	0	3	11	90	50	139	29.7	56.5	69.5	7.5	382.43	292.86	23.86	0.57	24.43	3.86	169.30	682.71
78	T81	1	3	13	109	61	141	37.7	64.5	72.5	4.5								
79	T82	0	2	9	102	55	130.5	29	56	67	13	136.00	401.17	188.00	36.83	224.83	123.67	862.70	762.00
80	T83	0	1	10	103	55	137.1	32.1	60	73	10	226.71	463.14	88.57	13.43	102.00	35.43	446.05	791.86
81	T84	1	1	15	128	66	168.5	69.6	84	97	6	347.33	374.17	45.50	1.50	47.00	8.83	238.55	784.00
82	T85	1	1	7	90	48	114.2	18.2	50.5	59	1.5								
83	T86	1	1	14	122	66	171	53.3	68.5	84.5	15	334.40	277.40	74.20	16.00	90.20	37.40	431.22	702.00
84	T87	1	3	7	97	62	122.4	25	60.5	61	6	198.29	412.57	113.00	0.86	113.86	35.86	422.36	724.71
85	T88	0	3	6	89	69	108	19	51.5	56.5	8								
86	T89	0	1	9	102	56	129	27.9	57	67	6								
87	T90	1	1	8	-	-	123.3	25.8	57.5	65.5	2	190.86	420.00	111.00	5.71	116.71	35.00	474.12	727.57

88	T91	1	3	7	-	-	123.2	22	50.5	57	-	53.86	385.43	245.00	10.43	255.43	108.14	879.48	694.43
89	T92	1	2	6	94	60	127.7	23.3	50.5	58.5	10.5	286.00	353.67	70.33	5.67	76.00	31.17	321.57	716.00
90	T93	1	1	12	109	72	163.5	47.5	68	80	8	231.29	399.00	152.86	21.86	174.71	97.14	640.49	804.86
91	T94	0	1	7	96	34	123.2	22.1	52	61	4	118.43	344.00	170.43	25.86	196.29	94.71	688.75	658.86