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Exploration of the Effects of Developmental Coordination Disorder on Skeletal Development from Childhood through to Early Adulthood

Jocelyn Tan

Exploration of the Effects of Developmental Coordination Disorder on Skeletal Development from Childhood through to Early Adulthood

Jocelyn Lee Kim Tan

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Declaration

I declare that this thesis is my own work and contains no material which has been accepted for the award of any other degree or diploma in any institution. This thesis is not known to contain any material previously published by another person, except in instances where this has been acknowledged.

Research presented and reported in this thesis was conducted in accordance with the National Health and Medical Research Council National Statement on Ethical Conduct in Human Research (2007, updated 2018). Each of the reported studies received institutional human research ethics approval by the Chief Investigator as follows:

Chapter 3: Skilled Kids Study and Active Family Study. Chief Investigator: A/Prof Arja Sääkslahti. University of Jyväskylä

Chapter 4: Arvo Ylppö Longitudinal Study.
Chief Investigator: Prof Aulikki Lano.
University of Jyväskylä.

Chapter 5: AMPitup Exercise and Bone Health Programs.
Chief Investigator: A/Prof Paola Chivers.
University Of Notre Dame Australia (010703F, 016120F)

Chapter 6: The Raine Cohort Study.
King Edward Memorial Hospital, Princess Margaret Hospital for Children, and the University of Western Australia (RA/4/20/5722).
Chief Investigator: A/Prof Paola Chivers.
University of Notre Dame Australia (019122F).

Appendix A: Bone Health of Adults with Poor Movement Coordination Pilot Study.
Chief Investigator: A/Prof Paola Chivers.
University of Notre Dame Australia (016120F).

Jocelyn Lee Kim Tan

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Abstract

This thesis examined bone development from childhood into early adulthood in individuals with developmental coordination disorder (DCD) using a life course health development framework. One systematic review was conducted, and four original research studies produced with retrospective data from four unique cohorts in childhood, adolescence, and adulthood. Physical activity was assessed via accelerometry in Finnish child and adult populations and via self-reporting in an Australian population at 17 and 20 years. Bone was assessed via peripheral quantitative computed tomography in adolescents and dual energy x-ray absorptiometry in adults at age 20 years in two Australian cohorts. Bone was assessed cross-sectionally in the adult cohort and longitudinally over six months in adolescents. A mixed model statistical approach was used across studies to account for effects of known physical activity and bone confounders.

Bone deficits were present in individuals with DCD until at least the time of peak bone mass and indicated to be related to reduced physical activity. DCD risk status was associated with deficits in physical activity across the lifespan that may relate to bone impairments, including reduced high impact peaks in boys (M_{age}=8.8 years) and increased sedentary light activity in adults aged 25 years. These patterns were influenced by other individual factors including individual motor skills and visuomotor impairment. Bone health improvements following engagement in an exercise program in adolescents showed that bone outcomes could be improved via osteogenic physical activity but also reinforced the importance of other aspects of movement on bone gains in this population.

Bone deficits differed by sex in accordance with physical activity differences whereby males showed larger differences based on DCD status than females. Notably, bone deficits were seen in early adulthood for males only. Physical activity patterns were indicative of a cause for this sex-based difference, with a relationship between loading from physical activity and bone only seen in males. These findings have important implications for the health and clinical management of individuals with DCD by confirming the continued vulnerability of this population for osteoporosis risk and fracture however they also provide a potential avenue for improvement via physical activity and exercise engagement.

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Statement of Authorship Contribution

I, Jocelyn Tan, led the projects reported within this thesis as per the requirements of the PhD program. I contributed to the associated publications via the generation of concept, data cleaning and analysis, manuscript preparation, revisions, and submission of manuscripts for publication. Other authors' contributions are detailed below with respect to each chapter.

Chapter 2: *Association of Developmental Coordination Disorder and Low Motor Competence with Impaired Bone Health: A Systematic Review*

Myles Murphy provided guidance for analysis and had first review of the paper. Ranila Bhoyroo and Paola Chivers participated in screening, data extraction and quality assessment. All authors revised the paper critically for intellectual content and approved the final version.

Chapter 3: *Motor Competence Indicators and Skeletal Loading Among Children*

Arja Sääkslahti designed the original study and Donna Niemistö collected the study data in Finland. Arto Laukkanen is the current data custodian and provided additional clarification of data. Timo Rantalainen assisted with data analysis to comply with European Union data sharing laws (ran data analysis scripts prepared by myself Jocelyn Tan). All authors revised the paper critically for intellectual content and approved the final version.

Chapter 4: *Effect of Childhood Developmental Coordination Disorder on Adulthood Physical Activity; Arvo Ylppö Longitudinal Study*

Anna-Mari Ylä-Kojola participated in the childhood data collection and assessments, Aulikki Lano and Johan G. Eriksson conceptualised the adulthood data collection, Minna K. Salonen and Niko Wasenius participated in accelerometery data collection. Timo Rantalainen and Harri Piitulainen assisted with the data analysis to comply with European Union data sharing laws (ran data analysis scripts prepared by myself Jocelyn Tan). All authors critically reviewed the manuscript for important intellectual content.

Chapter 5: *Impact of a Multimodal Exercise Program on Tibial Bone Health in Adolescents with Developmental Coordination Disorder*

Authors Aris Siafarikas, Timo Rantalainen, Nicolas Hart and Paola Chivers contributed to the bone analysis. Authors Fleur McIntyre and Beth Hands designed and contributed to the exercise intervention and data collection. All authors revised the paper critically for intellectual content and approved the final version.

Chapter 6: *Reduced Peak Bone Mass in Young Adults with Low Motor Competence*

Beth Hands and Kun Zhu were involved in the original Raine Cohort study planning, analysis and data cleaning of aspects of motor competence and bone variables respectively. Carrie-Anne Ng, David Scott and Marc Sim assisted with visualisation of the data. Paola Chivers provided specific Raine Cohort data cleaning and analysis advice. All authors revised the paper critically for intellectual content and approved the final version.

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List of Abbreviations

ADD	Attention Deficit Disorder
ADHD	Attention Deficit Hyperactivity Disorder
AIC	Akaike Information Criterion
AMPitup	Adolescent Movement Program run by the University of Notre Dame
AYLS	Arvo Ylppö Longitudinal Study
BMD	Bone Mineral Density
BMI	Body Mass Index
CI	Confidence Interval
d	Effect Size by Cohen's d
DAMP	Deficits in Attention, Motor Control and Perception
DCD	Developmental Coordination Disorder
DSM-V	Diagnostic and Statistical Manual of Mental Disorders. Edition 5.
DXA	Dual-Energy X-ray Absorptiometry
GEE	Generalised Estimating Equations
Gen1	Generation One of the Raine Cohort Study
Gen2	Generation Two of the Raine Cohort Study
GLM	General Linear Model
GRADE	Grading of Recommendations, Assessment, Development and Evaluation
HOI	High Intensity Osteogenic Index
ICC	Interclass Correlation Coefficients
IPAQ	International Physical Activity Questionnaire
IQR	Interquartile Range
KTK	Körperkoordinationstest für Kinder
LCHD	Life Course Health Development
LMC	Low Motor Competence
M	Statistical Mean
MAD	Mean Amplitude Deviation
MET	Metabolic Equivalent of Tasks

MAND	McCarron Assessment of Neuromuscular Development
Md	Median
MVPA	Moderate and Vigorous Physical Activity
N	Number
NDI	Neurological Developmental Index (scored according to the MAND)
OI	Osteogenic Index
OR	Odds Ratio
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analysis
pQCT	Peripheral Quantitative Computed Tomography
RM	Repetition Maximum
SD	Standard Deviation
SSI	Stress Strain Index
T1	Data Collection Time Point One in Chapter 3 (Skilled Kids Study)
T2	Data Collection Time Point Two in Chapter 3 (Active Family Study)
T4	Tibia measured at the 4^{th} percentile
T66	Tibia measured at the 66^{th} percentile
TGMD-3	Test of Gross Motor Development – 3^{rd} edition
U	Mann Whitney U Standardised Test Statistic
VMI	Visuomotor Integration
WHO	World Health Organisation
X3N	Fracture Load on the X Axis
Y3N	Fracture Load on the Y Axis

Definitions

Adolescence	Transitional stage of physical and psychological development between the age of 12 and 18 years
Adulthood	The period of the human lifespan after physical maturity has been attained, starting from the age of 18 years.
Bone Health	The vulnerability of a bone to fracture. This may be reflected through several different measures including density, architecture, and geometry
Childhood	The period of the human lifespan between infancy and adolescence, between the ages of 1 year and 12 years.
Competitive Sports	An organised sport in an environment which is orientated towards competition and achievement, rather than leisure.
Developmental Coordination Disorder	A neurodevelopmental disorder characterised by deficits in the acquisition and execution of coordinated motor skills. DCD is diagnosed according to American Psychiatric Association Diagnostic and Statistical Manual, version 5, criteria.
Early Adulthood	The period of adulthood from 18 years until 40 years
Exercise	Purposeful, prescriptive, programmed, and progressive activities targeting physiological outcomes
Loading	Strain received upon the bone from weight bearing and high acceleration impacts
Low Motor Competence	Individuals who perform in the diagnostic range for developmental coordination disorder on standardised motor tests, but for whom other diagnostic criteria can not be assessed
Odd Impact Activity	Activity for which an unusual strain pattern is anticipated typified by strains coming from multiple directions. Often used to describe activities such as team sports that take place on uneven or soft surfaces, for example soccer.
Osteogenic	The ability to induce bone formation
Organised Sports	Sports delivered by a club, association, or other organisational body
Osteogenic Physical Activity	Used in this thesis to refer to physical activity of high osteogenic potential
Osteopenia	Bone mineral and quality that is below normal levels but above that of osteoporosis. Defined as being one to two standard deviations below age and sex appropriate norms.

Osteoporosis	A reduction in bone mineral and quality to a level that the bone becomes brittle and fragile and so vulnerable to fracture
Paediatric	Period of the lifespan including infancy, childhood, and adolescence i.e., from birth through the age of 18.
Physical Activity	Any bodily movement produced by skeletal muscles that results in energy expenditure above a resting level
Sedentary Behaviour	Any waking behaviour categorised by a very low energy expenditure (less than 1.5 metabolic equivalents) while in a seated or reclining position.
Sports	Games and leisure activities that require physical effort and skill

Chapter 1

Introduction

1.1 Background

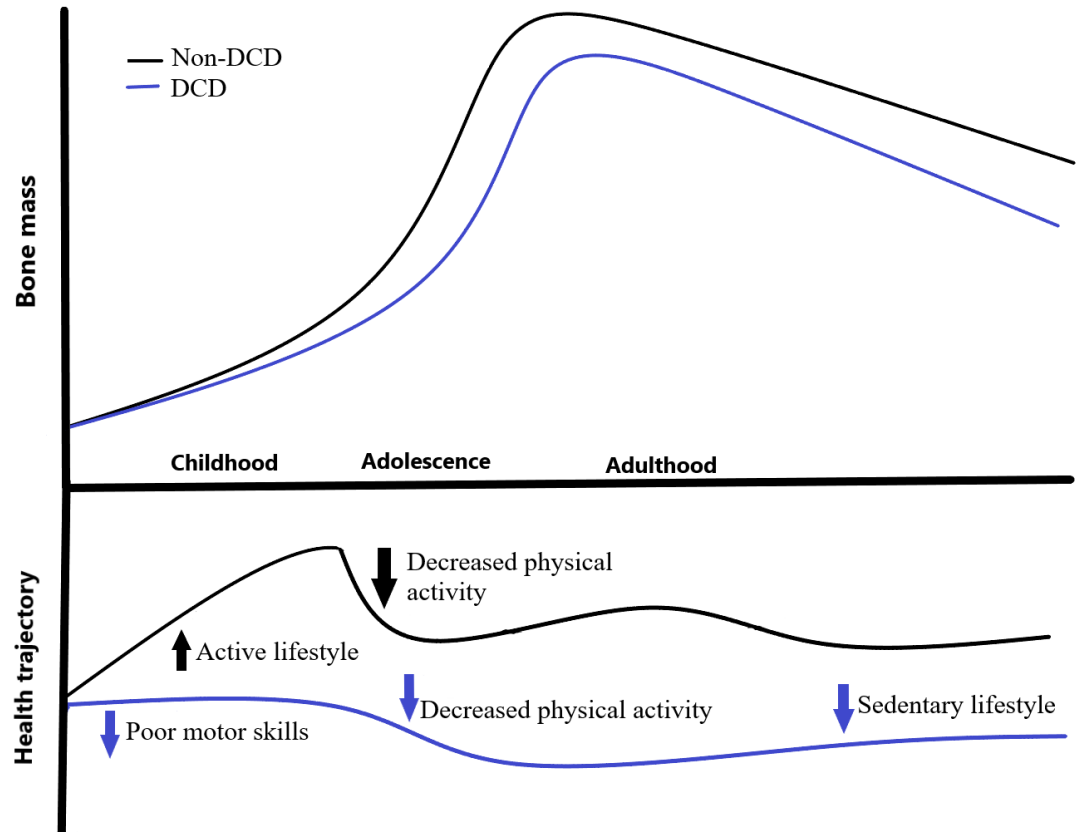
Developmental coordination disorder (DCD) is a neurodevelopmental condition typified by a difficulty in acquiring and executing coordinated motor skills to a degree that activities of daily living are impaired (American Psychiatric Association, 2013). Individuals with DCD have low levels of physical activity throughout their lifespan with an associated increased prevalence of health risk factors (Cairney, Hay, Veldhuizen, & Faught, 2011; Cairney, Hay, Veldhuizen, Missiuna, Mahlberg, et al., 2010; Hendrix, Prins, & Dekkers, 2014), including impaired bone health (Chivers et al., 2019; Fong et al., 2018; Ireland, Sayers, Deere, Emond, & Tobias, 2016; Jenkins et al., 2020; Tsang, Guo, Fong, Mak, & Pang, 2012). Bone health indicates the vulnerability of the bone to fracture and is indicated by measures including density, architecture, and geometry (Hart, Galvão, & Newton, 2017; Hart et al., 2020). Bone health deficits in individuals with DCD has been demonstrated in both architecture and density (Ireland et al., 2016). DCD continues into adulthood in most instances (Blank et al., 2019), however, it is not known if bone health deficits are similarly persistent, nor what factors contribute to its presence. One potential contributor is physical activity levels as physical activity is critical for bone development (Hart, Nimphius, et al., 2017). Physical activity levels are lower in individuals with DCD than their typically developing peers (A L Barnett, Dawes, & Wilmut, 2013; Cairney, Hay, Faught, Mandigo, & Flouris, 2005; Cairney, Hay, Faught, Wade, et al., 2005; Magalhães, Cardoso, & Missiuna, 2011; Rivilis et al., 2011). Effects of DCD on physical activity have been identified to be persistent over time (Cairney, Hay, Veldhuizen, Missiuna, & Faught, 2010) as have deficits in associated health indicators (Cairney et al., 2011; Cairney, Hay, Veldhuizen, Missiuna, Mahlberg, et al., 2010). Persistence of bone health deficits into adulthood is not established, however it is likely that they persist into adulthood reflecting a lifetime of suboptimal physical activity.

Given the lifelong deficits in motor skills and physical activity, deficits in bone health in a DCD population are best examined using a life course health development

(LCHD) framework. The LCHD framework views an individual's health as the result of a lifetime process whereby health is constantly acquired, optimised, and maintained from a combination of pre-existing and current risk factors and protective factors (Halfon, Larson, Lu, Tullis, & Russ, 2014). Although exposures in the developmental period of life are particularly important to optimal health outcomes (Bukata, Rosenthal, & Lacy, 2018), health in this framework is seen as fluid (Halfon et al., 2014). For example, as demonstrated in Figure 1.1, bone health is formed via a developmental trajectory of mineral accrual and growth through to early adulthood at which point growth ceases and peak bone mass is achieved (Foley, Quinn, & Jones, 2008; Hart et al., 2020). The bone development trajectory is influenced by individual health factors (e.g. prematurity, low birth weight) (Frysz et al., 2020; Ireland et al., 2018; C M Smith et al., 2011; Tobias et al., 2019) and external environmental factors, such as physical activity (Ireland, Rittweger, Schönau, Lamberg-Allardt, & Viljakainen, 2014) or sunlight for vitamin D generation (Holick, 2007). Exposures during important growth periods such as adolescence have a particularly strong impact on bone development (Bass et al., 2002; Farr, Laddu, & Going, 2014). Under the LCHD framework, bone changes during the sensitive time period of adolescence transforms the bone development trajectory with missed opportunities for improvement being harder to compensate for later in life (Halfon et al., 2014). Furthermore, the effects of environmental factors are amplified by the pre-existing health outcome trajectory (Halfon et al., 2014). For example, bone loss due to inactivity in adulthood will have a greater impact in an individual with low peak bone mass due to lifelong low levels of physical activity than an individual who was active in earlier life and thus developed a higher peak bone mass (Faulkner, 2007). As such lifetime physical activity levels result in a pre-disease state of vulnerable bone health, that will predate the onset of the disease state osteoporosis and osteoporotic fractures by many years. The LCHD framework considers the pre-disease state as modifiable, such that movement away from a disease state may occur via changed behaviour and other environmental exposures (Halfon et al., 2014). Potential pathways for bone development can be seen in Figure 1.1, where conceptually an individual with DCD has a trajectory of low levels of physical activity in pivotal periods in the lifespan, leading to a pre-disease state of sub-optimal bone health which makes them vulnerable to the ultimate disease state of osteoporosis and osteoporotic fractures.

Figure 1.1

Conceptual Examples of Differing Bone Development by Motor Competence Status as a Reflection of a Health Development Trajectory across the Life Course



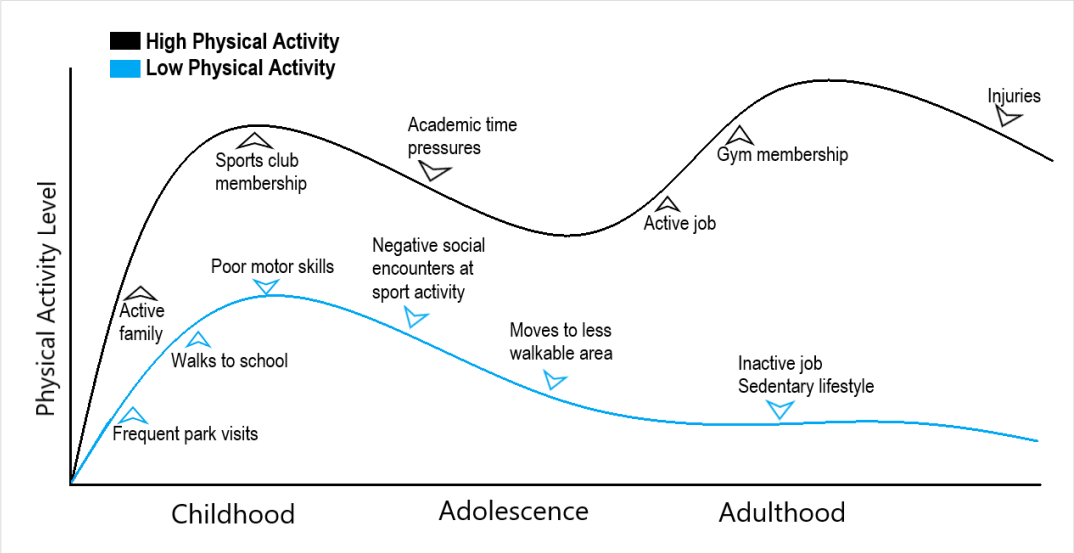
Adapted from Maternal and Child Health Life Course Research Network (2015).

The development of a pre-disease state, however, does not occur in isolation. Individuals with DCD will not follow the same trajectory. Some individuals will be more inclined to experience poor bone health due to genetics or the presence of other conditions, such as prematurity (Bronicki, Stevenson, & Spranger, 2015; Frysz et al., 2020). Additionally, DCD is a highly heterogeneous condition in terms of the motor skills impacted (Dewey, 2002; Williams, 2002) and co-occurrent conditions (Dewey, 2002; Jarus, Lourie-Gelberg, Engel-Yeger, & Bart, 2011). This heterogeneity may impact upon their physical activity participation. Individuals with DCD and attention deficit disorder or attention deficit hyperactivity disorder (ADD/ADHD), for example, are hypothesised to have higher physical activity than those with DCD without ADD/ADHD (James et al., 2021). Conversely, individuals with more severe motor difficulties have lower engagement in activities of daily living (Schoemaker, Lingam, Jongmans, van Heuvelen, & Emond, 2013) and so potentially lower physical activity.

Physical activity participation can also be considered to follow a trajectory influenced by internal and external factors, an example of which is shown in Figure 1.2. The trajectory of physical activity and its individual influences must be understood to fully understand the relationship between DCD and bone health development. Furthermore, physical activity needed to stimulate bone formation requires a diverse range of large mechanical loads or strain that is not always captured by conventional physical activity measurement. In keeping with a LCHD framework, it is necessary to examine the inter-dependent factors involved with the effect of physical activity upon the skeleton, such as the intensity of strain or diversity of physical activity.

Figure 1.2

Conceptual Examples of Physical Activity Lifetime Trajectories and Inter-Dependent Factors



This doctoral thesis reports on a body of work that examines bone development in individuals with DCD into early adulthood. It sought to confirm for individuals with DCD the continuance of bone detriments into early adulthood and the relationship between bone-specific (osteogenic) physical activity and bone development. It also examined the role of comorbidities and motor skill heterogeneity with physical activity to better understand the trajectory of bone development in individuals with DCD.

1.1.1 Aims and Objectives of the Thesis

The primary aim of this doctoral thesis was to examine bone development into early adulthood in individuals with DCD to determine the existence of a bone deficit.

A secondary aim of this doctoral thesis was to examine the role of motor competence, as well as specific motor impairments, on highly osteogenic physical activity to disentangle the role of physical activity on bone deficits in individuals with DCD. The LCHD framework was used to frame the research to examine potential contributors to bone health in individuals with DCD and the potential interplay of these factors upon bone measurements.

To address these factors, the following hypotheses were formulated:

1. Bone detriments will be present in individuals with DCD and LMC up until at least the time of peak bone mass.
2. The nature of bone detriments in individuals with DCD and LMC will reflect a lower level of engagement in physical activity.
3. Individuals with DCD who engage in a structured exercise intervention will show improvements in bone health.
4. Engagement in specific highly osteogenic physical activity will be lower in individuals with DCD. These differences will be present from childhood through to early adulthood.
5. Reduced osteogenic physical activity will be dependent upon individual factors, including the extent of motor impairment, the nature of motor impairment (i.e., the skills that are impaired) and the presence of other conditions.

As such the overarching research questions addressed in this doctoral thesis are:

1. Does DCD status impact upon bone health in adolescence and adulthood?
2. What is the relationship between DCD and osteogenic physical activity?

These research questions are further broken down into bone health and osteogenic physical activity. There related chapters are shown in brackets.

Bone Health.

1. What is the current evidence on the relationship between bone health and DCD? *(Chapter 2)*
2. What is the incidence of impaired bone health in a population with DCD? *(Chapter 2)*
3. What is the extent of impairment in bone health in a population with DCD? *(Chapter 2)*

4. What bone material, structure, and strength adaptations (measured by peripheral quantitative computed tomography) occur in adolescents with DCD participating in a longitudinal supervised exercise program? *(Chapter 5)*
5. Do young adults with DCD show an impairment in bone health at the time of peak bone mass compared to their typically developing peers? *(Chapter 6)*
6. Is there a relationship between engagement in physical activity and bone health impairments in individuals with DCD compared to their typically developing peers? *(Chapter 6)*

Osteogenic Physical Activity.

1. Is there a reduction in osteogenic physical activity in children with DCD compared to their typically developing peers? *(Chapter 3)*
2. Is there a reduction in physical activity in adults with DCD compared to their typically developing peers? *(Chapter 4)*
3. Are physical activity differences in individuals with DCD, seen when compared to their typically developing peers, impacted by the presence of specific motor skill impairments or the presence of visuomotor impairment? *(Chapter 3 and Chapter 4)*

1.1.2 Research Design

To achieve the forementioned aims, the research was broken into five separate studies. Research in this thesis (beyond the systematic review) involved retrospective analyses of datasets involving a DCD group, and physical activity or bone measurements. Datasets for analyses were chosen to reflect developmental timepoints across the lifespan from early childhood (age five years) to early adulthood (mean age 25 years). Cohorts from Finland and Western Australia were used reflecting a cross-cultural approach. Research design for each study is described in the methods section of each respective study chapter.

1.1.3 Study Delimitations

This body of work is limited to populations aged between five and 25 years and conclusions cannot be drawn for individuals outside of this age range. Bone health studies were based in adolescence and early adulthood. Although bone health at the time of peak bone mass is predictive of the age where osteoporosis occurs (Hernandez,

Beaupré, & Carter, 2003), factors affecting bone maintenance and loss in early adulthood could affect bone health in later adulthood and as such conclusions cannot be determined on later adulthood bone health outcomes. All studies involving bone health measurement were performed in Perth, Western Australia and may reflect features unique to this population and geographic region. Physical activity studies were performed in Australia and Finland, and results may not be applicable in other regions. DCD status was established using motor competence testing results, in accordance with DCD diagnostic criterion A (American Psychiatric Association, 2013). Due to testing limitations, the term low motor competence (LMC) is used in some chapters to describe the DCD population where it could not be confirmed that all participants fulfilled DSM-V diagnostic criteria. Limitations of individual studies are detailed in their relevant chapter.

The nature and direction of this body of work was impacted by the COVID-19 pandemic which occurred approximately six months following confirmation of candidature and persisted through-out the entirety of this doctoral work. Local government and institutions where preliminary research were taking place had restrictions which severely impacted the performance of health research. These restrictions led to in person measurements of physical activity and bone measurements not being able to be performed. In particular, participant recruitment and bone measurements for an adult bone health study were performed in January and February of 2020 but unable to be completed. The limited outcome data has been reported (Appendix A). Accordingly this doctoral thesis, utilised large data sets from previous and ongoing population wide studies to address the key questions underpinning the intention of the originally planned research work.

1.2 Significance

Information describing the bone health of people with DCD is necessary to confirm the presence of an association between DCD and compromised bone health. Current research in this area is limited by heterogeneity in motor measures and bone impairment measures, as well as diversity in age ranges assessed. Under a LCHD perspective, a compilation of studies from different stages in the life course are necessary to fully advance understanding of health issues (Bukata et al., 2018). A systematic review (Chapter 2) was thus required to provide a comprehensive understanding of bone health in a DCD population and where current gaps in knowledge are present.

Current evidence indicates that physical activity, which is an important driver of bone mass and strength, is impaired in individuals with DCD. Physical activity levels in individuals with DCD however has not been explored from an osteogenic point of view. As such, accelerometry data was used to fill gaps in knowledge about osteogenic physical activity at key timepoints in the lifespan (Chapter 3 and Chapter 4). Another key gap in knowledge was the objective assessment of physical activity in adults with DCD (Chapter 4) and the assessment of physical activity impairments in childhood using osteogenic specific measures (Chapter 3). Determining the existence of any physical activity related deficits in these areas is necessary to determine the aetiology of bone deficits in this population.

To further determine the impact of physical activity upon bone health in this population and inform research in this area, it was necessary to determine the impact of engagement in exercise on bone health (Chapter 5). An exercise intervention taking place during the critical adolescent time period for bone development was examined to determine whether exercise engagement leads to bone health improvements.

Finally, the combined impact of DCD and physical activity upon bone health in adults with DCD was examined (Chapter 6). There was an absence of any research reported in the literature on bone health and physical activity in an adult population. Long-term follow up studies investigating whether bone strength disadvantages persist in later years are crucial (V P Tan et al., 2014) under the LCHD framework to help understand the bone health trajectory in this population including possible influencing and or modifiable factors. The absence of this information therefore is a major gap in the understanding of the relationship between physical activity, bone health, and DCD status. This study aims to rectify this via studying the relationship between DCD status and bone health, as well as previous bone loading via physical activity.

Hence the body of work in this thesis aimed to provide a significant contribution to the understanding of bone outcomes for individuals with DCD by providing a cross-cultural understanding of physical activity variables and their relationship upon bone formation into early adulthood. The identification of the groups most likely to show deficits provides additional insight into the potential causation of bone deficits in a DCD population and all studies examine multiple influencing factors for this reason. Additionally, the empirical evidence of this body of work provides insight into potential solutions for improving bone health in the form of a generalised exercise intervention.

1.3 Structure of Thesis

The thesis is structured as follows:

Chapter 1 (the current chapter) provides a general introduction to the body of work undertaken as part of this doctoral thesis with respect to the bone health in a DCD population.

Chapter 2 presents a review of relevant literature on DCD and bone health. It includes three key sections: a systematic review of the current evidence on bone health in DCD populations (J Tan, Murphy, et al., 2022); review of the relationship between DCD and osteogenic physical activity; and a summary review on the theoretical framework underpinning the thesis research. The review on the current evidence on bone health in DCD populations is in manuscript format and has been published by Research in Developmental Disabilities (2022).

Chapter 3 reports on original research conducted on the relationship between individual motor competence and osteogenic physical activity in children. This chapter is in manuscript format, with the manuscript under review by Medicine and Science in Sports and Exercise at the time the thesis was submitted for examination.

Chapter 4 reports on original research on the relationship between DCD status in childhood and physical activity in adulthood (J Tan, Ylä-Kojola, et al., 2022). This chapter is in manuscript format and has been published by the Scandinavian Journal of Medicine and Science in Sports (2022).

Chapter 5 reports on the improvement of bone health in adolescents with DCD by engagement in a generalised physical activity intervention (J Tan et al., 2020). This chapter is in manuscript format and has been published by the Journal of Musculoskeletal and Neuronal Interactions (2020).

Chapter 6 reports on bone differences in young adults with DCD. This chapter is in a manuscript format and has been accepted for publication at the Journal of Bone and Mineral Research.

Chapter 7 discusses the collation of research outcomes. Overarching aims and research questions are reviewed, limitations examined, and conclusions from the body of work drawn. Suggestions for future research are discussed.

Due to this doctoral thesis being structured by publication, there is some unavoidable repetition of content although efforts have been taken to minimise this effect.

Chapter 2

Literature Review

Current literature associated with the undertaken research is outlined in this chapter. A brief overview regarding the importance of bone health and the relationship between physical activity and bone health is provided followed by a systematic review on what is known about bone health in individuals with DCD. As physical activity is a key determinant of bone health in this population, a description regarding what is known about the relationship between DCD and physical activity is subsequently provided. A review of the theoretical framework underpinning the research concludes this chapter.

2.1 Bone Health

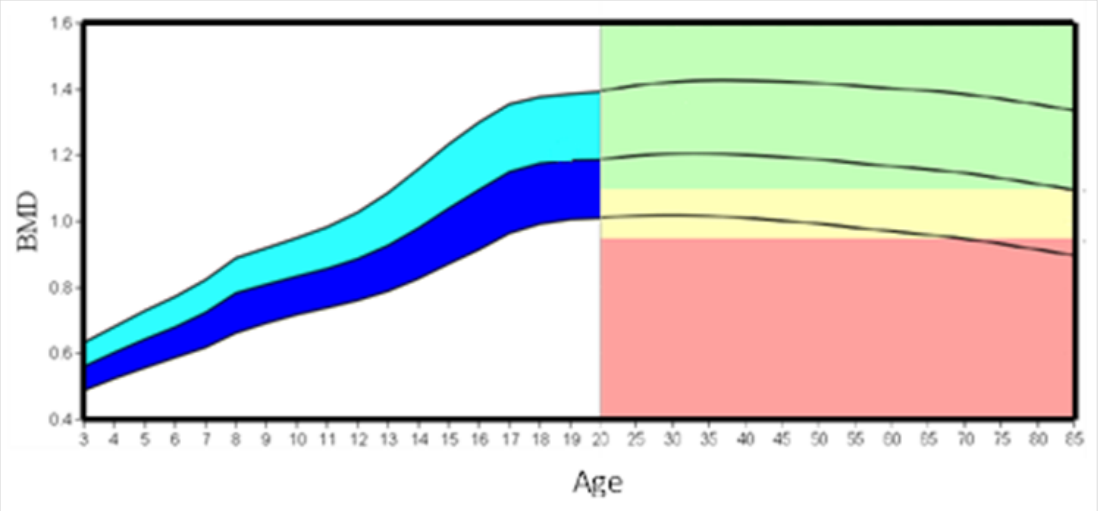
Bone health reflects the strength of bone in response to forces and as such its vulnerability to fracture. Bone health can be measured in the form of bone mass via bone mineral content or bone mineral density (BMD), or as measures of bone architecture (Hart et al., 2020). Ultimately deleterious changes in bone health reduces the structural strength of bone with a resulting increase in fracture risk. Fracture risk is associated with changes in bone mass and bone architecture (Bouxsein, 2005). For example, a one standard deviation reduction in the bone architecture measure of cortical thickness was significantly associated with an odds ratio for fracture of 1.63 for males and 1.65 for females with similar, although nonsignificant, odds changes for the architecture measure of trabecular density, trabecular number and trabecular thickness (Edwards et al., 2015). Bone mass measures are similarly associated, with a doubling of fracture risk for each standard deviation decrease in areal BMD (World Health Organization, 1994). These increases are significant when the substantial effect of osteoporotic fractures upon mortality and quality of life are considered. For example, a meta-analysis produced a relative hazard risk for mortality following a hip fracture of 5.75 for females and 7.95 for males in the first three months following fracture and, 1.96 and 1.79 respectively for ten years post-fracture. Increased rates of disability and depression are also reported following osteoporotic fracture as well as lower social participation (Cauley, 2013). As such the formation of a healthy bone phenotype during growth is a necessary goal in the maintenance of continued general

health. The formation of a bone phenotype is a dynamic process, involving complex interactions between genetic and hormonal factors as well as vitamin D, nutrition and mechanical loading from physical activity (V P Tan et al., 2014). Physical activity is an essential modifiable factor for bone formation and maintenance, with the dynamic forces stimulating the osteogenic cells to create bone in the area strained by the forces (Binkley, Berry, & Specker, 2008; Cech & Martin, 2002; Hart, Nimphius, et al., 2017).

Childhood and adolescence is a critical time for bone development as the majority of bone mass is accumulated (Binkley et al., 2008) and bone architecture established (Binkley et al., 2008; Hughes, 2007; Wren et al., 2014) over this period. This effect is illustrated in Figure 2.1. Adolescence in particular has a period of rapid bone gain, with an enhanced osteogenic effect from physical activity due to loading from activity as well as concurrent biochemical and hormonal changes related to puberty (Farr et al., 2014; Faulkner, 2007; L Santos, Elliott-Sale, & Sale, 2017; Wren et al., 2014). The timing of peak bone mass varies by site with the range for achievement being from the late teenage years to mid-twenties (Baxter-Jones, Faulkner, Forwood, Mirwald, & Bailey, 2011; Boot et al., 2010) after which further bone will not be accumulated and bone structural changes will predominate strength improvements (Hart, Nimphius, et al., 2017). These effects mean bone mass gains from physical activity in childhood and adolescence are long lasting compared to effects from physical activity in adulthood (L Santos et al., 2017). Hence, physical activity is particularly critical over adolescence for the maximisation of peak bone mass and bone architecture (Daly, 2007; Hughes, 2007; Stagi, Cavalli, Cavalli, De Martino, & Brandi, 2016) and the potential risk reduction of fragility or skeletal frailty in older adulthood.

Figure 2.1

Changes in Bone Mineral Density Through the Lifespan



From Hart et al., 2020. Normal levels of bone mass in later life are indicated as green, osteopenic as yellow and osteoporotic as red.

2.1.1 Bone and Physical Activity

A relationship between bone and physical activity has been long established, with benefits particularly noted in childhood and adolescence when bone is growing and bone shape established (Bland, Heatherington-Rauth, Howe, Going, & Bea, 2020; Brailey et al., 2022; Julián-Almárcegui et al., 2015). Cross-sectional studies have shown greater bone density in childhood athletes compared to non-athletes (Courteix et al., 1998) while longitudinal studies have shown benefits of childhood and adolescent physical activity up until midlife (MacKelvie, Khan, & McKay, 2002). For example, a large birth cohort study from Brazil found an association between BMD at age 30 years and reported physical activity at 15 years of age (Bielemann, Domingues, Horta, & Gigante, 2014). These benefits are likely from the effect of physical activity upon bone accrual particularly over the critical adolescent period. A study of changes in bone mass in children between eight and 16 years has shown that sports participation and fitness changes can be sufficient to change bone mass trajectory across tertiles, the only factors outside of medication use to be found to do so (Foley et al., 2008). Evidence from longitudinal studies of sustained benefits to bone do not necessarily indicate a causative relationship of physical activity on bone health due to the potential of unmeasured confounding factors related to both physical activity and bone strength, although studies such as Bielemann et al. (2014) did control for a number of factors.

However, these findings are supported by within individual studies that show bone variation due to loading differences between limbs, hence strongly indicating a direct sustained benefit from physical activity (Ducher, Bass, Saxon, & Daly, 2011; A.M. Weatherholt & Warden, 2015; A. M. Weatherholt & Warden, 2018). For example, examination of both arms in childhood tennis players (MacKelvie et al., 2002) and throwing athletes (A. M. Weatherholt & Warden, 2018) showed an improved bone architecture in the playing arm than the non-playing arm. (MacKelvie et al., 2002)

The effect of physical activity after the crucial period of bone development is less well established with evidence of benefits coming from cross-sectional studies and interventions. However, a study in older adults found higher BMD in 75-year-old women from engagement in physical activity in early and mid-adulthood (J Zhang et al., 2022). At a higher intensity of exercise, male former athletes were found to have a lower risk of hip fracture in later life compared to their non-athlete contemporaries (Korhonen et al., 2022). The causative effect of physical activity on bone over such a long time period is difficult to conclude due to the reciprocal relationship between physical activity and current health status, as well as the ongoing nature of physical activity such that prior physical activity impacts on current physical activity. This is particularly important for bone as adulthood physical activity reflects on physical activity during the critical timepoint of childhood and adolescence. Findings from Bielemann et al. (2014)'s longitudinal study however showed an effect on BMD from physical activity at 18 and 23 years of age regardless of previous physical activity status. Although this effect was smaller than what was demonstrated over the adolescent period it does indicate a continued benefit from engagement in physical activity (J Zhang et al., 2022).

2.1.1.1 Bone Loading Response Mechanism

Bone responds to the mechanical stimulation from physical activity by producing bone in the direction of the strain to reduce the force. This process has been well documented (Wolff, 1869, 1870, 1892). As a brief summary, bone responds to the strain from mechanical loading from both weight bearing and directional forces by stimulating the formation of new bone to reduce the strain (V P Tan et al., 2014). As the threshold for bone production is rapidly exhausted and there is a refractory period for bone regeneration, there is little additional benefit from increased length of activity

nor from activities repeated within a relatively short period of time. Rather the optimal activity pattern for bone stimulation is engagement in a diverse range of intense activities particularly during childhood and adolescence when bone is developing. How the bone responds to mechanical stimulation is not the focus of the current work, however a collaborative review summary (Hart et al., 2020) (Appendix B, Section B.1) was conducted by the candidate to inform the fundamental understanding of the role of physical activity as a mechanical stimulator.

2.1.1.2 Physical Activity Measurement

Physical activity is assessed in a variety of ways including self-report, caregiver report, direct observation, and device assessment. Self-report of physical activity is known to have reliability issues (Khan, 2001) including recall bias (Arts et al., 2022; Kohl, Fulton, & Caspersen, 2000). Validated measures are designed to limit the effects of these biases, for example the Bone Specific Physical Activity Questionnaire is partly based on the concept that activities reported were the most engaged in and thus had the largest impact on bone health (Weeks & Beck, 2008). However, such considerations do not account for social desirability bias, where activities and time of participation are reported in a manner that is more favourable to the participant (Brenner & DeLamater, 2014). For physical activity measurements this would likely mean over-reporting of physical activity and under-reporting of sedentary time, with high loading activities more likely to be over-reported due to these activities being more physically intensive.

Device-based assessment, although considered an objective measure, can be influenced by a number of factors from the participants, such as behavioural changes in response to measurement, as well as researchers' decisions such as analysis technique, measurement exclusion criteria, observation effects, and the limited time included in analysis (Borde, Smith, Sutherland, Nathan, & Lubans, 2017; Burchartz et al., 2020). The most commonly utilised forms of device assessment are accelerometry and pedometer, with accelerometry considered the most reliable (Burchartz et al., 2020). For accelerometry, the traditional form of analysis relies on devices designed to assess cardiovascular fitness, meaning that osteogenic specific physical activity is not well captured (Jämsä, Ahola, & Korpelainen, 2011). This deficit is amplified by differences in cut offs for moderate or vigorous activity which may affect study findings (Banda et al., 2016; Migueles et al., 2017; Nilsen et al., 2017). One aspect of

this effect is when activity categories are derived via metabolic equivalent of tasks (METs) as MET values do not necessarily reflect intensity of the movement, due to intensity changes depending upon the age of the individual (Arvidsson et al 2019). A similar effect can be seen from the length of epoch used for analysis with longer epochs causing short bouts of vigorous physical activity to be misclassified as a lower intensity. Aadland and Nilsen (2022) demonstrated this effect in evaluating activity with lower moderate-to-vigorous physical activity (MVPA) and higher light physical activity when 60 second epochs were used compared to a 1-second epoch. This change in classification had a resulting change in relationships between motor skill predictors and physical activity. Aadland and Nilsen (2022)'s study was in children and the impact in adolescents and adults is not yet established. Children have been consistently identified to engage in activity of extremely short duration (Aadland, Andersen, Anderssen, & Resaland, 2018; Bailey et al., 1995; Rowlands, Pilgrim, & Eston, 2007; Sanders, Cliff, & Lonsdale, 2014) while adolescents' and adults' activity is less sporadic. Accordingly, the impact could be theorised to be smaller in adolescents and adults. Notably however, Aadland and Nilsen (2022) found a stronger epoch effect in school age children than in preschool age children which they speculated was due to the intermittent nature of vigorous activity in organised sports. If this is the case, older groups for whom organised sports are a main driver of physical activity (Ikeda et al., 2022) may also be vulnerable to underreported physical activity.

The effect of epoch length is particularly important in considering the effect of physical activity upon bone. MVPA is used as a de facto indicator of osteogenic activity due to its association with high intensity activity (Brailey et al., 2022) and is vulnerable to epoch effects given the short bouts in which it is undertaken (Aadland et al., 2018; Sanders et al., 2014). As such, decisions on epoch lengths or MVPA thresholds (Banda et al., 2016; Migueles et al., 2017) may result in an underestimate of the effect of motor skills upon high intensity activity. This effect has been demonstrated in assessment of the numbers of bouts of activity engaged in, with a systematic review finding that engaging in MVPA in bouts of less than five minutes is associated with improved body composition and cardiometabolic measures (Poitras et al., 2016). However, these findings were limited to seven studies and lacked comparative information on other physical activity measures (Poitras et al., 2016). Lack of replication is an issue with the use of alternative techniques, however,

studies that use conventional and alternative analysis substantiate the differing relationship between physical activity and health variables between these techniques (e.g. Burden et al., 2022).

As such, there is evidence for an effect of physical activity upon bone beyond what has been previously reported and analysis techniques specific to osteogenic physical activity have been developed accordingly. The most used of these is osteogenic index (OI) (Ahola, Korpelainen, Vainionpää, & Jämsä, 2010; Deere, Sayers, Rittweger, & Tobias, 2012a), which evaluates vertical impacts of physical activity from accelerometry data with its accuracy in determining mechanical loading validated against ground reaction forces (Jämsä, Vainionpää, Korpelainen, Vihriälä, & Leppäluoto, 2006; Veras et al., 2022). OI is analysed in a variety of ways including on a continuum of measurement, within a range of accelerations signifying low, medium, or high intensities, or using only high intensity accelerations (peaks above 5.2g) (HOI) (Deere, Sayers, Rittweger, & Tobias, 2012b; Haapala, Rantalainen, Hesketh, Rodda, & Duckham, 2022; Vainionpää et al., 2007). OI is a predictor of bone health in adolescents (Deere et al., 2012b), and older adults (Ahola et al., 2010; Hannam et al., 2017; Savikangas, Sipilä, & Rantalainen, 2021; Vainionpää et al., 2007) and also has validity in paediatric populations (Rantalainen et al., 2021). A study of adolescents demonstrated the importance of using bone specific techniques, noting OI and HOI were stronger predictors of tibial bone health than MVPA (Haapala et al., 2022). There are small variations regarding grouping cut offs, particularly with differing age groups due to a lower level of OI in older adults (Savikangas et al., 2021) and this may impact upon interpretations. The use of bone-specific measures has also been suggested in interpreting self-report data due to bone health being better reflected when standardised physical activity measurement was transformed into a bone specific loading score than when it was interpreted as METs (Ng et al 2022).

2.1.2 Hormones and Bone

Bone is responsive to the effect of hormones. Puberty and menopause are particularly pivotal periods for bone growth, development, and its health trajectory (Venken, Callewaert, Boonen, & Vanderschueren, 2008). During puberty there are large gains in bone mineral due to height and weight changes as well as the direct effects from hormonal changes (Slemenda et al., 1994). Furthermore, for females,

hormonal changes during menopause cause high rates of bone loss (Sirola, Kröger, Honkanen, Jurvelin, et al., 2003; Sirola, Kröger, Honkanen, Sandini, et al., 2003).

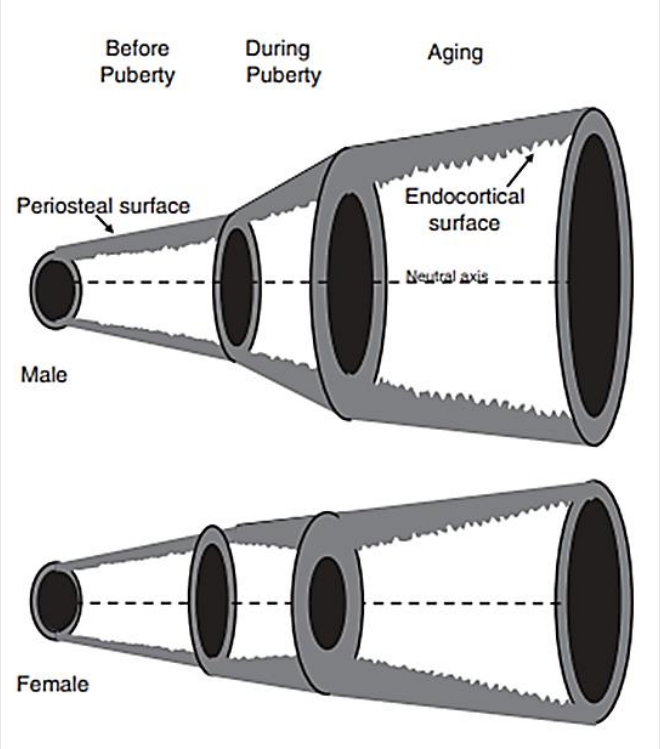
The effects of rapid gains in height and weight at the onset of puberty, stimulated by insulin-like growth factor 1 and growth hormone are strong drivers of bone changes. The fastest gains in bone mineral are in the time surrounding peak height velocity (Elhakeem, Frysz, Tilling, Tobias, & Lawlor, 2019; Nilsen et al., 2017) with approximately one third of skeletal mineral gained over those years (Slemenda et al., 1994). The effects of hormonal changes on bone health vary by body and bone location, with the femur and trabecular bone being particularly sensitive (Slemenda et al., 1994). As such bone health changes are highly sex specific, as shown in Figure 2.2, with males having an increase in bone width not seen in females and higher overall BMD (Elhakeem et al., 2019). Several differences in bone health between sexes, particularly length, width, mass and strength, emerge during puberty. Later onset of puberty in males result in larger appendicular bones in males due to the cessation of appendicular growth at puberty onset (Q Wang & Seeman, 2008). Additionally, hormonal differences between the sexes during puberty impact on bone mineral and architecture. For example, hormonal changes lead to an increase in periosteal apposition and endocortical resorption in males resulting in wider bones with an enlarged medullary cavity. In contrast females experience a decrease in periosteal apposition only leading to smaller bones and medullary cavity. As a result of these changes the same level of cortical thickness is present in both sexes but males will have a stronger, more robust bone due to the increase in bone width (Q Wang & Seeman, 2008). Additional to sex specific differences there are individual differences regarding timing of puberty that impact upon BMD. A later age at puberty will result in more rapid gain in bone mineral content and BMD when puberty occurs than is present for earlier onset puberty, but a lower BMD overall (Elhakeem et al., 2019). These pubertal changes mean it is necessary to know where an individual is in their pubertal development to interpret their bone strength. This is particularly important in the peak height velocity period as linear growth will outstrip bone mass accumulation resulting in a period of low BMD (Q Wang & Seeman, 2008).

Sex differences in bone health, established in adolescence, are cemented in middle-age due to bone losses from menopause. For females during the menopause period, hormonal changes in particular the loss of oestrogen causes the remodelling

balance for bone to become negative with more bone being resorbed than is deposited (Seeman, 2013). A longitudinal study found the greatest bone loss in women in the first menopausal years with bone loss slowing as menopause progresses (Sirola, Kröger, Honkanen, Jurvelin, et al., 2003). Bone loss was also variable by location with a greater loss being present in the spine than the femur (Sirola, Kröger, Honkanen, Jurvelin, et al., 2003). Individual factors play a part in mitigating the effects of sex differences on bone health including use of hormone replacement therapy (Komulainen et al., 1999; Morabito et al., 2002; Sirola, Kröger, Honkanen, Sandini, et al., 2003), weight (Guthrie et al., 1998; Komulainen et al., 1999; Sowers et al., 2013), and physical activity levels (Flores et al., 2022; Nakamura et al., 2019; Sirola, Kröger, Honkanen, Jurvelin, et al., 2003; Yasaku, Ishikawa-Takata, Koitaya, Yoshimoto, & Ohta, 2009).

Figure 2.2

Architectural Changes in Bone Mass Through the Lifespan



From Seeman & Delmas, 2006.

2.2 DCD and Bone Health

This section reports, as published, a systematic review (with published protocol presented in Appendix B, Section B.2) on the presence of bone health detriments in populations defined as DCD and LMC (J Tan, Murphy, et al., 2022). It reports on all known evidence in this area up until March 2021. An updated search, covering the intervening time between March 2021 and February 2023, found no additional literature not reported in this thesis.

Article Information

Title:	Association of Developmental Coordination Disorder and Low Motor Competence with Impaired Bone Health: A Systematic Review
Authors:	Jocelyn Tan, Myles Murphy, Nicolas H. Hart, Timo Rantalainen, Ranila Bhoyroo, Paola Chivers
Reference:	Tan, J., Murphy, M., Hart, N. H., Rantalainen, T., Bhoyroo, R., & Chivers, P. (2022). Association of developmental coordination disorder and low motor competence with impaired bone health: a systematic review. *Research in Developmental Disabilities*, *129*, 104324. https://doi.org/10.1016/j.ridd.2022.104324

Abstract

Aims. Individuals with developmental coordination disorder (DCD) and low motor competence (LMC) may be at increased risk of low bone health due to their lifetime physical activity patterns. Impaired bone health increases an individual's risk of osteoporosis and fracture; therefore, it is necessary to determine whether a bone health detriment is present in this group. Accordingly, this systematic review explores the association between DCD/LMC and bone health.

Methods and Procedures. Studies were included with assessment of bone health in a DCD/LMC population. Study bias was assessed using the JBI critical appraisal checklist. Due to heterogeneity, meta-analysis was not possible and narrative synthesis was performed with effect size and direction assessed via harvest plots.

Outcomes and Results. A total of 16 (15 paediatric[1]/adolescent) studies were included. Deficits in bone measures were reported for the DCD/LMC group and were more frequent in weight-bearing sites. Critical appraisal indicated very low confidence in the results, with issues relating to indirectness and imprecision relating to comorbidities.

Conclusions and Implications. Individuals with DCD or LMC are at increased risk of bone health deficits. Bone impairment locations indicate insufficient loading via physical activity as a potential cause of bone deficits. Results indicate a potential for earlier osteoporosis onset.

Keywords

Developmental disabilities, fracture, movement, inactivity, falls, bone.

[1] The word paediatric is used in this chapter to define a group between infancy and adolescence. This use of paediatric fits the definition of childhood, as listed in Definitions.

2.2.1 Introduction

Developmental coordination disorder (DCD) is a neurodevelopmental condition typified by difficulty in the acquisition and performance of motor skills impairing everyday functioning (American Psychiatric Association, 2013). Where diagnosis is not possible, DCD is often called low motor competence (LMC) (Blank et al., 2019). Individuals with DCD have been suggested to be at risk of a variety of health conditions, including impaired bone health (Cantell, Crawford, & Doyle-Baker, 2008; Hands, Chivers, et al., 2015; Tsang et al., 2012). Bone health indicates the vulnerability of the bone to fracture and is indicated by measures including density, architecture, and geometry (Hart, Galvão, et al., 2017; Hart et al., 2020). Bone health impairment may be considered present when bone measurements are more than one standard deviation below age-appropriate reference intervals (World Health Organization, 1994). However, no individual tool is currently able to assess all elements that make up bone health and hence completely assess fracture risk (Hart et al., 2020; Shalof, Dimitri, Shuweihdi, & Offiah, 2021). Bone health follows a lifelong trajectory of growth and development in childhood and adolescence followed by gradual decline in adulthood (World Health Organization, 1994).Therefore, bone health impairment at any age is predictive of early onset osteoporosis, and associated minimal trauma fractures (Bishop et al., 2014). As such, impaired bone health in populations with DCD may indicate a group at increased risk of fracture.

Individuals with DCD may be at increased risk of bone health impairment due to risk factors such as low birth weight (Blank, Smits-Engelsman, Polatajko, & Wilson, 2012; Cooper et al., 2006) or medication use for co-occurrent conditions such as ADD or ADHD (Feuer, Thai, Demmer, & Vogiatzi, 2016; Landgren, Fernell, Gillberg, Landgren, & Johnson, 2021). Additionally, individuals with DCD have been reported to have a lifetime physical activity pattern characterised by low levels of moderate and vigorous physical activity and high sedentary behaviour (Rivilis et al., 2011). Similar patterns are associated with impaired bone health in the general population (Faulkner, 2007; Foley et al., 2008; Hart et al., 2020). Physical activity creates mechanical strain which stimulates bone development depending on the type and degree of strain and the life stage in which it occurs (Kontulainen, 2007). The greatest benefits for bone development are observed from high levels of diverse physical activity during

childhood and adolescence (Hart, Nimphius, et al., 2017). As such, bone health impairments are anticipated in DCD individuals due to lifelong low levels of physical activity (Rivilis et al., 2011).

Individuals with DCD or LMC and bone health impairment may have a greater increase in fracture risk than would be anticipated for their level of bone impairment, due to a high rate of falls (Scott-Roberts & Purcell, 2018) and ADD/ADHD's increased injury risk (Chou, Lin, Sung, & Kao, 2014) given the high rates of comorbidity (James et al., 2021). Fractures have a substantial impact on quality of life (Fortington & Hart, 2021; Son et al., 2016), with osteoporotic fractures in particular having a high mortality rate (Cauley, 2013). Additionally, fractures have a substantial economic impact, with osteoporotic fractures alone being estimated to have a direct cost of more than 100 million dollars over 10 years (Briggs et al., 2015). Given the estimated population rate of DCD is between five to six percent (Blank et al., 2019), identification of bone health impairment in individuals with DCD is of public health interest.

To ascertain if DCD or LMC population is at increased risk of bone health impairments, it is necessary to determine its prevalence and severity. Hence, this systematic review aims to examine the association between DCD and LMC with bone health measures across the lifespan.

2.2.2 Methods

This systematic review was registered within PROSPERO[2]. It was performed in accordance with PRISMA guidelines for the reporting of systematic reviews (Page et al., 2021) and the JBI manual for studies of etiology and risk (Moola et al., 2017).

2.2.2.1 Eligibility Criteria.

2.2.2.1.1 Participants

Assessment of studies for inclusion was performed via two author assessment (JT and PC) of the DCD diagnostic criteria from the diagnostic and statistical manual, version five (DSM-V) (American Psychiatric Association, 2013).

[2] CRD42020167301

The criteria are:

A: Acquisition and performance of motor skills substantially below that expected given age and experience

B: Motor skill deficit affects age-appropriate activities of daily living, productivity, and leisure

C: Deficit present from early development

D: Another condition does not better explain the motor skill deficit

Studies were included as DCD if they met DSM-V criterion A, with studies not assessing the full criteria classified as LMC. Studies were excluded if participants had a movement limiting or bone affecting condition.

2.2.2.1.2 Study Design

Cross sectional studies and longitudinal single or multi-arm studies (including case studies, case series and clinical trials) were included in this review, provided they assessed bone health in human DCD/LMC populations. Only baseline data was extracted from intervention studies as change over time was not assessed. Book chapters were excluded based upon the assumption of no original empirical data. Review articles were not included but scanned for relevant articles as per the Cochrane Handbook in order to provide a comprehensive search. Conference publications and thesis were included. There were no exclusions based on language or publication date.

2.2.2.1.3 Outcome of Interest

Studies assessing bone health via any measure were included. Established measurement outcomes for bone health included dual-energy X-ray absorptiometry (DXA) for bone density measures (bone mineral density and content); peripheral quantitative computed tomography (pQCT) for macroscopic architecture, geometry, and bone density measurements (trabecular and cortical bone area, bone mineral content and density, periosteal and endosteal size, cortical thickness, bone mass, and bone strength indices) (Hart et al., 2020); quantitative ultrasound for overall bone health reflecting density and architecture (Binkley et al., 2008); and skeletal age assessment for bone maturity via hand and wrist sonography or radiography (Cavallo, Mohn, Chiarelli, & Giannini, 2021). Reliability issues have been reported in paediatric

use of bone measurement tools due to bone size variation (DXA, quantitative ultrasound), movement (pQCT) (Shalof et al., 2021) and ethnicity (skeletal age) (Mansourvar et al., 2013). DXA measurements in adults are used diagnostically to measure bone health using established reference norms (Hart et al., 2020) and a meta-analysis has reported correlation for DXA of 0.57 with pQCT results and quantitative ultrasound (Shalof et al., 2021). Fracture rates were assessed as a secondary indicator of bone health.

2.2.2.1.4 Information Sources

One study author (JT) performed a search (from inception to June 2020, updated in March 2021 and June 2022) of the following databases: PubMed, Cochrane Central Register of Controlled Trials, Informit Health Collection, and ScienceDirect. Grey literature was searched using OpenGrey, Trove, Digital Commons Network, Networked Digital Library of Theses and Dissertations, WorldCat (restricted to theses), DART-Europe E-these portal, EthOs, and Scopus. In addition, conference websites were searched for the American Society for Bone and Mineral Research, and International Conference on Children's Bone Health. International conferences for DCD (National Conference on Developmental Coordination Disorder, International Conference on Developmental Coordination Disorder) did not have comprehensive websites, however, the websites for each year's conference were searched when available. Google Scholar, WorldWideScience, and reference lists of key studies (Cantell et al., 2008; Chivers et al., 2019; Hands, Chivers, et al., 2015; Tsang et al., 2012) and relevant reviews were scanned for additional studies.

2.2.2.1.5 Search Strategy

The search strategy is provided in Table 2.1 and was amended to individual databases as needed (Supp 2A, Appendix C). For database searches, the search strategy was validated by its ability to identify key studies (Cantell et al., 2008; Chivers et al., 2019; Hands, Chivers, et al., 2015; Tsang et al., 2012) listed in the database. All records were exported into EndNote (Clarivate Analytics, 2018) and duplicate studies automatically removed. Study author (JT) uploaded remaining studies to Rayyan (Ouzzani, Hammady, Fedorowicz, & Elmagarmid, 2016) for screening. Studies where a translated English version was not available were translated via online translator ("Google Translate," 2021), with translation crosschecked (GmbH).

Table 2.1

Search Strategy

Number	Combiners	Terms
1	Problem of Interest	Bone health OR bone density OR fractures OR osteoporosis OR skeletal age OR pQCT OR bone mineral content
2	Participants	Developmental coordination disorder OR motor competence OR clumsiness OR apraxia OR dyspraxia OR motor difficulty OR physical awkwardness OR coordination impairment OR specific developmental disorder of motor function OR motorically awkward OR minimal cerebral dysfunction OR minimal brain dysfunction OR deficits in attention, motor control and perception
3		#1 AND #2
	Limitations	Human, study design as per inclusion criteria

2.2.2.1.6 Selection Process

Studies were screened for inclusion by title and abstract, and then full text by two pairs of authors (RB and JT or PC and JT) with disagreements resolved via discussion. Study exclusion reasons are in (Supp 2B, Appendix C).

2.2.2.2 Data Collection Process

JBI data extraction forms for systematic reviews of etiology and risk (https://tinyurl.com/2pxv2vmu), modified to include motor competence measures and mean (M) and standard deviation (SD) for outcomes, were used for data extraction. Data extraction was performed using an Excel form completed by two authors (JT and PC) working independently and crosschecked by JT for accuracy.

The following general study characteristics and demographic information were extracted to determine if studies were linked and the appropriateness of analysis: publication details; ethical approval details; date, duration, and location of data collection; recruitment procedure; motor competence terminology and assessment tool; and data analysis method. Furthermore, the following information was extracted where available for both the LMC/DCD and comparator group: participant number; age, sex, and puberty characteristics; motor competence measures; and comorbidity information. Where multiple studies represented a single cohort, all data was extracted and compared to determine the most representative study for sensitivity analysis.

2.2.2.2.1 Outcome Data Items

All reported measures presented in each study for bone health outcomes were extracted for the LMC/DCD and comparator group, including raw numbers, effect size, M or median (Md), SD, and 95% confidence interval (CI) and odds ratio (OR) for impairment or fracture rates. Data was extracted for all subgroups and models. Data representing the lowest 15th percentile was preferentially used for analysis in accordance with DCD recommendations (Smits-Engelsman, Schoemaker, Delabastita, Hoskens, & Geuze, 2015) as were models that controlled for confounding variables.

2.2.2.2.2 Dealing with Missing Data

Two studies did not report total group data. One study which reported gendered data only (Chivers et al., 2019), had complete data provided through PC as the original work's corresponding author. One paper provided correlation data only (Gustafsson et al., 2010) and the author provided unpublished total group data, when contacted.

2.2.2.2.3 Assessment of Study Quality

Study quality was independently assessed for each study using the JBI critical appraisal checklist for each study design (https://jbi.global/critical-appraisal-tools) by two authors (JT and PC) with disagreement resolved via discussion. The checklist for cross-sectional studies includes items on subject selection, incomplete reporting, and confounders, while the checklist for case series includes items on criteria and completeness of inclusion, and demographic and clinical information reporting. A judgement of overall study quality was performed using a method similar to that described by Hayden, van der Windt, Cartwright, Côté, and Bombardier (2013) based upon the number of missing measures and their relationship to study design. For example, failure to describe inclusion for the sample in detail may not affect study quality for a validated tool with established cut off points but would reduce the overall quality rating for a less established tool.

2.2.2.2.4 Reporting Biases

Publication bias was assessed visually using funnel plot asymmetry (Guyatt, Oxman, Montori, et al., 2011). Informal assessment of publication bias was performed by comparing harvest plots of unpublished results to that of published papers for effect size and direction. The influence of small study bias was addressed by the risk of bias

criterion ‘study size’ based on the number of DCD/LMC participants. Less than 50 participants was considered high risk, 50 to 200 moderate risk, and greater than 200 participants low risk (Dechartres, Trinquart, Boutron, & Ravaud, 2013).

2.2.2.2.5 Diversity and Heterogeneity

Clinical diversity in age, gender, and motor competence impairment was addressed by subgroup analyses. Other reasons for clinical diversity, such as comorbidities, were described narratively. For the intended meta-analysis, heterogeneity was assessed visually and via the X^2 and I^2 statistic.

2.2.2.3 Data Synthesis.

2.2.2.3.1 Eligibility for Synthesis

Data synthesis was performed using odd ratios for bone health impairment or fracture where outcomes were available from two different cohorts in the same body region. Reports that appeared to be of the same study were excluded from analysis. Ten studies were excluded in this manner, details of which are in Supp 2C, Appendix C. Two sets of papers and conference publications were considered as potentially from the same cohort based on author, population, and ethics details. The first set (Cohort 1) (Chivers et al., 2019; Hands, Chivers, et al., 2015; Jenkins et al., 2020; J Tan et al., 2020) was known to be of the same study cohort as PC and JT were authors. For the other paediatric cohort (Cohort 2) (Fong et al., 2018; A W W Ma et al., 2018; Yam & Fong, 2017) considered likely to be a shared cohort attempts to contact the author via email were unsuccessful, as the account was closed. No other contact information could be located for any of the authors via internet searches. Hence, the decision to link the studies was based on review authors’ decision due to similarities between the studies.

2.2.2.3.2 Preparation for Synthesis

Odds ratios were calculated preferentially using the number of reported cases in each population when presented (Hands, Chivers, et al., 2015; Hellgren, Gillberg, Gillberg, & Enerskog, 1993; Oettinger, 1975; Schlager, Newman, Dunn, Crichton, & Schulzer, 1974). The rates for the control population for Hands, Chivers, et al. (2015) paper was determined from the reference paper (Buntain et al., 2004). The fracture rates for Hellgren et al. (1993) paper were calculated by combining the motor deficiency and ADHD group with the motor deficiency only group and comparing

with the non-motor deficiency group. Comparison rates for skeletal age deficiency (Oettinger, 1975; Schlager et al., 1974) were derived from general population rates as defined by Acheson et al. (1963). Where number of reported cases were not presented, odds ratios were determined directly from effect size (Cantell et al., 2008; Fong et al., 2018; Tsang et al., 2012), and for one study via the inversion of the presented odds of being at low motor competence with impaired bone (Filteau et al., 2016). For all other included studies, odd ratios were calculated using a Z-score as detailed in Supp 2D, Appendix C (Borenstein, Hedges, Higgins, & Rothstein, 2009).

2.2.2.3.3 Statistical Synthesis

Maentel-Haenszel fixed effects and inverse variance random effects meta-analysis were performed using Review Manager 5.4 (Cochrane Collaboration, 2020) for fracture data and MetaXL plug in for Excel (Barendregt, Doi, Lee, Norman, & Vos, 2013) for bone health. Substantial heterogeneity (I^2 statistic greater than 50% when X^2 is smaller than 0.10) (Higgins & Green, 2008) remained following attempts to decrease. As such, meta-analysis results are included in Supp 2D, Appendix C but not reported in text. Vote counting was performed for evidence and direction of effect. Harvest plots (Ogilvie et al., 2008) were conducted to visualise the impact at both outcome and study level with the height of the bar dependent on degree of difference.

2.2.2.3.4 Heterogeneity Exploration

Sub-analyses were performed limiting analysis by age group, body region (whole, upper, lower), and DCD/LMC categorisation. Age group categorisation was based on established bone development trajectories, whereby paediatric refers to up to age 12, adolescent as 12 to 25, and adult as older than 25 years (Matkovic et al., 1994).

2.2.2.3.5 Sensitivity Analyses

Sensitivity analyses was performed to assess the effects of linking Cohort 1 (paediatric) (Fong et al., 2018; A W W Ma et al., 2018; Yam & Fong, 2017) and Cohort 2 (adolescent) (Chivers et al., 2019; Hands, Chivers, et al., 2015; Jenkins et al., 2020; J Tan et al., 2020). Harvest plots and tables were structured to visualise the effect of linked cohorts. Further analysis was performed limiting meta-analysis and harvest plots to the most representative paper from each cohort. The most representative paper was chosen based upon the most recent publication date and largest sample size with usable

information, including the presence of a comparator or number of bone measures. Based on this criteria Fong et al. (2018) and Chivers et al. (2019) were selected.

2.2.2.3.6 Assessment of the Certainty of the Evidence

Assessment for overall certainty of the evidence was performed using the Grading of Recommendation, Assessment, Development and Evaluation (GRADE) approach (Huguet et al., 2013) and a summary of findings created using GRADEPRO GDT (McMaster University, On, Canada) (Evidence Prime, 2015). GRADE considers risk of bias, effect estimate imprecision, indirectness of measures, and inconsistency in findings, as well as publication bias, effect size, plausible confounding, and dose response. Decisions were made in accordance with GRADE guidelines (Guyatt, Oxman, Akl, et al., 2011; Guyatt, Oxman, Kunz, Atkins, et al., 2011; Guyatt, Oxman, Kunz, Brozek, et al., 2011; Guyatt, Oxman, Kunz, Woodcock, Brozek, Helfand, Alonso-Coello, Falck-Ytter, et al., 2011; Guyatt, Oxman, Kunz, Woodcock, Brozek, Helfand, Alonso-Coello, Glasziou, et al., 2011; Guyatt, Oxman, Montori, et al., 2011; Guyatt, Oxman, Sultan, et al., 2011; Guyatt, Oxman, Vist, et al., 2011) by JT and crosschecked by PC, with disagreement resolved by discussion.

2.2.2.3.7 Deviations from Protocol

Provisionally, this review planned to include only studies which met DSM-V criterion B (J Tan, Hart, Rantalainen, & Chivers, 2021) (Supp 2C, Appendix C). As this was not assessed in the majority of studies screened the requirement was removed and sensitivity analysis performed to assess the impact of this decision.

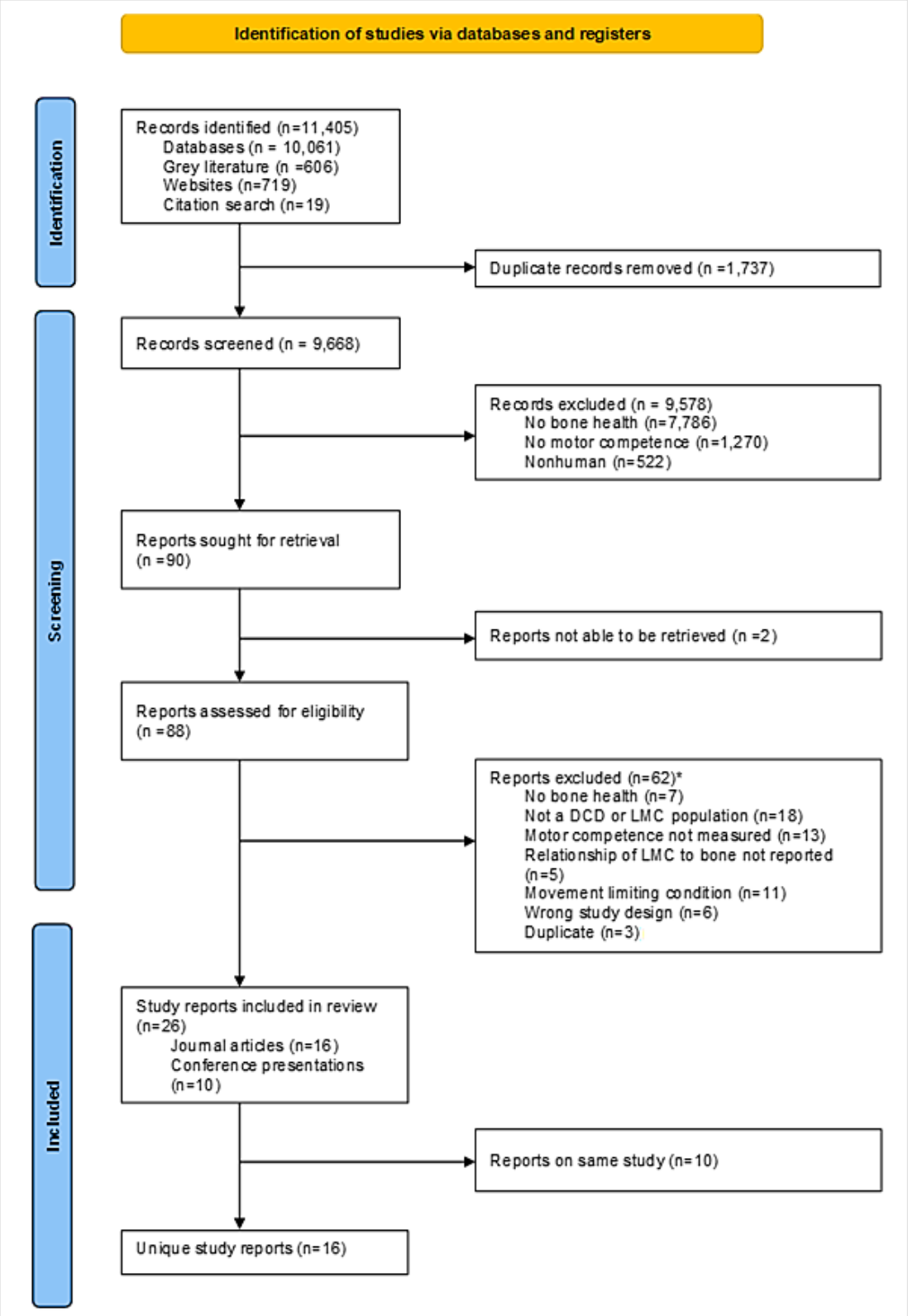
2.2.3 Results

2.2.3.1 Study Selection

The search provided 9688 articles, 16 studies of which were retained for review (Cantell et al., 2008; Chivers et al., 2019; Filteau et al., 2016; Fong et al., 2018; Gustafsson et al., 2008; Hands, Chivers, et al., 2015; Hellgren et al., 1993; Ireland et al., 2016; Jenkins et al., 2020; A W W Ma et al., 2018; D Ma, Morley, & Jones, 2004; Oettinger, 1975; Schlager et al., 1974; J Tan et al., 2020; Tsang et al., 2012; Yam & Fong, 2017). Figure 2.3 details exclusion numbers at each stage of screening.

Figure 2.3

Flow of Studies Through the Review



Adapted from PRISMA 2020 (Page et al., 2021).

2.2.3.1 Study Characteristics and Study Quality

2.2.3.1.1 Bone Health Impairment

Studies included in the review showed a broad range in exposure, outcomes, and participant characteristics (Table 2.2). Eight studies, from six cohorts, were of a paediatric population (M_{age} 5.0 to 8.4 years) (Filteau et al., 2016; Fong et al., 2018; Gustafsson et al., 2008; Oettinger, 1975; Schlager et al., 1974; Tsang et al., 2012), five studies from two adolescent cohorts (M_{age} 14.3 to 17.8 years) (Chivers et al., 2019; Hands, Chivers, et al., 2015; Ireland et al., 2016; Jenkins et al., 2020; J Tan et al., 2020), and one in adulthood (M_{age} 28.1 years) (Cantell et al., 2008). Paediatric studies predominantly used skeletal age as their main bone outcome (Fong et al., 2018; Gustafsson et al., 2008; A W W Ma et al., 2018; Oettinger, 1975; Tsang et al., 2012), but bone density via DXA (Fong et al., 2018; Tsang et al., 2012; Yam & Fong, 2017) and overall bone health via ultrasound (Filteau et al., 2016) was also reported. Adolescent studies reported on bone microarchitecture via pQCT (Chivers et al., 2019; Hands, Chivers, et al., 2015; Ireland et al., 2016; Jenkins et al., 2020). The tibia was the most frequent site for bone assessments with details of bone area by tool provided in Table 2.3.

Most studies used appropriate tools for assessment of motor skills. Only the Ages and Stages Questionnaire used by Filteau et al. (2016) has reported validity problems due to low specificity (King-Dowling, Rodriguez, Missiuna, & Cairney, 2016). Only three studies (Fong et al., 2018; A W W Ma et al., 2018; Tsang et al., 2012), all from the same research group, met all DSM-V criteria for DCD (Table 2.4). Six studies reported on comorbidity, specifically ADHD/ADD (Gustafsson et al., 2008; A W W Ma et al., 2018; Schlager et al., 1974; Tsang et al., 2012).

Table 2.2

List of Included Studies

Authors (date)	Title	Study design	Study population		Motor assessment	Bone assessment	Notes
			N	M age/ age range *(years)*			
Paediatric studies							
Schlager et al. (1974)	Bone age in children with minimal brain dysfunction	Case series	54	8.5	Minimal brain dysfunction diagnosis (Clements criteria)	Skeletal age (Greulich and Pyle)	Age range six to 12 years
Oettinger (1975)	Letter: Bone age and minimal brain dysfunction	Case series	105		Minimal brain dysfunction diagnosis	Skeletal age (Greulich and Pyle)	Letter to the editor Information on age not provided
Gustafsson et al. (2008)	ADHD symptoms and maturity a study in primary school children	Cross-sectional	208	8.4 (Md)	Motor Skill Development as a Basis of Learning	Skeletal age (Greulich and Pyle)	Age range seven to nine years
A. W. W. Ma et al. (2018)	Adapted taekwondo training for prepubertal children with developmental coordination disorder: a randomized, controlled trial	RCT	145	7.4/7.5	Bruininiks-Osteretsky Test of Motor Proficiency, or MABC[a]; DCD questionnaire	Ultrasonic bone age	Cohort 2 (linked paediatric cohort) Age range between six and nine years

Authors (date)	Title	Study design	Study population		Motor assessment	Bone assessment	Notes
			N	M age/ age range *(years)*			
Tsang et al. (2012)	Activity participation intensity is associated with skeletal development in pre-pubertal children with developmental coordination disorder	Cross-sectional	33	7.8	DCD diagnosis; MABC-2[a]	Ultrasonic bone age; DXA	Age range for recruitment six to 10 years
Fong et al. (2018)	Diversity of activity participation determines bone mineral content in the lower limbs of pre-pubertal children with developmental coordination disorder	Cross-sectional	52	7.5	Bruininiks-Osteretsky Test of Motor Proficiency or MABC	Ultrasonic bone age; DXA	Cohort 2 (linked childhood cohort) Age range for recruitment six to 10 years
Yam and Fong (2017)	A comparison of bone mineral density and body composition between children with developmental coordination disorder and typical development: Dual-energy X-ray absorptiometry	Cross-sectional	77	8.1	Physiotherapy assessment	DXA	Conference presentation. Cohort 2 (linked paediatric cohort) Age range not reported

Authors (date)	Title	Study design	Study population		Motor assessment	Bone assessment	Notes
			N	M age/ age range *(years)*			
Filteau et al. (2016)	Associations of vitamin D status, bone health and anthropometry, with gross motor development and performance of school-aged Indian children who were born at term with low birth weight	Cross-sectional	560	5.0	Ages and Stages Questionnaire	Quantitative ultrasound	Age range not reported
Adolescent studies							
Hands et al. (2015)	Peripheral quantitative computed tomography (pQCT) reveals low bone mineral density in adolescents with motor difficulties	Cross-sectional	33	14.3	MAND[b]	pQCT; Fracture rate	Cohort 1 (Linked adolescent cohort) Age range 12.5 to 17.6 years
Chivers et al. (2019)	Suboptimal bone status for adolescents with low motor competence and developmental coordination disorder: its sex specific	Cross-sectional	39	14.4	MAND[b]	pQCT	Cohort 1 (Linked adolescent cohort) Recruitment age range 12 to 18 years

Authors (date)	Title	Study design	Study population		Motor assessment	Bone assessment	Notes
			N	M age/ age range *(years)*			
Jenkins et al. (2020)	Characterisation of peripheral bone mineral density in youth at risk of secondary osteoporosis – A preliminary insight	Cross-sectional	51	14.3	MAND	pQCT	Cohort 1 (Linked adolescent cohort) Age range five to 18 years for control group and 12 to 18 years for DCD group
Tan et al. (2020)	Impact of a multimodal exercise program on tibial bone health in adolescents with Development Coordination Disorder: an examination of feasibility and potential efficacy.	Case series	28	14.1	MAND[b]	pQCT	Cohort 1 (Linked adolescent cohort) Age range 12 to 17 years
Ireland et al. (2016)	Motor competence in early childhood is positively associated with bone strength in late adolescence	Cross-sectional	443	17.8	Gross motor score at 18 months old	PQCT; DXA	Age range not reported

Authors (date)	Title	Study design	Study population		Motor assessment	Bone assessment	Notes
			N	M age/ age range *(years)*			
Hellgren et al. (1993)	Children with deficits in attention, motor control and perception (DAMP) almost grown up: general health at 16 years	Cross-sectional	59	16.5	Neurological and neuropsychological examinations	Fracture rate	Age range 16 to 17 years
D. Ma et al. (2004)	Risk-taking, coordination and upper limb fractures in children: a population based case-control study	Case-Control	642	12.0 to 13.5	MABC[a]	Fracture rate	Age range nine to 16 years
Adult studies							
Cantell et al. (2008)	Physical fitness and health indices in children, adolescents, and adults with high or low motor competence	Cross-sectional	66	28.1	MABC[a](experimental); DCD questionnaire	DXA	Age range 20 to 60 years

[a] Movement Assessment Battery for Children.
[b] McCarron Assessment of Neuromuscular Development

Table 2.3

Number of Studies by Body Region and Tool

	DXA	pQCT	QUS[a]	Total (including skeletal age)
By body region				
Total body	3	0	0	8
Lower body	3	4	1	8
Upper body	1	3	1	5
Individual location region				
Spine	1	0	0	1
Hip	2	0	0	2
Tibia	0	4	1	4
Fibula	0	1	0	1
Radius	0	3	1	4
Ulna	0	1	0	1

[a] quantitative ultrasound.
Numbers for individual location will not necessarily add up to total body region. Individual studies may measure multiple bone location, DXA measurements may report the total body only.

Table 2.4

DCD Diagnostic Criteria Assessment

	Criterion A	Criterion B	Criterion C	Criterion D	Classification
Paediatric					
Schlager et al. (1974)	Yes	No	No	Yes	LMC
Oettinger (1975)	Yes	Not reported	Not reported	Not reported	LMC
Gustafsson et al. (2008)	Yes	No	No	No	LMC
Tsang et al. (2012)	Yes	Yes	Yes	Yes	DCD
Filteau et al. (2016)	Yes	Partial[a]	No	No	LMC
Yam and Fong (2017)	Yes	No	No	No	LMC
Fong et al. (2018)	Yes	Yes	Yes	Yes	DCD
A W W Ma et al. (2018)	Yes	Yes	Yes	Yes	DCD
Adolescent					
Hellgren et al. (1993)	Yes	No	Yes	Yes	LMC
D Ma et al. (2004)	Yes	No	No	No	LMC
Hands et al. (2015)	Yes	Not exclusion	No	Yes	LMC
Ireland et al. (2016)	Yes	No	Yes	No	LMC
Tan et al. (2020)	Yes	Not exclusion	No	Yes	LMC
Jenkins et al. (2020)	Yes	Not exclusion	No	Yes	LMC
Adult					
Cantell et al. (2008)	Yes	Yes	No	Partial[b]	LMC

[a] Via Ages and Stages Questionnaire. [b] Intelligence testing only.

Critical appraisal indicated studies were mostly of high quality, however, causality due to confounding was a major concern (Table 2.5).

Table 2.5

Study Methodological Quality

	Overall bias	Study size bias	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8
DXA										
Cantell et al. (2008)	Low	High	X		X	X			X	X
Yam and Fong (2017)[c]	High	Moderate			U	U			X	X
pQCT										
Ireland et al. (2016)[e]	Low	Low	X	X	X	X	X	X	X	X
Jenkins et al. (2020)	Low	Moderate		X	X	X	X		X	X
Tan et al. (2020)[a]	Low	High	X	X	X	X	U	X	X	
Chivers et al. (2019)	Low	High	X	X	X	X	X		X	X
Skeletal age										
A W W Ma et al. (2018)	Low	Moderate	X	X	X	X	X	X	X	X
Fong et al. (2018)	Low	Moderate	X	X	X	X	X		X	X
Tsang et al. (2012)[e]	Low	High	X	X	X	X	X	X	X	X
Gustafsson et al. (2008)	Low	High	X	X	X				X	X
Schlager et al. (1974)[a]	Moderate	Moderate	X	X	X	X	U	X		
Oettinger (1975)[a,d]	High	Moderate		U					U	U
Qualitative ultrasound										
Filteau et al. (2016)	High	Low			X	X	X	X	X	
Fracture rates										
D Ma et al. (2004)[b]	Low	Moderate	X	X	X	X	U	U	X	U
Hellgren et al. (1993)	Low	High	X	X	X	X			X	X
Hands et al. (2015)[f]	Low	High	X	X	X	X	X	X	X	X

X=Present. U=Unclear. Cross-sectional questionnaire used unless specified a (case series) or b (case control); c=conference presentation; d=Letter to the editor; e=also DXA; f=also pQCT

Cross sectional. Q1: Inclusion criteria clear. Q2: Subjects and setting described in detail. Q3: Exposure measurement valid and reliable. Q4: Condition measurement used objective, standard criteria. Q5: Confounding factors identified. Q6: Confounding factor management stated. Q7: Outcome measurement valid and reliable. Q8: Appropriate statistical analysis.

Case series. Q1: Inclusion criteria clear. Q2: Condition measurement reliable and valid. Q3: Consecutive, complete inclusion of participants Q4: Clear demographic reporting. Q5: Clear clinical information reporting. Q6: Outcomes clearly reported. Q7: Presenting site(s) information clearly reported. Q8: Appropriate statistical analysis.

Case control. Q1: Groups comparable other than condition presence. Q2: Same identification criteria used for cases and controls, matching. Q3: Exposure measurement standard, valid and reliable. Q4: Exposure measured consistently for cases and controls. Q5: Confounding factors identified. Q6: Confounding factor management stated Q7: Outcomes assessment standard, valid and reliable. Q8: Appropriate statistical analysis.

The use of outcome measures were generally appropriate excepting the use of quantitative ultrasound in a paediatric population (Shalof et al., 2021). The appropriateness of the comparison group was an identified issue for the Jenkins et al. (2020) paper as the comparator population was significantly younger than the LMC group assessed (10.9 years [S.D=0.3] compared to 14.3 [SD =0.2]). Due to the trajectory of bone development this difference was likely to be clinically significant (Foley et al., 2008).

2.2.3.1.2 Fracture Rates

Three LMC studies reported on fracture rates in an adolescent population, with a mean age ranging from 12.0 (D Ma et al., 2004) to 16.5 years (Hellgren et al., 1993). Confounding was assessed in two papers, via assessment of ADD/ADHD (Hellgren et al., 1993) and risk-taking (D Ma et al., 2004). The absence of controlling for confounding was identified as a detriment in critical appraisal, particularly for the Hands, Chivers, et al. (2015) paper as fracture rates were assessed over different time periods for the study population and the comparator population (Buntain et al., 2004).

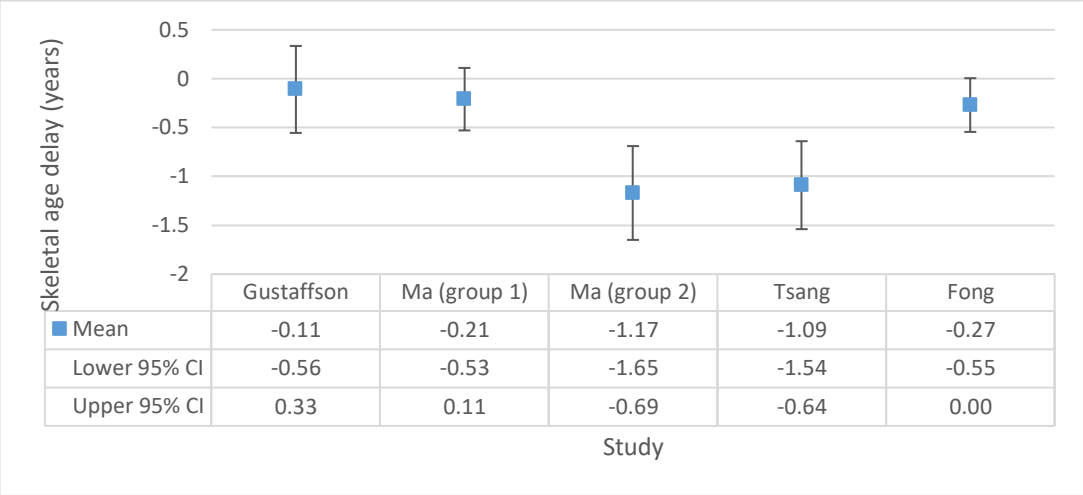
2.2.3.2 Summary Findings

2.2.3.2.1 Bone Health Impairment

Skeletal age was reported as being below chronological age for the DCD/LMC group, with a delay being reported in 50 to 66% of participants (Oettinger, 1975; Schlager et al., 1974). The mean skeletal age delay was between 0.1 (Gustafsson et al., 2008) and 1.2 years (A W W Ma et al., 2018). Range is shown in Figure 2.4. A skeletal age deficit was also reported in comparator groups with an additional deficit for the DCD group not conclusively shown. Tsang et al. (2012) and Gustafsson et al. (2008) reported neutral findings, while Fong et al. (2018) reported a deficit of 0.9 years. Larger deficits were reported for studies using the automated SunlightBonAge system than those using Greulich and Pyle standards with independent radiograph assessment. Whole body DXA studies (Fong et al., 2018; Yam & Fong, 2017) reported significantly lower bone mineral content but only Fong et al. (2018) reported significantly lower bone mineral density (d_{cohen} 3.0, 95% CI 2.5 – 3.5).

Figure 2.4

Delay in Skeletal Age by Study



(Fong et al., 2018; Gustafsson et al., 2008; A W W Ma et al., 2018; Tsang et al., 2012)

DXA studies in the lower body (Table 2.6) reported a deficit in BMD (Cantell et al., 2008; Fong et al., 2018; Ireland et al., 2016) for the DCD/LMC group. Studies which measured individual bone locations found no deficits in the fibula, while the tibia had significant deficits for the LMC group in a number of outcomes including cortical area (Chivers et al., 2019; Hands, Chivers, et al., 2015; Ireland et al., 2016), cross sectional moment of inertia (Ireland et al., 2016), and stress-strain index (Chivers et al., 2019; Hands, Chivers, et al., 2015). Effect size for statistically significant effects ranged from d_{Cohen} 0.1 (Cantell et al., 2008) to 8.9 (Jenkins et al., 2020).

Table 2.6

Lower Limb Effect Sizes

Study (year)	Bone outcome	d_{Cohen}	Confidence interval		P value
			Lower	Upper	
Fong et al. (2018)	Bone mineral content	4.8	4.0	5.5	.001
	BMD	6.0	5.1	6.9	<.001
Tibia					
Hands et al. (2015)	Trabecular density[b]	-0.3[a]	-0.8	0.2	.226
	Cortical density[b]	-0.2[a]	-0.6	0.3	.455
	Stress strain index[b]	0.7[a]	0.2	1.2	<.001
Filteau et al. (2016)		-0.1			

Study (year)	Bone outcome	d_{Cohen}	Confidence interval		P value
			Lower	Upper	
Ireland et al. (2016)	50% cortical area[b,c]	0.4	0.3	0.6	<.001
	50% cortical bone mineral content[b,c]	0.4	0.3	0.6	<.001
	50% cortical BMD[b,c]	0.04	-0.1	0.2	.216
	50% periosteal circumference[b,c]	0.3	0.2	0.5	<.001
	50% cortical thickness[b,c]	0.4	0.3	0.5	<.001
	50% endocortical circumference[b,c]	0.0	-0.1	0.1	.089
	50% cross-sectional moment of inertia[b,c]	-6.5	-6.8	-6.2	.003
Chivers et al. (2019)	Functional muscle-bone unit[b,c]	0.7	0.3	1.0	.214[d]
	Total area[b,c]	0.4	-0.04	0.8	.440[d]
	Stress-strain index[b,c]	0.5	0.02	0.9	.030[d]
	Robustness index[b,c]	0.4	0.001	0.9	.078[d]
	Cortical density[b]	-0.1	-0.5	0.2	.155
	Cortical area[b]	0.3	-0.1	0.6	.001
	Endocortical volumetric density [b,c]	-0.4	-0.9	-0.01	.063
	Midcortical volumetric density[b,c]	-0.3	-0.7	0.2	.353
	Pericortical volumetric density[b,c]	0.1	-0.3	0.5	.458
Jenkins et al. (2020)	4% cortical density	7.4	6.7	8.0	>.05
	4% cortical area	-6.4	-7.0	-5.8	>.05
	4% stress strain index	-6.5	-7.1	-5.9	>.05
	4% total area	-12.1	-13.1	-11.0	>.05
	4% compressive bone strength	-0.4	-0.7	-0.1	>.05
	4% pericortical radius	-12.6	-13.7	-11.5	>.05
	4% trabecular density	6.7	6.0	7.3	>.05
	66% cortical density	-4.6	-5.1	-4.1	>.05
	66% cortical area	-8.9	-9.7	-8.1	.011
	66% stress strain index	-9.7	-10.6	-8.9	>.05
	66% total area	-11.8	-12.8	-10.8	>.05
	66% compressive bone strength	-6.7	-7.3	-6.1	>.05
	66% midcortical ring density	-0.6	-0.9	-0.3	>.05
	66% endocortical ring density	-11.7	-12.7	-10.7	>.05
	66% pericortical ring density	-12.6	-13.6	-11.5	>.05

Study (year)	Bone outcome	d_{Cohen}	Confidence interval		P value
			Lower	Upper	
Tan et al. (2020)	4% trabecular density[b]	0.1[a]	-0.4	0.6	
	66% cortical area[b]	0.8[a]	0.3	1.4	
	66% cortical density[b]	0.03[a]	-0.5	0.6	
	Stress-strain index[b]	0.7[a]	0.1	1.2	
Hip					
Cantell et al. (2008)	Hip t-scores	0.1[a]			.03
Ireland et al. (2016)	Cross-sectional moment of inertia[c]	0.3	0.2	0.4	<.001
	BMD[c]	0.2	0.1	0.3	
Fibula					
Jenkins et al. (2020)	4% cortical density	-3.9	-4.4	-3.5	>.05
	4% cortical area	-7.2	-7.9	-6.6	>.05
	4% stress strain index	-7.7	-8.4	-7.0	>.05
	4% total area	-9.2	-9.9	-8.4	>.05
	4% compressive bone strength	-6.3	-6.9	-5.7	>.05
	4% pericortical radius	-9.0	-9.8	-8.3	>.05
	4% trabecular density	1.6	1.3	1.9	>.05
	66% cortical density	-5.8	-6.3	-5.2	>.05
	66% cortical area	-8.1	-8.9	-7.4	>.05
	66% stress strain index	-7.5	-8.1	-6.8	>.05
	66% total area	-9.1	-9.8	-8.3	>.05
	66% compressive bone strength	-8.1	-8.9	-7.4	>.05
	66% pericortical radius	-10.0	-10.9	-9.2	>.05
	66% midcortical radius	-7.2	-7.9	-6.6	>.05

[a] Values presented in text, otherwise calculated.
[b] No comparator group, population norm comparison.
[c] Males only.
[d] Total group (gendered data).

Studies in the upper body were limited to studies from Cohort 2 (adolescent) and a paediatric ultrasound study. Significant deficits were reported for the LMC group for the entire upper body, radius, and ulna. Deficits included measures of density (Hands, Chivers, et al., 2015) and stress-strain index (Chivers et al., 2019; Hands, Chivers, et al., 2015; Jenkins et al., 2020). Findings on all measures are reported in Table 2.7.

Table 2.7

Upper Limb Effect Sizes

Study (year)	Bone outcome	d_{Cohen}	Confidence interval		P value
			Lower	Upper	
Fong et al. (2018)	Bone mineral content	0.4	0.1	0.8	.150
	BMD	3.0	2.5	3.5	.012
Radius					
Hands et al. (2015)	4% trabecular density[b]	0.3[a]	-0.2	0.8	.106
	4% total density[b]	0.9[a]	0.4	1.4	<.001
	66% cortical density[b]	0.7[a]	0.2	1.2	.038
	66% stress strain index[b]	1.0[a]	0.5	1.5	<.001
Filteau et al. (2016)	Quantitative ultrasound Z score	-0.1			
Chivers et al. (2019)	Functional muscle bone unit[c]	0.6	0.2	1.1	.300
	Total area[c]	0.7	0.2	1.1	.053
	Stress strain index[c]	0.7	0.2	- 1.1	.040
	Robustness index[c]	0.6	0.2	1.0	.092
	Cortical density	-0.4	-0.7	-0.1	.071
	Cortical area	0.2	-0.1	0.6	.243
	Endocortical volumetric density	-0.3	-0.6	0.1	.342
	Midcortical volumetric density	-0.5	-0.8	-0.1	.010
Jenkins et al. (2020)	4% cortical density	0.3	-0.02	0.6	.854
	4% cortical area	-5.9	-6.5	-5.3	1.000
	4% stress strain index	-8.1	-8.8	-7.3	1.000
	4% total area	-12.8	-13.9	-11.7	1.000
	4% compressive bone strength	-3.0	-3.4	-2.6	.251
	4% pericortical radius	-13.4	-14.5	-12.3	1.000
	4% trabecular density	9.2	8.4	10.0	.512
	66% cortical density	-9.3	-10.1	-8.5	1.000
	66% cortical area	-6.7	-7.4	-6.1	.043
	66% stress strain index	-4.8	-5.3	-4.3	<.001
	66% total area	-5.2	-5.7	-4.7	.010
	66% midcortical ring density	-2.9	-3.3	-2.5	.315
	66% endocortical radius	-2.5	-2.9	-2.1	.134
	66% pericortical radius	-5.5	-6.0	-4.9	.007

Study (year)	Bone outcome	d_{Cohen}	Confidence interval		P value
			Lower	Upper	
Ulna					
Jenkins et al. (2020)	4% cortical density	1.3	0.9	1.6	.754
	4% cortical area	-11.9	-12.9	-10.9	1.00
	4% stress strain index	-10.2	-11.0	-9.3	1.00
	4% total area	-12.7	-13.8	-11.7	1.00
	4% compressive bone strength	-4.8	-5.3	-4.4	1.00
	4% pericortical radius	-12.1	-13.1	-11.1	1.00
	4% trabecular density	4.1	3.6	4.5	1.00
	66% cortical density	-8.3	-9.0	-7.5	1.00
	66% cortical area	-6.3	-6.9	-5.7	.046
	66% stress strain index	-4.9	-5.4	-4.4	<.0001
	66% total area	-4.9	-5.4	-4.4	.032
	66% compressive bone strength	-8.2	-8.9	-7.5	.842
	66% midcortical ring density	-0.2	-0.5	0.1	.086
	66% endocortical radius	-2.0	-2.4	-1.7	.156
	66% pericortical radius	-5.6	-6.1	-5.1	.021

[a] Values presented in text, otherwise calculated.
[b] No comparator group, population norm comparison.
[c] Males only.

2.2.3.2.2 Fracture Rates

Increased fractures were reported in two out of three studies reporting fracture rates, Odds ratios for fracture occurrence for the whole body was between 3.1 (95% CI 1.2 to 7.9) (Hands, Chivers, et al., 2015) and 8.3 (95% CI 1.0 to 70.5) (Hellgren et al., 1993). The arm was reported to be the most common fracture site (57 to 90% of fractures respectively). D Ma et al. (2004)'s study, however, was confined in the upper limb and reported no increased risk for LMC individuals with odds ratios between 1.16 (95% CI 0.16 to 4.01) in the upper arm and 1.25 (95% CI 0.56 to 2.81) in the hand.

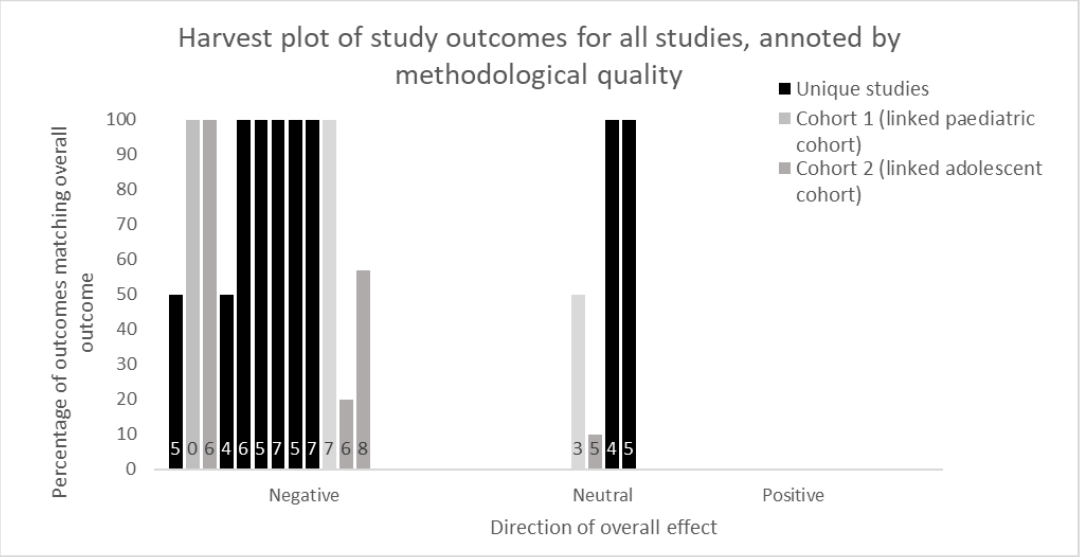
2.2.3.2.3 Data Syntheses

Study level comparisons using harvest plots found an overall detrimental impact of DCD/LMC upon bone health as indicated in Figure 2.5. Two paediatric studies reported no effect (Gustafsson et al., 2008; D Ma et al., 2004). One adolescent study using pQCT (Jenkins et al., 2020) reported bone outcome benefits for the LMC group compared to the healthy comparator group on 87% of measures. The comparator

group for this study was significantly younger and differences were found prior to statistical adjustment for age, sex, and bone length. Similar findings were not reported in studies from the same cohort where a different comparator group was used.

Figure 2.5

Harvest Plot for Overall Outcomes by Study

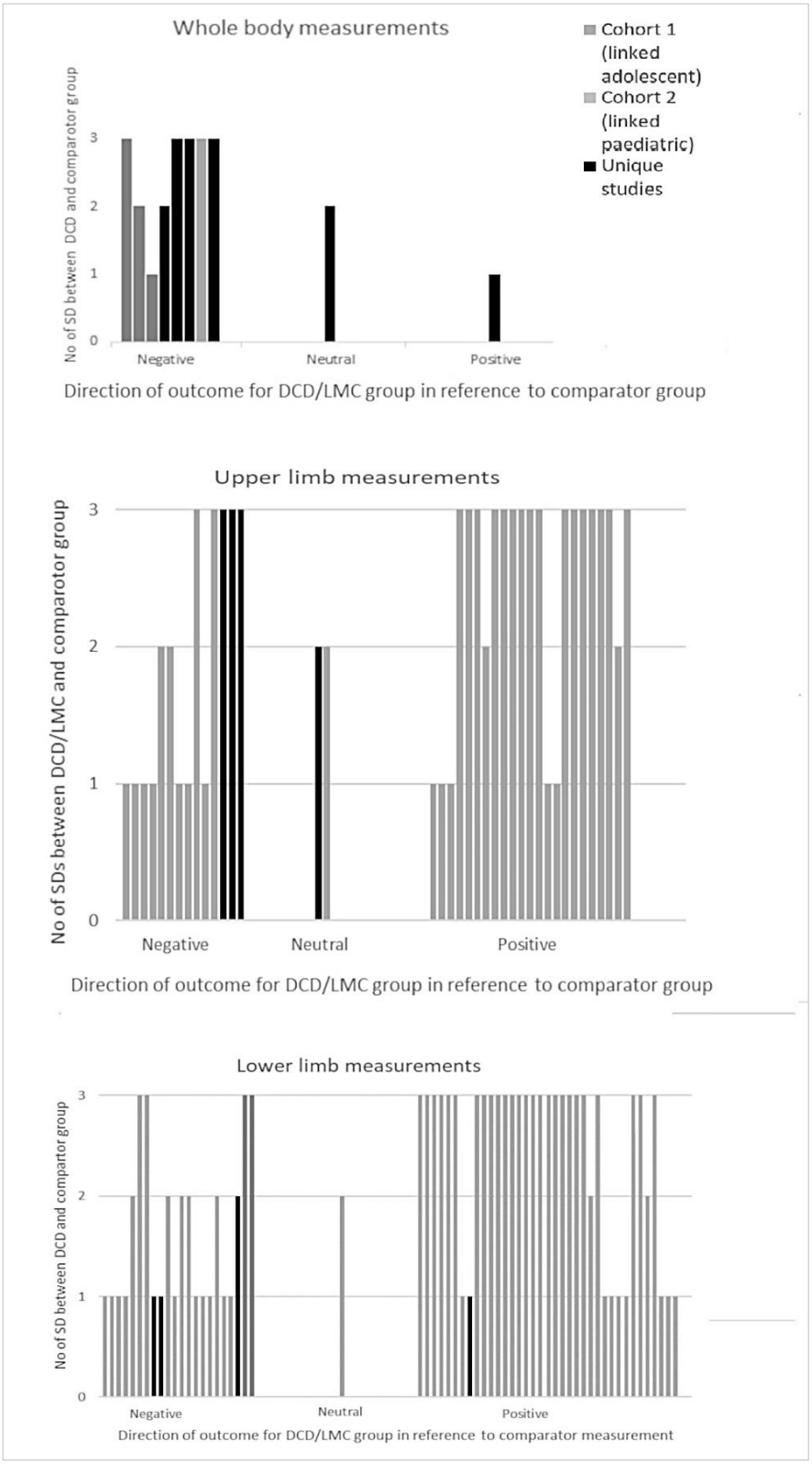


Cohort 1 (linked adolescent cohort) dark grey, Cohort 2 (linked paediatric cohort) light grey, unique studies black. Each bar is annotated with the number of methodological criteria met for the study. Negative label indicates an overall bone deficit for DCD/LMC group. Neutral indicates balance of outcomes is inconclusive. Positive indicates an overall bone deficit for comparator group.

Harvest plots for individual outcomes (Figure 2.6) showed variability between individual outcomes by bone area with whole body measurements the most likely to report a detriment for the DCD/LMC group. Bone health detriment for the DCD/LMC group can be seen to be larger for loading sites than non-loading sites, although detriments occur at roughly the same rate. Findings from pQCT studies on bone architecture found more detriments for the LMC group in areas responsive to bone loading e.g., trabecular density. Where bone detriments were present measurements were between one and two standard deviations lower than the comparator group.

Figure 2.6

Harvest Plots of Individual Measurement Outcomes by Body Region

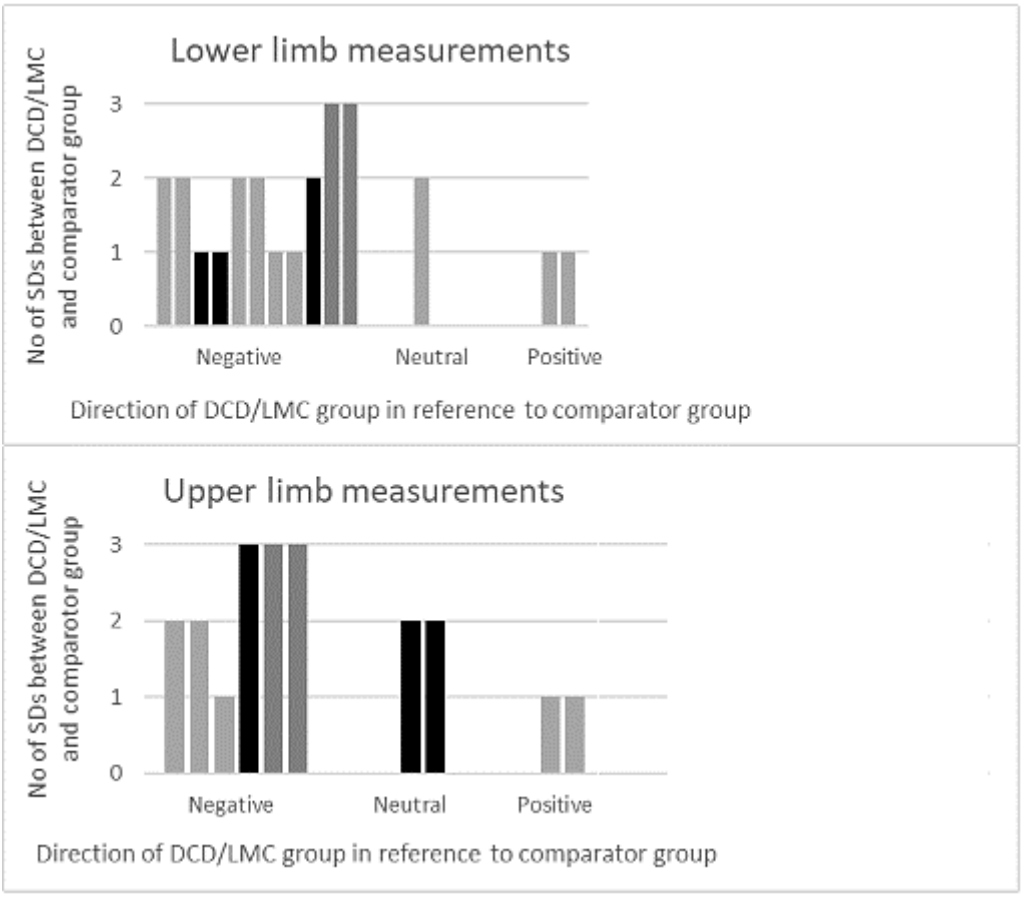


Linked cohort studies are grey, unique studies are black. Negative label indicates bone measures are lower for DCD/LMC group than comparator. Neutral indicates no or extremely small difference. Positive indicates bone measures ae higher for DCD/LMC group than comparator. Except in neutral category, height represents degree of difference 1≤ 1 SD, 2 = 1 to 2 SD, 3 ≥2 SD.

Analysis indicated that including studies from the same cohort may have been influencing results. For example, examination of the upper limb outcomes in Figure 2.6 shows positive outcomes are mostly from a linked cohort that used pQCT analysis. By comparison whole body outcomes include fewer linked cohort studies and have a largely negative result. To examine this, a sensitivity analysis was performed to examine the effects of including studies from the same cohort by limiting Cohort 1 and 2 to one study that best represented the study, selected as detailed in Section 2.2.2.3.1. For Cohort 1 (adolescent) (Chivers et al., 2019; Hands, Chivers, et al., 2015; Jenkins et al., 2020; J Tan et al., 2020) more bone detriments were found overall for the LMC group, via the reduction of beneficial bone health outcomes (Figure 2.7). Limiting Cohort 2 (paediatric) to one representative paper reduced the number of bone detriments for the DCD/LMC whole body measurements only. Sensitivity analyses on the effect of including studies that did not fulfil DSM-V criterion B found a reduction in negative outcomes for whole body measurements and no effect for upper and lower body outcomes.

Figure 2.7

Sensitivity Analysis of Lower and Upper Limb Outcomes for the Effect of Including Linked Cohorts



Outcomes from the representative study from Cohort 1 (adolescent) is grey, other studies are black bars. Negative label indicates bone measures are lower for DCD/LMC group than comparator. Neutral indicates no or extremely small difference. Positive indicates bone measures are higher for DCD/LMC group than comparator. Except in neutral category, height represents degree of difference 1≤ 1 SD, 2 = 1 to 2 SD, 3 ≥2 SD.

2.2.3.2.4 Heterogeneity of Studies

Meta-analysis of bone health outcomes found a high level of heterogeneity (I^2 = 94%). Separate sub-analyses found heterogeneity was higher for adolescent studies (I^2 = 97%), than childhood (I^2 = 50%). Restricting paediatric analysis to skeletal age did not improve heterogeneity (I^2 between 55 and 71%) nor did sensitivity analysis removing linked cohorts. Examination of individual outcomes found that negative outcomes were not confined to a particular age group and no difference was found between age groups in the overall rate of bone health detriments. Paediatric populations had a higher proportion of males (between 71.7% and 83.5% male) than the adolescent population (40.4% to 75.5% male) which may have influenced the

results. Importantly, some adolescent studies reported a gender effect on bone outcomes with the greatest detriments reported in males. No paediatric studies reported gender specific data.

Sub-analyses based on DCD versus LMC status, found more negative outcomes for DCD populations, with neutral and positive outcomes being confined to LMC studies (Cantell et al., 2008; Chivers et al., 2019; Filteau et al., 2016; Gustafsson et al., 2008; Hands, Chivers, et al., 2015; Hellgren et al., 1993; Ireland et al., 2016; Jenkins et al., 2020; D Ma et al., 2004; Oettinger, 1975; Schlager et al., 1974; J Tan et al., 2020). DCD studies, however, were few, confined to a paediatric population, and reported fewer outcomes.

The impact of other factors such as physical activity and comorbidities could not be assessed due to insufficient studies reporting on these outcomes.

2.2.3.2.5 Reporting Biases

Publication bias was not considered to be present as the grey literature did not show a different rate of findings than published literature. Funnel plots did not show evidence of asymmetry for total outcomes, skeletal age, or fractures. Missing results were considered unlikely as studies reported outcomes anticipated for the tool and body area, excepting pQCT studies which reported different outcomes between studies. It was considered possible that fracture rates were underreported given the ease of acquiring this information. As an example, Hands, Chivers, et al. (2015) paper is part of Cohort 1 (adolescent), none of whom have reported on fracture rates.

2.2.3.2.6 Certainty of Evidence

Assessment of the body of evidence using the GRADE system produced a very low rating for certainty of evidence, indicating the true effect may be substantially different from that presented. Summary of findings is presented in Table 2.8, with rationale for ratings in Supp 2E, Appendix C.

Table 2.8

GRADE Summary of Findings

Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Overall certainty of evidence
Bone health					
Serious	Serious	Serious	Not serious	None	Very low
Fracture rate					
Serious	Serious	Serious	Serious	Publication bias suspected Strong association	Very low

Ratings explanation in Supp 2E, Appendix C.

2.2.4 Discussion

2.2.4.1 Interpretation

Outcomes of this systematic review indicate that DCD and LMC are associated with deficits in bone health. These detriments were between one and two standard deviations below the comparator group mean which may indicate low bone health or osteopenia (World Health Organization, 1994). These findings indicate that individuals with DCD and LMC, while not having clinically important bone impairments at the time of study may be at increased risk of osteoporosis in later life. Findings regarding fracture risk were mixed, however, the bone health detriments determined by the study do indicate a potential for increased risk of fractures. In particular, decreased skeletal age and bone density were commonly reported in paediatric samples and are known to be associated with increased paediatric fracture rate (G Jones & Ma, 2005). Additionally, bone microarchitecture changes reported (Chivers et al., 2019; Ireland et al., 2016; J Tan et al., 2020) suggest increased fracture potential via decreased bone strength measurements, such as fracture load. The absence of clinically significant findings is not unexpected as studies were performed prior to the age when bone loss would occur.

Although effect size was unable to be determined due to heterogeneity in measurement sites, the location of bone impairments is suggestive of loading causality. Studies examining weight-bearing locations, particularly the tibia and the hip, reported

more deficits for the DCD/LMC group than non-weight bearing locations such as the fibula (Jenkins et al., 2020) and ulna (Ireland et al., 2016). Measures of bone architecture found more deficits in areas responsive to loading such as cortical area (Chivers et al., 2019; Ireland et al., 2016; J Tan et al., 2020) and trabecular density (Chivers et al., 2019). Combined, this indicates bone deficits in a DCD or LMC population may be due to bone loading variations. Further research is required to establish causation of bone differences in the DCD and LMC group, especially given that most research was in a paediatric population and the effects of physical activity in determining optimal bone structure in children and adolescents is not established in the general population (Bland et al., 2020).

Bone deficits found in this review may be compensated in later life (Shalof et al., 2021) as all but one study was performed prior to peak bone mass attainment. Bone detriments, however, were consistent between paediatric and adolescent studies in keeping with longitudinal studies on bone development which showed bone impairments continued into at least late adolescence (Wren et al., 2014). Furthermore, habitual physical activity patterns established in childhood tend to continue into adulthood in individuals with DCD (Missiuna, Moll, King, Stewart, & Macdonald, 2008), which may indicate that bone deficits are unlikely to be regained over the adolescence and young adulthood period. Therefore, it is anticipated that adults with DCD would have similar or greater bone impairments, with associated clinical implications.

2.2.4.2 Limitations of Evidence

The evidence was limited by heterogeneity in bone health measurements and issues related to the use of bone measurements tools in the population being studied. Quantitative ultrasound and DXA for paediatric populations tend to produce inconsistent results compared to other modalities due to confounding by bone size (Shalof et al., 2021) and pQCT results in adolescents with LMC are known to be impacted by motion artefact (Rantalainen et al., 2018). Furthermore, methodological review indicated low certainty in the results. The majority of studies did not comment on comorbidities, particularly ADD/ADHD which may have impacted on bone health measures due to increased fracture risk (Chou et al., 2014; S W Zhang, Shen, & Yan, 2021) and bone affecting medication use (Feuer et al., 2016). As ADD/ADHD was not

accounted for in most studies and is estimated to occur in 50% of individuals with DCD (Kaplan, Dewey, Crawford, & Wilson, 2001) bone impairments found in this review may reflect ADD/ADHD rather than DCD or LMC. A similar effect may be seen for other conditions not measured such as autism or hypermobility. Furthermore, inconsistency in how the DCD/LMC population was identified, although common (Smits-Engelsman et al., 2015), is of particular concern in assessing bone health measures. As such further work is required to differentiate bone impairments in a clinical DCD population rather than a LMC population.

2.2.4.3 Limitations of Review Process

Search terms used were extensive to include all studies in this area but may have increased heterogeneity. The decision to deviate from protocol and include studies that did not assess criterion B of DSM-V may also have increased heterogeneity. Individual perception of motor competence, reflected by criterion B, rather than motor test performance has been reported to be the strongest influencer of physical activity (Utesch et al., 2021) and so may impact bone health. Sensitivity analysis however did not show an impact of including studies that did not fulfil criterion B.

This review did not include clinical trial registries, outside of the Cochrane Central Register, therefore some unpublished studies may not have been reported.

2.2.4.4 Implications and Future Research

Identified detriments in bone health may have clinical implications, particularly regarding the increased risk of fracture. Due to the impact of fractures upon quality of life (Hough, Boyd, & Keating, 2010) this is an important area for further investigation. Findings suggested impaired bone health was linked to reduced physical activity and responsive to interventions to increase physical activity. Although findings of this review indicate a continuance into adulthood, there is an absence of research in this age group. Clinical implications of impaired bone health in later adulthood could be significant and further research is required in this age group. Longitudinal studies to determine bone change in this population would also be valuable.

Findings of this review were limited by high heterogeneity between studies. This indicates the need for studies to use reliable tools, appropriate comparator populations, and report on comorbidities and DSM-V diagnostic criteria. Clarification is needed in future studies as to whether bone impairments are unique to DCD to shape research and treatment recommendations.

2.2.5 Conclusion

DCD and LMC show an association with impaired bone health on multiple measures in childhood and adolescence. These detriments are such that they appear to be due to physical activity variations. There is currently insufficient evidence as to the continuation of bone health detriments into adulthood, with a complete absence of information in later adulthood. Further evidence is also required as to whether the presence of bone health impairment has clinical implications.

2.2.6 Registration and Protocol

This systematic review was prospectively registered within PROSPERO (CRD42020167301). The protocol for this review is published and can be accessed at https://doi.org/0.11124/JBIES-20-00112 (Supp 2B, Appendix C)

2.3 DCD and Physical Activity

2.3.1 Physical Activity Levels in DCD

Physical activity levels in individuals with DCD are frequently hypothesised to be a potential cause for bone deficits (Chivers et al., 2019). However, there are only two studies (Ireland et al., 2016; Tsang et al., 2012) that have investigated the relationship between bone deficits and physical activity levels in individuals with DCD. These studies have differences in methodologies that may have impacted upon their interpretation of the contribution of physical activity to bone health differences in a DCD population. Therefore, it is necessary to examine the role of DCD on physical activity levels to understand the justification for it as a potential cause of bone deficits. Although physically capable of performing physical activity, children with DCD lack the skills to perform the required motor movements at the level needed for proficient performance of many social physical activities and sports (Hands, Kendall, Larkin, Rose, & Parker, 2009; Williams, 2002). As such low to moderate deficits in physical activity, particularly MVPA, have been reported throughout childhood (King-Dowling

et al., 2019). It is hypothesised that physical activity deficits in individuals with DCD will increase over time as motor skill demands for physical activity increase (Cairney, Hay, Veldhuizen, Missiuna, & Faught, 2010). Particularly, as individuals with DCD are unable to easily adapt their movements to failed task attempts (Martini, Wall, & Shore, 2004) or environmental demands (Larkin & Parker, 2002; Williams, 2002) and so struggle to improve in physical activity performance. Additionally, physical and emotional barriers can inhibit physical activity including early fatigue (Williams, 2002), exarcabated by inefficient muscle movements leading to energy use excessive to that required by the tasks, and low physical self efficacy (Viholainen et al., 2022).

Decreased physical activity in children with DCD occurs early in development from parental reports (May-Benson, Ingolia, & Koomar, 2002). However, studies of early childhood activity showed no evidence of a physical activity difference at the age of five years on either accelerometry or activity participation rates, including diversity and intensity (King-Dowling et al., 2019; Soref et al., 2012). Objective reports of physical activity differences were seen in King-Dowling et al. (2019)'s study with activity patterns indicating inefficient movements and a lower level of stamina. Thus, King-Dowling et al. (2019)'s study implies the beginning of a detrimental activity pattern in early childhood. As physical activity demands at this point in development are low this negative pattern is indicative of the beginning of physical activity deficits in keeping with the activity deficit hypothesis.

As children reach school age, reports on activity deficits become more frequent. A systematic review evaluating activity and participation for children with DCD reported frequent concerns about physical activity limitations across a range of different activities, including bike riding, organised sports and social play (Magalhães et al., 2011). Although the impact upon bone is not clear these findings are indicative of a reduction in diversity of movement. Other studies have shown a similar reduction in self-reported social leisure time and organised sports, but importantly found that DCD status did not limit engagement in school sports and season dependent activity (Cairney, Hay, Faught, Mandigo, et al., 2005). The limiting of physical activity deficits to certain aspects of physical activity explains the findings of a study on six to 10 year old children in Hong Kong which found that although children with DCD self-reported lower leisure activity, particularly social leisure activity, accelerometry analysis showed a lower sedentary behaviour and higher engagement in light and moderate

physical activity in children with DCD than typically developing children (Sit, Yu, Capio, Masters, & Abernethy, 2022). This finding likely indicates an alteration in physical activity patterns, rather than a direct detriment, such that children with DCD are substituting other physical activity for those physical activities they choose to not engage in. Although Sit et al. (2022)'s findings of an increase in device assessed physical measurements in children with DCD are atypical, device assessed deficits in physical activity in children tend to be quite small with the largest detriment being in vigorous physical activity to the order of an 8.6% decrease (Rivilis et al., 2011). These deficits are smaller than would be anticipated given the physical activity patterns reported by children with DCD of playing less team or organised sports, and engaging in less free play (Rivilis et al., 2011).

As children with DCD enter into adolescence, they continue to report a different physical activity pattern than their typically developing peers with a notable decrease in engagement in leisure activities (Rivilis et al., 2011). They also continue to demonstrate a deficit in physical activity levels although the deficit is smaller than what was demonstrated in childhood (Rivilis et al., 2011). This pattern appears to continue into adulthood, although information at this point in the lifespan is scarce. Objective studies of physical activity in adults with DCD are limited to Lloyd, Saunders, Bremer, and Tremblay (2014)'s longitudinal study which showed no difference in physical activity in individuals who had motor competence difficulties at the age of six years. However, it is unclear if this was a true DCD population as adult motor competence testing determined motor issues were not ongoing (Lloyd et al., 2014), indicating they no longer meet the DSM-V criterion A and B (American Psychiatric Association, 2013).

The lack of continuance of motor problems is in contrast to what is known about DCD in the general population (Blank et al., 2019). Cantell, Smyth, and Ahonen (1994) has previously identified that activity patterns for adolescents with childhood DCD whose motor problems resolved by adolescence was comparable to that of typically developing adolescents, while adolescents with motor problems had decreased engagement particularly in social sports. As such, Lloyd et al. (2014)'s study is likely to have underestimated the physical activity difference associated with adulthood DCD. However, the findings are in keeping with those of earlier time points of a deficit in physical activity on self -report (Fitzpatrick & Watkinson, 2003;

Missiuna et al., 2008; Scott-Roberts & Purcell, 2018) not demonstrated by objective accelerometry data (Lloyd et al., 2014). Self-report interview studies involving individuals with DCD found frequent reports of negative experiences and concerns related to physical activity, specifically concerns about social embarrassment (Fitzpatrick & Watkinson, 2003; Missiuna et al., 2008; Scott-Roberts & Purcell, 2018). These concerns would likely reduce physical activity engagement. Additionally, some participants in Missiuna et al. (2008)'s study became less concerned about their physical activity levels due to their peers becoming more sedentary as they aged which may reduce their motivation to engage in physical activity. Scott-Roberts and Purcell (2018)'s interviews of a clinical sample of individuals with DCD who were registered with a treatment group found additional concerns on factors that may have reduced their physical activity such as fear of falling while walking on steep surfaces or walking the dog. Fear of injury has been associated with decreased physical activity in other populations (Okuda et al., 2022). Fatigue, also associated with decreased physical activity levels (Koh et al., 2022), has also been shown to be high in individuals with DCD. Individuals with DCD have been shown to have a level of fatigue midway on the continuum between that of healthy adults and adults with chronic fatigue (M Thomas & Christopher, 2018). Importantly however, Scott-Roberts and Purcell (2018) conclusion was that participants modified their physical behaviour to minimise the impact of motor deficits such that functional mobility was likely unaffected. For example, many participants reported spending their leisure time with family members, so they did not have to worry about social embarrassment and some participants chose to wear different shoes to prevent their mobility from being impeded. Additionally, although Fitzpatrick and Watkinson (2003)'s study reported participants avoiding certain aspects of other activities, they would still engage in other aspects and would sometimes move more due to trying to avoid certain actions. For example, participants reported moving around a lot during ball games to avoid being in a position to catch the ball. There is no information on physical activity engagement in adults with DCD after middle adulthood (early 40s) and so the presence of detriments in later adulthood has not been determined.

As such, physical activity deficits can be seen to be present in children with DCD. However, in contrast to the activity deficit hypothesis these differences decrease in size through adolescence and appear to be no longer present in adulthood although

more evidence is needed. Physical activity patterns however appear to be more negative in individuals with DCD with these differences persisting throughout the lifespan.

2.3.1.1 Physical Activity Measurement in DCD

Complexity concerning the interpretation of physical activity among individuals with DCD is compounded by the multiple methods of physical activity assessment used (Rivilis et al., 2011). Additionally, physical measures do not routinely have information reported on their reliability or validity within the DCD popualtion with Rivilis et al (2011) noting that some self-report tools for physical activity did not have validition information. Physical activity assessment in DCD populations are usually via either self-report or parental report, including interviews, with the period of physical activity assessed varying from one week to total lifetime activity. Validity and reliability are particular issues for parental report questionnaires, with a systematic review finding a complete absence of sufficient validity and reliability data and criterion validity against the accelerometry gold standard in only one measure (Arts et al., 2022). Parental reports of physical activity may also not be reflective of child self-reported physical activity as agreement between child and adult reports are low for other health related questionnaires (Schoemaker & Houwen, 2021). As such, parental reports of physical activity may be reflective of the reporting parent's values and biases and should not be considered a substitute for the child's self-reported information (Schoemaker & Houwen, 2021). Additionally, while some studies use established questionnaires, such as the International Physical Activity Questionnaire (Hallal & Victora, 2004; IPAQ Research Committee, 2005), or the Bone Specific Physical Activity questionnaire (Weeks & Beck, 2008), others use non-validated questions including proxy measurements of physical activity such as sports membership. These non-validated questions have been identified to be insufficiently comprehensive to reflect physical activity as an overall concept (Arts et al., 2022). Additionally, as such questions fail to gather information about physical activity outside of sports, problems in physical activity may be overestimated (Rivilis et al., 2011). Such lack of validity is an important consideration given the frequency of these reporting techniques in evaluating physical activity in the DCD population.

Evidence from the literature using both self-report and objective physical activity measurement indicates that physical activity levels are underestimated in self-

reports by individuals with DCD. Although, overestimation is the more common error in self-report data, underestimation has been reported in individuals who are less active, of poorer health, and believe that others want them to be more active (Godino et al., 2014), while parental underestimation may be related to the desire for their child to increase activity and the effect of parental anxiety on reporting negative outcomes in children (Najman et al., 2000). Examples of the incongruity in reporting can be seen from Rivilis et al. (2011)'s systematic review which showed a smaller difference in physical activity from studies using device assessment or observation than was shown in self and parental reported physical activity. Self and parental report showed lower levels of energy used, fewer physical activity guidelines met, and lower participation in intense exercise than their typically developing peers, while device assessment and observation found the main deficit was in vigorous physical activity (Rivilis et al., 2011). Similar findings were found in a cross-cultural analysis with parental reports of high sedentary activity not being verified by accelerometry measurements (Cermak et al., 2015).

Identified issues with objective measurements of physical activity, however, may also disproportionately affect adolescents with DCD. Aadland and Nilsen (2022)'s study found epoch effects continued into middle childhood despite activity becoming less erratic. This may be due to activity being dependent on sports where movements are often intense but of short duration. Adolescents with DCD are less likely to engage in organised sports than their peers (Cantell et al., 1994; Fitzpatrick & Watkinson, 2003; Fransen et al., 2014), such that epoch effects may only underestimate physical activity for typically developing individuals resulting in the groups appearing more similar in physical activity than they are. Individuals with DCD may also be disproportionally affected by analysis decisions, such as the criteria for a minimum amount of measured time for study inclusion. This was observed in King-Dowling et al. (2019)'s study where more participants with motor impairment were excluded for failing to reach activity thresholds than typically developing participants. This indicates a need for consideration of the effects of motor difficulties in analysis decisions as well as the need for alternative forms of analysis. King-Dowling et al. (2019)'s study shows the importance of these alternative analysis techniques, King-Dowling included the use of triaxial movements (mediolateral, anterio-posterior, and vertical) in physical activity assessment in addition to the conventional vertical

movements. The use of these alternative techniques allowed for the detection of a maladaptive physical activity pattern associated with increased movement in the mediolateral axis (towards and away from the midline of the body) and shorter bouts of activity accumulation. Such additional movements indicate inefficient movement patterns likely contributing to the lower levels of stamina shown by short bouts of activity and so provides important additional information not shown by conventional techniques. Alternative techniques, however, are rarely used in assessing physical activity in a DCD population, and Ireland et al. (2016)'s study in a 17 year old cohort of high intensity impacts from accelerometry is the only known study to use a bone specific measure. The use of alternative techniques may be of particular benefit to the DCD population due to the differences in movement patterns that have been identified from self-report and interview studies. In a similar manner to King-Dowling's identification of inefficient movements, the amount of bone stimulation received in a DCD population from MVPA could be theoretically lower than in a typical population and health benefits may as such be underestimated.

2.3.2 Relationship Between Physical Activity and Motor Competence

Motor competence can be considered to exist upon a spectrum, where individuals with DCD are at the bottom end (American Psychiatric Association, 2013). As such to fully understand the effects of DCD on physical activity levels, it is necessary to look at motor competence as a continuous variable. The relationship between physical activity and general motor competence can be conceptualised using Stodden et al. (2008) which proposes a relationship between motor competence and physical fitness via physical activity with the relationship strengthening with increasing age due to the impact of motor competence on physical self-efficacy. This model conceives lower motor competence as acting on physical activity both directly and indirectly via self-constraining of physical activity due to fear of social embarrassment. As such this model is in keeping with the activity deficit hypothesis. The applicability of Stodden et al. (2008)'s model of the relationship between motor competence and physical activity has been confirmed from numerous review articles (L M Barnett et al., 2021; Figueroa & An, 2016; D Jones, Innerd, Giles, & Azevedo, 2020).

Evidence of a relationship between physical activity and motor competence is present throughout the lifespan with a systematic review indicating strong evidence

for a relationship between total motor competence and overall physical activity (L M Barnett et al., 2021). A specific role has been shown in childhood, with systematic reviews finding a correlation between motor competence and both MVPA and overall physical activity in early childhood (D Jones et al., 2020), and an inverse correlation with sedentary behaviour in middle childhood and early adolescence (G D Santos et al., 2021). However, longitudinal studies in Santos's review indicated an effect of sedentary behaviour upon motor competence levels as well as the inverse relationship which may have impacted study outcomes (G D Santos et al., 2021) and was not considered in the interpretation of the review. Although a review of longitudinal studies found no evidence for an inverse relationship between motor competence and physical activity, the potential bidirectionality of the relationship between motor competence and physical activity variables is an identified issue for cross sectional studies due to motor competence and physical activity co-occurring and hence causation unable to be determined (L M Barnett et al., 2021). Additionally, the presence of mediating factors interfering with the relationship between motor competence and physical activity are rarely assessed in studies in this area and may lead to an overestimation of the strength of the relationship.

Cardiorespiratory fitness measures, for example, may be a mediator of the relationship between motor competence and physical activity (L M Barnett et al., 2021). Kaiglou et al (2022) for example indicated that in middle childhood motor competence only predicted physical activity via its effect upon cardiorespiratory fitness. This potential pathway is further complicated by evidence of the reverse pathway with motor competence affecting physical fitness via its effect on physical activity being present predominantly in early childhood (Hands & Larkin, 2002; King-Dowling et al. 2019). Additionally, the presence of conditions such as DCD which co-occur with LMC may impact upon the relationship between physical activity and motor competence. A hypothesis from Seefeldt (1979) considered there to be the presence of a proficiency barrier in motor skills which must be overcome in order for motor skills to affect physical activity. This theory may be supported by a cross-sectional study in early adulthood finding no significant relationship between motor competence and MVPA (Li, Chirico, Graham, Kwan, & Cairney, 2020). As well as evidence showing significant differences in physical activity are only present at the highest tertile, perhaps indicating that the proficiency barrier is higher than expected

(L Smith, Fisher, & Hamer, 2015). Despite this indicating an issue with assessing motor competence on a continuum by skewing from the top and bottom percentile, the impact of individuals with extremely high motor competence and its inverse DCD status are rarely assessed.

A factor that has been investigated is the role of individual motor skills constituting total motor competence. This is particularly important when considering the effects of DCD since it is a heterogeneous condition. L M Barnett et al. (2021)'s systematic review found no evidence for the impact of individual motor skills upon physical activity from childhood to adolescence and adulthood. This study assessed strength of association by dividing the number of positive associations by the total numbers of analyses, rather than counting individual associations. This alternative analysis technique was presented as the reason for the difference between Barnett's findings and those of other reviews (L M Barnett et al., 2021). However, differences in physical activity measurement may also explain the difference, with most studies in L M Barnett et al. (2021) review using self-report measures. A review article using accelerometry measures as an outcome found individual motor skills, particularly locomotor skills, were predictive of MVPA with this association present across multiple cohorts across more than one country, including Finland and Australia (Cohen et al., 2014). Additionally, research in this area is limited by only being performed in the paediatric time frame with the assumption that physical activity trajectories will carry into adulthood. Although continuity in physical activity occurs into adolescence (Loprinzi, Davis, & Fu, 2015), the continuance of the trajectory into adulthood is not well established.

Importantly, there is limited evidence that DCD status may impact upon the effects of motor skill performance in individuals with DCD with only two studies indicating an effect. Yu, Capio, Abernethy, and Sit (2021) found that decreases in MVPA associated with running performance was present in typically developing children but not children with DCD, while catching performance affected MVPA and sedentary behaviour in typically developing girls and not girls with DCD. These findings are important as they indicate a need to examine the effects of motor competence in the DCD community separately to that of the general population. Examination of factors by DCD status, may lead to different associations as demonstrated in Yu et al. (2021) study or may cause relationships to cease to exist.

The latter effect was demonstrated in King-Dowling et al. (2019) where relationships between individual motor skills (aiming, catch, balance) with MVPA ceased to exist when groups were divided by DCD status. The effect before dividing by DCD status was small, making it possible that this finding was due to sample size however the possibility that effects of individual motor skills upon physical activity is a result of their relationship with DCD status is important to confirm.

2.3.3 Role of Co-occurrent Conditions in DCD

Co-occurrent conditions occur frequently in individuals with DCD (Kaplan, Wilson, Dewey, & Crawford, 1998) and may play an independent role in activities of daily living. The effect of co-occurrent conditions however has only been acknowledged in the most recent diagnostic criteria and is rarely considered in assessment (American Psychiatric Association, 2013). The most common co-occurrent condition is ADD/ADHD with a 50% co-occurrence rate (American Psychiatric Association, 2013; Kaiser, Schoemaker, Albaret, & Geuze, 2015). Language disorders, autism, and internalising conditions are also commonly co-occurrent (American Psychiatric Association, 2013). Additionally, individuals with DCD often have specific deficits such as in executive functioning and visuo-motor integration (VMI) (Lalanne, Falissard, Golse, & Vaivre-Douret, 2012; Lust et al., 2022; Wilson, Ruddock, Smits-Engelsman, Polatajko, & Blank, 2013). Co-occurrent conditions may occur in clusters with differing effects on daily living skills (American Psychiatric Association, 2013).

The only co-occurrent conditions to be considered in evaluating physical activity in a DCD population is that of ADD/ADHD (James et al., 2021). In James et al. (2021) study in children, there was no effect found from DCD for physical activity until ADD symptoms were controlled for. Once ADD symptoms were controlled for, there was a significant decrease in physical activity compared to typically developing children (James et al., 2021). This relationship is likely due to the positive effect that ADD symptoms have upon MVPA, and as such co-occurrent DCD and ADD has the effect of reducing DCD's impact upon physical activity. This potential protective effect for bone for people with co-occurrent DCD and ADD may be mediated by the use of symptom controlling medications, particularly stimulants, which are detrimental to the bone (Feuer et al., 2016; S W Zhang et al., 2021). Although James et al. (2021)'

s study indicates the importance of controlling for co-occurrent conditions, controlling for ADD has rarely been performed in research studies and other co-occurrent conditions, including those that could feasibly affect physical activity such as VMI impairment, have not been explored.

2.3.4 Sex Differences in Physical Activity in DCD

Sex differences are known to be present in the effect of DCD on physical activity, with males showing a decrease in MVPA that is not seen in females (Green et al., 2011). These differences in physical activity levels provide a potential explanation for bone health deficits in DCD being restricted to males (Chivers et al., 2019). A greater effect for boys has also been noted for the impact of motor competence upon physical activity (Figueroa & An, 2016). Differences present in physical activity in girls may be due to unaccounted mediating factors, such as physical fitness which was shown to be completely mediating in females but only partial in males (L M Barnett et al., 2021). Gender differences in the types of physical activity engaged in may be reflected in the differing effect of individual motor skills by sex, with object control skills being a stronger predictor in males and locomotor skills in females up until late childhood (L M Barnett et al., 2021; Logan, Kipling Webster, Getchell, Pfeiffer, & Robinson, 2015). As such, although physical activity detriments are the largest in males with DCD compared to females there are many potential causations for this that has not as yet been established.

2.4 Physical Activity and Bone Health in a DCD Population

Only two studies, one in childhood (Tsang et al., 2012) and one in adolescence (Ireland et al., 2016), have assessed the relationship between physical activity and bone health in individuals with DCD. Tsang et al. (2012)'s study of children between six and 10 years of age found self-reported physical activity and overall activity of the DCD group was significantly lower than that of typically developing children. The role of these differences upon bone variation based on DCD status was found to be significant for overall intensity of activity but not for physical activity intensity. This may potentially reflect on the difference in activity accrual in individuals with DCD as well as the age of the group being assessed. In school children it is likely that much intense physical activity is accrued through organised sports, particularly in school, which will not differ in self-report based on DCD status, although actual level of

engagement during the activity may be lower. Other activities are more variable in intensity and so better reflect an altered physical activity pattern.

One reason for this difference in significance, is that individuals with DCD have reported using techniques to avoid participation in physical activity even while performing a sport (Missiuna et al., 2008), and as such self-reported physical activity may not accurately capture the intensity of physical activity engaged in. For this reason, Ireland et al. (2016)'s study investigating the relationship between physical activity and bone health in adolescents with motor impairment is critical as it uses a device assessed intensity measure. However, Ireland et al. (2016)'s study did not fully explore the differences in physical activity between the LMC and non-LMC group, nor did they explicitly categorise DCD according to the DSM-V. The effect of motor competence on physical activity was instead assessed with motor competence as a continuous variable. This analysis found that physical activity at the age of 17 years increased with increasing motor competence at 18 months. Physical activity levels were also found to attenuate the effect of motor competence on bone health measures. Although this effect was only weak, Ireland et al. (2016)'s study used physical activity measures taken concurrently to the bone health measures and as such may have not given the bone sufficient time to mineralise (Dumith, Gigante, Domingues, & Kohl, 2011). The presence of lean muscle measures accounting for more variation in physical activity, indicates that there may be a larger role from prior physical activity than is seen from the association between current physical activity and bone measures.

Combined the findings from Ireland et al. (2016) and Tsang et al. (2012) study indicate that physical activity plays a mediating role between that of motor competence and bone health. The role of physical activity is likely underestimated due to physical activity being measured concurrently with bone health as bone changes are likely also from previous exposures. Due to the differences in the age being assessed and the method of physical activity assessment more evidence is needed to determine the role of physical activity upon bone health. Additionally, the evidence on the role of physical activity on bone health in a DCD population is limited, with no evidence post mid-adolescence.

2.5 Theoretical Framework

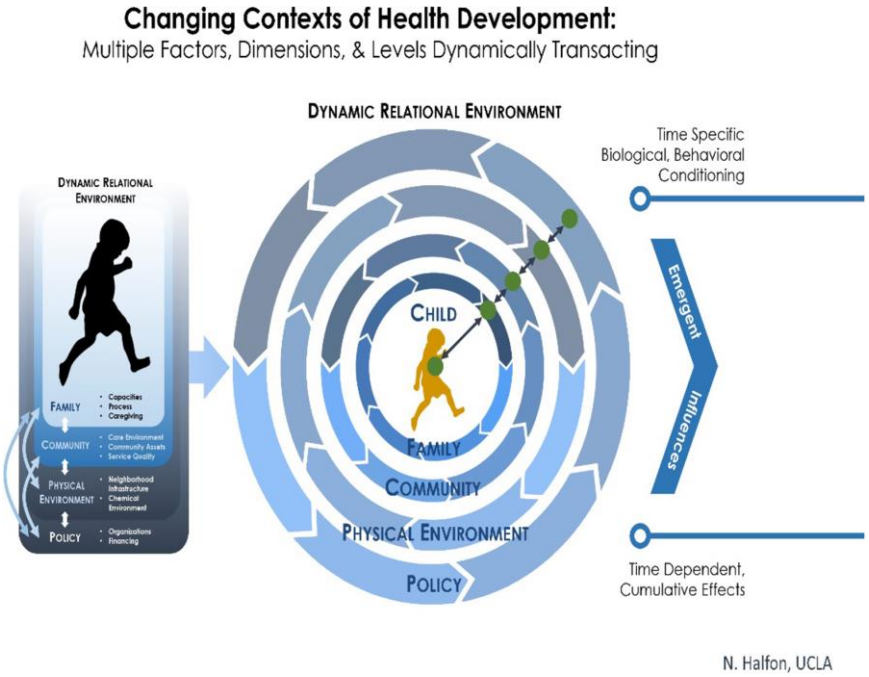
The LCHD Framework was used to guide the methodological approach of the research. The LCHD framework has been primarily used as a framing mechanism in review articles discussing the developmental origins and epidemiology for many health conditions and has been identified as being particularly relevant for chronic health conditions. Given that DCD begins early in development and persists throughout the lifespan, the LCHD framework provides an appropriate framing mechanism. For example, G Wang, Bartell, and Wang (2018) used the methodology to describe the impact of early life factors, including maternal health, on offspring metabolic risk associated with obesity and diabetes as well as that of future generations. Such models are useful given the growing evidence on the effect of early life exposures on lifetime health and disease (Gluckman, Hanson, Cooper, & Thornburg, 2008). It is particularly valuable in explaining conditions of neurodiversity, such as premature infants or individuals with autism, where it has identified gaps in the literature (Halfon et al., 2018). It is recognised that individuals with vulnerabilities and disparities in childhood are likely to have poor health in adulthood due to their lifetime health trajectory. As very few studies follow all factors along the lifespan, the LCHD framework is primarily used to describe the aetiology of health conditions rather than potential solutions. However, given that the LCHD framework considers health a constantly emerging phenomenon it emphasises the prevention of future disease via health asset development (Fraser, Catov, Lawlor, & Rich-Edwards, 2018), a theory that is well aligned to the investigation of bone health across the life course.

Growing acceptability of the framework has led to policies and interventions using similar methods to those advocated in the LCHD framework. Health measures are increasingly framed as health promotion throughout the lifespan for the optimisation of all individual's health rather than being aimed at a particular health goal (G Wang et al., 2018). For example, cardiovascular health research and treatment now use models where health is seen as a continuous factor rather than an endpoint and as a result have begun intervening earlier in the lifespan. Such actions recognises the existence of pre-disease states where remedial action with modifiable factors can result in meaningful changes to an individual's health (Fraser et al., 2018). However, many studies still have gaps in addressing the multifaceted aspects predicting an

individual's health outcomes, including sex specific considerations. The LCHD framework does recognise the importance of environmental and social factors (Hertzman, 1999) and the multifactorial nature of the framework provides a flexibility such that these factors can be incorporated into the lifetime trajectories. Overall, the LCHD framework has facilitated the transition of studies from a less optimal single factorial assessment to an improved multifactorial approach. For example, studies aiming to improve the management of insulin dependent diabetes now include multi-behavioural aspects, including weight change, insulin management and exercise programs, with great success (Halfon & Hochstein, 2002). Similar models could be conceived for managing physical activity and bone health.

Figure 2.8

Schematic Indicating the Major Factors in the Life Course Health Development Framework



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Interventions and studies canvassing physical activity and bone health, particularly focus on the importance of early life factors and the clustering of risk factors whereby one exposure leads to another (Ben-Shlomo & Kuh, 2002). However, other aspects of the LCHD framework including the importance of family and social factors, shown in Figure 2.8, and critical time points are often overlooked. Under a

LCHD framework, the importance of family resources and strategies are identified as the most important indicator of children's future success (Elder, 1998). However, studies examining physical activity and DCD are usually focused entirely on the child, while family interventions to improve physical activity have been trialled in other settings (Foster, Moore, Singletary, & Skelton, 2018). Furthermore, physical activity research in DCD does not consider critical time points and the relevance of these times. Critical time points for physical activity could be when the child is entering school; around the age of nine years when most children have begun participating in competitive sports: age 11 to 12 years when the child enters secondary education; age 16 to 18 years when physical education in school ceases to be compulsory; and early adulthood where individuals are starting employment. For bone health, the most critical time points are the years surrounding the occurrence of peak height velocity which is variable for each individual but has overlap with the critical adolescent time periods for physical activity. These critical time points represent the opportune moment to alter trajectories, as transition points put stress upon existing systems leading to the creation of new response patterns more aligned to the new influences and routines. This means actions at critical time points have a non-linear impact upon health. As such, they are an ideal point for an intervention. Additionally, since critical time points often occur where there is additional hormonal, physiological, and social developmental changes any health behaviours that are altered at this time may have additional effects upon health and be critical for long term life outcomes (Elder, 1998; Halfon et al., 2018).

These models are often not considered within the field of physical activity or bone health as most knowledge in this area relies on single time point assessments as a proxy of an individual's activity and health over an extended time period (Mielke, 2022). Such methodology results in information gaps. Even in instances where there is a longitudinal study, physical activity engagement is often not repeatedly measured and so change over critical time points is not reflected, nor the influence of other factors upon physical activity, or the interaction with bone. By using a LCHD framework in guiding this thesis, a more complete picture of physical activity over the lifespan can be presented as well as the factors that may change an individual's activity level.

2.6 Summary

The literature canvassing physical activity in individuals with DCD indicates the presence of some impairments in physical activity, although the scale of impairment varies depending on the age group and measurement technique used. Physical activity impairments may increase over adolescence and then decrease in adulthood, but this trajectory is limited by the scarce evidence on physical activity effects in adulthood. Device-based assessment of adulthood impairments of physical activity in the DCD population are scarce and inconclusive, with more evidence required. There are only two studies that have assessed the relationship between physical activity and bone, one using self-reporting in childhood and another using accelerometry measurements in adolescence. These studies show a limited role of physical activity upon bone but findings, such as the importance of muscle area, imply a greater role than detected. Tsang et al. (2012) and Ireland et al. (2016) use of measures assessing diversity and intensity of physical activity indicate the importance of including measurements of these two elements of mechanical stimulation in order to accurately assess bone health. Further information is still required on the relationship between physical activity and bone in the DCD population. In particular, there is more information needed on the relationship between physical activity and bone in adulthood as well as the presence of detriments of physical activity in older age groups and osteogenic physical activity at all age levels.

Chapter 3

Motor Competence Indicators and Skeletal Loading among Children: The Skilled Kids and Active Family Studies

Research Synthesis

As identified in the previous chapter, physical activity deficits have been shown to be present in children with DCD. Although reduced physical activity is believed to be the reason for identified bone deficits in DCD, the nature of these deficits and how they relate to bone development is not fully understood. This chapter of the thesis aimed to address this gap by examining physical activity differences in children with DCD using an osteogenic specific measure of physical activity. Furthermore, given the heterogenous nature of deficits in DCD the relationship with individual motor skills on osteogenic physical activity was explored.

Article Information

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Authors:	Jocelyn Tan, Timo Rantalainen, Nicolas H. Hart, Paola Chivers, Arto Laukkanen, Donna Niemistö, and Arja Sääkslahti

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Abstract

Motor competence skills are necessary for the performance of physical activity needed for healthy bone development. Individuals with motor competence impairment, in the form of Developmental Coordination Disorder (DCD), have bone health impairments which are attributed to decreased physical activity. However, the impact of individual motor skills on osteogenic physical activity in children is unknown. This study used accelerometry impact peak analysis to determine the impact of individual motor skills (hopping, skipping, bouncing a ball, overhand throw, sideways jump) and DCD risk status on osteogenic physical activity levels.

Five-hundred and forty-three children (277 girls, 266 boys; mean age = 8.8 [SD=1.1] years) from a longitudinal cohort had motor competence assessed via items from the Test of Gross Motor Development and the Körperkoordinationstest für Kinder and wore waist accelerometers for 7 days. Accelerometery data was assessed as number of acceleration peaks in low (up to 2.1g), moderate (2.1 to 4.3g) and high (above 4.3g) impact categories and daily osteogenic index, along with mean daily duration in sedentary, light, moderate, and vigorous activity. A cross sectional analysis used general linear models to examine the impact of motor skills on osteogenic physical activity variables, as well as daily duration, number of bouts and bout duration in sedentary, light, moderate and vigorous activity, while controlling for sex, body mass index Z-score, and age. General linear model showed a significant association for only sideways jumping and overhand throw in osteogenic physical activity measurements. No association was detected for DCD risk. Study findings suggest that osteogenic physical activity participation in children is related to performance ability of specific motor skills rather than DCD risk, which may explain bone health disparity in individuals with DCD.

Keywords

Accelerometery, bone, developmental coordination disorder, motor competence, paediatric.

3.1 Introduction

Physical activity stimulates bone growth and development via increases in bone mass and bone structure (Hart, Nimphius, et al., 2017). The mechanical forces acting upon the bone during physical activity stimulates bone formation, with activity of high intensity or which is weight-bearing known to be particularly beneficial to the bone (osteogenic physical activity) (Erickson & Vukovich, 2010). As bone development follows a trajectory, the greatest benefits of physical activity upon bone can be seen during childhood (Hart, Nimphius, et al., 2017). High levels of physical activity in childhood and adolescence will result in a high peak bone mass delaying the age of onset of osteoporosis and osteoporotic fracture (Bonjour, Chevalley, Ferrari, & Rizzoli, 2009). Optimal development of bone from physical activity however depends upon the nature of the physical activity engaged in. Diverse high impact activities such as jumping will result in the greatest bone gains (Hart, Nimphius, et al., 2017). Engagement in such activities requires the ability to perform complex movement skills, the combined ability of which is referred to as motor competence. Motor competence can be grouped into object control (e.g., catch, kick, throw), locomotor (e.g., run, hop, jump), and balance skills (Robinson et al., 2015). Physical activity levels and associated health outcomes have been linked to overall motor competence and individual motor skill performance (L M Barnett et al., 2021; Robinson et al., 2015; Yu et al., 2021). As such, low motor skill performance may act as a barrier to engagement in osteogenic physical activity. The effect of individual motor skill performance on bone development has not been previously assessed, although very low motor competence, such as is seen in the neurodevelopmental condition Developmental Coordination Disorder (DCD), has been linked to bone health impairments (Chivers et al., 2019; Tsang et al., 2012).

Individuals with DCD have low levels of physical activity which may provide a potential explanation for reported bone deficits (Ireland et al., 2016). Differences in osteogenic activity (as measured by acceleration impact peaks above 3g) has been previously reported in adolescents with motor competence impairment (Ireland et al., 2016). Similarly, a study of children with diagnosed DCD found that their decreased bone health when compared to typically developing children was partly accounted for by decreased diversity in self-reported total activity (Tsang et al., 2012). As such, differences in osteogenic physical activity in children with DCD or its undiagnosed form low motor competence (LMC) are likely to exist but need to be confirmed via device

assessment. Studies assessing the effect of DCD upon bone health, however, assess motor competence as a single entity despite DCD being heterogenous in which motor skills are impaired (Blank et al., 2019). Given that studies in children in the general population show a variable relationship between motor skills and physical activity levels depending on which motor skill is being assessed (Logan et al., 2015), it is likely that individual aspects of motor competence affect osteogenic physical activity differently. The relationship between motor skills and osteogenic physical activity is however not established in either the general population or individuals with DCD or LMC.

In addition, previous research on motor competence and physical activity does not provide information on osteogenic activity. Classification methods used in standard physical activity analysis is based upon the cardiovascular demands of the activity, and as such, can be a poor indicator of osteogenic effect (Brailey et al., 2022; Weeks & Beck, 2008). For example, the vigorous physical activity of running has an effective bone load rating far closer to walking (i.e., light physical activity) than jumping (i.e., vigorous physical activity) (Weeks & Beck, 2008). Furthermore, the time period used for accelerometry classifications can mean osteogenic activity of short duration, such as a single jump, is not captured (Migueles et al., 2017). This particularly affects the accuracy of physical activity measurement in children (Rantalainen et al., 2021). Osteogenic index (OI) is an alternative analysis technique designed to capture osteogenic physical activity using accelerometry (Ahola et al., 2010), however OI has not been thoroughly investigated in children. The OI summary score, derived from daily acceleration peaks or impacts in accelerometry assessment, has been found to be associated with bone size, quality, and strength in adults (Ahola et al., 2010). Additional analysis using acceleration peaks within intensity bands from loading (Ahola et al., 2010) has found quantity of vigorous peaks to be associated with bone traits in adolescents (Deere et al., 2012b) and adults (Vainionpää et al., 2006). An association between acceleration peaks and bone traits in children is not known, however, a study looking at acceleration intensity has indicated the majority of children's activity accumulation is at low intensity levels (Rantalainen et al., 2021). Although the sample size in the study was small, this finding indicates the need to use OI and acceleration peak analysis, along with conventional accelerometery to provide a more complete understanding of the osteogenic effect of childhood daily activity.

The lack of conclusive research exploring the link between osteogenic physical activity and motor competence in children means it is not possible to determine

causation for identified bone health deficits in individuals with DCD or LMC. As such, the use of an alternative form of accelerometery analysis provides necessary information in determining this relationship. Furthermore, although physical activity findings vary according to the skill being assessed (L M Barnett et al., 2021), it is not known which motor skills (i.e., locomotor, object control, balance) have the greatest impact on OI. Hence, this study aimed to explore the impact of motor competence measures upon bone affecting physical activity by examining the individual motor skill impact on osteogenic physical activity measures, as well as the effect of previously established motor competence impairment in the form of DCD risk.

3.2 Methods

3.2.1 Experimental Design

This is a retrospective analysis of participants from the Skilled Kids Study (T1) and the Active Family Study (T2). T1 was a geographical cluster-randomised study examining motor competence in families with three- to seven-year-old children between 2015 and 2016 (Laukkanen et al., 2018), and T2 was a follow-up study of the T1 participants including motor and physical activity factors conducted three years later. The current study uses cross-sectional analysis to explore the impact of motor competence on osteogenic physical activity at six to ten years of age. A subgroup analysis for the effects of DCD risk at T1 was also performed.

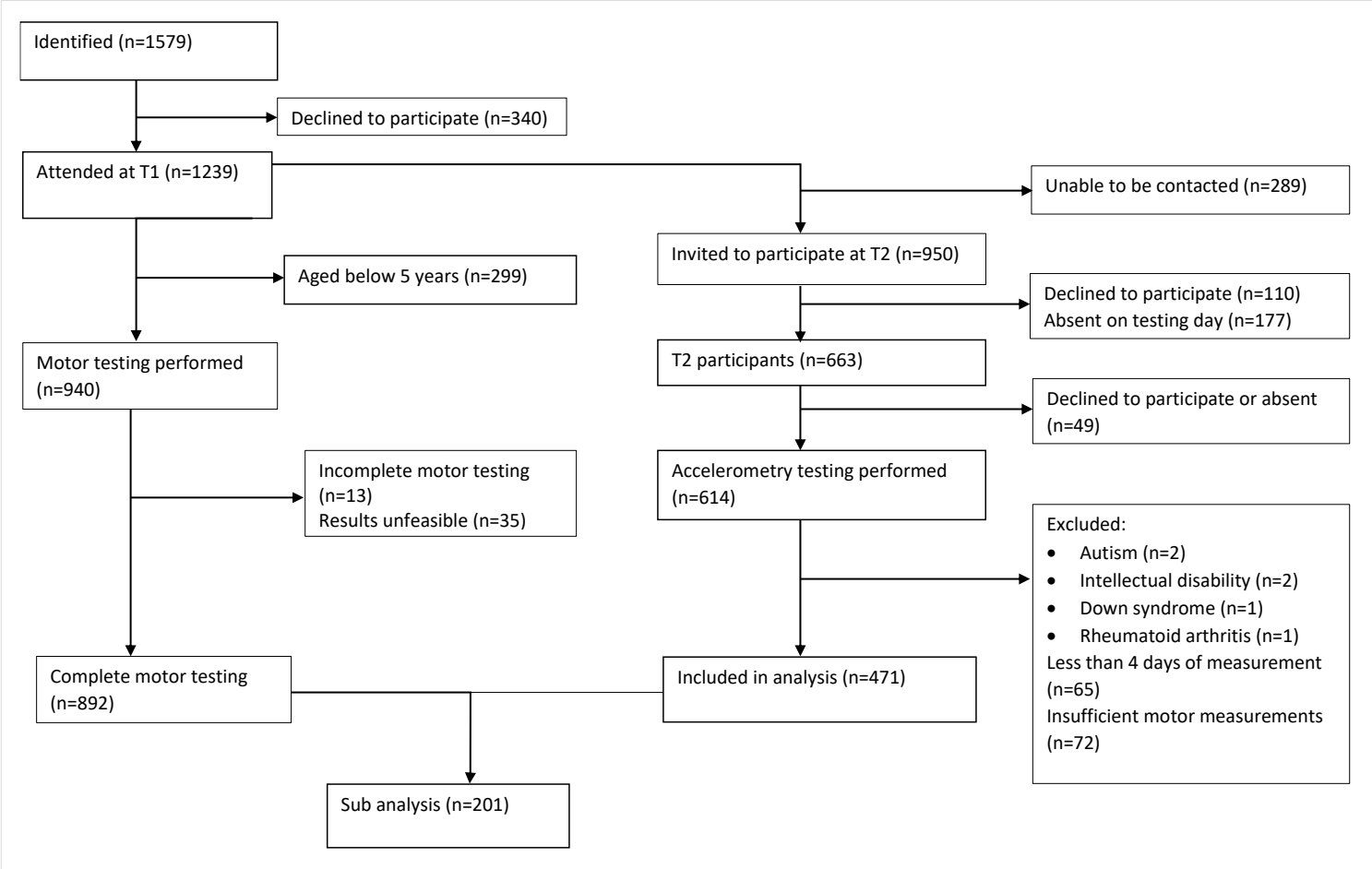
3.2.2 Participants

Guardians (n=1579) of three- to seven-year-old children attending 37 childcare centres in Finland were invited to participate in T1, of which 1239 guardians consented to participation. Centres were identified from a national registry of early educators and then selected using random-cluster sampling based upon the postal codes with weighting based upon population size. Full details of the sampling method and protocol for T1 are reported elsewhere (Laukkanen et al., 2018). Three years later, 950 eligible participants were contacted for participation in T2 through 97 primary schools. Ethics approval for the T1 and T2 studies were received from the University of Jyväskylä. Informed consent was signed by children's guardians for both studies. To aid in the identification of DCD risk and in line with diagnostic criteria (American Psychiatric Association, 2013), participants were excluded if a condition with the

potential to affect their motor skills had been reported at T1. Reasons for exclusion included intellectual disability and rheumatoid arthritis (see Figure 3.1).

Figure 3.1

Participant Flow Through the Study



3.2.3 Assessment Measurement and Tools

3.2.3.1 Quantification of Physical Activity

Physical activity was measured using triaxial accelerometers at a sampling rate of 100hz (UKK RM42, UKK Terveyspalvelut Oy, Tampere, Finland). Participants were given verbal and written instructions to wear the device for seven consecutive days on the anterior waistline in a firmly secured adjustable elastic belt during waking hours, excepting water-based activities. A study diary was provided for the recording of any relevant information (e.g., sick days). Participants were excluded if they had less than four days wear or less than 480 total minutes of accelerometry recorded (Migueles et al., 2017). Accelerometry data was assessed based upon 1 minute non-overlapping mean amplitude deviation (MAD) epochs. In accordance with published protocol (Verswijveren et al., 2021), data was classified as non-wear if there were continuous bouts of zero counts for a period of at least 20 minutes. MAD intensity epochs were used to divide the remaining data into five categories of physical activity (sedentary, light, moderate, vigorous, and very vigorous) using published cut offs (Verswijveren et al., 2021). A moderate-vigorous (MVPA) category was created by pooling moderate, vigorous, and very vigorous categories. Bouts of activity was determined based upon one-minute MADs as continuous bouts within the MVPA intensity. Outcome data were reported as mean duration in minutes per day, except for number of bouts which were reported as mean bouts per day, and MAD which is an arbitrary unit.

OI was calculated following the procedure introduced by Ahola et al. (2010) wherein all peaks above 1.3g (corresponding to the threshold for detecting movement above standing) were identified and allocated to one of 32 bins based on amplitude. The sum of the logarithm of peaks in a bin was multiplied by the lower cut off for the applicable bin and summed for all bins to create a daily OI score (Ahola et al., 2010). Validity has been established for impact peaks and OI against ground impact forces (Vainionpää et al., 2006). Bins were further compressed for analysis into low impact for peaks up to 2.1, moderate impact from 2.1 to 4.3, and high impact for peaks above 4.3 (Deere et al., 2012a, 2012b). Impact peaks are defined according to the work of Witzke and Snow (2000), with low impact corresponding to approximately two times body weight, moderate as two to four times body weight, and high impact as above four times body weight. Cut off points for categorisation was based on the work of

Deere et al. (2012b) in adolescents, with the high impact cut off being increased from 4.2 to 4.3 based on pre-existing cut offs in the data. Thus, data were reported as OI and as number of peaks in each impact category.

3.2.3.2 Motor Competence Assessment

Motor skills were assessed at T1 and T2 using items from the Test of Gross Motor Development – 3rd edition (TGMD-3) (Ulrich, 2017) and the Körperkoordinationstest für Kinder (KTK) (Kiphard & Schilling, 1974). As the KTK is standardised for only five- to 14-year-olds, participants who were under five at T1 were not assessed by KTK.

The KTK is a product-orientated tool that assesses performance on the following items: walking backwards, hopping for height, jumping sideways, and moving sideways (Kiphard & Schilling, 1974). The KTK has been shown to have validity in differentiating between children with typical and atypical motor development, moderate correlations with other movement tests (Movement Assessment Battery for Children, Bruininks-Osertsky Test of Motor Proficiency), and a test-retest coefficient of 0.89 to 0.94 for total score (Iivonen, Sääkslahti, & Laukkanen, 2015). Concurrent validity has also been shown with the DCD Screening Questionnaire in identifying children with Developmental Coordination Disorder (Asunta, Viholainen, Ahonen, & Rintala, 2019). The TGMD-3 is a process-orientated measure that assesses the quality of performance for 13 different motor skills in the subcategories of locomotor (running, galloping, hopping, skipping, horizontal jumping, sliding) and object control (two hand strike of a stationary ball, one hand forehand strike, one hand stationary dribble, two hand catch, kicking a stationary ball, overhand throw, underhand throw). TGMD-3 is validated for use in children between three and 10 years of age (Wagner, Webster, & Ulrich, 2017). Validity and reliability for the TGMD-3 has been established in different populations, with internal consistency ranging from 0.74 to 0.96 and test-retest reliability being between 0.95 to 0.97 (Field, Esposito Bosma, & Temple, 2020). As such using measures from both the KTK and TGMD-3 provides both product and process assessments.

For testing at T2, four items were selected from the TGMD-3 based upon prior factor structure analysis (Rintala, Sääkslahti, & Iivonen, 2016) and one item from the KTK. Items were selected to represent all aspects of motor competence including

locomotor (hopping, skipping), object control (throwing, bouncing a ball) and balance (jumping sideways). The appropriateness of these items was confirmed by principal factor analysis (unpublished) using data from 150 seven- to ten-year-old children (Rintala et al., 2016). A moderate correlation was shown between the jumping sideways scores at T2 and T1 (r = 0.65) as well as with overall KTK score at T1 (r = 0.63). Motor skill assessments were performed by a trained researcher (DN at T1, AL at T2) and research assistants. Research assistants were sport science students or graduates who the researchers had educated on measurement techniques in a two-to-three-hour training session. Interrater reliability was assessed on a sample of 167 children with a resulting ICC of 0.88 (95% CI = 0.85 to 0.92) (Niemistö, Finni, Cantell, Korhonen, & Sääkslahti, 2020). Children were tested in their childcare centres with a familiar staff member present. The tests were administered in the same order using the same instructions for all participants. Test performance was evaluated against pre-established performance criteria.

3.2.3.3 Anthropometric Measures

Height (Charder HM 200P) and body mass (Seca 877) were measured to the nearest millimetre and 0.1kg respectively by researchers in the childcare centres. Body mass index (BMI) was calculated using the formula mass(kg)/height(m)^2, with weight classifications determined via the World Health Organisation standards for age and sex (Onis, 2006). To standardise BMI results for growth, BMI Z-scores were calculated for BMI for age using macros provided by the World Health Organisation (World Health Organization, 2023).

3.2.4 Statistical Analysis

Analysis was performed in IBM SPSS, version 26. Alpha was set at .05. Missing data was assessed and found to be missing at random with physical activity variables being largely unaffected by missing motor competence data. Data was described using mean (M), standard deviation (SD), and median (Md). All variables were assessed for normality using visual assessment and Shapiro-Wilk test. As data was non-parametric between group differences were assessed using the Mann Whitney U test with the standardised test statistic (U) reported.

The effect of motor competence measures on the outcome variables of physical activity and OI was explored using a general linear model (GLM). Model covariates were sex (male/female), BMI Z-score, age, and motor skill variables (hopping, skipping, bouncing a ball, overhand throw, sideways jumping). Outcome data was transformed via natural log as visual assessment of residual plots for each model showed they violated the normality assumption (Aadland, Andersen, Migueles, Ortega, & Kvalheim, 2020). Model residuals for the transformed data were normally distributed with some deviation in the tail, except for the models for very vigorous activity, vigorous bouts, and vigorous bout time which showed significant skew. These models were not presented in text as they were not considered sufficiently robust. Models were tested for multicollinearity and had a variance inflation factor of between 1.03 and 1.44.

Sub-analysis was performed to examine the role of DCD risk using scores from T1 KTK assessment. DCD risk was defined as being present in scores between 56 and 85, with scores 86 and above classified as not at risk (Kiphard & Schilling, 1974). Scores under 56 were classified as unfeasible and excluded from sub-analysis. Between group difference tests (Mann-Whitney U) were performed for DCD risk categories, and additional GLMs performed with DCD risk category as an additional covariate, as well as a DCD by sex interaction effect. The interaction effect was included based on previous work indicating that the effects of DCD on bone health outcomes differed by sex (Chivers et al., 2019). Due to the method of participant recruitment, additional mixed models were performed to control for the effects of the family, kindergarten, and school of origin. Two models were run, one with family and kindergarten ID as nested fixed effects, and one with family and school ID. Due to the sample size, nesting was not able to be investigated across all models and as such all models were not presented. Additionally, GLMs were performed including only DCD status, sex, BMI, and age which are reported as supplementary material (Supp 3A, Appendix C).

3.3 Results

3.3.1 Overall Sample Descriptive Data

Participants (277 girls, 266 boys) ranged in age from 6.7 to 11.4 years with a mean age of 8.9 years (SD=1.1). The majority (76%) of participants were in the healthy

BMI category with 20% overweight and 4% obese. The most common health or developmental concerns reported by guardians were learning disabilities (n = 5), attention deficit and hyperactivity disorder (ADHD) (n = 7), and asthma (n = 7). Significant differences were present between sexes at T2 motor testing, except for sideways jumping and hopping, and T1 motor testing, with girls having a higher locomotor score (Md = 31.00 compared to 28.00, U = -3.39, d_{cohen} = 0.31, p = .001), lower object control score (Md = 23.00 compared to 28.00, U = 6.86, d_{cohen} = 0.65, p < .001), and lower total scores (Md = 53.00 compared to 57.00, U = 2.62, d_{cohen} = 0.23, p = .009). Results of sex analysis are available in Supp 3B, Appendix C.

Participants wore their accelerometer for a mean of 6.64 days (SD = 1.02) constituting a total of 760.19 minutes (SD = 64.59), over a mean of 4.88 weekdays (SD = 0.81) and 1.76 weekend days (SD = 0.65). A mean of 52% of recorded time was spent in sedentary behaviour and 19% in MVPA. Activity was undertaken over a mean total of 120.40 bouts a day, with the number of bouts decreasing as intensity increased. Physical activity characteristics are detailed in Table 3.1.

Table 3.1

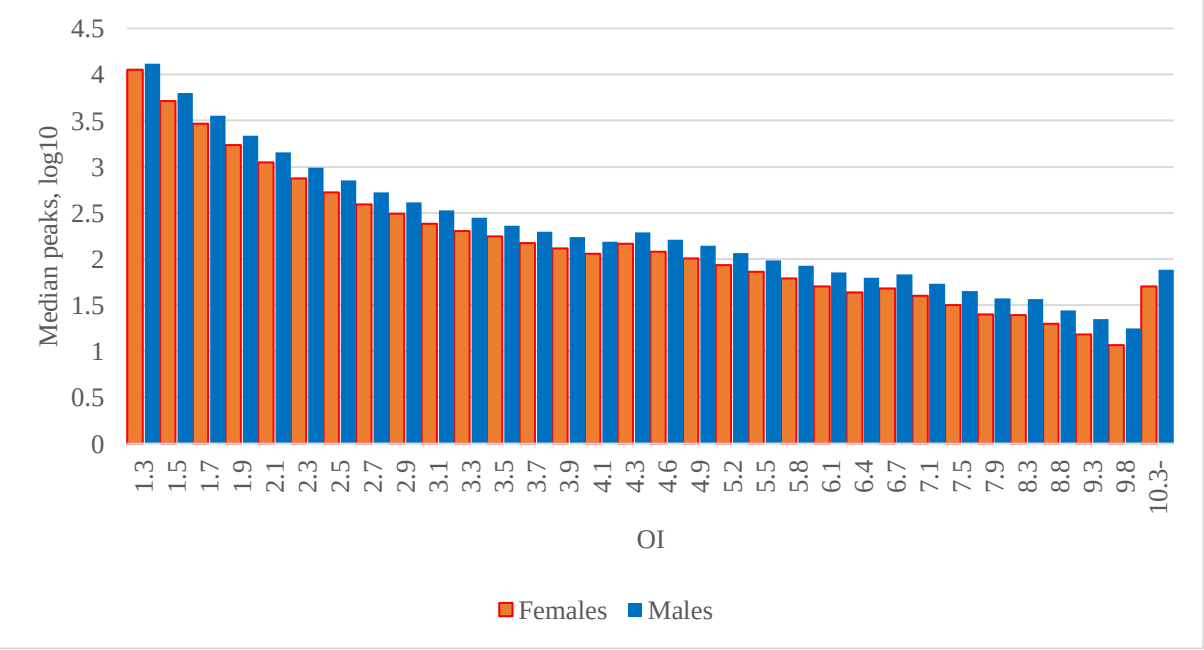
Descriptive Data for the Entire Group

		95% Confidence Interval	
Variable	**M(SD)[Md]**	**Lower**	**Upper**
Age	8.9 (1.1)[8.9]	8.8	8.9
BMI	16.3(1.7)[16.0]	16.1	16.4
Motor competence variables			
Sum of 2 rounds hopping	5.6(1.7)[6.0]	5.5	5.8
Sum of 2 rounds skipping	3.4(1.9) [4.0]	3.3	3.6
Bouncing a ball	3.6(1.9)[4.0]	3.4	3.7
Overhand throw	4.9(2.2)[5.0]	4.7	5.1
Jumping sideways	52.0(13.5)[52.0]	50.9	53.2
Accelerometry			
Sedentary (minutes/day)	397.6(67.2)[392.3]	391.9	403.2
Light (minutes/day)	216.5(34.9)[216.8]	213.5	219.4
Moderate (minutes/day)	125.3(27.2)[123.9]	123.0	127.5
Vigorous (minutes/day)	20.4(10.2)[18.7]	19.6	21.3
Very vigorous (minutes/day)	0.5(0.8)[0.2]	0.4	0.6
MVPA (minutes/day)	146.2(34.8)[145.4]	143.2	149.1
MAD	0.04 (0.01)[0.04]	0.04	0.04
Sedentary bouts (bouts/day)	92.3(18.3) [91.4]	90.8	93.9
Light bouts (bouts/day)	14.0(5.8)[13.4]	13.5	14.4
Moderate bouts (bouts/day)	13.0(5.0)[12.6]	12.5	13.4
Vigorous bouts (bouts/day)	1.1(1.4)[0.7]	1.0	1.3
Sedentary bout duration (minute/ bouts)	254.7(68.4)[250.4]	248.9	260.5
Light bout duration (minute/bouts)	34.4(20.7)]29.8]	32.6	36.1
Moderate bout duration (minute/bouts)	22.5(10.0)[21.5]	21.6	23.3
Vigorous bout duration (minute/bouts)	1.9(2.5)[1.0]	1.6	2.1
Sedentary breaks (breaks/day)	691.6(106.6)[692.1]	682.7	700.6
Daily OI	658.9(99.6)[664.5]	650.5	667.3
Low impact peaks (N/day)	23405.8(6200.7)[22746.1]	22883.1	23928.5
Medium impact peaks (N/day)	4963.2(1938.1)[4609.3]	4799.9	5126.6
High impact peaks (N/day)	1251.0(703.8)[1111.8]	1191.7	1310.4

Analysis of accelerometery peaks (Figure 3.2) shows a deviation from the anticipated steady decrease with peaks increasing compared to the prior bin for 4.3 to 4.6, 4.6 to 4.9, and 6.7 to 7.1. An anticipated increase was also shown at 10.3 and above which constituted all remaining bins. OI was significantly higher for males than for females (Md = 692.66 compared to 639.54, U = 5.99, d_{cohen} = 0.51, $p < .001$), and males had significantly more peaks in all bins. These changes were reflected in physical activity patterns with females performing significantly higher light physical activity (Md = 213.79) than males (Md = 219.44) (U = -3.13, d_{cohen} = -0.29, $p = .002$), but lower MVPA (Md = 134.64 compared to 155.65, U = 6.58, d_{cohen} = 0.59, $p < .001$). The overall pattern of physical activity engaged in was significantly different with females having more sedentary breaks a day (Md = 712.50 compared to 667.27 in males, U = 4.78, d_{cohen} = -0.42, $p < .001$) and fewer and shorter bouts of moderate activity, with a median of 11.17 bouts of 20.62 minutes, compared to 14.00 bouts of 24.35 minutes in males (U = 6.55, d_{cohen} = 0.59 $p < .001$; U = 4.42, d_{cohen} = 0.38, $p < .001$).

Figure 3.2

Osteogenic Index Bins by Sex



3.3.2 Effect of Motor Competence on Physical Activity

GLM modelling (Table 3.2) showed two motor skill measures (sideways jumping and overhand throw) were significantly associated with OI and number of impact peaks. Sideways jumping was significant for OI (β = 0.002, 95% CI 0.000 to 0.003, p = .010) and number of low (β = 0.004, 95% CI 0.002 to 0.005, p = .001), moderate (β = 0.006, 95% CI 0.003 to 0.009, p < .001), and high impact peaks (β = 0.006, 95% CI 0.002 to 0.011, p = .007). Overhand throw was significant for moderate impact peaks (β = 0.018, 95% CI 0.003 to 0.033, p = .020). These relationships were such that OI and number of peaks increased as sideways jumping and overhand throw scores increased. For example, an 8-year-old girl, BMI 16, with mean motor skill performance but overhand throwing and sideways jumping score at the bottom of the 95% CI, will have 198.29 less low impact peaks, 98.87 less moderate impact peaks and 23.46 less high impact peaks than a girl with the same characteristics but overhand throwing and sideways jumping scores at the top of the 95% CI.

For other physical activity variables, motor skills were significantly associated with time in light, moderate, vigorous, and MVPA as well as activity patterns via number of light and moderate bouts and time spent in moderate bouts. Sideways jumping and overhand throw reported a significant effect in the models for moderate (β = 0.003, 95% CI 0.001 to 0.004, p = .004; β = 0.017, 95% CI 0.008 to 0.026, p < .001 respectively), vigorous (β = 0.007, 95% CI 0.004 to 0.011, p < .001; β = 0.020, 95% CI 0.001 to 0.039, p = .037 respectively), and MVPA (β = 0.003, 95% CI 0.001 to 0.005, p < .001; β = 0.017, 95% CI: 0.008 to 0.027, p < .001 respectively), with hopping also reporting a significant effect in vigorous physical activity models (β = 0.027, 95% CI 0.002 to 0.053, p = .037). Overhand throw was also a significant predictor in number of moderate bouts (β = 0.020, 95% CI 0.005 to 0.035, p = .010), while sideways jumping increased the number of light bouts (β = 0.004, 95% CI 0.001 to 0.007, p = .015) as well as overall light physical activity (β = 0.001, 95% CI 0.000 to 0.003, p = .040). Combined these relationships indicate that as overhand throw and sideways jumping scores increase so did the total amount of physical activity (light, moderate, vigorous, MVPA), with activity patterns also changing such that more moderate bouts occur with increased overhand throw score and more light bouts with increased sideways jump score. The models for sedentary physical activity did not detect an impact for any motor skills, except skipping which was inversely associated

with sedentary breaks (β = -0.011, 95% CI -0.019 to -0.003, p = .008) such that the number of sedentary breaks decreased as skipping skill increased. The motor skill bouncing a ball did not have a significant effect in any model. Controlling for nesting did not alter results, except the loss of significance for overhand throw and hopping for vigorous activity and an additional significance for skipping in moderate bout duration (β = 0.024, 95% CI 0.000 to 0.047, p = .046). Nesting models are reported in Supp 3C, Appendix C.

Table 3.2

General Linear Model for Physical Activity and OI Variables

			95% Confidence Interval		
	Beta	**S.E.**	**Lower**	**Upper**	**P**
Sedentary behaviour (Ln)					
Intercept	5.568	0.063	5.445	5.691	<.001
Sex†	-0.002	0.016	-0.034	0.030	.909
Age	0.048	0.008	0.033	0.063	<.001
BMI Z score	0.025	0.008	0.009	0.040	.002
Hopping	0.003	0.005	-0.006	0.012	.558
Skipping	0.000	0.004	-0.008	0.009	.969
Bouncing a ball	0.000	0.004	-0.008	0.008	.964
Overhand throw	-0.005	0.003	-0.012	0.001	.124
Sideways jumping	0.000	0.001	-0.002	0.001	.658
Light activity (Ln)					
Intercept	5.747	0.062	5.626	5.868	<.001
Sex†	0.049	0.016	0.018	0.081	.002
Age	-0.051	0.008	-0.066	-0.035	<.001
BMI Z score	0.000	0.008	-0.016	0.015	.972
Hopping	-0.004	0.005	-0.013	0.005	.369
Skipping	-0.004	0.004	-0.013	0.004	.285
Bouncing a ball	0.001	0.004	-0.007	0.009	.829
Overhand throw	0.002	0.003	-0.005	0.008	.650
Sideways jumping	0.001	0.001	0.000	0.003	**.040**

			95% Confidence Interval		
	Beta	**S.E.**	**Lower**	**Upper**	**P**
Moderate activity (Ln)					
Intercept	5.136	0.085	4.970	5.302	<.001
Sex†	-0.092	0.022	-0.134	-0.049	<.001
Age	-0.057	0.011	-0.077	-0.036	<.001
BMI Z score	-0.006	0.011	-0.027	0.015	.593
Hopping	0.002	0.006	-0.011	0.014	.780
Skipping	-0.003	0.006	-0.014	0.008	.633
Bouncing a ball	0.001	0.006	-0.010	0.012	.833
Overhand throw	0.017	0.005	0.008	0.026	**<.001**
Sideways jumping	0.003	0.001	0.001	0.004	**.004**
Vigorous activity (Ln)					
Intercept	3.845	0.176	3.500	4.191	<.001
Sex†	-0.162	0.046	-0.251	-0.073	<.001
Age	-0.165	0.022	-0.208	-0.122	<.001
BMI Z score	-0.045	0.022	-0.089	-0.002	.042
Hopping	0.027	0.013	0.002	0.053	**.037**
Skipping	-0.017	0.012	-0.040	0.007	.159
Bouncing a ball	0.020	0.012	-0.003	0.044	.085
Overhand throw	0.020	0.010	0.001	0.039	**.037**
Sideways jumping	0.007	0.002	0.004	0.011	**<.001**
MVPA (Ln)					
Intercept	5.358	0.091	5.180	5.536	<.001
Sex†	-0.104	0.023	-0.150	-0.058	<.001
Age	-0.071	0.011	-0.094	-0.049	<.001
BMI Z score	-0.011	0.012	-0.033	0.012	.343
Hopping	0.005	0.007	-0.008	0.018	.442
Skipping	-0.005	0.006	-0.017	0.007	.461
Bouncing a ball	0.004	0.006	-0.008	0.015	.562
Overhand throw	0.017	0.005	0.008	0.027	**<.001**
Sideways jumping	0.003	0.001	0.001	0.005	**<.001**

			95% Confidence Interval		
	Beta	**S.E.**	**Lower**	**Upper**	**P**
MAD					
Intercept	-2.909	0.084	-3.073	-2.745	<.001
Sex†	-0.078	0.022	-0.121	-0.036	<.001
Age	-0.074	0.011	-0.094	-0.053	<.001
BMI Z score	-0.013	0.011	-0.033	0.008	.233
Hopping	0.008	0.006	-0.004	0.020	.182
Skipping	-0.006	0.006	-0.018	0.005	.255
Bouncing a ball	0.005	0.006	-0.006	0.016	.392
Overhand throw	0.013	0.005	0.004	0.022	**.005**
Sideways jumping	0.004	0.001	0.002	0.005	**<.001**
Number of sedentary bouts (Ln)					
Intercept	3.964	0.075	3.817	4.111	<.001
Sex†	-0.022	0.019	-0.060	0.016	.267
Age	0.070	0.009	0.052	0.089	<.001
BMI Z score	0.029	0.010	0.010	0.047	.003
Hopping	-0.002	0.006	-0.013	0.009	.740
Skipping	0.004	0.005	-0.006	0.013	.489
Bouncing a ball	-0.003	0.005	-0.012	0.007	.619
Overhand throw	-0.005	0.004	-0.013	0.003	.216
Sideways jumping	-0.001	0.001	-0.002	0.001	.308
Number of light bouts (Ln)					
Intercept	2.805	0.155	2.501	3.109	<.001
Sex†	0.026	0.040	-0.052	0.105	.510
Age	-0.040	0.019	-0.078	-0.002	.040
BMI Z score	0.044	0.020	0.006	0.083	.025
Hopping	-0.017	0.012	-0.040	0.005	.134
Skipping	0.003	0.011	-0.018	0.023	.800
Bouncing a ball	-0.006	0.010	-0.026	0.015	.595
Overhand throw	0.001	0.009	-0.016	0.017	.935
Sideways jumping	0.004	0.002	0.001	0.007	**.015**

			95% Confidence Interval		
	Beta	**S.E.**	**Lower**	**Upper**	**P**
Number of moderate bouts (Ln)					
Intercept	2.251	0.141	1.975	2.527	<.001
Sex†	-0.203	0.036	-0.274	-0.131	<.001
Age	0.026	0.018	-0.009	0.060	.146
BMI Z score	0.024	0.018	-0.011	0.059	.176
Hopping	-0.003	0.010	-0.024	0.017	.769
Skipping	0.017	0.010	-0.001	0.036	.070
Bouncing a ball	-0.014	0.009	-0.032	0.005	.146
Overhand throw	0.020	0.008	0.005	0.035	**.010**
Sideways jumping	0.002	0.002	-0.001	0.005	.139
Sedentary bout duration (Ln)					
Intercept	4.685	0.100	4.488	4.881	<.001
Sex†	-0.034	0.026	-0.085	0.016	.182
Age	0.094	0.013	0.069	0.118	<.001
BMI Z score	0.044	0.013	0.019	0.069	<.001
Hopping	0.008	0.007	-0.007	0.022	.296
Skipping	0.007	0.007	-0.006	0.021	.281
Bouncing a ball	0.000	0.007	-0.013	0.013	.961
Overhand throw	-0.006	0.006	-0.017	0.004	.236
Sideways jumping	-0.001	0.001	-0.003	0.001	.549
Light bout duration (Ln)					
Intercept	3.862	0.40	3.393	4.332	<.001
Sex†	-0.101	0.062	-0.223	0.020	.101
Age	-0.065	0.030	-0.124	-0.006	.031
BMI Z score	0.067	0.030	0.007	0.126	.028
Hopping	-0.016	0.018	-0.050	0.019	.382
Skipping	0.026	0.016	-0.006	0.058	.111
Bouncing a ball	-0.015	0.016	-0.046	0.017	.357
Overhand throw	-0.006	0.013	-0.032	0.019	.629
Sideways jumping	0.004	0.003	-0.001	0.009	.106

			95% Confidence Interval		
	Beta	**S.E.**	**Lower**	**Upper**	**P**
Moderate bout duration (Ln)					
Intercept	2.676	0.175	2.332	3.019	<.001
Sex†	-0.190	0.045	-0.278	-0.101	<.001
Age	0.034	0.022	-0.009	0.077	.119
BMI Z score	0.030	0.022	-0.014	0.073	.184
Hopping	-0.009	0.013	-0.034	0.017	.501
Skipping	0.023	0.012	0.000	0.047	**.047**
Bouncing a ball	-0.020	0.012	-0.043	0.003	.088
Overhand throw	0.017	0.010	-0.002	0.036	.079
Sideways jumping	0.003	0.002	-0.001	0.006	.135
Sedentary breaks (Ln)					
Intercept	6.815	0.060	6.698	6.933	<.001
Sex†	0.069	0.016	0.039	0.099	<.001
Age	-0.034	0.008	-0.049	-0.019	<.001
BMI Z score	-0.012	0.008	-0.027	0.003	.117
Hopping	-0.002	0.004	-0.010	0.007	.694
Skipping	-0.011	0.004	-0.019	-0.003	**.008**
Bouncing a ball	0.002	0.004	-0.006	0.010	.647
Overhand throw	-0.001	0.003	-0.007	0.006	.827
Sideways jumping	0.000	0.001	-0.001	0.002	.493
OI (Ln)					
Intercept	6.919	0.060	6.802	7.036	<.001
Sex†	-0.064	0.015	-0.094	-0.034	<.001
Age	-0.060	0.008	-0.075	-0.045	<.001
BMI Z score	-0.006	0.008	-0.021	0.009	.418
Hopping	0.004	0.004	-0.005	0.013	.362
Skipping	-0.005	0.004	-0.013	0.003	.212
Bouncing a ball	0.004	0.004	-0.004	0.012	.328
Overhand throw	0.004	0.003	-0.002	0.010	.229
Sideways jumping	0.002	0.001	0.000	0.003	**.010**

			95% Confidence Interval		
	Beta	**S.E.**	**Lower**	**Upper**	**P**
Low impact peaks (Ln)					
Intercept	10.625	0.096	10.437	10.814	<.001
Sex†	-0.145	0.025	-0.194	-0.097	<.001
Age	-0.092	0.012	-0.116	-0.069	<.001
BMI Z score	-0.037	0.012	-0.061	-0.014	.002
Hopping	0.003	0.007	-0.011	0.017	.635
Skipping	0.001	0.007	-0.012	0.014	.904
Bouncing a ball	0.001	0.007	-0.012	0.014	.867
Overhand throw	0.018	0.005	0.007	0.028	**.001**
Sideways jumping	0.004	0.001	0.002	0.005	**.001**
Moderate impact peaks (Ln)					
Intercept	9.557	0.140	9.283	9.830	<.001
Sex†	-0.237	0.036	-0.308	-0.167	<.001
Age	-0.166	0.018	-0.200	-0.132	<.001
BMI Z score	-0.059	0.018	-0.094	-0.024	.001
Hopping	0.006	0.010	-0.014	0.026	.573
Skipping	-0.003	0.009	-0.022	0.015	.737
Bouncing a ball	0.008	0.009	-0.010	0.026	.395
Overhand throw	0.018	0.008	0.003	0.033	**.020**
Sideways jumping	0.006	0.002	0.003	0.009	**<.001**
High impact peaks (Ln)					
Intercept	8.684	0.222	8.249	9.120	<.001
Sex†	-0.291	0.057	-0.403	-0.179	<.001
Age	-0.239	0.028	-0.294	-0.185	<.001
BMI Z score	-0.016	0.028	-0.071	0.040	.580
Hopping	0.022	0.017	-0.011	0.054	.192
Skipping	-0.010	0.015	-0.040	0.019	.485
Bouncing a ball	0.019	0.015	-0.010	0.048	.207
Overhand throw	0.013	0.012	-0.010	0.037	.267
Sideways jumping	0.006	0.002	0.002	0.011	**.007**

† Where female is the comparison group and β=1.

3.3.3 DCD Sub-analysis

The DCD risk group (n = 54) was significantly younger than the not at risk group (n = 170) (Md = 9.1 years compared to 9.6, U = 4.25, d_{cohen} = 0.74, p < .001), with no significant difference in BMI or the frequency of comorbidities. Participants at risk of DCD had significantly lower scores on all motor skills, except for overhand throw. Between group analysis showed no significant difference on any physical activity variable based on DCD risk status (Supp 3D, Appendix C).

DCD risk status had no significant association for any physical activity variable when added as a covariate to previously reported GLMs (Table 3.3 and Table 3.4). The OI and low impact peak models including DCD risk showed no significant effect for motor skills. Additionally, overhand throw was no longer significant in the moderate impact peak model leaving sideways jumping the only significant motor skill; while for the high impact peak model, sideways jumping ceased to be significant but hopping reported a significant effect (β = -0.005, 95% CI 0.000 to 0.009, p = .044). Motor skills also ceased to play any significant role in the models for light activity, number of light bouts, and sedentary breaks. As such, the only motor skill showing a significant role were overhand throw in the model for moderate activity (β = 0.015, 95% CI 0.003 to 0.028, p = .016) and MVPA (β = 0.016, 95% CI 0.002 to 0.029, p = .025), sideways jumping in vigorous activity (β = 0.007, 95% CI 0.001 to 0.013, p = .021) and MAD (β = -0.003, 95% CI 0.000 to 0.006, p = .040), hopping in MAD (β = -0.019, 95% CI 0.000 to 0.038, p = .049), and skipping in number of moderate bouts (β = 0.029, 95% CI 0.020 to 0.056, p = .035). Models examining the DCD risk by sex interaction did not detect a significant effect due to the presence of overlapping confidence intervals. Examination of estimated marginal means, however, showed a lower level of medium and high impact peaks for boys at risk of DCD than was seen in boys not at risk of DCD for models including DCD risk, BMI, and age only. These results are shown in Supp 3B, Appendix C.

Table 3.3

General Linear Model Including DCD Status

			95% Confidence Interval		
	Beta	**S.E.**	**Lower**	**Upper**	**P**
Sedentary behaviour (Ln)					
Intercept	5.475	0.155	5.170	5.780	<.001
Sex†	0.003	0.026	-0.049	0.055	.913
DCD‡	0.058	0.030	-0.001	0.117	.055
Age	0.047	0.015	0.017	0.078	.002
BMI Z score	0.032	0.012	0.009	0.056	.007
Hopping	0.005	0.008	-0.009	0.020	.465
Skipping	-0.011	0.007	-0.025	0.003	.114
Bouncing a ball	0.004	0.007	-0.009	0.017	.505
Overhand throw	-0.004	0.005	-0.014	0.007	.474
Sideways jumping	0.001	0.001	-0.001	0.003	.292
Moderate activity (Ln)					
Intercept	5.443	0.192	5.064	5.821	<.001
Sex†	-0.118	0.033	-0.182	-0.053	<.001
DCD‡	0.001	0.037	-0.072	0.075	.971
Age	-0.080	0.019	-0.118	-0.042	<.001
BMI Z score	-0.020	0.015	-0.049	0.009	.170
Hopping	0.005	0.009	-0.013	0.023	.604
Skipping	0.006	0.009	-0.011	0.024	.697
Bouncing a ball	-0.008	0.008	-0.024	0.008	.341
Overhand throw	0.016	0.007	0.003	0.028	**.019**
Sideways jumping	0.002	0.001	-0.001	0.004	.237
Vigorous activity (Ln)					
Intercept	4.046	0.433	3.188	4.904	<.001
Sex†	-0.249	0.075	-0.396	-0.101	.001
DCD‡	0.092	0.084	-0.074	0.258	.275
Age	-0.199	0.043	-0.284	-0.114	<.001
BMI Z score	-0.090	0.034	-0.157	-0.023	.009
Hopping	0.056	0.021	0.014	0.097	**.009**
Skipping	0.010	0.020	-0.030	0.049	.634
Bouncing a ball	0.009	0.019	-0.028	0.046	.624
Overhand throw	0.013	0.015	-0.017	0.043	.406
Sideways jumping	0.007	0.003	0.001	0.013	**.027**
MVPA (Ln)					
Intercept	5.658	0.210	5.244	6.072	<.001

			95% Confidence Interval		
	Beta	**S.E.**	**Lower**	**Upper**	**P**
Sex†	-0.136	0.036	-0.207	-0.066	<.001
DCD‡	0.014	0.041	-0.067	0.094	.735
Age	-0.097	0.021	-0.138	-0.056	<.001
BMI Z score	-0.029	0.016	-0.061	0.002	.068
Hopping	0.012	0.010	-0.008	0.032	.220
Skipping	0.007	0.010	-0.012	0.026	.458
Bouncing a ball	-0.007	0.009	-0.024	0.011	.457
Overhand throw	0.016	0.007	0.002	0.030	**.029**
Sideways jumping	0.002	0.001	-0.001	0.005	.115
MAD					
Intercept	-2.648	0.202	-3.047	-2.249	<.001
Sex†	-0.120	0.035	-0.188	-0.052	.001
DCD‡	0.023	0.039	-0.054	0.100	.555
Age	-0.100	0.020	-0.140	-0.060	<.001
BMI Z score	-0.033	0.016	-0.063	-0.002	.037
Hopping	0.018	0.010	-0.001	0.038	.064
Skipping	0.008	0.009	-0.010	0.027	.375
Bouncing a ball	-0.004	0.009	-0.021	0.013	.665
Overhand throw	0.012	0.007	-0.002	0.025	.095
Sideways jumping	0.003	0.001	0.000	0.006	.064
Number of sedentary bouts (Ln)					
Intercept	3.838	0.183	3.478	4.199	<.001
Sex†	-0.015	0.031	-0.077	0.046	.631
DCD‡	0.062	0.035	-0.008	0.132	.083
Age	0.072	0.018	0.036	0.108	<.001
BMI Z score	0.033	0.014	0.006	0.061	.018
Hopping	0.002	0.009	-0.016	0.019	.855
Skipping	-0.008	0.008	-0.025	0.008	.316
Bouncing a ball	-0.000	0.008	-0.015	0.015	.974
Overhand throw	-0.004	0.006	-0.016	0.009	.569
Sideways jumping	0.001	0.001	-0.002	0.003	.525
Sedentary bout duration (Ln)					
Intercept	4.492	0.239	4.018	4.965	<.001
Sex†	-0.010	0.041	-0.091	0.071	.807
DCD‡	0.089	0.046	-0.003	0.180	.058
Age	0.099	0.024	0.052	0.146	<.001

			95% Confidence Interval		
	Beta	**S.E.**	**Lower**	**Upper**	**P**
BMI Z score	0.061	0.019	0.024	0.097	.001
Hopping	0.013	0.012	-0.010	0.036	.251
Skipping	-0.012	0.011	-0.033	0.010	.294
Bouncing a ball	0.003	0.010	-0.017	0.024	.746
Overhand throw	-0.002	0.008	-0.018	0.015	.817
Sideways jumping	0.001	0.002	-0.002	0.005	.473
Sedentary breaks (Ln)					
Intercept	6.893	0.149	6.599	7.187	<.001
Sex†	0.051	0.026	0.001	0.102	.046
DCD‡	0.004	0.029	-0.061	0.053	/902
Age	-0.045	0.015	-0.074	-0.015	.003
BMI Z score	-0.024	0.011	-0.047	-0.001	.039
Hopping	-0.002	0.007	-0.017	0.012	.739
Skipping	-0.011	0.007	-0.025	0.002	.108
Bouncing a ball	0.003	0.006	-0.009	0.016	.606
Overhand throw	-0.006	0.005	-0.016	0.005	.283
Sideways jumping	0.001	0.001	-0.001	0.004	.177
OI (Ln)					
Intercept	7.005	0.130	6.734	7.276	<.001
Sex†	-0.107	0.023	-0.153	-0.061	<.001
DCD‡	0.011	0.025	-0.041	0.063	.653
Age	-0.066	0.013	-0.093	-0.039	<.001
BMI Z score	-0.017	0.011	-0.039	0.005	.139
Hopping	0.006	0.007	-0.007	0.020	.340
Skipping	0.005	0.006	-0.007	0.018	.405
Bouncing a ball	0.000	0.006	-0.012	0.013	.938
Overhand throw	0.001	0.005	-0.008	0.011	.763
Sideways jumping	0.001	0.001	-0.001	0.003	.205
Moderate impact peaks (Ln)					
Intercept	10.062	0.326	9.416	10.708	<.001
Sex†	-0.329	0.056	-0.440	-0.218	<.001
DCD‡	0.071	0.063	-0.054	0.196	.263
Age	-0.215	0.032	-0.279	-0.151	<.001
BMI Z score	-0.102	0.026	-0.153	-0.051	<.001
Hopping	0.016	0.016	-0.015	0.048	.306
Skipping	0.019	0.015	-0.011	0.049	.213

			95% Confidence Interval		
	Beta	**S.E.**	**Lower**	**Upper**	**P**
Bouncing a ball	0.014	0.014	-0.014	0.042	.333
Overhand throw	0.013	0.011	-0.009	0.036	.247
Sideways jumping	0.004	0.002	-0.001	0.009	.087
High impact peaks (Ln)					
Intercept	8.816	0.477	7.784	9.848	<.001
Sex†	-0.461	0.086	-0.635	-0.287	<.001
DCD‡	0.111	0.092	-0.085	0.307	.247
Age	-0.251	0.046	-0.356	-0.146	<.001
BMI Z score	-0.048	0.042	-0.131	0.035	.258
Hopping	0.036	0.024	-0.014	0.085	.154
Skipping	0.035	0.023	-0.011	0.082	.132
Bouncing a ball	0.012	0.023	-0.034	0.058	.610
Overhand throw	0.002	0.018	-0.035	0.038	.924
Sideways jumping	0.005	0.004	-0.002	0.012	.185

† Where female is the comparison group and β=1.
‡ Where DCD is the comparison group and β=1.

General Linear Model Including DCD Status

			95% Confidence Interval		
	Beta	**S.E.**	**Lower**	**Upper**	**P**
Sedentary behaviour (Ln)					
Intercept	5.492	0.154	5.190	5.793	<.001
Sex†	-0.006	0.029	-0.062	0.049	.823
DCD‡	0.051	0.039	-0.024	0.127	.183
Age	0.047	0.015	0.017	0.077	.002
BMI Z score	0.033	0.012	0.010	0.056	.005
Hopping	0.007	0.007	-0.007	0.022	.316
Skipping	-0.011	0.007	-0.025	0.003	.123
Bouncing a ball	0.004	0.007	-0.009	0.017	.520
Overhand throw	-0.004	0.005	-0.014	0.006	.448
Sideways jumping	0.001	0.001	-0.001	0.003	.431
DCD-sex interaction	0.017	0.051	-0.083	0.118	.734
Light activity (Ln)					
Intercept	5.984	0.157	5.676	6.292	<.001
Sex†	0.034	0.029	-0.023	0.091	.241
DCD‡	-0.026	0.039	-0.103	0.051	.514

			95% Confidence Interval		
	Beta	**S.E.**	**Lower**	**Upper**	**P**
Age	-0.072	0.016	-0.103	-0.042	<.001
BMI Z score	-0.012	0.012	-0.035	0.011	.317
Hopping	-0.004	0.008	-0.018	0.011	.636
Skipping	0.003	0.007	-0.011	0.017	.692
Bouncing a ball	-0.004	0.007	-0.017	0.009	.586
Overhand throw	-0.002	0.005	-0.012	0.009	.740
Sideways jumping	0.001	0.001	-0.001	0.003	.278
DCD-sex interaction	-0.019	0.052	-0.122	0.083	.712
Moderate activity (Ln)					
Intercept	5.443	0.188	5.074	5.812	<.001
Sex†	-0.118	0.035	-0.187	-0.050	.001
DCD‡	-0.004	0.047	-0.097	0.088	.924
Age	-0.080	0.019	-0.117	-0.043	<.001
BMI Z score	-0.020	0.014	-0.048	0.008	.170
Hopping	0.005	0.009	-0.013	0.023	.603
Skipping	0.006	0.009	-0.012	0.023	.527
Bouncing a ball	-0.008	0.008	-0.024	0.007	.307
Overhand throw	0.015	0.006	0.003	0.028	**.016**
Sideways jumping	0.002	0.001	-0.001	0.004	.198
DCD-sex interaction	0.008	0.063	-0.114	0.131	.893
Vigorous activity (Ln)					
Intercept	4.195	0.438	3.337	5.052	<.001
Sex†	-0.253	0.081	-0.412	-0.094	.002
DCD‡	0.031	0.109	-0.184	0.245	.779
Age	-0.215	0.044	-0.300	-0.129	<.001
BMI Z score	-0.087	0.033	-0.152	-0.022	.009
Hopping	0.061	0.021	0.019	0.102	**.004**
Skipping	0.004	0.020	-0.036	0.044	.845
Bouncing a ball	0.006	0.018	-0.030	0.042	.748
Overhand throw	0.015	0.015	-0.015	0.044	.328
Sideways jumping	0.007	0.003	0.001	0.013	**.021**
DCD-sex interaction	0.078	0.146	-0.207	0.363	.592
MVPA (Ln)					
Intercept	5.664	0.296	5.259	6.068	<.001
Sex†	-0.139	0.038	-0.214	-0.064	<.001
DCD‡	0.001	0.052	-0.103	0.100	.978
Age	-0.097	0.021	-0.138	-0.057	<.001
BMI Z score	-0.028	0.016	-0.059	0.002	.070

			95% Confidence Interval		
	Beta	**S.E.**	**Lower**	**Upper**	**P**
Hopping	0.013	0.010	-0.007	0.032	.207
Skipping	0.006	0.010	-0.013	0.025	.547
Bouncing a ball	-0.007	0.009	-0.024	0.010	.393
Overhand throw	0.016	0.007	0.002	0.029	**.025**
Sideways jumping	0.003	0.002	0.000	0.005	.081
DCD-sex interaction	0.024	0.069	-0.110	0.159	.722
MAD					
Intercept	-2.623	0.200	-3.016	-2.230	<.001
Sex†	-0.122	0.037	-0.195	-0.050	.001
DCD‡	-0.004	0.050	-0.102	0.095	.942
Age	-0.103	0.020	-0.142	-0.063	<.001
BMI Z score	-0.031	0.015	-0.061	-0.002	.039
Hopping	0.019	0.010	0.000	0.038	**.049**
Skipping	0.006	0.009	-0.013	0.024	.553
Bouncing a ball	-0.005	0.008	-0.022	0.011	.545
Overhand throw	0.012	0.007	-0.002	0.025	.085
Sideways jumping	0.003	0.001	0.000	0.006	**.040**
DCD-sex interaction	0.037	0.067	-0.093	0.168	l.574
Number of sedentary bouts (Ln)					
Intercept	3.852	0.180	3.50	4.204	<.001
Sex†	-0.028	0.033	-0.093	0.037	.399
DCD‡	0.042	0.045	-0.047	0.130	.356
Age	0.072	0.018	0.037	0.107	<.001
BMI Z score	0.034	0.014	0.007	0.061	.012
Hopping	0.003	0.009	-0.014	0.020	.696
Skipping	-0.009	0.008	-0.026	0.007	.266
Bouncing a ball	-0.001	0.008	-0.016	0.014	.891
Overhand throw	-0.004	0.006	-0.016	0.008	.518
Sideways jumping	0.001	0.001	-0.002	0.003	.595
DCD-sex interaction	0.043	0.060	-0.074	0.160	.472
Number of light bouts (Ln)					
Intercept	3.326	0.399	2.544	4.108	<.001
Sex†	0.050	0.074	-0.095	0.194	.503
DCD‡	-0.091	0.100	-0.287	0.105	.362
Age	-0.084	0.040	-0.162	-0.007	.033
BMI Z score	0.040	0.030	-0.019	0.099	.188

			95% Confidence Interval		
	Beta	**S.E.**	**Lower**	**Upper**	**P**
Hopping	-0.029	0.019	-0.067	0.009	.133
Skipping	0.015	0.019	-0.021	0.051	.419
Bouncing a ball	-0.003	0.017	-0.036	0.029	.836
Overhand throw	0.004	0.014	-0.023	0.030	.777
Sideways jumping	0.002	0.003	-0.003	0.008	.397
DCD-sex interaction	-0.003	0.133	-0.264	0.257	.979
Number of moderate bouts (Ln)					
Intercept	2.859	0.293	2.285	3.434	<.001
Sex†	-0.272	0.054	-0.378	-0.165	<.001
DCD‡	-0.014	0.073	-0.157	0.130	.851
Age	-0.023	0.029	-0.080	0.034	.437
BMI Z score	0.008	0.022	-0.036	0.052	.716
Hopping	-0.017	0.014	-0.044	0.011	.242
Skipping	0.029	0.014	0.020	0.056	.035
Bouncing a ball	-0.017	0.012	-0.041	0.007	.169
Overhand throw	0.016	0.010	-0.004	0.035	.118
Sideways jumping	0.002	0.002	-0.002	0.006	.303
DCD-sex interaction	-0.023	0.098	-0.214	0.168	.814
Sedentary bout duration (Ln)					
Intercept	4.538	0.240	4.067	5.008	<.001
Sex†	-0.025	0.045	-0.112	0.062	.578
DCD‡	0.079	0.060	-0.039	0.196	.190
Age	0.095	0.024	0.048	0.142	<.001
BMI Z score	0.061	0.018	0.025	0.097	.001
Hopping	0.017	0.012	-0.006	0.039	.149
Skipping	-0.011	0.011	-0.033	0.011	.333
Bouncing a ball	0.003	0.010	-0.017	0.023	.764
Overhand throw	-0.002	0.008	-0.018	0.014	.847
Sideways jumping	0.001	0.002	-0.003	0.004	.664
DCD-sex interaction	0.028	0.080	-0.128	0.185	.722
Light bout duration (Ln)					
Intercept	4.636	0.596	3.468	5.804	<.001
Sex†	-0.177	0.110	-0.394	0.039	.108
DCD‡	-0.117	0.149	-0.409	0.176	.434
Age	-0.107	0.059	-0.223	0.009	.071
BMI Z score	0.064	0.045	-0.025	0.153	.157

			95% Confidence Interval		
	Beta	**S.E.**	**Lower**	**Upper**	**P**
Hopping	-0.035	0.029	-0.091	0.022	.227
Skipping	0.048	0.028	-0.006	0.103	.082
Bouncing a ball	-0.034	0.025	-0.083	0.016	.180
Overhand throw	-0.006	0.020	-0.046	0.033	.754
Sideways jumping	0.000	0.004	-0.008	0.009	.933
DCD-sex interaction	0.035	0.198	-0.353	0.424	.858
Moderate bout duration (Ln)					
Intercept	3.297	0.384	2.544	4.049	<.001
Sex†	-0.252	0.071	-0.391	-0.112	<.001
DCD‡	0.022	0.096	-0.167	0.210	.822
Age	-0.004	0.038	-0.079	0.071	.916
BMI Z score	0.018	0.029	-0.039	0.075	.534
Hopping	-0.034	0.019	-0.071	0.002	.065
Skipping	0.031	0.018	-0.005	0.066	.088
Bouncing a ball	-0.023	0.016	-0.055	0.009	.152
Overhand throw	0.011	0.013	-0.015	0.036	.405
Sideways jumping	0.002	0.003	-0.003	0.008	.366
DCD-sex interaction	-0.074	0.128	-0.324	0.177	.563
Sedentary breaks (Ln)					
Intercept	6.896	0.148	6.605	7.187	<.001
Sex†	0.051	0.028	-0.003	0.105	.066
DCD‡	0.009	0.037	-0.064	0.082	.810
Age	-0.045	0.015	-0.073	-0.016	.003
BMI Z score	-0.024	0.011	-0.046	-0.002	.031
Hopping	-0.001	0.007	-0.015	0.013	.861
Skipping	-0.010	0.007	-0.023	0.004	.157
Bouncing a ball	0.004	0.006	-0.009	0.016	.575
Overhand throw	-0.006	0.005	-0.016	0.004	.263
Sideways jumping	0.001	0.001	-0.001	0.003	.289
DCD-sex interaction	-0.022	0.049	-0.119	0.075	.654
OI (Ln)					
Intercept	7.084	0.144	6.802	7.366	<.001
Sex†	-0.114	0.027	-0.166	-0.062	<.001
DCD‡	0.005	0.036	-0.065	0.075	.890
Age	-0.075	0.014	-0.103	-0.047	<.001
BMI Z score	-0.016	0.011	-0.037	0.006	.152

			95% Confidence Interval		
	Beta	**S.E.**	**Lower**	**Upper**	**P**
Hopping	0.009	0.007	-0.004	0.023	.189
Skipping	0.006	0.007	-0.007	0.019	.357
Bouncing a ball	0.000	0.006	-0.012	0.012	.969
Overhand throw	0.003	0.005	-0.007	0.013	.549
Sideways jumping	0.001	0.001	-0.001	0.003	.321
DCD-sex interaction	0.014	0.048	-0.079	0.108	.762
Low impact peaks (Ln)					
Intercept	10.920	0.215	10.498	11.342	<.001
Sex†	-0.189	0.040	-0.267	-0.110	<.001
DCD‡	0.000	0.054	-0.105	0.106	.996
Age	-0.114	0.021	-0.156	0.072	<.001
BMI Z score	-0.060	0.016	-0.092	-0.028	<.001
Hopping	0.009	0.010	-0.011	0.030	.366
Skipping	0.012	0.010	-0.008	0.032	.230
Bouncing a ball	-0.005	0.009	-0.023	0.012	.549
Overhand throw	0.013	0.007	-0.002	0.027	.080
Sideways jumping	0.002	0.002	-0.001	0.005	.152
DCD-sex interaction	0.019	0.072	-0.122	0.159	.796
Moderate impact peaks (Ln)					
Intercept	10.111	0.330	9.465	10.757	<.001
Sex†	-0.331	0.061	-0.450	-0.211	<.001
DCD‡	0.007	0.083	-0.154	0.169	.928
Age	-0.220	0.033	-0.284	-0.156	<.001
BMI Z score	-0.099	0.025	-0.015	-0.050	<.001
Hopping	0.017	0.016	-0.014	0.049	.272
Skipping	0.012	0.014	-0.018	0.042	.431
Bouncing a ball	0.011	0.014	-0.016	0.038	.431
Overhand throw	0.013	0.011	-0.009	0.035	.233
Sideways jumping	0.005	0.002	0.000	0.009	**.044**
DCD-sex interaction	0.086	0.110	-0.129	0.301	.432
High impact peaks (Ln)					
Intercept	9.233	0.543	8.169	10.297	<.001
Sex†	-0.480	0.101	-0.677	-0.283	<.001
DCD‡	-0.010	0.136	-0.276	0.256	.940
Age	-0.295	0.054	-0.401	-0.189	<.001
BMI Z score	-0.042	0.041	-0.123	0.038	.304
Hopping	0.051	0.026	0.000	0.102	.052

			95% Confidence Interval		
	Beta	**S.E.**	**Lower**	**Upper**	**P**
Skipping	0.026	0.025	-0.023	0.076	.297
Bouncing a ball	0.005	0.023	-0.040	0.050	.823
Overhand throw	0.008	0.019	-0.028	0.044	.673
Sideways jumping	0.004	0.004	-0.003	0.012	.254
DCD-sex interaction	0.159	0.181	-0.195	0.513	.377

† Where female is the comparison group and β=1.
‡ Where DCD is the comparison group and β=1.

3.4 Discussion

3.4.1 Osteogenic Index and Accelerometery Peaks

Accelerometry peaks in this study were higher than has been previously shown in adolescents (Deere et al., 2012a, 2012b) reflecting the presence of high levels of osteogenic activity in children. Activity was undertaken in multiple bouts, with short bouts of vigorous activity and very vigorous activity unlikely to be detected by conventional accelerometery analysis. This reinforces the need to use alternative accelerometery analysis when assessing childhood physical activity. OI peaks showed an increase in activity at the start of high impact classification followed by a slower decline than seen in the low to moderate impact levels. This trend was particularly notable for males and likely reflects on sporadic high impact activity undertaken by children. It is likely that such activity will have a positive impact upon bone development, as this has been previously demonstrated in adolescents (Deere et al., 2012a). However, as this study did not directly assess bone measurements further research is required to confirm this relationship.

3.4.2 Role of Motor Skills Upon OI and Accelerometery Outcomes

Performance of some motor skills was shown to predict engagement in osteogenic activity via OI and numbers of accelerometery peaks. In particular, sideways jumping score was shown to predict overall OI and the number of peaks in all impact categories, while overhand throw provided an estimate of effect for the number of moderate impact peaks. These findings were also reflected in conventional accelerometery models with sideways jumping and overhand throw positively associated with moderate and vigorous physical activity. Locomotor measures showed

a role in more models than object control measures and remained present in models for osteogenic measures when DCD risk was included. This would indicate that object control skills are not a good indicator of osteogenic activity in middle childhood, contrasting with prior reports on the strength of object control skills for predicting physical activity (Yu et al., 2021). However, these findings particularly object control skills ceasing to be significant in osteogenic activity when DCD risk is included, would support Melby et al. (2021)'s suggestion that the contribution of object control skills to physical activity is due to their role in organised sports involvement, which individuals with DCD participate less in (Blank et al., 2019). Additionally, organised sports activity that is enhanced by object control skills, may be of lower intensity in middle childhood engagement than organised sports that do not require object control skills (e.g., athletics, gymnastics), and correspondingly less osteogenic.

Findings of our study indicate that locomotor factors particularly those involving dynamic balance are the best predictors for osteogenic activity. Although this needs to be confirmed in childhood, the suggestion that jumping skills contribute most to bone health outcomes is supported by work in pre-schoolers which found standing broad jump to be the strongest predictor of relative skeletal age above other motor skills (Ke et al., 2021). In the current study, other locomotive measures including hopping and skipping did not play a role in predicting osteogenic physical activity and played a lesser role in all physical activity. This may reflect on the dynamic balance aspect of sideways jumping as being the best single indicator of engagement in osteogenic activity.

3.4.3 Impact of DCD Risk Status Upon OI and Other Accelerometery Outcomes

When DCD risk was included in the statistical models, the role of overhand throw and sideways jumping was diminished for osteogenic accelerometery variables, with the only estimate of effect being from sideways jumping in moderate impact peaks and hopping in high impact peaks. Studies in adolescents show the number of moderate impact peaks is not associated with bone outcomes (Deere et al., 2012b; Laukkanen et al., 2018), although the higher levels of impact peaks demonstrated in this study as well as the differing developmental stages of a paediatric group may mean some bone outcomes are linked to overhand throw. The greatest bone changes however are likely to be linked to hopping skills when DCD risk is considered in children.

Changes in models for conventional accelerometery analysis of physical activity did not completely account for changes in osteogenic activity. For example, sideways jumping had an estimate of effect for vigorous activity but not for high impact peaks, demonstrating that the vigorous activity linked to sideways jumping was of a lower impact level that was unlikely to be osteogenic. This reinforces the importance of using alternate accelerometery analyses when osteogenic effect is being assessed. Furthermore, the continued role of hopping, and to a lesser extent sideways jumping, in predicting osteogenic activity when DCD risk was controlled for indicates that locomotor and balance skills play a role above that of motor competence alone in predicting physical activity in children. Given the heterogeneity in motor skill impairment in individuals with DCD (Blank et al., 2019), this finding may indicate the presence of a subgroup of individuals with DCD who are particularly vulnerable to bone health impairment due to lower levels of physical activity. DCD subtypes, in the form of visual-motor impairment, has been previously shown to effect physical activity in children with DCD (Jarus et al., 2011). If a similar role is present for locomotor and balance skills it may explain some variability in bone health and other health measures in children with DCD (Rivilis et al., 2011). Additionally, Yu et al. (2021) reported that motor skills play a different predictive role for physical activity in children with DCD compared to typically developing children, which combined with the findings of the current study indicates the importance of identifying DCD prior to assessing the role of individual motor skills on physical activity and fitness variables.

Our current study, however, did not find a role for DCD risk status in predicting any osteogenic physical activity outcome. Examination of estimated marginal means for DCD risk by sex suggested that there may be a sex specific role for DCD risk status in osteogenic measures, particularly for boys. Although this effect was not statistically significant in the current study, the sex difference in physical activity would provide an explanation for the findings of Chivers et al. (2019) in Australian adolescents that bone changes due to DCD risk status were confined to males. As the findings of the current study contrasts with previous research in adolescents which found a reduction in osteogenic activity in adolescents with DCD (Ireland et al., 2016) it may be considered that osteogenic physical activity differences due to DCD risk occur later in life than middle childhood. Although not statistically significant, the absence of differences in estimated marginal means when motor competence was controlled for

could indicate that psychological and social barriers to physical activity known to decrease physical activity engagement in individuals with DCD (Logan et al., 2015) were not present during the childhood period studied. Bone health changes in childhood may instead be due to an increase in sedentary activity for which DCD risk had a non-significant role in this study and which is known to be predictive of bone health changes (Gabel, Macdonald, Nettlefold, & McKay, 2017). As such, bone health impairments in individuals at risk of DCD may be attributable more to an increase in sedentary behaviour than differences in physical activity, at least in middle childhood.

3.4.4 Strengths and Limitations

This study used a large cohort of children who were randomly selected using sampling designed to be nationally representative of residences within Finland. Combined with active recruitment of participants the study provides a good representation of motor competence and physical activity within Finnish children. The presence of motor competence and anthropological measures over multiple years helped to strengthen the study by providing insight into the consistency of these measures over time. As this analysis is predominantly cross sectional, causation cannot be stated and the possibility that physical activity levels improved scores on motor skills cannot be eliminated. However, previous meta-analysis has found an absence of evidence for a physical activity to motor competence directional relationship (L M Barnett et al., 2021), and analysis of participants who had motor measurements at both time points found a moderate correlation between motor scores at T1 and T2. The inclusion of the subgroup who had motor testing performed at T1 strengthens the study, as although there was a weakened role for motor competence measures when T1 motor competence was included, the findings overall supported those of the larger sample. Physical fitness measures are a known mediator between motor competence levels and physical activity levels (Stodden et al., 2008; Utesch, Bardid, Büsch, & Strauss, 2019) and were not assessed in the study. The role of physical fitness performance on osteogenic physical activity is outside the scope of this study, however, although motor competence is known to impact on physical fitness there is indeterminate evidence of the reverse relationship (L M Barnett et al., 2021) and hence it is considered unlikely that fitness variables would diminish the results demonstrated in this study particularly in this age range.

The findings of this study may reflect sociocultural factors specific to a Finnish population. In particular, children in middle childhood in Finland are engaged in active transportation, organised sports, and physical activity during the school day at levels above those seen in other countries (Tammelin et al., 2016). Such activity may have increased osteogenic activity and it is noted that this study reported a MVPA higher than that reported in other studies of children of similar ages (Purslow, Hill, Saxton, Corder, & Wardle, 2008). These results are likely to have also affected the interpretation of OI and a more substantial effect of motor skills on physical activity may be seen in populations with lower general physical activity. Twenty four percent of children at T1 were identified to be at risk of DCD, which is higher than the general incidence rate (Blank et al., 2019) although similar to prevalence reported in countries with inactive populations (Tsiotra et al., 2006). As such, motor skills were unlikely to be higher than in other studies and higher levels of MVPA may be a reflection of sociocultural factors, such as higher education levels (Niemistö et al., 2019), or differences in accelerometery measurement and analysis (Brailey et al., 2022). The potential for accelerometery variability to be due to measurement differences has been decreased by the combined use of conventional analysis and osteogenic specific analysis which widens the applicability of the results. However, it should be noted that OI has not been thoroughly validated in pre-pubertal children having been previously investigated only once, also in a Finnish population (Rantalainen et al., 2021). Validation of the relationship between OI and bone has not been established in a paediatric population, nonetheless the use of accelerometery output specific to osteogenic characteristics, rather than cardiovascular demands, strengthens the findings by providing information on osteogenic outcomes that are not conventionally captured.

3.4.5 Conclusion

Osteogenic physical activity in children is influenced by motor competence. Locomotor and balance measures were the most important contributors to participation in osteogenic activity, suggesting that suboptimal locomotor and balance skills may hinder bone development via its effect on physical activity. As this is the first study to investigate the effect of individual motor competence variables on osteogenic physical activity further investigation is needed. However, these findings suggest a potential focal point for future clinical interventions. This study was also the first to investigate

osteogenic physical activity in children at risk of DCD and found that individual motor skills were more important for osteogenic outcomes than DCD risk status. Assessment of individual motor skills is as such essential when considering the impact on physical activity of DCD risk.

Chapter 4

Effect of Childhood Developmental Coordination Disorder on Adulthood Physical Activity; Arvo Ylppö Longitudinal Study

Research Synthesis

Chapter 3 reported the investigation of physical activity patterns in children indicating the beginning of a negative lifetime physical activity pattern. This suggests that the detrimental negative physical activity pattern for individuals with DCD, discussed in Chapter 2, extends to osteogenic measures. The continuance of detrimental physical activity patterns into adulthood, however, is not well established. This is an important gap in the literature since physical activity differences in adulthood are important for the maintenance of bone health. Additionally, in Chapter 3 it was reported that individual motor skills impacted upon physical activity levels. The Tan et al. study (J Tan, Ylä-Kojola, et al., 2022) reported in this chapter expands upon this by looking at the effect of another co-occurrent condition on physical activity levels in adulthood.

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Effect of childhood developmental coordination disorder on adulthood physical activity; Arvo Ylppö longitudinal study

Jocelyn L. K. Tan[1,2] | Anna-Mari Ylä-Kojola[3] | Johan G. Eriksson[4,5,6,7] | Minna K. Salonen[4,8] | Niko Wasenius[4,5] | Nicolas H. Hart[2,9,10,11] | Paola Chivers[2,9,10] | Timo Rantalainen[2,9,10,12] | Aulikki Lano[3] | Harri Piitulainen[13,14]

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Authors:	Jocelyn L.K. Tan, Anna-Mari Ylä-Kojola, Johan G. Eriksson, Minna K. Salonen, Niko Wasenius, Nicolas H. Hart, Paola Chivers, Timo Rantalainen, Aulikki Lano, Harri Piitulainen
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Abstract

Individuals at risk of Developmental Coordination Disorder (DCD) have low levels of physical activity in childhood due to impaired motor competence, however physical activity levels in adulthood have not been established. This study sought to determine the impact of DCD risk on physical activity levels in adults using accelerometry measurement.

Participants (n=656) from the Arvo Ylppö Longitudinal Study cohort had their motor competence assessed at the age of five years, and their physical activity quantified via device assessment at the age of 25 years. Between group differences were assessed to differentiate physical activity measures for individuals based on DCD risk status, with general linear modelling performed to control for the effects of sex, body mass index (BMI), and maternal education.

Participants at risk of DCD were found to have a lower total number of steps (d = 0.3, p = .022) than those not at risk. Statistical modelling indicated that DCD risk status increased time spent in sedentary light activity (β = 0.1, 95% CI 0.02 to 0.3, p = .026) and decreased time spent in vigorous physical activity via interaction with BMI (β = 0.04, 95% CI 0.001 to 0.1, p = .025). Sensitivity analysis found that visuomotor impairment did not significantly impact physical activity but did increase the role of DCD risk status in some models.

This 20-year-longitudinal study indicated that DCD risk status continues to negatively impact on levels of physical activity into early adulthood.

Keywords

Motor competence, developmental disability, accelerometery.

4.1 Introduction

Individuals with motor difficulties, manifesting clinically as DCD in approximately five percent of the population, have difficulties with the performance of their motor skills to a degree that is impactful upon everyday functioning (Blank et al., 2019). In 75 to 80% of cases with DCD motor difficulties recognised in childhood persist into adulthood (Blank et al., 2019) and although natural variation of motor competence in early childhood prevents diagnosis of DCD prior to the age of five, the presence of motor difficulties indicating DCD risk in preschool aged children has been shown to be a good indicator of persistent motor difficulties (Pless, Carlsson, Sundelin, & Persson, 2002).

Preschool aged children at risk of DCD have been identified to have physical activity deficits (Silva-Santos et al., 2021), similar to those reported throughout childhood and adolescence for individuals with DCD (Blank et al., 2019; Cairney, Hay, Veldhuizen, Missiuna, & Faught, 2010; Kwan, Cairney, Hay, & Faught, 2013). As motor deficits associated with DCD usually continue into adulthood, along with negative physical activity beliefs (Kwan et al., 2013) and the use of avoidance based coping mechanisms (Missiuna et al., 2008) continued detriment of physical activity into adulthood would be anticipated. Although this has been reported via self-report (Missiuna et al., 2008), there is currently an absence of device-assessed measures of physical activity in this group. This absence is particularly pertinent, as studies in paediatric populations have reported a discrepancy between self-report and device-assessed measures of physical activity in children with DCD (Rivilis et al., 2011) and as such self-reports in adults need confirmation. Due to the prevalence of DCD, continued low physical activity could have population level health repercussions given the increased risk of sedentary behaviour related chronic conditions later in life (Cermak et al., 2015; Proper, Singh, van Mechelen, & Chinapaw, 2011), and markers for these conditions have been reported in adults with DCD (Cantell et al., 2008). As such, the absence of device-assessed measures of physical activity in an adult population with DCD is a significant gap in the literature with the potential for significant health implications.

In quantifying the differences in physical activity in adults with childhood DCD risk, the role of specific areas of impairment as a barrier to physical activity is a necessary avenue for investigation. Studies of physical activity in paediatric

populations report varying levels of deficit (Rivilis et al., 2011), which may in part be due to the impact of a variety of factors known to impact upon physical activity such as gender, body mass index (BMI), and socioeconomic factors (Elhakeem, Cooper, Bann, & Hardy, 2015). However, a specific area affecting physical activity for individuals at risk of DCD is the frequent co-occurrence of impairments outside of pure motor competence issues (Blank et al., 2019), which may also act to impair physical activity. A common deficit among individuals at risk of DCD is in VMI (Debrabant et al., 2016; Wilson et al., 2013), the coordination of visual and motor related neuronal processing known to impact behaviour and perception (Debrabant et al., 2016). Individuals with DCD and VMI deficits have been shown to have different areas of motor deficit than those with motor competence impairment only (Lalanne et al., 2012; Vaivre-Douret et al., 2011) and decreasing diversity and intensity of physical activity with increasing VMI deficits has been shown in children with DCD (Jarus et al., 2011). It is not known whether VMI plays a similar role for adults with a history of DCD risk, however prior work using the Arvo Ylppö Longitudinal Study (AYLS) population established a link between decreased VMI and negative health outcomes in the form of increased body fat percentage and increased BMI (Kumpulainen et al., 2016) of which lower levels of physical activity could be a causative factor. The potential for VMI impairments to reduce physical activity indicates a need for further investigation of the role of VMI on physical activity in a DCD population.

This study aims to describe the relationship between childhood DCD risk status and VMI deficits defined at the age of approximately five years, and physical activity levels recorded at the age of 25 years in a young adult population by addressing the following two questions:

1. Does early DCD risk status have an impact upon physical activity levels into early adulthood?
2. Does early VMI impairment have an impact upon physical activity levels into early adulthood, either independently or in combination with DCD?

It was hypothesised that both DCD risk status and VMI impairment will have a negative long-term effect on the physical activity levels (increased sedentary behaviour, decreased moderate to vigorous physical activity compared to non-affected referents) that would still be evident at the age of 25 years.

4.2 Methods

4.2.1 Experimental Design

This is an analysis of participants from the AYLS, a longitudinal prospective cohort study (Riegel, Ohrt, Wolke, & Österlund, 1995). The current study explores the impact of DCD status and VMI impairment at the age of approximately five years on physical activity at the age of 25 years using data from birth, 56 months, and 25 years. DCD risk status via motor competence assessment and VMI using the Beery scale were assessed at the age of 56 months. Participants had anthropometry assessment (height and weight) and accelerometry performed at the age of 25 years.

4.2.2 Participants

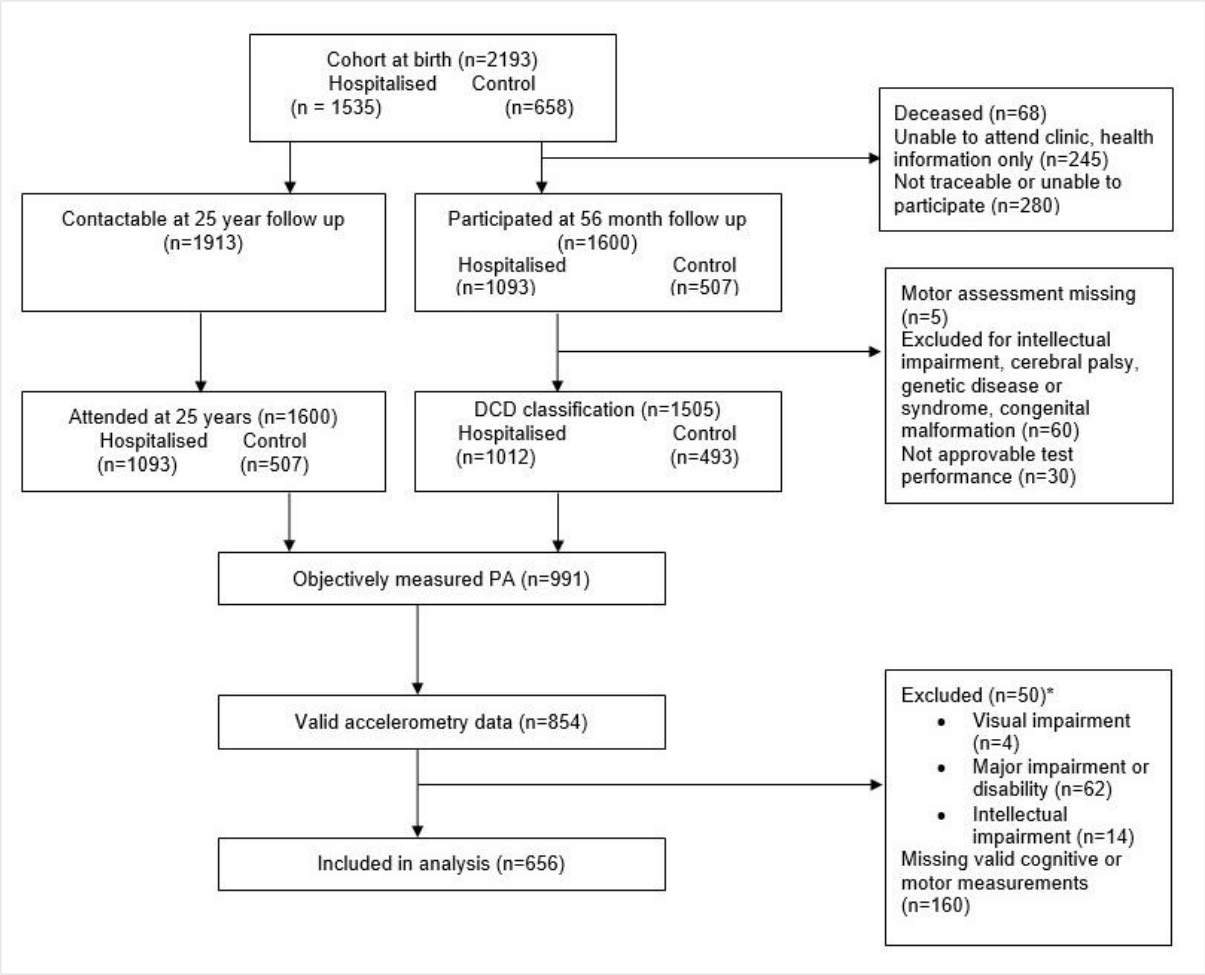
The AYLS comprised of infants born alive from seven maternity hospitals in the county of Uusimaa, Finland between March 15th 1985 and March 14th 1986. A total of 1535 participants were recruited who had been admitted to neonatal wards of obstetric units or the Neonatal Intensive Care Unit of Children's Hospital, Helsinki University Hospital, Finland within ten days of their birth, with an additional 658 healthy control infants prospectively and randomly recruited via three maternity hospitals. Participants were invited to clinical follow up visits at age 56 months and 25 years. As shown in Figure 4.1, some participants attended at one clinical follow up visit only, with about twenty percent of those with valid accelerometery data not attending at the age of 56 months which is considered to be due to the mobility of the sample. Missing data analysis of participants who had valid accelerometery data at the age of 25 years found no significant differences in gender, hospitalisation rate, parental education level, birth weight, gestational age, or in sum scores for obstetric or neonatal optimality when assessed based upon attendance at 56 months. However, participants who were included in DCD classification at 56 months but did not have accelerometery performed at the age of 25 years were found to be more frequently male (57.5% compared to 48.9%, $\chi^2 = 11.2$, $p < .001$), hospitalised following birth (70.5% compared to 63.5%, $\chi^2 = 8.4$, $p = .004$), and had parents with a lower education level (maternal $\chi^2 = 20.2$ $p < .001$; paternal $\chi^2 = 12.7$ $p = .005$). The childhood protocol was approved by the ethics committees of the Women's Hospital and Children's Hospital of Helsinki University Hospital, the Helsinki City Maternity Hospital, and Jorvi Hospital, and in adulthood by the Coordinating Ethics Committee of the Helsinki and Uusimaa

Hospital District. Informed consent was provided by parents in childhood and participants in adulthood.

The current study reports on a subsample of 695 participants drawn from the AYLS cohort. Participants were excluded from analysis if they had an impairment that could impact upon their motor skills in accordance with criterion D of the DSM-V criteria for DCD diagnosis (American Psychiatric Association, 2013) as reported by parents or their medical records. Reasons for exclusion included intellectual impairment, cerebral palsy, genetic disease, and congenital malformations (Figure 4.1). An additional four cases were excluded as they had visual impairment to a degree that may have impacted upon their VMI score.

Figure 4.1

Participant Flow Through Study, Including Exclusion Points



Some participants qualified for exclusion on more than one criterion.

4.2.3 Assessment Measures and Tools

4.2.3.1 Motor Competence Testing

Motor competence was assessed by four experienced paediatricians (incl.AL) of the research team using a quantitative test of motor competence developed for the AYLS study. The test contained items similar to the Zurich Neuromotor Assessment (Largo et al., 2001) and each child was scored on whether their performance on each item was within normal range. Individual test items are listed in Supp 4A, Appendix C. The Zurich Neuromotor assessment is designed for use in children from the age of five years, although adjusted versions of the test have been found to be reliable in children aged three to five (Kakebeeke et al., 2016). Test-retest correlations are between 0.66 to 0.8 in children aged between five and 10 years of age and convergent validity with other motor tests established (Kakebeeke et al., 2016).

As some children refused to perform all tasks, a percentage sum score of successful tasks to attempted tasks ($\frac{n(succesful\ tasks)}{n(attempted\ tasks)} * 100$) (Aylward, Pfeiffer, Wright, & Verhulst, 1989) was used to define the child's motor competence (Lano, 2002). For children who made insufficient task attempts (less than seven), the calculated percentage score on attempted tasks was only used if the score was outside of normal range, children who had insufficient attempts but whose percentage score was within normal range were excluded from analysis (Lano, 2002). DCD risk status was established based on the cut off points where five percent and 15 percent of the healthy control subjects in the original AYLS study population (n= 493) failed, equivalent to a score of 68.75 and 78.95, respectively. Due to the children being below diagnostic age for DCD at the time of testing the groups were classified as 'at risk of DCD' (DCD5) at the five percent cut off and 'probably at risk of DCD' (DCD15) at the 15 percent cut off (Smits-Engelsman et al., 2015). The impact of motor skills upon activities of daily living was assessed via parental clinical interviews at child age 4.7 years, including questions on age-appropriate activities of daily living (e.g., buttoning, dressing self), social relationships, play skills and motor skill performance (running, catching a ball, riding a bike).

4.2.3.2 Visuomotor Integration (VMI) Testing

VMI was assessed using 12-items of Beery-Buktenica Developmental Test of Visual Motor Integration where children are instructed to copy geometric forms which increase in complexity (Beery & Beery, 2010). Test scores were corrected for exact age at measurement and converted to have a mean of 100 and a standard deviation of 15, such that standardised scores represent the difference from the mean for healthy children born at term. The Beery VMI has convergent validity with other tests of visual perception (Martin, 2006) and a reported inter-rater reliability of 0.92, internal consistency of 0.96 and test re-test reliability of 0.89 (Beery & Beery, 2010). For consistency with DCD categorisations, VMI scores were categorised into the bottom fifth percentile, and fifth to 15th percentile of scores, corresponding to cut off scores of 75.6 and 82.6, respectively.

4.2.3.3 Quantification of Physical Activity

Physical activity was measured with SenseWear Pro 3 Armband (Body Media, Inc, Pittsburgh, PA, USA), a multisensory body monitor including a two-way axis accelerometer (Salonen et al., 2015). The SenseWear Armband has been found to be valid for physical activity measurements in young adults in resting conditions, exercise conditions and field monitoring (Fruin & Rankin, 2004; Welk, McClain, Eisenmann, & Wickel, 2007). Participants were instructed to wear the armband on their right triceps for 10 consecutive days. Participants were included if they had more than three valid days, weekday, or weekend, with a valid day having more than 10 hours of wear. This criterion was designed to maximise sample size while providing measurement reliability (Burchartz et al., 2020; Trost, McIver, & Pate, 2005). The device logged physical activity based on the acceleration recordings minute by minute, which was combined with subject's characteristics such as gender, age, and BMI to estimate intensity of physical activity, distance of data points from the mean (MAD), and number of steps, using manufacturer algorithms (SenseWear Professional Software, v6.1)[1]. Following the removal of any measurements indicated by the device to be sleep, each minute was classified into sedentary light (under 3 metabolic equivalent [MET]), moderate (3 to under 6 MET), vigorous (6 to under 9 MET), or very vigorous (above 9 MET) (Salonen et al., 2015). Vigorous and very vigorous minutes were

[1] Algorithms have been validated (Farooqi, Slinde, Håglin, & Sandström 2013).

pooled into the vigorous category, and a MVPA category created by pooling moderate and vigorous categories. The mean durations (minutes) per day are reported as the outcome. Physical activity was assessed as minutes per day, and percentage of total wear time. Minutes per day for MVPA was converted to a weekly duration by multiplying by seven, which was then categorised to determine if participants met World Health Organisation (WHO) Guidelines for physical activity. Cut offs for meeting guidelines were set at 150 minutes for MVPA, covering minimum requirements for moderate and vigorous activity (World Health Organization, 2020).

4.2.3.4 Anthropometric and Background Measures

Researchers collected information about pre-, peri- and neonatal conditions from medical records on daily ward visits. Information about parental educational status was collected via parental interviews at wards and 56-month clinical visits. Anthropometric measures for height in centimetres and weight in kilograms were taken by trained research nurses during clinical visits at 56 months and 25 years. Height was measured to the nearest 0.1cm and weight in light indoor clothing to the nearest 0.1kg. As some participants did not attend at the exact age for each visit, corrections were made for exact age by linear regression. BMI was calculated as weight(kg)/height(m)^2 and categorised into weight status for age and gender using the WHO standards for childhood measures (Onis, 2006) and the Centre for Disease Control standards for adult measurements (NHLBI Obesity Education Initiative, 1998).

4.2.4 Data Analysis

All analysis was performed in IBM SPSS, version 26, excepting effect size measures which used the Psychometrica online calculator (Lenhard & Lenhard, 2016). Alpha was set at .05. All variables were assessed for normality using visual assessment and Shapiro-Wilk test. Data was assessed to be missing at random. Descriptive between group differences for confounders by risk group were assessed using either an independent t-test, Kruskal-Wallis, Mann-Whitney U or Chi square tests. Between group differences were assessed for age, BMI, and accelerometery via Mann-Whitney U as the data had a non-parametric distribution. BMI categories, change in BMI categories between time points, and meeting of physical activity guidelines were assessed via Chi-Square analysis. Age, BMI, and accelerometery measurements were described using mean (M), median (Md) and standard deviation (SD). Parental age,

birth weight, gestational age, and VMI scores were described with M and SD. Pre-, peri and neonatal risk factors as well as socioeconomic factors as reflected by parental (paternal and maternal) education level were described as frequencies in each risk category. Motor competence measures were described as both group frequencies for anomalous measures and M, Md, and SD for continuous scores. Cohen's d effect sizes were calculated and classified as small d=0.2, medium d=0.5 and large d=0.8. As following assessment, no significant difference was shown between the DCD5 and DCD15 categories, and in accordance with International Clinical Practice recommendations where the 16th percentile is set as a cut off for DCD (Blank et al., 2019), the groups were combined into a single risk category (DCD) and general linear modelling was done at this level. Accelerometery and BMI measurements were performed for the entire risk group, as well as at the fifth and 15th percentile, while confounder assessment was done at the fifth and 15th percentile only.

The relationship of VMI and DCD category with physical activity levels was explored using a general linear model. Predictors included in the final model were sex, BMI, socioeconomics as reflected by mother's educational attainment, DCD or VMI category, and an interaction variable between risk category and BMI. Three other models were also conducted: model one included predictors of sex and risk category only, model two included predictors of sex, BMI, and risk category, and model three contained predictors of sex, BMI, mother's educational attainment, and risk category. The interaction variable predictor was included after prior models indicated that the addition of BMI removed the effect of risk category. Figures of the interaction effect were derived from the final model presented in the manuscript. All other predictors were chosen as significant predictors for physical activity via accelerometery in young adults based on prior literature (Elhakeem et al., 2015), with mother's educational attainment included as it is the most commonly used indicator of socioeconomic status (Sherar et al., 2016). Age was not included in the model as the mean between group difference in age at time of accelerometery was 0.7 months and hence not clinically relevant at the age of 25 years. The final model was chosen based on Akaike information criterion (AIC), with the most complex model showing the best AIC fit. Residual plots for each model were visually assessed and determined to violate the assumption of normality and as such, accelerometery data were transformed via natural log. Model residuals for the transformed data showed no violations although slight

deviations were seen in the tails of some models. Due to reported sex effects on physical activity in this group (Cairney, Hay, Veldhuizen, Missiuna, & Faught, 2010), subgroup analysis was performed limiting the analysis by sex. A sensitivity analysis was also performed to determine the effects of using a minimum of three rather than four days as inclusion criteria in order to maximise sample size.

4.3 Results

4.3.1 Motor Competence

4.3.1.1 Motor Competence Measures

Motor competence testing indicated 30 participants (23 male, seven female) as DCD5, with an additional 53 participants (43 male, 10 female) being categorised as DCD15, and 575 participants (250 male, 325 female) as no-risk. Both risk groups (DCD5 M = 88.1 [SD = 13.91, MD = 89.7]; DCD15 M = 97.0 [SD = 11.9, Md = 96.8]) showed detriments in their VMI score compared to the no-risk group (M = 102.1 [SD = 14.1, Md = 103.9]). These differences were statistically significant when compared at the fifth percentile ($t = -4.9$, $p < .001$) and the 15th percentile ($t = -4.8$, $p < .001$) to the no-risk group. DCD risk groups were shown to have increased difficulty with motor skill performance at five years old with a higher proportion of the at-risk group being reported to have difficulties in ball catching (DCD5 36.7%; DCD15 30.2% compared to 14.1% in no-risk, $\chi^2 = 18.4$, $p < .001$) and running (16.7% DCD5; 5.7% DCD15 vs 2.6% in no-risk, $\chi^2 = 17.5$, $p < .001$).

4.3.1.1 Background Variables

Motor competence groups were of similar health levels at birth with no differences detected in infant or maternal risk factors (Table 4.1), including gestational age. No differences between DCD groups were detected for parental education maternally ($\chi^2 = 3.9$, $p = .685$) or paternally ($\chi^2 = 5.4$, $p = .496$). No difference in adiposity as assessed by BMI was found between groups in either score or corresponding category at either five or 25 years of age, although the group as a whole increased in adiposity with a total of 32.7% being overweight or obese at age 25 compared to 15.8% at age five. Change in adiposity as indicated by BMI category change between five-year assessment and 25-year assessment did not detect a

difference for the DCD5 group (χ^2 = 1.1, p = .896) nor the DCD15 group (χ^2 = 2.7, p = .604). Between group differences at five years of age are shown in Table 4.2.

Table 4.1

Prenatal, Perinatal, and Neonatal Characteristics by DCD Risk Category

	DCD5	DCD15	Not at risk	Group Difference	
	%	*%*	*%*	*χ2*	*p*
Pre and Perinatal Risk Factors					
Maternal severe chronic illness	6.7	9.4	5.6	1.3	.513
Multiple pregnancy	6.7	1.9	4.9	1.2	.539
Pre-eclampsia	23.3	11.3	12.0	3.4	.180
Fetal distress during pregnancy	10.0	5.7	7.3	0.5	.766
Fetal distress during birth	26.7	15.1	16.2	2.4	.307
Small for gestational age	6.7	3.8	6.1	0.5	.780
Neonatal Risk Factors/Complications					
Hospitalized	56.7	69.8	62.3	1.7	.437
Intubation or ventilator treatment	10.0	7.5	9.4	0.2	.898
Suspicion/verified septic infection	6.7	5.7	5.7	0.05	.977
Surgical operation	3.4	1.9	1.2	1.1	.588
Severe anemia requiring blood transfusion	6.7	3.8	4.0	0.5	.767
Apnea	6.7	3.8	2.3	2.5	.283
Clinical seizures	0.0	0.0	1.6	1.3	.518
IVH grade 1-2	3.3	0.0	1.1	2.0	.364

Table 4.2

Characteristics at 56 Months Follow Up

	DCD5	DCD15	Not at risk	Group Difference	
	M (SD)	*M (SD)*	*M (SD)*	*H*	*p*
Age (yr)	4.7 (0.05)	4.7 (0.03)	4.7 (0.04)	1.2	.547
Weight (kg)	18.5 (3.3)	18.4 (2.5)	18.2 (2.5)	20.0	**<.001**
BMI	15.7 (2.1)	15.5 (1.5)	15.4 (1.3)	0.6	.748
VMI (% sum score)	88.1 (13.9)	97.0 (11.9)	102.1 (14.1)	32.2	**<.001**
	M (SD)	*M (SD)*	*M (SD)*	*H*	*p*
Hardly able to catch a ball	4.7 (0.05)	4.7 (0.03)	4.7 (0.04)	1.2	.547
Running, only slowly	18.5 (3.3)	18.4 (2.5)	18.2 (2.5)	20.0	**<.001**

BMI Grouping					
Underweight	3.3	1.9	1.4	9.5	.149
Healthy	73.3	76.9	83.9		
Overweight	13.3	19.2	12.4		
Obese	10.0	1.9	2.3		

4.3.2 Visuomotor Integration (VMI) Measures

4.3.2.1 Visuomotor Integration (VMI)

Division of groups based on VMI testing found 23 participants (16 male, 7 female) in the bottom fifth percentile, 32 (18 male, 14 female) in the fifth to 15th percentile and 579 above the 15th percentile (272 male, 309 female), with no difference in motor competence (<fifth percentile M = 98.2[SD = 4.0], fifth to 15th percentile M = 99.0 [SD = 2.3], >15th percentile M = 99.2 [SD = 2.5], H = 5.0, p = .083).

4.3.2.2 Background Variables

The VMI groups showed some significant differences in risk factors in the neonatal period with those with lower scores having more neonatal complications and a lower gestational age. These differences are shown in Supp 4B, Appendix C. VMI category did not impact on BMI or BMI category but impacted upon BMI change, with a significant difference being found for those in the bottom 15th percentile of VMI compared to those above the 15th percentile. The ≤15th percentile group were more likely to change category both down (18.8% ≤15th percentile vs 10.6% >15th percentile) and up (30.2% ≤15th vs 26.5% >15th percentile) compared to those above the 15th percentile (χ^2 = 15.0 p = .005).

4.3.3 Physical Activity

At 25 years of age between group difference tests for the entire DCD group showed fewer steps taken compared to the no-risk group (Md = 9083.4 compared to Md = 9927.9, d = 0.3, U = 20161.0, p = .022). The entire DCD group spent a higher proportion of time in sedentary light physical activity than the no-risk group constituting a mean of 62.8% of their total measured time (SD = 6.0, Md = 63.7) compared to 61.2% for the no-risk group (SD = 6.4, Md = 61.8) (U = 20205.0, d = -0.3, p = .024). This difference in sedentary physical activity was also found in the DCD15 group for proportion of time in sedentary light activity (Md = 63.7 compared to Md 61.8, d = -0.3, U = 20205.0, p = .024) and total sedentary physical activity (M = 872.1 minutes [SD = 92.6, Md = 877.5] vs M = 836.5 [SD = 105.3, Md = 853.7]) (d

= -0.3, U = 12272.0, p = .019). No other differences in physical activity measures were detected between the DCD5 and no-risk group. No differences were found between risk groups in the frequency of participants meeting WHO physical activity guidelines for MVPA (World Health Organization, 2020). Subgroup analysis restricting by sex found that no physical activity differences were statistically significant based on DCD risk status for either sex when analysed separately. Between group difference measures are reported in Table 4.3 and Table 4.4. Of the eight participants with three days measurement, one was in the DCD5 group and two in the DCD15 group, however there was no significant difference between risk groups for number of days included or total number of minutes recorded. A sensitivity analysis removing participants with less than four recorded days found no significant effect on any analysis, aside from the model for DCD risk and sedentary light activity. Results from sensitivity analysis are detailed in Supp 4G, Appendix C

Table 4.3

Accelerometry Differences Between DCD Risk Groups

	DCD5	**DCD15**	**Not at risk**	**Group Difference**	
	M (SD)	*M (SD)*	*M (SD)*	*H*	*p*
Sedentary Light (mins/day)	843.2 (120.8)	872.1 (92.6)	836.5 (105.3)	5.4	.067
Moderate (mins/day)	129.6 (69.3)	130.7 (65.5)	139.1 (79.0)	0.4	.802
Vigorous (mins/day)	5.4 (6.3)	6.4 (7.8)	6.6 (8.2)	0.2	.889
MVPA (mins/day)	135.0 (71.1)	137.0 (68.3)	145.7 (82.5)	0.5	.796
% Sedentary light activity	62.9 (6.2)	62.8 (5.9)	61.2 (6.4)	5.2	.074
% Moderate activity	9.5 (4.8)	9.4 (4.6)	10.2 (5.7)	0.7	.713
% Vigorous activity	0.4 (0.5)	0.5 (0.6)	0.5 (0.6)	0.2	.918
% MVPA	9.9 (5.0)	9.8 (4.8)	10.7 (6.0)	0.7	.714
Steps	9136.1 (3205.3)	9436.9 (3430.3)	10335.8 (3642.4)	5.3	.070
MAD	0.96 (0.3)	0.96 (0.3)	0.99 (0.3)	0.9	.633

Table 4.4

Accelerometry Group Difference Between DCD (DCD5 and 15) and Not at Risk

	DCD N=83	**Not at risk** N=573	**Group Difference**		
	M (SD)	*M (SD)*	d_{Cohen}	*U-statistic*	*p*
Age (yr)	24.9 (0.6)	24.8 (0.7)	-0.1	-1.1 †	.267
BMI	25.1 (5.1)	23.9 (4.2)	-0.03	20342.0	**.030**

	DCD N=83	**Not at risk** N=573	**Group Difference**		
Sedentary light (mins/day)	861.7 (103.9)	836.5 (105.3)	-0.2	20831.0	.061
Moderate (mins/day)	130.3 (66.5)	139.1 (79.0)	0.1	22827.0	.522
Vigorous (mins/day)	6.0 (7.3)	6.6 (8.2)	0.07	23522.0	.833
MVPA (mins/day)	136.3 (68.9)	145.7 (82.5)	0.1	22796.5	.510
% Sedentary light activity	62.8 (6.0)	61.2 (6.4)	-0.3	20205.0	**.024**
% Moderate activity	9.4 (4.7)	10.2 (5.7)	0.1	22646.0	.452
% Vigorous activity	0.4 (0.5)	0.5 (0.6)	0.2	23444.0	.796
% MVPA	9.9 (4.8)	10.7 (6.0)	0.05	22613.0	.440
Steps	9328.2 (334.2)	10335.8 (3642.4)	0.3	20161.0	**.022**
Mean amplitude deviation	0.96 (0.3)	0.99 (0.3)	-0.03	22352.0	.351

† t-test

GLM modelling of physical activity variables showed a significant role for the DCD group in sedentary light physical activity ($\beta = 0.1$, $p = .027$) when sex, BMI, DCD risk, maternal education, and BMI-to-DCD interaction were included in the model, as shown in Supp 4C, Appendix C. A statistically significant role was also seen in the sedentary light model for BMI ($\beta = 0.01$, $p < .001$) and a non-significant effect for BMI-to-DCD interaction ($\beta = -0.01$, $p = .057$). The BMI-to-DCD effect became significant in sensitivity analysis when participants with less than four recorded days were removed ($\beta = -0.01$, $p = .048$). The interaction, depicted in Figure 4.2, was such that the non-DCD group increased time spent in sedentary light activity at a faster trajectory than the DCD group. The model for vigorous physical activity suggested a role for DCD via its interaction with BMI ($\beta = 0.04$, $p = .050$), although not significant, with an additional non-significant role for DCD risk category ($\beta = -0.9$, $p = .062$). This model, shown in Figure 4.2, showed time spent in vigorous physical activity decreased at differing rates between groups with the non-DCD group losing more time in vigorous physical activity as BMI increased than the DCD group.

Models including VMI as a continuous variable, shown in Supp 4D, Appendix C, found a statistically significant effect for DCD risk in more models, although no significant effect was detected for VMI. DCD had a statistically significant effect in the models for sedentary light activity ($\beta = 0.2$, $p = .007$), moderate activity ($\beta = -0.6$, $p = .020$) and MVPA ($\beta = -0.7$, $p = .014$) such that sedentary light activity levels were higher for those in the DCD group while moderate and MVPA levels were lower. A DCD-to-BMI interaction was seen in models for sedentary light activity ($\beta = -0.01$, $p = .019$), moderate activity ($\beta = 0.03$, $p = .027$) and MVPA ($\beta = 0.03$, $p = .018$),

illustrated in Figure 4.2, which resulted in a more rapid reduction/increase in physical activity with increasing BMI.

Sensitivity analysis to determine if VMI risk had similar impact to DCD status on accelerometry found that the <fifth percentile group indicated less vigorous activity (Md = 1.1 compared to Md = 3.8 minutes a day) when compared to the >15th percentile group (d = 0.2, U = 4780.0, p = .021), while the fifth to 15th percentile showed reduced moderate physical activity compared to the >15th percentile group (Md = 156.9 minutes a day compared to Md = 121.2, d = 0.3, U = 7349.0, p = .046). Combining the groups to <15th percentile found no significant differences on any physical activity measure. No significant differences were found between risk groups in frequency of meeting physical activity guidelines. Subgroup analysis by sex found differing physical activity effects for each sex, with the vigorous activity effect for the < fifth percentile group being only significant for males, and the fifth to 15th percentile reduced moderate physical activity differences only being significant for females. Additional significant effects were found for females only at the fifth to 15th percentile of reduced MVPA, percentage time in moderate and MVPA, and total steps (Supp 4F, Appendix C). GLM modelling of <15th percentile did not detect a significant role for VMI risk in any model, although VMI-to-BMI interaction effect was significant in the model for mean amplitude deviation, such that mean amplitude deviation decreased more rapidly with increasing BMI for the VMI risk group. Between group difference test and model results for VMI scores can be found in Supp 4E, Appendix C.

Figure 4.2

Interaction Effect Between DCD Risk Status and BMI for GLM Models for Physical Activity, Both With and Without VMI as a Continuous Variable, Showing a Slower Rate of Change in Physical Activity for Participants Classed as DCD Compared to Non-DCD

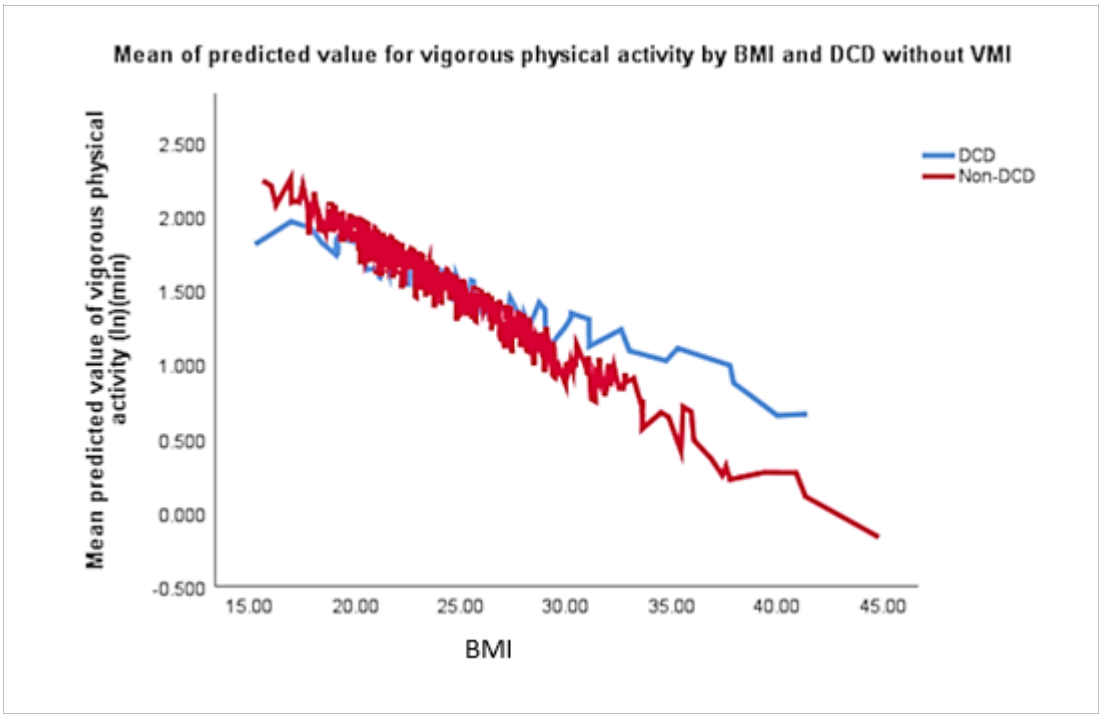
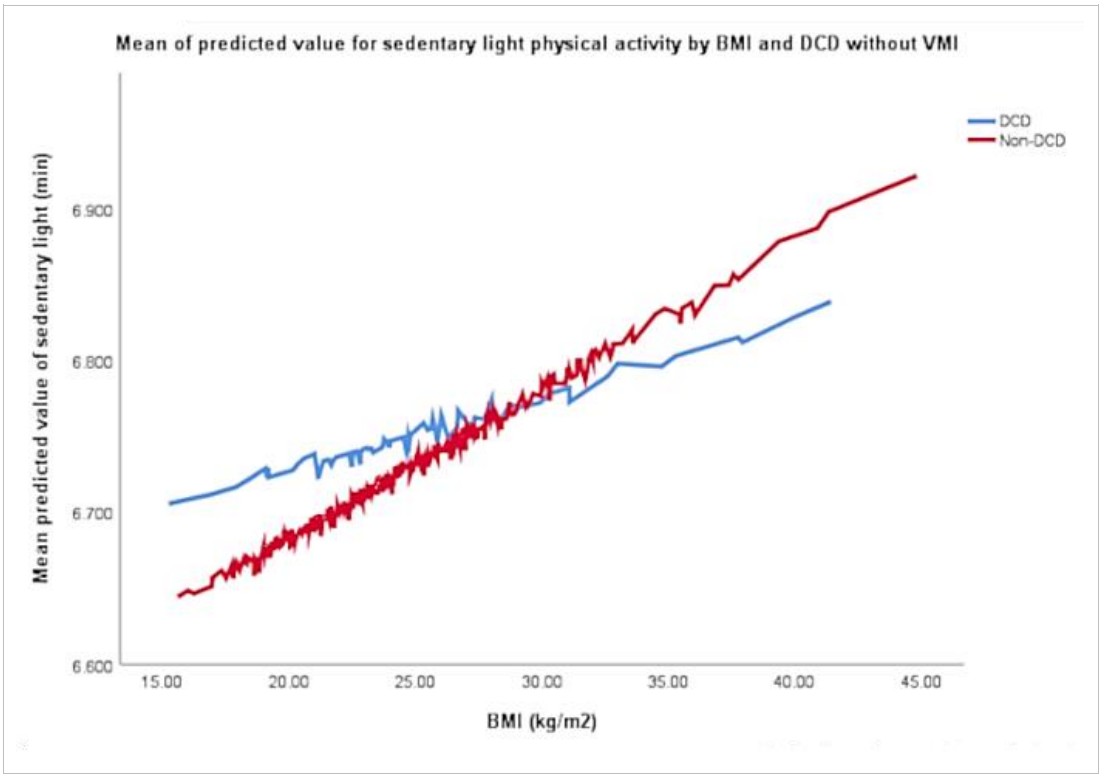
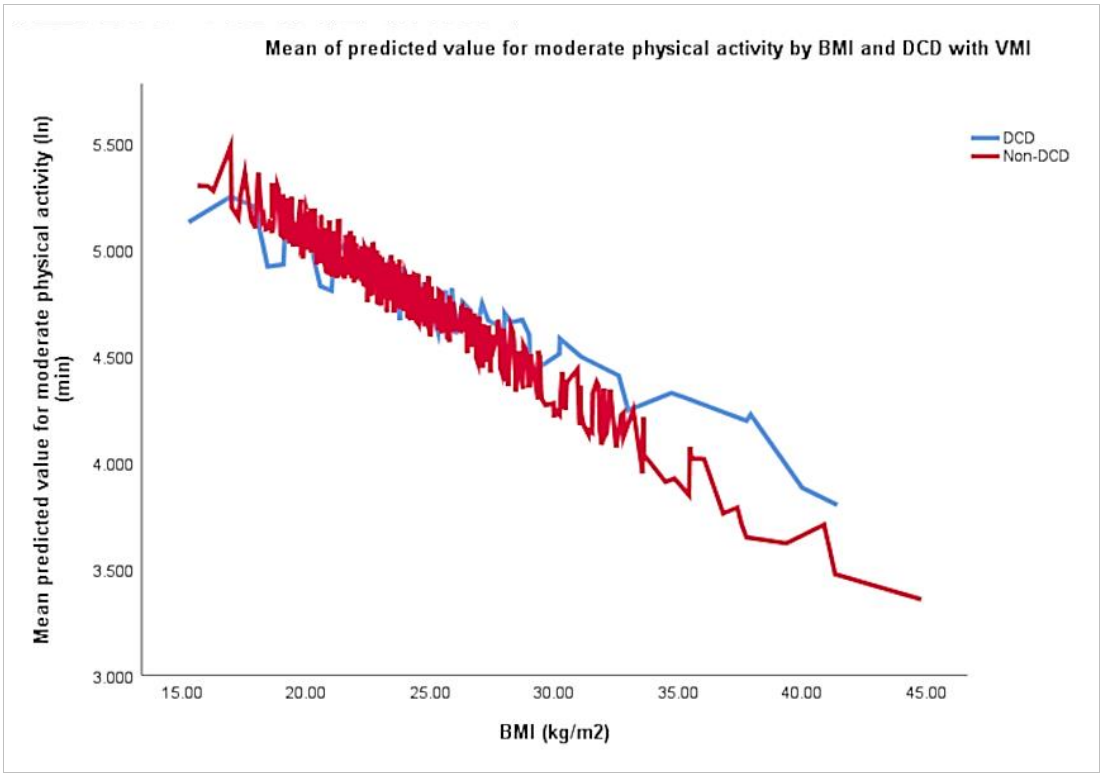


Figure 4.2
(continued)





Sedentary light and vigorous models include VMI. Moderate model does not include VMI.

4.4 Discussion

DCD risk status in early childhood was found to impact upon some aspects of physical activity in early adulthood, with a small to medium effect on total steps and sedentary light physical activity. Controlling for VMI impairment further increased the role of DCD risk in statistical models but an independent role for VMI was not shown. As such, DCD risk status in childhood appears to have a role in impairing some aspects of physical activity and individuals which may be influenced by the co-occurrence of detriments in VMI.

4.4.1 Does Early DCD Risk Status Impact Upon Physical Activity Levels at the Age of 25?

This study found DCD risk status in childhood impacted upon some aspects of physical activity in early adulthood. Between group differences were evident for the entire DCD risk group who took fewer total steps and spent a higher percentage of their day in sedentary-light activity compared to their non-DCD counterparts. Statistical modelling controlling for the effects of sex, BMI, and maternal education also found an increase in the number of minutes per day in sedentary light physical activity for the DCD group. These findings extend what has been found in paediatric DCD accelerometery studies (Baerg et al., 2011; Kwan et al., 2013; Rivilis et al., 2011) providing device measured evidence to confirm that the physical activity pattern shown in individuals at risk for DCD during childhood extends into at least early adulthood. Deficits in motor competence were found to be concentrated in the fifth to 15th percentile of motor competence with the most profoundly affected group showing no physical activity detriments. This may indicate that physical activity participation in adulthood is not due to continuing motor difficulties and are instead a continuation of physical activity patterns from childhood. Although not measured in this study, it is also possible that the most severely impaired individuals received more concerted outside effort, such as interventions, to increase their motor skills than the less impaired group, placing them on a more positive physical activity trajectory for adulthood. International studies have found that individuals with more severe motor skill impairment are more likely to show problems, such as handwriting issues, that result in intervention than those with more moderate motor impairments (Blank et al., 2019). This also offers a potential explanation for why physical activity differences found in this study are smaller than what has been reported in previous paediatric

accelerometery studies (Baerg et al., 2011; Cermak et al., 2015). Individuals with DCD may also be less affected by the decrease in MVPA that has been reported to occur in much of the general population in young adulthood (Kwon, Janz, Letuchy, Burns, & Levy, 2015). As a relationship has been demonstrated between decrease in physical activity and reduction in organised physical activity as individuals age (Kwon et al., 2015), individuals with DCD may be less affected as they engage less in team and competitive physical activity programs in favour of solitary exercise (Missiuna et al., 2008). The absence of any significant differences when the DCD risk groups were analysed by gender may support this theory, as gender specific effects reported in other studies have been hypothesised to be due to gender specific differences in activity play, sports and similar physical activities (Cairney, Hay, Veldhuizen, Missiuna, & Faught, 2010). Cultural effects, specific to physical activity in Finland (Elhakeem et al., 2015; Laukkanen et al., 2020) may also be a factor. Studies of Finnish children have found that motor competence did not impact upon cardiorespiratory fitness measures in this population (Haapala et al., 2020).

Statistical modelling indicated an increased role for DCD risk upon physical activity via its interaction with BMI. Non-DCD individuals were more affected by BMI changes than the DCD group, with the minutes per day in MVPA decreasing and minutes per day in sedentary light activity increasing at a greater rate as BMI increased. The lesser effect of BMI on physical activity for the DCD group may be due to their physical activity patterns being impacted by their pre-existing motor competence difficulties and related factors such as avoidance coping strategies, making them less affected by movement difficulties associated with increasing BMI which decreases physical activity in non-DCD individuals (Chivers, Larkin, Rose, Beilin, & Hands, 2013). Additionally, as movement of individuals with DCD is less efficient, they use more metabolic energy during physical activity (Baerg et al., 2011). Hence individuals with DCD may use the same amount of energy at lower levels of physical activity than is seen in nonaffected individuals such that their BMI reflects the energy efficiency of their movement. The absence of any difference in BMI measurements between DCD risk groups despite physical activity differences would support the idea of differential energy efficiency being a factor in the BMI-to-DCD interaction effect, although other casual factors upon BMI were not measured in this

study. The differential effect of BMI upon physical activity has not been previously investigated and is an important avenue for further research.

Inefficiency of locomotion effects on BMI cannot be extended to other adverse health outcomes of inactivity. Although no significant differences were found in percentage of participants meeting physical activity guidelines, with MVPA levels being currently sufficient to meet physical activity guidelines, the association of higher levels of sedentary behaviour with adverse health outcomes (Proper et al., 2011) is worth noting, with the physical activity pattern seen in this study with increased sedentary behaviour and decreased vigorous physical activity being particularly detrimental to cardiovascular (Shiroma & Lee, 2010) and bone health (Koedijk et al., 2017). Bone health detriments are reported in individuals with DCD, potentially due to a detrimental physical activity pattern (Tsang et al., 2012). The current study provides further support for this hypothesis, as although the changes reported in this study are small, with small to medium effect sizes, it is likely that they would result in bone changes, particularly for vigorous physical activity as only a small amount of vigorous physical activity is required to stimulate the formation of bone mineral (Koedijk et al., 2017). Previous paediatric studies have found a change of -0.5 to –0.7% in bone measurements for every additional hour of sedentary time or reduction of 18 minutes of MVPA (Koedijk et al., 2017), which if applied to adults in this study could amount to a 0.2 to 0.3 difference in bone measurements, which would be clinically significant on a population level. Further research, directly measuring physical activity levels and bone health in adult DCD populations are required to confirm these findings, however, it may indicate an important area of focus for future research and therapeutic options.

4.4.2 Does VMI Impact Upon Physical Activity Levels at the Age of 25?

Sensitivity analysis of VMI did not show an impact of VMI detriments upon physical activity levels at the 15th percentile level, although lower levels of vigorous physical activity were shown in between group differences at the highest level of detriment (fifth percentile). Statistical models including VMI as both a categorical and continuous variable did not show a significant role for VMI in affecting physical activity apart from mean amplitude deviation although risk status for DCD and the DCD-to-BMI interaction did become significant in the models for moderate and

MVPA. This contrasts with Jarus et al. (2011)'s work in a paediatric population that showed VMI acting as an independent inhibitor of physical activity, however Jarus's study measured the type of physical activity (i.e., diversity, intensity, sociality) engaged in rather than total physical activity. This study particularly the significant BMI-to-VMI interaction effect for MAD and the increased role for DCD risk status in models including VMI, indicate a change in choice of physical activity due to VMI in this population and supports Jarus' findings. Since such physical activity choices would not necessarily affect overall energy expenditure it is unlikely that these changes would impact upon BMI and body fat and so the current study did not provide an explanation for the previous findings from this population that VMI was linked to increased BMI and body fat percentage in early adulthood (Kumpulainen et al., 2016), although it supported the findings in regards to differences in BMI and BMI trajectory based on VMI risk status. Given the higher rate of some medical interventions and neonatal complications in this group, it is possible that VMI reflects differences in development which independently relate to BMI and body fat, as the current study did not find a causal pathway with physical activity, nor does it appear to be via its impact on motor competence. Examination of motor competence scores in this group, showed that although the DCD groups showed detriments in VMI scores similar to what has been reported in other studies (Vaivre-Douret et al., 2011) the reverse was not the case and VMI as measured by the Beery test, did not offer sufficient sensitivity to be used as a marker for DCD. As such, evidence for VMI's role in predicting health outcomes was not found and does not appear to be related to its association with DCD or its impact on physical activity.

4.4.3 Strengths and Limitations

The longitudinal nature of this study, including follow up over a 20-year period, is a strength as longitudinal measures provide an additional insight into the effects of motor competence on physical activity. This study by measuring motor competence at five years and then physical activity in adulthood shows the long-term implications of impaired motor competence in early life, rather than showing the effects on motor competence of inactivity. This is particularly an issue for studies on motor competence in adulthood as these studies are often cross-sectional and thus likely to be confounded by the effects of prior experience, BMI, and increased body stature on performance on motor competence test items (Chivers et al., 2013). This study did not re-evaluate motor

competence at the age of 25 years, however most of the group would be anticipated to continue to have motor competence issues into adulthood (Blank et al., 2019); with this study focused only on the effect of childhood low motor competence as is seen in DCD on adulthood physical activity. This study did not assess physical activity at age five years and as such it is not known whether the reported physical activity patterns were established in childhood or occurred later in life.

Cross-cultural issues related to physical activity, should be considered in interpreting the results from this study as Finland has a high level of leisure physical activity participation with less reliance on organised sports or structured environments than present in other countries (Elhakeem et al., 2015). Given that adults with DCD report less physical activity in organised sports and structured environments and more exercise that is solitary or with their immediate social group (Missiuna et al., 2008), a smaller difference in physical activity may be present in this population than is found cross culturally. The type of physical activity was not collected for this study, however, the likely low levels of organised sports participation in the non-DCD group provides an opportunity to examine leisure based physical activity in DCD which is likely the largest contributor to their physical activity levels. Furthermore, as specific facilitators and barriers to physical activity may be present in different environments and cross-cultural studies have indicated a cross-cultural effect on physical activity in DCD (Cermak et al., 2015), validation and applicability of these findings in other countries is warranted.

The AYLS cohort is a longitudinal observational study, and as such, causality cannot be assigned. In addition, although many health confounders were examined, confounding by other unmeasured variables is still a risk. A particular concern for confounding is from the effects of ADD, particularly the hyperactive form (ADHD), which is commonly comorbid in individuals with DCD (Blank et al., 2019), and for which data was not available for this study. Paediatric studies have shown that children with both DCD and ADHD have a smaller deficit in activity levels compared to their typically developing peers than children with DCD alone (Lenhard & Lenhard, 2016), and so failing to control for this factor may have resulted in underestimating the degree of deficit in activity levels in individuals with DCD.

4.5 Conclusion

Early DCD risk status was associated with lower levels of physical activity in young adults, providing device measured evidence that deficits in physical activity shown in childhood and adolescence in individuals with DCD extends into adulthood. Childhood DCD status appeared to moderate[2] the role of BMI upon physical activity, such that individuals with DCD did not show as much decrease in physical activity with increasing BMI, potentially due to higher energy requirements for movement in individuals with DCD. However, the physical activity pattern demonstrated if continued through the lifespan is likely to place this population at an increased risk of sedentary related adverse health outcomes and highlights a continued need for physical activity interventions to improve physical activity into adulthood.

[2] Original sentence in published manuscript was Childhood DCD status appeared to mediate the role of BMI upon physical activity

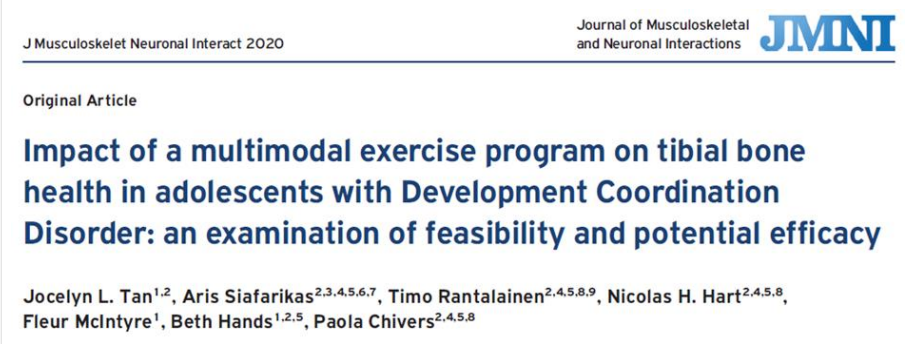
Chapter 5

Impact of a Multimodal Exercise Program on Tibial Bone Health in Adolescents with Development Coordination Disorder: An Examination of Feasibility and Potential Efficacy

Research Synthesis

Previous chapters have indicated the presence of a detrimental physical activity pattern in individuals with DCD. The relationship between physical activity and bone development in a DCD population is however not determined. As such, this study sought to determine if bone health in individuals with DCD could be improved via engagement in an exercise intervention. Since the systematic review (Chapter 2) showed the presence of bone detriments in an adolescent population, this study examined the impact of an exercise intervention at this time point (J Tan et al., 2020). Adolescence is also a critical time point under the life course health development model and so a critical time for interventions to target.

Article Information



Title:	Impact of a Multimodal Exercise Program on Tibial Bone Health in Adolescents With Development Coordination Disorder: An Examination of Feasibility and Potential Efficacy
Authors:	Jocelyn L. Tan, Aris Siafarikas, Timo Rantalainen, Nicolas H. Hart, Fleur McIntyre, Beth Hands, Paola Chivers
Reference:	Tan, J. L., Siafarikas, A., Rantalainen, T., Hart, N. H., McIntyre, F., Hands, B., & Chivers, P. (2020). Impact of a multimodal exercise program on tibial bone health in adolescents with Development Coordination Disorder: an examination of feasibility and potential efficacy. *Journal of Musculoskeletal & Neuronal Interactions*, *20*(4), 445–471.

Abstract

Objectives. Developmental coordination disorder (DCD) compromises bone health purportedly due to lower levels of physical activity. The potential of an exercise intervention to improve bone health parameters in adolescents with DCD has not previously been studied. This study thus aimed to determine the impact of a multimodal exercise intervention on bone health in this population at-risk of secondary osteoporosis.

Methods. Twenty-eight adolescents (17 male, 11 female) aged between 12 and17 years (M_{age}= 14.1) with DCD participated in a twice weekly, 13-week generalised multimodal exercise intervention. Peripheral quantitative computed tomography scans of the tibia (4% and 66%) were performed over a six month period. Generalised estimating equations were used to examine the impact of fitness measures on bone parameters over time.

Results. An overall improvement trend was observed for bone health, with significant increases at the 66% tibial site for bone mass (4.12% increase, d_{cohen} = 0.23, p = .010) and cortical area (5.42% increase, η^2 =12.09, p = .014). Lower body fitness measures were significantly associated with improvements in bone health parameters, tempered by the degree of motor impairment.

Conclusion. A multimodal exercise intervention may be effective in improving bone health of adolescents with DCD. Given the impact of motor impairments, gains may be greater over an extended period of study.

Keywords

Developmental coordination disorder, bone health, exercise, physical activity, developmental disorder.

5.1 Introduction

Developmental coordination disorder (DCD) is a neurodevelopmental disorder typified by the slow acquisition and poor performance of motor skills across an individual's lifespan (American Psychiatric Association, 2013). Persons with DCD tend to have low levels of physical activity (Cairney, Hay, Veldhuizen, Missiuna, & Faught, 2010; Haga, 2009; Hands, 2008) which has been purportedly linked to detrimental bone health (Tsang et al., 2012), including bone health impairments (Cantell et al., 2008; Chivers et al., 2019; Fong et al., 2018; Hands, Chivers, et al., 2015; Jenkins et al., 2020) and increased rates of fracture (Hands, Chivers, et al., 2015; D Ma et al., 2004) placing them at risk of osteoporotic fractures later in life. Furthermore, suboptimal bone health is not just a consequence of reduced overall physical activity in childhood DCD populations, but also from a lack of diversity in activities engaged (Fong et al., 2018), such that childhood DCD populations appear to benefit most from physical activity that is diverse and intense (A W W Ma et al., 2018). As diverse mechanical loading modalities, methods, and intensity are known to be an essential part of all osteogenic activities (Hart, Nimphius, et al., 2017) it is likely that a similar association between incidental physical activity and prescribed exercise with bone-specific outcomes also applies to adolescent and adult DCD populations, however this has not as yet been established. Furthermore, while physical activity (i.e., incidental and/or nonspecific activities requiring bodily movement) appears to improve bone health in DCD populations, exercise (i.e. purposeful, prescriptive, programmed and progressive activities targeting physiological outcomes) is likely to produce even greater benefits (Hart, Nimphius, et al., 2017).

No studies, to our knowledge, have investigated the relationship between physical activity or exercise and bone health in adolescents with DCD. Weight bearing activity is known to have a particularly strong osteogenic effect during the early to mid-puberty time frame due to the velocity of bone growth and endocrine changes seen at this age (Hind & Burrows, 2007; MacKelvie et al., 2002) with significant improvements noted in bone health from a broad range of exercise interventions within adolescent populations (Bernardoni et al., 2014; Blimkie et al., 1996; Nichols, Sanborn, & Love, 2001; Vlachopoulos, Barker, Ubago-Guisado, Williams, & Gracia-Marco, 2018; Xu, Lombardi, Jiao, & Banfi, 2016). Exercise interventions are known to be particularly effective in populations who are relatively inactive (Ireland &

Rittweger, 2017), with a substantial benefit anticipated for the typically inactive DCD population (Cairney, Hay, Veldhuizen, Missiuna, & Faught, 2010; Haga, 2009; Hands, 2008). The benefits of exercise interventions in this age group, however, are heavily influenced by the types of activities or exercise modalities used (Bernardoni et al., 2014; Nikander, Sievänen, et al., 2010; Xu et al., 2016). Given the difficulties of motor skill acquisition and performance inefficiency inherent with DCD (American Psychiatric Association, 2013; Martini et al., 2004) it is likely there will be specific challenges concerning the implementation of prescribed exercise interventions in DCD populations. Thus, it is not yet known whether adolescents with DCD can engage in exercise interventions to a degree that would induce improvements in muscle and bone parameters. Indeed, to have an osteogenic effect, physical activity and/or exercise is required to be frequent, with a variety of different loading types, and be progressive through increasing magnitudes and rates of loading (Hart, Nimphius, et al., 2017). However, as individuals with DCD have a slower rate of mastering movements and a lower level of engagement in physical activity (Yu, Burnett, & Sit, 2018) such effects may be impeded. Accordingly, this study examined whether participating in a multimodal exercise intervention designed to address the general needs of adolescents with DCD, shown to improve the physical fitness (Hands, Chivers, Grace, & McIntyre, 2018) and self-perception of physical abilities among adolescents with DCD (McIntyre, Chivers, Larkin, Rose, & Hands, 2015), would also have the capacity to produce improvements in bone health parameters.

5.2 Materials and Methods

5.2.1 Experimental Design

A longitudinal, single-cohort study design was used to explore the feasibility and preliminary efficacy of a 13-week exercise program in adolescents with DCD to improve tibial bone health outcomes. All participants attended two testing sessions, six months apart, for anthropometry and lower-limb muscle bone morphology, with the first session taking place immediately prior to the commencement of the exercise program. Participants attended the local tertiary paediatric hospital to have their anthropometry (height, weight, and tibial length) and lower limb muscle-bone morphology measures taken. Lower limb fitness assessments and motor performance tests were performed at The University of Notre Dame Australia's exercise clinic on

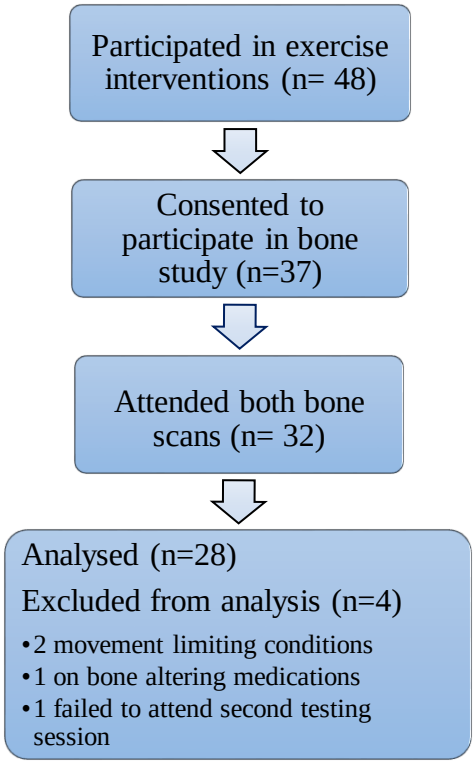
the first and last session of the exercise intervention. Bone measurements were performed approximately three months following the completion of the exercise program to allow time for bone adaptation. Participants were also required to attend the exercise clinic two days per week throughout the program to complete their supervised exercise sessions.

5.2.2 Participants

Participants were recruited from the Adolescent Movement Program (AMPitup: www.movegrowengage.com.au/ampitup/), a research program providing an exercise intervention for adolescents with movement difficulties (Hands, 2008; Hands et al., 2018; McIntyre et al., 2015). The program is aimed at adolescents aged 12 to 18 years with a reported history of movement difficulties below what would be expected for their age that has impacted upon their activities of daily living as per the diagnostic criteria for DCD (American Psychiatric Association, 2013). Participants in the study are recruited through referral from allied health professionals (e.g., Occupational Therapists, Physiotherapists) or through word of mouth. All participants in the Adolescent Movement Program were offered the opportunity to participate in this bone health study. Participants whose movement difficulties did not occur early in the developmental period or were due to an intellectual or physical disability were excluded from this analysis in keeping with the diagnostic criteria for DCD (American Psychiatric Association, 2013). As indicated in Figure 5.1, two participants were excluded for this reason, with another participant being excluded due to use of bone affecting medication for epilepsy. The study had ethics approval from the Human Research Ethics Committee of the University of Notre Dame Australia (Reference 011004F, 09004F, 09050F, 09039F) and written informed consent was provided by participants and their caregivers prior to participation. The study and its procedures conformed to the World Medical Associations' Declaration of Helsinki for Medical Research Involving Human Subjects.

Figure 5.1

Inclusion of Participants for Bone Health Analysis



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5.2.3 Intervention

A multimodal exercise intervention was undertaken as part of the AMPitup program. Participants received individualised exercise training over thirteen weeks consisting of two 90-minute sessions per week after school, overseen by an accredited exercise physiologist (AEP; Exercise and Sport Science Australia) and clinically experienced academics. Each participant received one to one coaching from physiotherapy and exercise sport science undergraduate students, together with exercise physiology postgraduate students. The use of one to one coaching has been found to increase the participants engagement in the intervention (McIntyre et al., 2015) and also allows for individualised feedback on technique. Each participant had two assigned trainers through-out the intervention, one for each exercise session of the week, to encourage variability in exercise routines. The AMPitup program is general and broad in focus, thus activities are not explicitly targeting osteogenesis. All exercise sessions include a combination of aerobic training (cardiorespiratory fitness), resistance training (muscle and strength development) and other activities aimed at improving motor skills and balance. Stretching and flexibility activities, core strength and postural exercises, were also included dependent on the participant's individual

[1] Corrected from the published paper.

fitness interests, goals and needs. Fitness games and group activities were often included to improve participant's engagement and enjoyment of physical activity. A full list of activities used are included in Table 5.1. The volume and intensity of exercises were prescribed as recommended by Faigenbaum et al. (2009), and Falk et al. (2010), relative to participant's physical abilities and fitness. Progression in sets, repetitions and weight occurred after proper technique was achieved as determined by the trainer (Bernhardt et al., 2001).

Table 5.1

List of Activities Performed by Participants

Cardiovascular exercises		
Arm ergometer	Hula hooping	Stair run
Bike	Mountain climbers	Step aerobics combinations
Boxing	Rower	Walk
Cross-trainer	Running	
Core strength and flexibility		
Abdominal crunch	Heel slide	Plank
Ball rollouts	Hover	Rotary torso
Dead bugs	Leg lifts	Stretches
Farmers walk	Oblique leg slide	Wheelbarrow
Fit ball knee tucks	Oblique twist	
Glute bridge	Pilates Machine	
Motor and postural skills		
Balance on beam	Heel-toe walk	Throwing into bucket/bin/net
Balance on bosu	Kicking	Throwing while balancing
Balance on one leg	Obstacle course	Throwing while standing on one leg
Catching	Star excursion balance	
Fitball balance on all fours	Throwing over object	
Resistance training (for lower body)		
Bear crawls	Heel raises	Reverse leg curls
Burpees	Leg curl	Side kicks
Calf raises	Leg extension	Squats
Chair sit to stand	Leg press	Travelling lunges
Climbing frame	Leg raises	Tricep dip
Heel press	Lunges	Tricep extension
Resistance training (general)		
Arnold dumbbell press	Deadlifts	Pectoral fly
Arm raises	Dead row	Pelvic lift
Arm extension	Dumbbell snatches	Pull up
Bridge	High pull	Push press

Back extension	Kettlebell swings	Rope climbing
Bent over barbell row	Lateral pulldown	Seated cable row
Bicep curl	Lateral shoulder raise	Shoulder press
Bicep extension	Medicine ball passes	Shoulder shrug
Cable pull down	Medicine ball slam	Supine rows
Chest press	Medicine ball twist	
Chin ups	Overhead press	
Plyometrics		
Body weight jump squat	Side to side hops/jumps	Dodgeball
Bounding	Skipping	Four square
Box jumps	Star jumps	Frisbee
Broad jumps	Toe taps	Kick to kick
Hopping	Vertical jump	Piggy in the middle
Hopscotch	Group and partner games	Soccer
Horizontal jumps	Baseball	Tennis
Hurdles	Basketball	Two square
Jump over board	British bulldog	
Lateral jump	Circuit of park equipment	

5.2.4 Measures

5.2.4.1 Musculoskeletal Morphology

Tibial scans were performed using peripheral Quantitative Computed Tomography (pQCT; Stratec XCT-3000, Stratec GmbH; slice thickness 2.3 mm, pixel size 0.4 × 0.4 mm) at proximal (66% of tibial length, T66) and distal (4% of tibial length, T4) sites of the tibia, of the non-dominant side as reported by the participant. Participants sat on a height-adjustable chair with their lower limb fully extended through the acrylic cylinder and central gantry of the pQCT machine and secured to the foothold attachment under the supervision of a trained bone densitometry hospital technician. A 30-mm scout scan was produced at the base of the malleolus in order to identify the talocrural joint, as an internal reference point from which the scan commenced to measure cross-sectional slices at 4% (T4) and 66% (T66) of tibial length. Scans per participant spanned approximately five minutes and were performed approximately six months (20.4 (8.4) weeks) after baseline testing; approximately three months following the completion of the 13-week exercise program. Following scan completion, total tibial mass (g/cm) and cross-sectional area (mm^2) were assessed at both sites. In addition, total density (mg/cm^3) and trabecular density (mg/cm^3) were assessed at the T4 site, and cortical density (mg/cm^3), cortical area (mm^2), stress strain

index (mm^3), fracture load on the X and Y axis (N), muscle and fat cross-sectional area were assessed at T66. SSI and fracture load were used as surrogates for bone strength. To account for the absence of a concurrently assessed control group, Z-scores were calculated using height and sex-specific means and standard deviations from the Stratec reference database (Version 6.20, Stratec, Stratec GmbH) (Ashby et al., 2009) using the formula $z = \frac{x-\mu}{\sigma}$ where x is the individual value, μ is the sex and height specific mean and σ is the associated standard deviation.

5.2.4.2 Anthropometry

Stature was recorded to the nearest 0.1 cm using a wall-mounted stadiometer (Mentone Educational Centre), with body weight recorded to the nearest 0.1 kg using an electronic scale (Homedics). Tibial length of the non-dominant leg was assessed using a retractable measuring tape, defined as the tibial plateau at the knee joint (proximal end) to the medial malleolus (distal end), recorded to the nearest 0.1 cm. BMI was subsequently calculated using weight (kg) / height $(m)^2$.

5.2.4.3 Pubertal Status

Pubertal status was assessed using the Pubertal Developmental Scale, a non-invasive self-report scale which covers five aspects of pubertal development including sex specific questions (Brooks-Gunn, Warren, Rosso, & Gargiulo, 1987). Items are scored on a scale of one to five, with five indicating a mature stage. The scale can be converted to correspond to five categories of pubertal development (Peterson et al 1998 in Bond et al. (2006)). Validity has been established against physical exams and self-report measures of puberty (Brooks-Gunn et al., 1987), with a Kappa concordance of 0.5 with self-reported Tanner stage (Bond et al., 2006). Reliability has been established in rural and urban populations (Robertson et al., 1992).

5.2.4.4 Motor Performance

Motor performance was assessed using the McCarron Assessment of Neuromuscular Development (MAND) (McCarron, 1997) as part of the screening process for the AMPitup program. The MAND is a ten-item test designed for the assessment of gross and fine motor skills in adolescence and young adults. Scores from the ten items are scaled and summed to produce a Neuromuscular Developmental Index (NDI), with a mean of 100 and standard deviation of 15. Lower

NDI scores indicate poorer performance of motor skills and as such a greater degree of motor impairment. An NDI of more than one standard deviation below the mean (85) was required in order to be eligible for participation in the intervention, however participants with an NDI above 85 were included if a substantial history of motor difficulties impacting on their daily life was reported. The MAND has a test-retest of 0.99 after one month and concurrent validity to a number of different motor skill tests (McCarron, 1997).

5.2.4.5 Lower Limb Fitness Measures

Lower limb fitness was measured using three assessments: the standing broad jump, vertical jump, and a one-repetition maximum (1RM) leg press. All measures are reliable forms of evaluation of lower limb fitness validated under similar conditions to their use in this study. The standing broad jump has an intraclass correlation coefficients (ICC) from test-retest of 0.98 in an adolescent population (C Thomas, Dos'Santos, Comfort, & Jones, 2017), while the vertical jump, as measured by the Vertec system, has an 0.91 ICC in college aged females (M_{age}=19.5, SD=1.3), and 0.94 in college aged males (M_{age}=19.7, SD=1.5) (Nuzzo, Anning, & Scharfenberg, 2011). The 1RM leg press has a test-retest ICC of 0.95 in college aged athletes (M_{age}=18.9, SD =1.2) (Kraemer et al., 2000) and 0.99 in untrained adults (Levinger et al., 2009). The measures were taken for each participant at the first and last session of the thirteen-week exercise intervention. The standing broad jump was measured as the horizontal distance achieved by the participant jumping forwards from a standing stationary position, by drawing a line behind their heels following the landing point. Each participant had three attempts with the best achieved jump being recorded in inches (in) (McCarron, 1997). The vertical jump was measured as the maximum vertical height achieved in a standing jump (Vertec, Sports Imports, Hilliard) by determining the difference in the number of vanes between the participant's standing reach and jump reach at peak height. Vanes are spaced 1.27 cm apart with vertical jump height in centimetres calculated as the number of vanes multiplied by 1.27. Each participant was provided with multiple attempts with short rests of about a minute until a plateau in performance was observed, with the best achieved jump retained for analysis (Hands et al., 2018). Leg strength was assessed using 1RM leg press, recording the maximum weight that could be lifted through a full range of motion in kilograms (kg). Failure was defined as an incomplete range of motion through

execution, or an inability to lift the weight in two attempts (Faigenbaum, Milliken, & Westcott, 2003). Due to technical specifications of the leg press machine, increase of weight was in five kilogram increments. Fitness procedures were performed in the same set pattern for all participants with the 1RM leg press being performed last.

5.2.5 Statistical Analysis

All statistical calculations, except effect sizes, were completed using SPSS (IBM Corporation). Effect sizes were calculated using Psychometrica online calculator (Lenhard & Lenhard, 2016). Normality of data distribution was explored using a Shapiro-Wilk test. Full statistical analysis was performed for bone measurements in both the raw data and Z-scores. Baseline and post intervention differences in bone parameters and fitness assessments were explored using paired sample t-tests for parametric variables or Wilcoxon signed rank tests for non-parametric variables. Effect sizes were calculated using Cohen's d for parametric variables and eta squared for non-parametric variables. Sex differences for bone parameters, fitness measures, and descriptive characteristics were determined via independent t-tests for parametric variables and Mann Whitney U tests for non-parametric variables. Generalised estimating equations (GEE) were used to identify determinants of bone parameters. Sex, puberty score, age, height, and weight were included in the GEE model as they were considered likely influencers of improvements in bone health in this age group. Physical fitness measures were included in order to evaluate the impact of the intervention. Separate GEE models were performed including age^2 to assess for the effects of growth but did not substantially alter the results (Supp 5B, Appendix C), and due to sample size the simpler model was retained and reported. As participants who had prior fitness intervention exposure were included in the sample, a sensitivity analysis was conducted to determine any differences in baseline bone parameters and fitness measures as well as differences in changes over the course of the intervention. The impact of age between the intervention groups was explored using a two-way between groups analysis of variance. Alpha of <.05 were considered statistically significant. Sample size was not formally calculated as participation in the bone health study was offered to all participants of AMPitup. The program is limited to a maximum of 25 participants per semester for accommodation purposes (McIntyre et al., 2015).

5.3 Results

5.3.1 Baseline

The sample comprised 28 participants, 17 male and 11 female, ranging in age between 12.6 and 17.6 years with a mean age of 14.1 (SD=1.3) years. The mean pubertal score was 6.4 (SD=1.8) with conversion of pubertal scores to categories indicating that the majority (92.9%) were in a mid or post-pubertal stage. Fourteen participants were mid-pubertal, 12 were post-pubertal and two were pre-pubertal. Four participants (14.8%) changed pubertal category over the course of the intervention, two moved from pre-pubertal to mid-pubertal and two moved from mid-pubertal to post-pubertal. There were no statistically significant differences between sexes for age, puberty score, height, weight, BMI or NDI. Baseline descriptive characteristics of the sample are presented in Table 5.2. Eleven participants had taken part in the 13-week intervention program at least once prior to bone parameter measurements being taken. Prior participants had completed between one and five programs, with a mean prior attendance of 2.2 (SD=1.1) programs.

Table 5.2

Descriptive Characteristics of the Total Sample, Males and Females

Characteristic	Total sample (n=28		Male (n=17)		Female (n=11)	
	M	*SD*	*M*	*SD*	*M*	*SD*
Age (years)	14.1	1.3	14.0	0.9	14.2	1.8
Height (cm)	163.8	10.6	163.9	10.0	163.7	11.9
Weight (kg)	61.4	14.9	61.1	16.2	61.9	13.6
Puberty score	6.4	1.8	6.4	2.0	6.5	1.4
NDI	66.3	17.9	68.1	17.9	63.5	18.3

Baseline measurements of bone parameters indicated a deficit in bone health with Z-scores indicating the deficit was also present when compared to sex and height matched norms (Table 5.3). The 11 participants who had previously taken part in the fitness intervention (intervention-experienced participants) had higher baseline parameters on all measurements of bone health than those who had never previously taken part (intervention-naïve participants). The differences between groups based on prior intervention engagement were statistically significant for all bone health parameters except total area (T4 and T66), fracture load on the Y-axis (Y3N),

trabecular density and the Z-scores for SSI and cortical density. Fitness parameters, however, were not significantly different between groups based on prior participation status, apart from the 1RM leg press which was significantly higher in the intervention-experienced group (61.8% increase, d_{cohen}= 1.35, t = -3.01, p = .008). All baseline measurements for both groups are presented in Table 5.3 and Table 5.4.

As the intervention-experienced participants were significantly older (15.1 years compared to 13.4 years respectively) (η^2 = 12.13, t = -3.62, p <.001), a two-way between groups analysis of variance was conducted in order to explore the impact of prior intervention and age. The interaction effect between age and intervention status was not statistically significant for any variable. There was a statistically significant main effect for age only for fracture load F (5, 20) = 3.26, p= .026, η_p^2 = 0.45. A statistically significant main effect for intervention was found only for T4 trabecular density score, F (1, 15) = 5.34, p = .025, partial eta squared = 0.26.

Table 5.3

Intervention Group Difference

	Intervention – Naive (n=17)		**Intervention – Experienced (n=11)**					
	M	*SD*	***M***	*SD*	d_{cohen}	*d 95% Confidence Interval*	*T test*	*P- value*
Age (years)	13.38	0.53	15.11	1.40	12.13[b]		-3.62[a]	<.001
Height (cm)	161.27	11.39	167.73	8.07	0.25	-0.28 to 0.78	1.63	.116
Weight (kg)	57.88	13.66	66.84	15.82	12.10[b]		1.53[a]	.134
T4								
Total area (mm2)	2.87	0.52	3.54	0.61	1.18	0.61 to 1.75	-3.14	**.004**
Total density (mg/cm3)	1100.74	164.81	1211.21	199.90	0.60	0.07 to 1.14	-1.59	.123
Trabecular density (mg/cm3)	261.19	29.28	293.55	24.20	4.93	3.88 to 5.98	-3.05	**.005**
Trabecular density Z-score	224.86	35.50	249.75	22.18	0.84	0.29 to 1.39	-2.07	**.048**
Total area (mm2)	0.38	1.58	0.25	1.05	-0.10	-0.62 to 0.43	-1.28	.212
T66								
Mass (g/cm)	2.88	0.52	3.57	0.49	1.37	0.78 to 1.95	-3.56	**.001**
Total area (mm2)	616.58	161.00	612.00	122.12	12.11[b]		-0.21[a]	.853
Cortical density (mg/cm3)	1022.87	49.65	1061.69	44.79	12.12[b]		-2.19[a]	**.029**
Cortical area (mm2)	207.11	58.15	278.50	36.68	12.13[b]		-3.65[a]	**<.001**
SSI (mm3)	1639.67	323.05	1910.04	374.69	0.77	0.23 to 1.32	-2.03	.050
Fracture load X3N	4112.75	883.31	5038.25	1188.45	0.88	0.34 to 1.43	-2.36	**.026**
Fracture load Y3N	3215.80	765.04	3540.28	727.05	0.44	-0.10 to 0.97	-1.12	.274

	Intervention – Naive (n=17)		**Intervention – Experienced (n=11)**					
	M	*SD*	***M***	*SD*	d_{cohen}	*d 95% Confidence Interval*	*T test*	*P- value*
Cortical density Z-score	-0.33	1.44	0.45	0.87	0.66	0.12 to 1.19	-1.79	.084
Cortical area Z-score	-1.72	1.72	-0.25	1.11	1.02	0.46 to 1.57	-2.75	**.011**
SSI Z-score	-0.71	1.00	-0.52	0.95	0.20	-0.33 to 0.72	-0.50	.619
Fitness parameters								
1RM leg press (kg)	59.33	20.17	96.00	32.86	1.35	0.77 to 1.93	-3.01	**.008**
Vertical jump (cm)	33.39	11.59	34.52	7.78	0.11	-0.41 to 0.64	-0.28	.779
Standing broad jump (in)	41.71	15.50	47.00	15.13	0.35	-0.18 to 0.87	-0.89	.381

[a] Mann-Whitney U test standardized test statistic.
[b] eta squared

Table 5.4

Pre-Post Group Difference on Fitness Measures

	Baseline		**Post-intervention**					
	M	***SD***	***M***	***SD***	d_{cohen}	*d 95% Confidence Interval*	*T test*	*P- value*
1 RM leg press (kg)	68.50	28.14	83.00	26.77	0.53	-0.01 to 1.06	-3.68	**.002**
Standing broad jump (in)	43.79	15.30	46.14	15.10	0.16	-0.37 to 0.68	-2.74	**.011**
Vertical jump (cm)	33.84	10.11	35.61	12.60	0.16	-0.37 to 0.68	-1.21	.235

5.3.2 Intervention

Participants attended between 15 through to 25 out of a possible 26 sessions during the 13-week intervention, with a median attendance of 22 sessions (95% CI 20.6 to 22.6). All fitness measures improved on average over the course of the intervention; 1 RM leg press increased by 21.1% (d_{cohen} = 0.53, p = .002), standing broad jump by 5.4% (d_{cohen} = 0.16, p = .011), and vertical jump by 5.2% (d_{cohen} = 0.16, p = .235) (Table 5.4).

An improvement trend in bone health measurements was observed over the course of the 13- week intervention, with a statistically significant increase present for T66 measurements for bone mass (4.1% increase, d_{cohen} = 0.23, t = – 2.75, p = .010) and cortical area (5.4% increase, η^2 =12.09, t = 2.45, p = .014) as seen in Table 5.5. A sensitivity analysis to limit analyses to only intervention-naïve participants indicated similar results for bone health parameters, except for the change in T66 mass which was no longer statistically significant (p = .065). Non-statistically significant improvements were seen in the Z-scores for cortical area and cortical density.

As the intervention-experienced participants were significantly older (15.1 years compared to 13.4 years respectively) (η^2 = 12.13, t = -3.62, p <.001), a two-way between groups analysis of variance was conducted in order to explore the impact of prior intervention and age. The interaction effect between age and intervention status was not statistically significant for any variable. There was a statistically significant main effect for age only for fracture load F (5, 20) = 3.26, p= .026, η_p^2 = 0.45. A statistically significant main effect for intervention was found only for T4 trabecular density score, F (1, 15) = 5.34, p = .025, partial eta squared = 0.26.

Table 5.5

Pre-Post Group Difference on pQCT Bone Health Parameters

	Intervention – Naive (n=17)		**Intervention – Experienced (n=11)**					
	M	*SD*	***M***	*SD*	d_{cohen}	*d 95% Confidence Interval*	*T test*	*P- value*
Age (years)	14.06	1.28	14.45	1.25	12.07[b]		4.62[a]	<**.001**
Height (cm)	163.81	10.55	165.89	10.05	0.20	-0.32 to 0.73	-0.75	.454
Weight (kg)	61.40	14.94	63.75	14.78	12.10[b]		0.64 [a]	.523
Fat/Muscle area ratio	60.75	42.29	35.16	2.08	-0.86	-1.40 to -0.31	0.90	.534
Bone/ Muscle area ratio	40.72	52.86	35.11	42.19	-0.12	-0.64 to 0.41	1.07	.363
T4								
Total area (mm^2)	3.14	0.64	3.17	0.58	0.05	-0.48 to 0.57	-0.46	.647
Total density (mg/cm^3)	1144.14	184.16	1159.49	178.54	0.09	-0.44 to 0.61	-0.69	.497
Trabecular density (mg/cm^3)	273.89	31.37	273.79	34.48	-0.00	-0.53 to 0.52	0.03	.976
Trabecular density Z-score	-0.13	1.41	-0.65	2.16	-0.29	-0.81 to 0.24	1.07	.290
T66								
Mass (g/cm)	3.15	0.61	3.28	0.53	0.23	-0.30 to 0.75	-2.75	**.010**
Cortical area (mm^2)	235.15	61.35	247.89	47.49	12.09[b]		2.45[a]	**.014**
Total area (mm^2)	614.78	144.53	595.00	103.56	12.10[b]		0.48[a]	.633
Cortical density (mg/cm^3)	1038.12	50.76	1049.26	38.45	0.25	-0.28 to 0.77	-0.93	.359
SSI (mm^3)	1745.89	363.21	1745.31	478.77	-0.00	-0.53 to 0.52	0.01	.992

	Intervention – Naive (n=17)		**Intervention – Experienced (n=11)**					
	M	*SD*	***M***	*SD*	d_{cohen}	*d 95% Confidence Interval*	*T test*	*P- value*
Fracture load X3N	4476.34	1094.24	4609.13	1312.96	0.11	-0.41 to 0.63	-1.31	.202
Fracture load Y3N	3343.28	754.31	3230.69	853.56	-0.14	-0.66 to 0.39	0.93	.363
Cortical area Z-score	-1.14	1.66	-0.96	1.18	0.13	-0.40 to 0.65	-0.47	.638
Cortical density Z-score	-0.03	1.29	0.18	0.86	0.19	-0.33 to 0.72	-0.69	.495
SSI Z-score	-0.64	0.97	-0.81	1.13	-0.16	-0.69 to 0.36	0.61	.546
Cortical area to total area ratio	21.43	5.99	22.55	5.09	0.20	-0.32 to 0.73	-1.86	.071

[a] Related samples Wilcoxon signed rank test, b=eta squared

GEE modelling indicated that the improvement in T4 total area became statistically significant when the effect of sex, puberty score, age, height, weight, degree of motor impairment, and improvement in lower fitness measures was accounted for (β = -54.02, p = .017). A statistically significant influence was found in the model for sex (β = 116.94, p = .007), height (β = 6.29, p = .014), and NDI score (β = 2.29, p = .044), with vertical jump measurements not statistically significant (β = 6.69, p = .060). The model was such that T4 total area increased as height and vertical jump performance increased, improvements were greater for those with a lower degree of motor impairment as measured by NDI, and for males compared to females. Vertical jump also had a statistically significant impact in the model for T66 cortical area (β = 2.01, p = .043) and T66 cortical area Z score (β = 0.02, p = .037). The only other fitness measure that had a statistically significant impact on any model was 1RM leg press in the model for T66 cortical density (β = 0.56, p = .015), and cortical density Z score (β = 0.02, p = .037) as well as a negative impact on fracture load on the Y axis (β = -13.51, p = .033). The degree of motor impairment as indicated by NDI was a statistically significant influencer in some of the models (T4 total area, total density, trabecular density, and trabecular density Z score; T66 mass) with the direction of influence varying between models. A positive association was found such that bone gains increased as NDI score increased (motor impairment decreased) in T4 total area (β = 2.29, p = .044) and T66 mass (β = 0.01, p = .044) and a negative association such that bone gains decreased as NDI score decreased (motor impairment increased) in T4 total density (β = -0.64, p = .044), T4 trabecular density (β = -0.69, p = .028) and T4 trabecular density Z score (β = -0.04, p = .049). Growth as indicated by age, height and weight were found to be statistically significant influences in only some of the models (T4 trabecular density, T4 trabecular density Z-score, T66 mass and T66 cortical area; T4 total area; T4 total density, T4 trabecular density and T4 trabecular density Z-score) as was sex (T4 total area, T66 mass, T66 cortical density and fracture load X3N respectively). The increase in bone mass for both T66 mass and cortical area ceased to be statistically significant after controlling for confounders. GEE models for parameters found to have a statistically significant effect in pre and post modelling, as well as models for Z-scores, are presented in Table 5.6 with results for all GEE models presented in Supp 5A, Appendix C.

Table 5.6

GEE Modelling Showing Relationships Between Changes in Bone Health and Potential Mediators

	β Estimate	S.E.	β 95% Confidence Interval	p-value
T4 Total Area				
Pre/post[a]	-54.02	22.68	-98.47 to -9.57	**.017**
Sex[b]	116.94	43.42	31.84 to 202.04	**.007**
Puberty score	-23.64	15.15	-53.34 to 6.06	.119
Age	20.28	39.61	-57.36 to 97.91	.609
Height	6.29	2.56	1.29 to 11.31	**.014**
Weight	-1.23	2.26	-5.66 to 3.21	.587
1RM leg press	-1.09	0.83	-2.72 to 0.53	.188
Vertical jump	6.69	3.57	-0.29 to 13.69	.060
Standing broad jump	-4.14	3.87	-11.72 to 3.44	.285
NDI	2.29	1.14	0.06 to 4.53	**.044**
T66 Mass				
Pre/post[a]	-0.02	0.08	-0.18 to 0.14	.783
Sex[b]	-0.40	0.17	-0.74 to -0.07	**.019**
Puberty score	0.00	0.06	-0.13 to 0.12	.949
Age	0.58	0.17	0.25 to 0.91	**<.001**
Height	-0.01	0.01	- 0.03 to 0.01	.281
Weight	0.01	0.01	-0.01 to 0.03	.357
1RM leg press	-0.01	0.004	-0.01 to 0.00	.137
Vertical jump	0.01	0.01	-0.01 to 0.03	.373
Standing broad jump	-0.01	0.01	-0.03 to 0.01	.302
NDI	0.01	0.01	0.00 to 0.02	**.044**
T66 Cortical Area				
Pre/post[a]	-3.38	9.50	-21.99 to 15.24	.722
Sex[b]	-27.19	16.82	-60.17 to 5.78	.106
Puberty score	-2.48	7.70	-17.57 to 12.62	.748
Age	34.23	15.72	3.41 to 65.04	**.029**
Height	0.60	1.16	-1.68 to 2.88	.607
Weight	0.66	0.92	-1.14 to 2.46	.473
1RM leg press	-0.21	0.36	-0.91 to 0.49	.557
Vertical jump	2.01	0.99	0.06 to 3.95	**.043**
Standing broad jump	-0.71	0.77	-2.24 to 0.81	.359
NDI	0.53	0.59	-0.62 to 1.69	.366

	β Estimate	S.E.	β 95% Confidence Interval	p-value
T4 Trabecular Density Z Score				
Pre/post[a]	0.72	0.81	-0.87 to 2.32	.374
Puberty score	-0.28	0.22	-0.70 to 0.14	.190
Age	-0.83	0.40	-1.61 to -0.04	**.039**
Weight	0.05	0.02	0.01 to 0.09	.016
1RM leg press	0.03	0.02	-0.01 to 0.06	.105
Vertical jump	0.07	0.06	-0.06 to 0.19	.304
Standing broad jump	0.00	0.03	-0.06 to 0.06	.997
NDI	-0.04	0.02	-0.08 to 0.00	**.049**
T66 Cortical Density Z Score				
Pre/post[a]	-0.06	0.27	-0.58 to 0.47	.835
Puberty score	0.02	0.14	-0.26 to 0.31	.869
Age	-0.06	0.26	-0.46 to 0.57	.831
Weight	-0.02	0.02	-0.06 to 0.02	.335
1RM leg press	0.02	0.01	0.001 to 0.03	**.037**
Vertical jump	0.03	0.04	-0.04 to 0.10	.382
Standing broad jump	0.01	0.02	-0.03 to 0.06	.635
NDI	-0.02	0.01	-0.04 to 0.01	.246
T66 Cortical Area Z Score				
Pre/post[a]	-0.16	0.31	-0.77 to 0.45	.613
Puberty score	-0.08	0.26	-0.58 to 0.43	.764
Age	0.16	0.52	-0.86 to 1.18	.758
Weight	0.02	0.03	-0.04 to 0.08	.597
1RM leg press	0.01	0.01	-0.02 to 0.03	.655
Vertical jump	0.07	0.04	-0.01 to 0.14	.081
Standing broad jump	-0.02	0.03	-0.07 to 0.03	.467
NDI	0.01	0.02	-0.03 to 0.05	.736
T66 SSI Z Score				
Pre/post[a]	0.28	0.22	-1.04 to 0.35	.203
Puberty score	0.04	0.17	0.30 to 0.38	.824
Age	-0.35	0.35	-1.04 to 0.35	.327
Weight	0.02	0.02	-0.02 to 0.06	.270
1RM leg press	0.00	0.01	-0.02 to 0.02	.804
Vertical jump	0.03	0.03	-0.03 to 0.09	.290
Standing broad jump	0.00	0.02	-0.05 to 0.05	.998
NDI	0.00	0.02	-0.03 to 0.03	.909

[a] Where pre-intervention is the comparison group and β=1.
[b] Where male is the comparison group and β=1; SE=standard error.

A sensitivity analysis of only intervention-naïve participants found that the changes in T66 total area (β = 168.54, p = .013), SSI (β = 164.65, p = .024), and fracture load X3N and Y3N (β = 369.08, p = .025; β = 590.86, p = .022) became statistically significant when the effect of other variables was controlled for statistically. The models for these parameters as well as T66 mass, T66 cortical area, and all Z scores are presented in Table 5.7, GEE models for other variables are presented in Supp 5C, Appendix C. Fitness measures in this group were implicated in more models than when intervention-experienced participants were included. Vertical jump was implicated in T4 mass (β = 0.03, p = .002), T4 total area (β = 9.46, p = .015), T4 trabecular density (β = 1.77, p = .030), T66 total area (β = -9.43, p = .002), T66 cortical area (β = 2.80, p = .006), T66 cortical area Z-score (β = 0.07, p = .034) and an effect nearing significance in T66 cortical density (β = 2.89, p = .067); 1RM leg press in T4 total area (β = -2.28, p = .038) and T66 total area (β = 2.70, p = .011); and standing broad jump showed a statistically significant influence in T4 total density (β = 1.04, p = .033). NDI, however, had a primarily negative effect in modelling for this sample with bone gains decreasing as motor impairment decreased in models for T4 total density (β = -0.91, p < .001), T4 trabecular density (β = -1.04, p = .001), T66 cortical density (β = -1.03, p = .023), T4 trabecular density Z-score (β = -0.05, p = .010) and T66 cortical density Z-score (β = -0.03, p = .038) while a positive effect was seen only for T66 total area (β = 3.39, p < .001).

Table 5.7

GEE Modelling Showing Relationships Between Changes in Bone health and Potential Mediators for Intervention-Naive Participants Only

	β Estimate	S.E.	β 95% Confidence Interval	p-value
T66 Mass				
Pre/post[a]	-0.07	2.73	-9.61 to 1.09	.119
Sex[b]	-0.42	0.15	-0.72 to -0.12	**.005**
Puberty score	-0.04	0.07	-0.18 to 0.10	.579
Age	0.67	0.29	0.09 to 1.24	**.022**
Height	-0.02	0.01	- 0.03 to 0.002	.090
Weight	0.02	0.01	0.002 to 0.03	**.022**
1RM leg press	-0.01	0.01	-0.02 to 0.00	.130
Vertical jump	0.01	0.01	-0.02 to 0.03	.588
Standing broad jump	0.00	0.01	-0.02 to 0.02	.864
NDI	0.01	0.05	0.00 to 0.02	.079

	β Estimate	S.E.	β 95% Confidence Interval	p-value
T66 Total Area				
Pre/post[a]	168.54	67.93	35.40 to 301.69	**.013**
Sex[b]	70.55	36.58	-1.15 to 142.25	.054
Puberty score	-14.01	23.37	-59.82 to 31.81	.549
Age	136.09	53.60	31.04 to 241.14	**.011**
Height	-0.77	1.31	-3.34 to 1.80	.555
Weight	-0.51	1.87	-4.18 to 3.16	.785
1RM leg press	2.70	1.07	0.61 to 4.79	**.011**
Vertical jump	-9.43	2.30	-15.31 to -3.56	**.002**
Standing broad jump	-0.94	1.45	-3.78 to 1.90	.516
NDI	3.39	0.80	1.82 to 4.95	**<.001**
T66 Cortical Area				
Pre/post[a]	-27.02	19.80	-65.84 to 15.96	.799
Sex[b]	-26.41	14.30	-54.43 to 1.62	.065
Puberty score	-2.39	9.36	-20.73 to 15.96	.799
Age	16.62	32.85	-47.76 to 81.00	.613
Height	0.38	0.99	-1.56 to 2.32	.699
Weight	1.79	0.71	0.39 to 3.18	**.012**
1RM leg press	-0.61	0.56	-1.70 to 0.48	.274
Vertical jump	2.80	1.03	0.79 to 4.81	**.006**
Standing broad jump	0.12	0.80	-1.37 to 1.62	.874
NDI	0.57	0.50	-0.93 to 1.04	.910
T66 SSI				
Pre/post[a]	164.65	79.93	22.72 to 307.59	**.024**
Sex[b]	63.19	144.82	-220.65 to 347.02	.663
Puberty score	32.82	46.83	-58.97 to 124.60	.483
Age	27.16	239.47	-442.20 to 496.51	.910
Height	9.96	8.20	-6.12 to 26.04	.225
Weight	4.79	5.01	-5.02 to 14.60	.339
1RM leg press	2.76	3.40	-3.91 to 9.42	.418
Vertical jump	-1.28	10.36	-21.59 to 19.03	.902
Standing broad jump	2.19	9.27	-15.97 to 20.35	.813
NDI	5.08	4.18	-3.11 to 13.27	.224

	β Estimate	S.E.	β 95% Confidence Interval	p-value
T66 Fracture Load X3N				
Pre/post[a]	369.08	164.29	47.09 to 691.08	**.025**
Sex[b]	-270.67	312.20	-882.57 to 341.23	.386
Puberty score	-81.70	96.43	-270.70 to 107.31	.397
Age	409.16	521.97	-613.88 to 1432.20	.433
Height	10.60	17.24	-23.19 to 44.39	.539
Weight	17.84	10.38	-2.51 to 38.19	.086
1RM leg press	7.99	7.54	-6.79 to 22.77	.289
Vertical jump	5.14	17.79	-29.72 to 39.99	.773
Standing broad jump	13.72	16.98	-19.56 to 47.01	.419
NDI	8.40	9.24	-9.71 to 26.50	.363
T66 Fracture Load Y3N				
Pre/post[a]	590.86	258.79	83.65 to 1098.07	**.022**
Sex[b]	-224.60	292.11	-347.94 to 797.13	.442
Puberty score	123.73	124.84	-120.95 to 368.41	.322
Age	409.16	521.97	-613.88 to 1432.20	.433
Height	12.97	17.80	-21.92 to 47.85	.466
Weight	0.52	13.19	-25.33 to 26.38	.968
1RM leg press	-0.32	6.63	-13.32 to 12.68	.962
Vertical jump	-20.33	26.03	-71.35 to 30.68	.435
Standing broad jump	6.06	18.08	-29.38 to 41.49	.738
NDI	14.31	10.53	-6.33 to 34.94	.174
T4 Trabecular Density Z score				
Pre/post[a]	0.92	1.25	-1.54 to 3.38	.463
Puberty score	-0.38	0.30	-0.96 to 0.20	.201
Age	-1.01	0.75	-2.48 to 0.47	.181
Weight	0.08	0.03	0.04 to 0.13	**<.001**
1RM leg press	0.04	0.03	-0.02 to 0.09	.171
Vertical jump	0.09	0.07	-0.03 to 0.22	.151
Standing broad jump	-0.01	0.04	-0.09 to 0.06	.781
NDI	-0.05	0.02	-0.09 to -0.01	**.010**

	β Estimate	S.E.	β 95% Confidence Interval	p-value
T66 Cortical Density Z Score				
Pre/post[a]	-0.48	0.53	-1.52 to 0.56	.366
Puberty score	0.11	0.23	-0.33 to 0.56	.616
Age	-0.41	0.61	-1.60 to 0.79	.506
Weight	-0.01	0.02	-0.05 to 0.03	.476
1RM leg press	0.01	0.01	-0.01 to 0.03	.339
Vertical jump	0.06	0.04	-0.03 to 0.14	.174
Standing broad jump	0.02	0.02	-0.03 to 0.06	.500
NDI	-0.03	0.01	-0.05 to -0.001	**.038**
T66 Cortical Area Z Score				
Pre/post[a]	-1.02	0.75	-2.48 to 0.44	.172
Puberty score	0.29	0.31	-0.33 to 0.90	.360
Age	1.21	0.86	-2.91 to 0.48	.161
Weight	0.02	0.03	-0.04 to 0.07	.609
1RM leg press	0.00	0.02	-0.05 to 0.04	.865
Vertical jump	0.07	0.03	0.01 to 0.13	.034
Standing broad jump	0.00	0.03	-0.06 to 0.05	.934
NDI	0.01	0.02	-0.03 to 0.05	.735
T66 SSI Z Score				
Pre/post[a]	0.39	0.21	-0.02 to 0.80	.061
Puberty score	0.28	0.11	0.05 to 0.50	.015
Age	-0.66	0.35	-1.35 to 0.02	.057
Weight	-0.01	0.02	-0.04 to 0.02	.541
1RM leg press	0.01	0.01	-0.01 to 0.03	.188
Vertical jump	-0.01	0.02	-0.06 to 0.03	.547
Standing broad jump	0.00	0.02	-0.05 to 0.04	.961
NDI	0.02	0.01	-0.01 to 0.05	.148

[a] Where pre-intervention is the comparison group and β=1.
[b] Where male is the comparison group and β=1.

To compensate for the non-linear effect of age on growth, models were also run using age^2 as a growth estimate. While recognising that the models are likely underpowered, models which included age^2 as an estimate of growth found a statistically significant influence for growth, as indicated by age^2, age, height or weight, for the following measures T4 mass, T4 total area, T4 total density, T4 trabecular density, T4 trabecular density Z-score, T66 mass, T66 SSI, T66 cortical area, and T66 fracture load X3N. Models including age^2 also showed a stronger role for fitness measures which were additionally implicated in T4 mass, T4 total area, T4

total density, T4 trabecular density, and cortical density Z scores (Supp 5B, Appendix C). It was not possible to run models including age^2 in the intervention naïve group only due to the smaller sample size.

5.4 Discussion

This study explored whether a prescribed multimodal exercise intervention established to improve physical abilities among adolescents with DCD (Hands et al., 2018; McIntyre et al., 2015) could also improve measures of bone health. Positively, AMPitup Program improved fitness parameters over the 13-week intervention, with improvements in bone parameters subsequently observed in bone scans conducted during the follow-up assessment period (approximately six months post-intervention). Prior research on fitness improvements in AMPitup have found that fitness gains tend to return to baseline over the break between interventions and thus can be attributed to the intervention rather than due to growth (Hands et al., 2018). Statistical modelling also indicated that improvements in bone health parameters were related to improvements in fitness measures and gains were above what could be attributed to growth. Considering the short intervention time and sample size, these findings indicate that participation in a generalised multimodal exercise intervention may be effective in improving bone health of adolescents with DCD.

Bone parameters indicated an impairment at baseline and improvement over the course of the intervention, with the group overall moving towards a healthier bone phenotype. The size of the gains demonstrated in this study appear similar to what has been shown in other exercise interventions in comparable age groups, which have shown increases of between one and eight percent in bone strength at the loaded sites (Hind & Burrows, 2007; Nikander, Sievänen, et al., 2010). The pattern of changes in bone parameters were primarily in bone mass and cortical area as would be anticipated for changes during an exercise intervention in a peri pubertal population (Gabel et al., 2017; Haapasalo et al., 2000; Hind & Burrows, 2007; MacKelvie et al., 2002), since loading in this age group results in reshaping of bone cross-sectionally along with a redistribution of bone minerals to the cortical area (Gabel et al., 2017; Haapasalo et al., 2000; Hind & Burrows, 2007) .

GEE modelling indicated that improvements in physical fitness contributed to changes in bone parameters beyond the effects of growth as indicated by age, height,

weight, age^2 and pubertal stage, with vertical jump and 1RM leg press being implicated in several models. Fitness measures had a stronger role in models of only intervention-naïve participants, which likely reflects a low level of baseline physical activity in this population. Individuals who have lower baseline physical activity levels tend to show more substantial bone changes in response to an exercise intervention (Ireland & Rittweger, 2017). A low baseline of physical activity may also explain the finding in many models that bone gains increased as motor impairment increased (lower NDI). Physical activity has been found previously to decrease as motor impairment increases (Wrotniak, Epstein, Dorn, Jones, & Kondilis, 2006) and as such it is probable that those with greater motor impairment had lower baseline levels of physical activity. Some bone measures however, had an inverse finding with bone gains found to increase as degree of motor impairment decreased (higher NDI). This may reflect the impact of motor impairment on exercise performance with improvements in fitness being more limited in those that have more motor impairment which is then reflected in bone gains.

The role of motor impairment upon bone gains is also implicated by the smaller scale of change in muscle strength than would be anticipated based on other similar exercise interventions (Blimkie et al., 1996; Nichols et al., 2001; Nikander, Sievänen, et al., 2010). Although this could reflect on the osteogenic potential of the program, it may also indicate that the impact of exercise interventions on bone parameters is somewhat less effective in this population. It was noted in this study that exercise progression, including increasing loading, was slow for many participants with some participants remaining at the same level of loading throughout the intervention. Other studies have found that gains in fitness are more limited in individuals with DCD when compared to individuals without DCD (Rivilis et al., 2011) and have indicated the need for a longer learning period (Yu et al., 2018). As increased loading and variety are required to stimulate osteogenic change (Hart, Nimphius, et al., 2017), a slower exercise progression will limit the osteogenic potential of the exercise program. A longer time frame therefore may be needed by individuals with DCD to learn and effectively execute the exercise tasks before the osteogenic effects can be accurately observed and assessed.

This study had the advantage of including intervention experienced participants and sensitivity analysis supported the need for a longer intervention period by showing continued improvement in those participants. This would seem to indicate

that once necessary motor skills are acquired for the exercise program modalities, participants are then able to achieve the increased loading and variety required to stimulate osteogenic change (Hart, Nimphius, et al., 2017). The study was strengthened by the use of a program specifically designed for individuals with DCD and already established to improve strength in an adolescent population with DCD (Hands et al., 2018), however it is likely that the 13 week program in this study was insufficient to allow for skill mastery. A longer study period would also allow more time for bone adaptation, however the five to seven-month epoch between the scans should have been sufficient to allow bone remodelling to occur (Allen & Burr, 2014). The study was conspicuously limited by the absence of a control group, however the use of sex and height-matched Z-scores derived from the Stratec reference values (Ashby et al., 2009) and statistical modelling to control for variables related to growth provided the advantage of being able to indicate that the effect of the exercise interventions on changes in bone outcomes were possibly above what would be anticipated from growth. Future research should include a control group to determine the impact of DCD specific impairments upon exercise intervention. The impact of the exercise program upon other exercise benefits such as improved muscle function and balance was beyond the reach of this study, however these are likely to magnify the benefits of the found small gains in bone mass (Hind & Burrows, 2007; Kemmler, von Stengel, Engelke, Häberle, & Kalender, 2010). Combined benefits, including improvements in muscle function and balance, as well as clinical benefits such as fracture rates are a potential avenue for future research along with confirmation of improvements in bone parameters.

The outcomes of this study are promising in relation to the ability of the intervention to be effective in improving muscle and bone parameters in adolescents with DCD. The changes detected in this study are small but reasonable given the timing of the study and the motor difficulties of the individuals with DCD. Further research should be undertaken over a longer period to determine whether bone improvements can be achieved and sustained to promote maximal bone mass accrual closer to the normal range during this critical developmental period. This is important for the prevention of future bone-health related adverse outcomes, particularly as this group reports a higher falls rate.

Chapter 6

Reduced Peak Bone Mass in Young Adults with Low Motor Competence

Research Synthesis

Prior chapters (Chapter 3 and 4 (J Tan, Ylä-Kojola, et al., 2022)) reported the presence of a detrimental physical activity pattern in a manner that is indicative of a lifetime physical activity detriment. Further, the systematic review reported in Chapter 2 (J Tan et al., 2021) as well as baseline findings reported in Chapter 5 (J Tan et al., 2020) have indicated that bone detriments are present in children and adolescents with DCD. However, Chapter 2 also reported an identified a gap in knowledge as to the presence of bone detriments at the time of peak bone mass (J Tan et al., 2021). It is important to address this gap, as results reported in Chapter 5 (J Tan et al., 2020), have shown that physical activity engagement can increase bone health measures in adolescents with DCD so making it possible that bone health detriments may have resolved by the time of peak bone mass. Accordingly, this chapter reports on the examination of the presence of bone health detriments, as measured by BMD, at the time of peak bone mass and its relationship to physical activity (J Tan et al., In press).

Article Information

Title:	Reduced peak bone mass in young adults with low motor competence *(In press)*
Authors:	Jocelyn Tan, Carrie-Anne Ng, Nicolas Hart, Timo Rantalainen, Marc Sim, David Scott, Kun Zhu, Beth Hands, Paola Chivers
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Abstract

Although suboptimal bone health has been reported in children and adolescents with low motor competence (LMC), it is not known whether such deficits are present at the time of peak bone mass. We examined the impact of LMC on bone mineral density (BMD) in 1043 participants (484 females) from the Raine Cohort Study. Participants had motor competence assessed using the McCarron Assessment of Neuromuscular Development at 10, 14, and 17 years, and a whole body dual-energy X-ray absorptiometry scan at 20 years. Bone loading from physical activity was estimated from the International Physical Activity Questionnaire at the age of 17. The association between LMC and BMD was determined using general linear models that controlled for sex, age, body mass index, vitamin D status, and prior bone loading. Results indicated LMC status (present in 29.6% males and 21.9% females) was associated with a 1.8 to 2.6% decrease in BMD at all load-bearing bone sites. Assessment by sex showed that the association was mainly in males. Osteogenic potential of physical activity was associated with increased BMD dependent on sex and LMC status, with males with DCD showing a reduced effect from increasing bone loading. As such, although engagement in osteogenic physical activity is associated with BMD, other factors involved in physical activity e.g. diversity, movement quality, may also contribute to BMD differences based upon LMC status. The finding of lower peak bone mass for individuals with LMC may reflect a higher risk of osteoporosis, especially for males, however, further research is required.

Keywords

DXA, other disorders related to bone, exercise, fracture prevention, screening.

6.1 Introduction

Poor motor skills or low motor competence (LMC) which impairs the ability to participate in age appropriate activities of daily living, are a key feature of the neurodevelopmental movement disorder developmental coordination disorder (DCD) (American Psychiatric Association, 2013). LMC in the clinical form of DCD affects about 5% of the population (American Psychiatric Association, 2013), with prevalence rates in some geographical regions being as high as 20% on standard motor assessments (Tsiotra et al., 2006). Typically diagnosed in developing children, this motor impairment often persists into adulthood (Blank et al., 2019), with studies showing reduced overall health in adulthood for people with LMC (Engel-Yeger, 2020; Kirby, Williams, Thomas, & Hill, 2013), including impairment in bone mineral density (Cantell et al., 2008). Suboptimal bone mass and geometry increases the risk of osteoporosis and related fragility fracture in later adulthood (Autier et al., 2000; Briggs et al., 2015). Accordingly, there is a need to identify factors that increase the risk of secondary osteoporosis, including prior diagnosis of LMC.

The status of bone health in adults with LMC has only been reported once (Cantell et al., 2008), although findings of bone health deficits in this study are supported by findings of lower bone health throughout childhood and adolescence (Chivers et al., 2019; Fong et al., 2018; Ireland et al., 2016; Jenkins et al., 2020; Tsang et al., 2012). However, the applicability of these studies is limited by restricted predictive power of early bone measurements (Buttazzoni et al., 2015; Matkovic et al., 1994). Bone measures at the time of peak bone mass, when bone accrual and development ceases, by contrast, are strong predictors of bone health in later life and age of osteoporosis occurrence (Hernandez et al., 2003). The timing of peak bone mass varies by sex and by bone region. Although there is a peak for whole body BMD of 19.9 (95% confidence interval 17.4 to 22.4) years in females and 23.1 (95% confidence interval 20.8 to 25.5) years in males (Boot et al., 2010), some sites peak as early as 16 years in females and 18 in males (Buttazzoni et al., 2015; Heaney et al., 2000; Kang et al., 2015). For studies of the LMC community, only Ireland et al. (2016) finding of decreased hip BMD and bone structure changes in 17 year old's with LMC has the potential to reflect bone health at the time of peak bone mass. Further verification is thus required as to the presence of bone deficits in LMC populations at the age where peak bone mass would be expected to occur.

Reasons for bone health deficits in individuals with LMC are not well established. One potential cause is lower levels of physical activity in a LMC population (Cairney, Hay, Veldhuizen, Missiuna, & Faught, 2010; Hagen Vist, Håvard, Hermundur, & Haga, 2022; Rivilis et al., 2011; Robinson et al., 2015; J Tan, Ylä-Kojola, et al., 2022) due to reduced habitual mechanical loading from physical activity underpinning bone formation (Beck & Snow, 2003; Hart et al., 2020; Hart, Nimphius, et al., 2017). Bone deficits noted in individuals with LMC are located primarily in load-bearing sites (Cantell et al., 2008; Chivers et al., 2019; Ireland et al., 2016; Jenkins et al., 2020). However, the relationship between physical activity and bone health changes in individuals with LMC has shown to be weak (Ireland et al., 2016) or non-significant (Tsang et al., 2012). Given that adaptations to bone mass and strength can take up to 12 months to be detectable following exercise (Weaver et al., 2016) other studies may have provided insufficient time for adaptation and physical activity measures may provide a stronger explanation should physical activity measures be taken from an earlier time point.

The aim of this study was to determine whether there are differences in BMD in young adults with and without LMC, and whether the association between physical activity loading and BMD differs between these groups.

6.2 Methods

6.2.1 Experimental Design

The Raine Study is a prospective multigenerational observational study from Western Australia monitoring growth and development through the lifespan (Dontje, Eastwood, & Straker, 2019). The current analysis explores the association of LMC status on measures of BMD, as well as the impact of bone loading from physical activity. Participants were grouped based on LMC status via motor competence assessments performed at follow up visits at 10, 14 and 17 years of age. BMD measures were assessed using dual energy X-ray absorptiometry (DXA) at approximately 20 years of age. Bone loading outcomes were determined from self-reported physical activity recorded at 17 years of age.

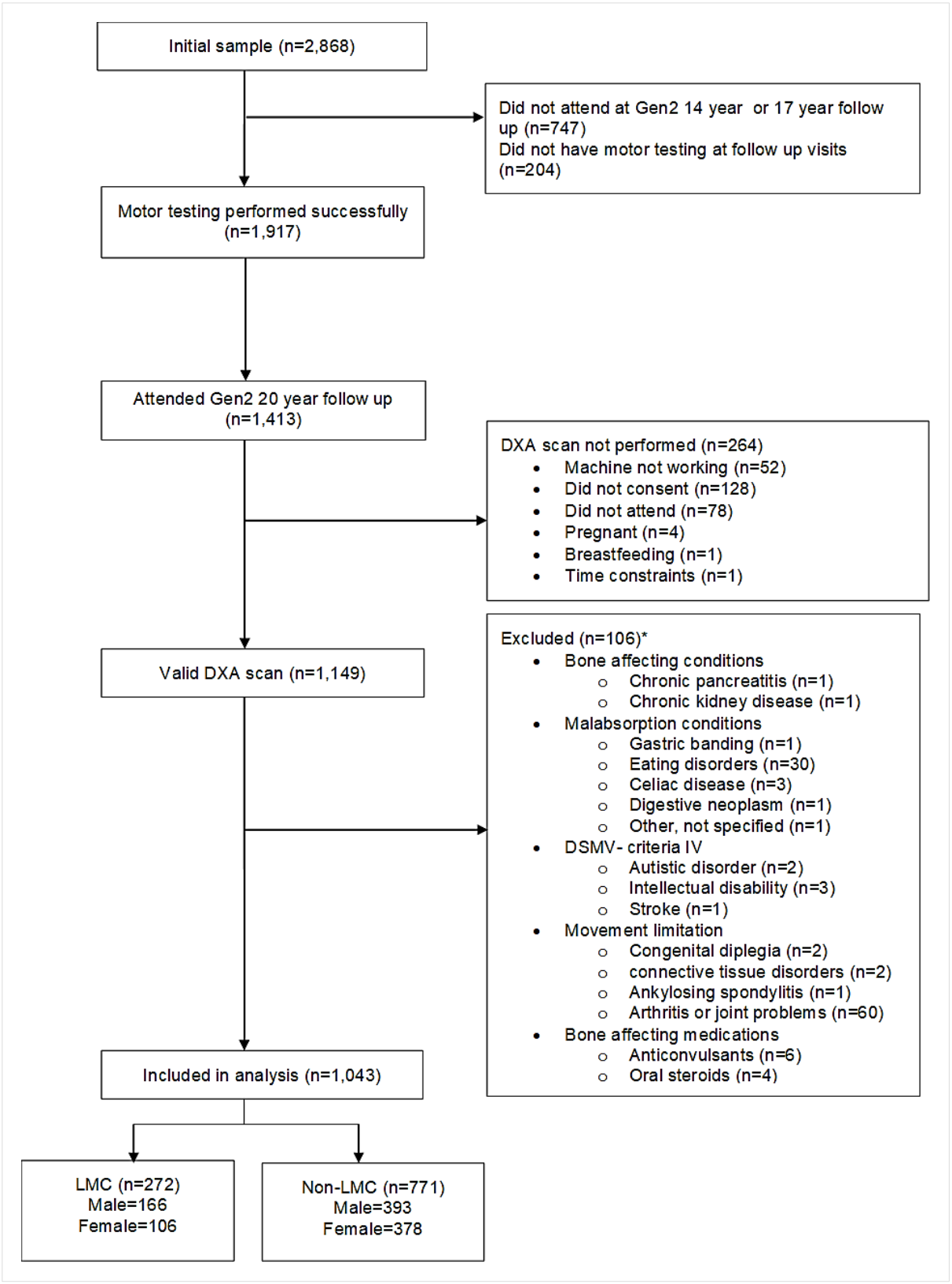
6.2.2 Participants

The Raine Study recruited pregnant women (Gen1) expecting to deliver at a maternity hospital in Perth, Western Australian (King Edward Memorial Hospital) between 1989 and 1991. A total of 2900 women were recruited, with 2730 participants giving birth to 2868 children (Gen2) between 1989 and 1992. Gen2 was assessed on eleven occasions since birth at the age of 1, 2, 3, 5, 8, 10, 14, 17, 18, 20, and 22 years. Flow of participants through the study was previously reported by Straker et al. (2017). Comparisons of the Raine Study cohort to state government data at five timepoints found that the cohort was mostly representative of the Western Australian population, but were more likely to be Caucasian, first time parents, and unmarried, with births more likely to be complicated and via caesarean section (Dontje et al., 2019). Attrition analysis found infant characteristics were constant across participants and nonparticipants at each time point (Straker et al., 2017). The original study and follow up studies were approved by the Human Research Ethics Committees at King Edward Memorial Hospital, Princess Margaret Hospital for Children, and the University of Western Australia. Informed consent was provided by Gen1 or another parent, until Gen2 reached 17 years of age at which point they provided consent.

Gen2 participants classified as LMC or non-LMC based upon motor competence testing at visits between 10, 14 and 17 years, and who had a whole body DXA scan at the 20 year follow up were included in this analysis. Participants were excluded if they had a medical condition that was likely to be bone affecting either directly (e.g., corticoadrenal insufficiency) or via malabsorption of nutrients (e.g., coeliac disease), or who were on medication that was bone affecting (e.g., anticonvulsants, steroids). The clinical expertise of a paediatric endocrinologist was sought to guide these decisions. To assist in the classification of the LMC group, participants were excluded if they had a cognitive disability that may have affected their motor skills. Participants with a condition that was movement limiting (e.g., cerebral palsy) were excluded due to the impact on both motor skills and bone. Exclusion reasons are detailed in Figure 6.1.

Figure 6.1

Participant Flow Through the Study



*Some participants are in multiple categories. LMC=Low motor competence. DXA=Dual-energy X-ray absorptiometry

6.2.3 Assessment Measures and Tools

6.2.3.1 Bone Measurements

Participants had a single whole-body DXA scan (Norland XR-36; Norland Medical Systems, Inc., Fort Atkinson, WI, USA) at the 20 year follow up (Zhu et al., 2014). Scan analysis was performed using built-in software (version 4.3.0) according to the manufacturer's protocol to provide estimates of total body and regional BMD (g/cm^2). The machine was calibrated prior to each scanning session and had an interscan coefficient of less than two percent. BMD measures used for analysis were whole body, head, pelvis, arms, and legs. Legs and arms were analysed as separate limbs (preferred and non-preferred) due to the potential for loading asymmetry. The preferred limb was identified from the patient's reported preferred hand during motor testing. The head was included to provide a representation of a non-loading site. Data on total body fat mass and lean mass were also obtained from the whole-body DXA scan. Lifetime occurrence of fractures was obtained via self-report on a medical history questionnaire at 17 and 20 year follow up.

6.2.3.2 Motor Assessment

Motor performance was assessed using the McCarron Assessment of Neuromuscular Development (MAND), a ten item test assessing five gross and five fine motor skills (McCarron, 1997). Fine motor skill tests involved placing beads in a box within a time frame, threading beads on a row (eyes open and shut), screwing a nut onto a bolt, and sliding an object along a horizontal plane with control (rod slide). Gross motor skill tests involved assessment of hand strength using a dynamometer, the touching of finger to nose and an outstretched finger with eyes open and shut, heel to toe tandem walking, standing broad jump, and balancing on one foot with eyes open and shut (McCarron, 1997). Testing was performed by trained administrators using standardised demonstrations and instructions and following standardised scoring. A senior researcher trained research staff in the MAND protocol for each of the timepoints, oversaw the data acquisition, and conducted the data cleaning and normative scoring. Some item scores include marks for the quality of movement as well as the quantity or speed of achievement. MAND has a very high test-retest reliability ($r = 0.99$), and concurrent validity with the Bruininks-Oseretsky Test of Motor Proficiency, a commonly used alternative motor performance test (Hands,

Licari, & Piek, 2015). MAND is validated for individuals aged between three and 36 years, although the potential for validity to be impacted by ceiling effects has been identified for older adolescents and adults (Hands, Licari, et al., 2015). Items were scaled for age and summed to produce a total score, the Neuromuscular Developmental Index (NDI). The NDI is normalised with a mean score of 100, and as such individuals were classified as LMC when they had an NDI of lower than 85 (McCarron, 1997).

Gen2 participants were tested at the 10, 14, and 17 year follow up time points, however, only 66% of participants had complete motor testing at all time points. Twenty five percent of participants had a change in LMC status between time points, 10% changed classification from LMC to non-LMC and 15% went from non-LMC to LMC. Previous work in the Raine Study cohort found a moderate correlation between NDI scores and Z-scores on subsequent follow up testing (Hands, Larkin, & Rose, 2013). Missing value assessment showed participants who missed at least one measurement had significantly lower NDIs (e.g., participants who missed their 10 year follow up had a median NDI of 93.0 at 14 years of age compared to 97.7) and were slightly younger (e.g. participants who missed their 10 year follow up had a median age of 14.1 compared to 14.2 at 14 year follow up) than those who completed all assessments. In accordance with diagnostic criteria (American Psychiatric Association, 2013) and to avoid the potential for ceiling effects on test items (Hands, Licari, et al., 2015), participants were classified based upon their first available MAND score.

6.2.3.3 Bone Loading

Physical activity levels were assessed via self-report at the Gen2 17 and 20 year follow ups, using the International Physical Activity Questionnaire (IPAQ), and via device-assessment using a pedometer (Yamax Digiwalker SW200, Yamax, Shropshire, UK) at the 17 year follow up visit. IPAQ is a self-report measure that has been developed and tested for use in adults aged between 15 and 69 years. It assesses the frequency, in days, and duration, in minutes, of physical activity over the past seven days in a range of areas (leisure, occupation, domestic work, transport) and their associated intensities (walking, moderate, vigorous). The total duration spent in each activity's intensity was multiplied by the associated metabolic equivalent of tasks (METs) to obtain scores for walking, moderate and vigorous activities (MET-min/wk), which were summed to create an overall IPAQ score (MET-min/wk) (IPAQ Research

Committee, 2005). Short- and long-form versions of the IPAQ were administered with the long form administered at the 17 year follow up, and the short form administered at 20 year follow up. IPAQ scores were converted into a loading score to assess the osteogenic potential of the physical activity. This score (effective loading rating over the week) was calculated as the frequency of the activity multiplied by the activity's effective load rating and summed across physical activity areas, using the method detailed by Ng et al. (2022)(Appendix B, Supp 3.B). The predictive ability of loading scores on BMD has been assessed in this cohort with an association shown in whole body and leg BMD (Ng et al., 2022)(Appendix B, Supp 3.B). An additional sedentary behaviour score in minutes per week was calculated from the total number of minutes spent sitting and lying over the course of a week. Types of activities engaged in were also assessed via self-report of membership to physical activity clubs (sports, exercise, outdoor recreation) at the 17 year follow up.

For pedometer measurements, the Yamax Digiwalker SW200 was worn on the right hip for seven days during waking hours. A minimum of three valid weekdays and one weekend day was required for data inclusion, with a valid day having between 1,000 and 40,0000 steps. The Yamax Digiwalker SW200 pedometer has established reliability in distance walked, with a 1% difference between measured distance and actual distance walked and 100% accuracy in number of steps (Bassett et al., 1996).

6.2.3.4 Vitamin D Status

Participants provided a blood sample for analysis of serum 25-hydroxyvitamin D [25(OH)D] concentration following an overnight fast at the Gen2 17 and 20 year follow up. Samples were stored at –80C until analysed via liquid chromatography-tandem mass spectrometry (RDDT; vivoPharm Co.; Bundoora, Victoria, AUS) using an established protocol (Maunsell, Wright, & Rainbow, 2005) with confirmed validity and reliability (Rappold, 2022). As blood samples were collected year-round, results were de-seasonalised using a published methodology (van der Mei et al., 2007). Vitamin D was defined as deficient when results were under 50 nmol/L and insufficient at between 50 to 74.9 nmol/L (Saggese et al., 2015). Vitamin D reflected deseasonlised serum 25(OH)D3 concentration sample at the 20 year follow up, as serum 25(OH)2 concentrations were rarely detectable in the sample.

6.2.3.5 Anthropometric and Other Measures

Weight was measured to the nearest 0.1kg using calibrated digital scales (Wedderburn; Ingleburn, NSW, AUS) and height measured using a calibrated stadiometer (Holtain; Crosswell, Crymych, UK) to the nearest 0.1cm at each follow up visit. BMI was calculated as weight(kg)/ height(m^2). Weight categories were determined based upon National Institution of Health categorisations (NHLBI Obesity Education Initiative, 1998) with overweight being defined as a BMI of 25.0 to 29.9 and obese as being above 30.0. Information on medical history (diagnosis, medication use, accidents, or injuries) were collected at the 17 and 20 year follow up via questionnaire. Protein (g/day), mineral (calcium, phosphorous, magnesium, potassium, zinc) in mg/day, and alcohol consumption (g/day) was determined from self-report using a semi-quantitative Food Frequency Questionnaire at the 20 year follow up. This questionnaire has been validated in Australia against weighted food records (Hodge, Patterson, Brown, Ireland, & Giles, 2000). Puberty data was collected via self-report questionnaire at 14 year and 17 year follow up appointments. Puberty was assessed via the Tanner stages of pubic hair development for males and females which is a five stage scale (Marshall & Tanner, 1969, 1970).

6.2.4 Statistical Analysis

Statistical analyses were performed using IBM SPSS version 26 (IBM Corp., USA). Alpha was set at 0.05. Data were assessed to be missing at random. Normality was assessed using Kolmogorov-Smirnov and visual assessment. As no variable was normally distributed, non-parametric between group difference tests were performed using Mann-Whitney U, and X^2 tests for medical condition frequency. X^2 or the standardised test statistic is reported (U). Data are reported as mean (M), standard deviation (SD) and median (Md), interquartile range (IQR) or as proportion (%) in each category.

The relationship between LMC status and BMD (outcome) was assessed using general linear models (GLM). A preliminary model was performed controlling for current sex, age, BMI, and vitamin D status, as well as prior bone loading (fixed effects). Variables for inclusion in this model were established based on literature (Alswat, 2017; Beck & Snow, 2003; Heaney et al., 2000; Ng et al., 2022). The bone loading score derived from the Gen2 17 year follow up visit was used as the time-point

of comparison to BMD at the 20 year follow up visit due to the established effect of prior habitual physical activity on DXA-derived bone health (Bland et al., 2020). BMD measures were log transformed due to non-normality in residuals (Aadland et al., 2020), with resulting residuals being normal barring some minor deviation in the tails. Additional models were performed adding LMC to sex interaction (model two), using a sedentary behaviour score rather than the loading score (model three), adding a puberty variable (model four), a LMC to loading interaction variable (model five) and including a body composition variable in the form of lean mass for each body part (model six). Additionally, a simple model including only sex, age, BMI, and LMC status was examined. Estimated marginal means for sex and LMC status were derived from model two. Sex separated models were also examined. All models are described in full in supplementary material (Supp 6B, Appendix C).

From model one of the GLMs, BMD at each site were predicted based on loading score at 17 year follow up, and BMI, age, and serum 25(OH)D levels at 20 year follow up. These predicted values were graphed in R (version 4.0.3; R Foundation for Statistical Computing) to depict the relationships between bone loading and BMD by sex and LMC status. Likelihood ratio tests indicated that the models were linear and as such data was plotted as a GLM. For visual simplicity, the x-axis was truncated at three SD, with the shaded area representing the 95% confidence interval.

6.3 Results

6.3.1 Participant Characteristics

Of the 1043 participants, 272 (166 male, 106 female) were categorised as LMC. A higher proportion of males were classified as LMC compared to females. LMC participants more frequently chose the left side as their preferred limb compared to non-LMC participants (16.3% compared to 11.1%, $X^2 = 4.73$, $p = .030$). Both males and females classified as LMC had lower lean mass on DXA than their typically developing peers (Md = 54.1 kg compared to 56.7 and 34.9 compared to 36.3, U = -3.94 and -2.21, $p < .001$ and .027 respectively) with females also having a significantly higher fat mass (25.2 kg compared to 23.4, U = 1.97, $p = .049$). There were no differences between groups for age or BMI, however a significantly higher frequency of participants classified as LMC were in an overweight or obese category (24.1% compared to 20.8% and 14.3% to 8.7% respectively, $X^2 = 9.70$, $p = .021$).

Between-group differences for variables with the potential to affect bone outcomes are detailed in Table 6.1. Significant differences were seen in vitamin D status and physical activity. Lower levels of serum 25(OH)D were seen at 20 year follow up (U = -2.90, p = .004), with a lower proportion of participants classified as LMC having sufficient vitamin D status (above 75nmol/L) at both time points (17 years: 44.5% vs 47.2%, $X^2 = 5.49$, p = .064; 20 years: 33.8% vs 45.8%, $X^2 = 11.44$, p = .003 respectively). Sex-specific analysis of height differences found that LMC males were significantly shorter at 17 year follow up compared to non-LMC (Md = 176.0cm [IQR: 171.4 to 182.1] compared to Md = 178.4 cm [IQR=174.1 to 183.4], U = -3.02, p = .003) with no significant difference at 20 year follow up. Puberty analysis showed a lower frequency of puberty category five (full maturity) at the age of 17 years for the LMC group (78.6% compared to 88.4%, $X^2 = 6.86$, p = .032). No significant differences were observed between motor competence groups on health measures that may have impacted physical activity (depression, anxiety, joint problems, back or neck pain, respiratory problems) or usage of potentially bone affecting medication such as hormonal contraceptives. The only significant difference in dietary intake was in alcohol consumption with individuals with LMC consuming less (7.2 g/day compared to 10.8 g/day, U = -3.13, p = .007). For physical activity variables, detailed in Table 6.2, the only significant differences found at the 17 year follow up were a lower level of moderate physical activity (Md = 15.0 compared to 30.0 in non-LMC, U = -2.03, p = .042) and lower frequency of moderate and vigorous physical activity engagement in the last week for the LMC group (42.4% and 33.5% respectively for LMC compared to 53.9% and 46.1% for non-LMC, $X^2 = 7.66$ and 4.48, p = .006 and .034). For the 20 year follow up visit the only significant difference in physical activity was a lower level of moderate physical activity (Md = 20.00 compared to 30.00, U = -2.02, p = .004) for individuals with LMC. Membership of sports clubs was lower by 9% for the LMC than the non-LMC group ($X^2 = 3.90$, p = .048), but there was no significant differences in exercise club or outdoor recreation club membership. Expanded information on demographic and physical activity differences are presented in Supp 6A, Appendix C, Table A1, with differences by gender in Tables A2 and A3.

Table 6.1

Participant Characteristics at 17 and 20 Years

	17 year				20 year			
	LMC *M (SD)* *[Md] {IQR}*	**Non-LMC** *M (SD)* *[Md] {IQR}*	**U**	**P**	**LMC** *M (SD)* *[Md] {IQR}*	**Non-LMC** *M (SD)* *[Md] {IQR}*	**U**	**P**
Participant characteristics								
Height (cm)	172.1 (8.7) [172.0] {166.4 to 178.0}	172.7 (8.9) [172.2] {165.8 to 178.9}	-0.61	.542	173.3 (9.0) [173.0] {167.0 to 180.0}	172.7 (9.4) [172.5] {165.4 to 179.7}	-1.00	.315
BMI (kg/m^2)	22.8 (4.4) [22.0] {19.8 to 24.6}	22.4 (3.7) [21.8] {20.0 to 23.9}	-0.5	.610	24.6 (5.0) [23.5] {21.2 to 26.6}	23.9 (4.3) [23.2] {21.0 to 25.7}	-1.55	.121
Total number of injuries	0.6 (1.0) [0.0] {0.0 to 1.0}	0.7 (1.3) [0.0] {0.0 to 1.0}	-1.66	.097	0.4 (0.8) [0.0] {0.0 to 1.0}	0.5 (0.8) [0.0] {0.0 to 1.0}	-0.85	.394
Total fat mass (kg)					21.2 (10.5) [19.7] {12.5 to 28.0}	20.4 (9.7) [18.7] {13.3 to 25.3}	-0.73	.467
Total lean mass (kg)					46.7 (1.2) [47.8] {37.0 to 55.4}	46.2 (11.7) [44.0] {35.8 to 56.4}	-0.47	.639
Vitamin levels								
Deseasonalised 25(OH)D3 (nmol/L)	73.0 (26.1) [71.0] {55.4 to 86.3}	75.8 (24.8) [73.6] {58.7 to 89.3}	-1.64	.100	70.1 (24.6) [68.3] {53.2 to 81.9}	74.6 (23.2) [72.7] {58.7 to 88.5}	-2.90	.004
Dietary intake								
Protein (g/day)					106.0 (81.1) [88.4] {67.6 to 121.1}	103.6 (59.1) [92.2] {66.5 to 124.0}	-0.43	.670
Calcium (mg/day)					947.2 (488.1) [842.2] {647.9 to 1147.0}	912.0 (396.0) [850.0] {638.1 to 1098.1}	-0.07	.948
Alcohol (g/day)					15.5 (19.8) [7.2] {1.6 to 23.4}	17.7 (19.1) [10.8] {3.8 to 24.5}	-3.13	.002

	17 year				20 year			
	%	%	X^2	P	%	%	X^2	P
Health								
Diagnosis	29.4	28.9	1.1	.787	19.0	17.0	1.5	.693
Asthma	8.5	11.0	2.9	.412	11.7	13.1	0.8	.859
Back pain	4.2	5.5	1.1	.798	4.8	6.0	3.9	.273
Neck pain	7.5	3.2	10.0	**.019**	5.2	3.7	2.5	.478
Attentional problems	38.3	44.7	2.6	.106	29.2	32.9	1.0	.320
Any accidents or injury since last follow up	29.4	28.9	1.1	.787	19.0	17.0	1.5	.693
Medication use								
Any prescription medication use in last 6 months	50.2	55.9	2.1	.149	52.1	58.1	2.3	.127
Oral contraceptives	22.7	32.5	3.9	.146	41.7	47.8	2.5	.282
Roaccutane	1.0	3.6	2.2	.326	1.9	3.2	1.8	.411
Other medication	7.3	2.5	6.8	**.034**	4.7	5.0	0.4	.828
Any non-prescription medication use in the last 6 months	72.5	73.2	0.0	.847	28.3	20.8	5.1	**.023**
Antacids	0.0	0.4	0.7	.724	0.0	0.4	0.6	.743
Vitamins	23.6	31.8	3.8	.148	5.3	10.2	3.4	.186

Note: LMC=Low motor competence. M=Mean, SD=Standard deviation, Md=Median, U=Mann Whitney U standardised score.

Table 6.2

Physical Activity Differences Based Upon LMC Status

	17 year				20 year			
	LMC *M (SD)* *[Md] {IQR}*	**Non-LMC** *M (SD)* *[Md] {IQR}*	**U**	**P**	**LMC** *M (SD)* *[Md] {IQR}*	**Non-LMC** *M (SD)* *[Md] {IQR}*	**U**	**P**
Physical activity								
Walking *(min/day)*	65.5 (69.8) [30.0] {0.0 to 120.0}	60.0 (63.1) [30.0] {10.0 to 120.0}	-0.28	.782	83.4 (68.6) [60.0] {25.0 to 180.0}	73.8 (62.3) [60.0] {30.0 to 120.0}	-1.13	.257
Moderate activity *(min/day)*	44.3 (60.2) [15.0] {0.0 to 60.0}	53.3 (64.3) [30.0] {0.0 to 87.5}	-2.03	**.042**	50.6 (61.9) [20.0] {0.0 to 75.0}	60.2 (65.2) [30.0] {0.0 to 120.0}	-2.02	**.044**
Vigorous activity} *(min/day)*	53.4 (64.1) [30.0] {0.0 to 90.0}	58.6 (60.6) [45.0] {0.0 to 90.0}	-1.71	.088	59.7 (64.9) [42.5] {0.0 to 120.0}	62.4 (60.6) [60.0] {0.0 to 90.0}	-1.02	.306
IPAQ total score *(METs/wk)*	4229.1 (4434.3) [2467.0] {1078.5 to 6168.0}	4302.0 (4051.6) [3099.0] {1593.0 to 5514.0}	-1.73	.079	3536.9 (4200.4) [2125.5] {560.0 to 4320.0}	3644.6 (3623.4) [2520.0] {933.0 to 5040.0}	-1.69	.092
Loading score *(ELR/wk)*	148.7 (176.9) [71.4] {4.40 to 238.9}	157.4 (154.9) [113.5] {17.6 to 248.3}	-1.83	.067	159.7 (140.7) [139.2] {15.6 to 276.5}	170.5 (133.7) [166.2] {56.2 to 275.0}	-1.33	.185
Sedentary behaviour *(min/day)*	1820.8 (385.5) [1800.0] {1530.0 to 2040.0}	1820.8 (370.1) [1800.0] {1620.0 to 2040.0}	-0.98	.326				
Pedometer total *(steps/day)*	9564.3 (3192.5) [9303.0] {7002.0 to 12078.8}	9771.6 (3893.9) [9717.9) {7063.0 to 11528.3}	-0.16	.876				

	17 year				20 year			
	%	**%**	**X^2**	**P**	**%**	**%**	**X^2**	**P**
Performed moderate activity for leisure	33.5	42.1	4.48	**.034**				
Performed vigorous activity for leisure	42.4	53.9	7.66	**.006**				
Sports club membership	21.3	30.3	3.90	**.048**				
Exercise club membership	13.4	15.5	0.34	.560				
Outdoor recreation club membership	14.2	12.8	0.15	.696				

Note: LMC=Low motor competence. METS=Metabolic equivalent of tasks. ELR=Effective loading rating. M=Mean, SD=Standard deviation, Md=Median, U=Mann Whitney U standardised score.

6.3.2 Differences in Bone Measures by Motor Competence Status

Between group difference tests on bone measurements showed significantly lower bone measures for males with LMC. No significant differences were seen in females, except for the preferred arm with a deficit of 0.021 g/cm^2 for LMC females compared to non-LMC (U = -2.33, p = .020) (Table 6.3). Between group difference tests did not show an increased frequency of fractures for individuals with LMC (p = .903). In the whole sample, when controlling for sex, age, BMI, vitamin D status, and bone loading, LMC status showed a significant estimate of effect for all measured regions except the head (Supp 6B, Appendix C, Table B1). Simple models, controlling only for the effects of age, sex, and BMI showed a larger regression β co-efficient than were seen when vitamin D status and bone loading were also controlled for, except in the models for the head and non-preferred leg (Supp 6B, Appendix C, Table B2). The relationship was such that individuals with LMC had lower BMD at these regions compared to non-LMC individuals, that would be equivalent to a 0.024 g/cm^2 difference for a whole-body BMD between LMC and non-LMC males. Additional models controlling for the lean mass showed a significant estimate of effect only for the preferred arm and non-preferred leg (Supp 6B, Appendix C, Table B3) while models controlling for puberty did not impact on the findings for LMC status (Supp 6B, Appendix C, Table B4).

Table 6.3

Unadjusted Between Group Differences for Dual-Energy X-ray Absorptiometry Measures

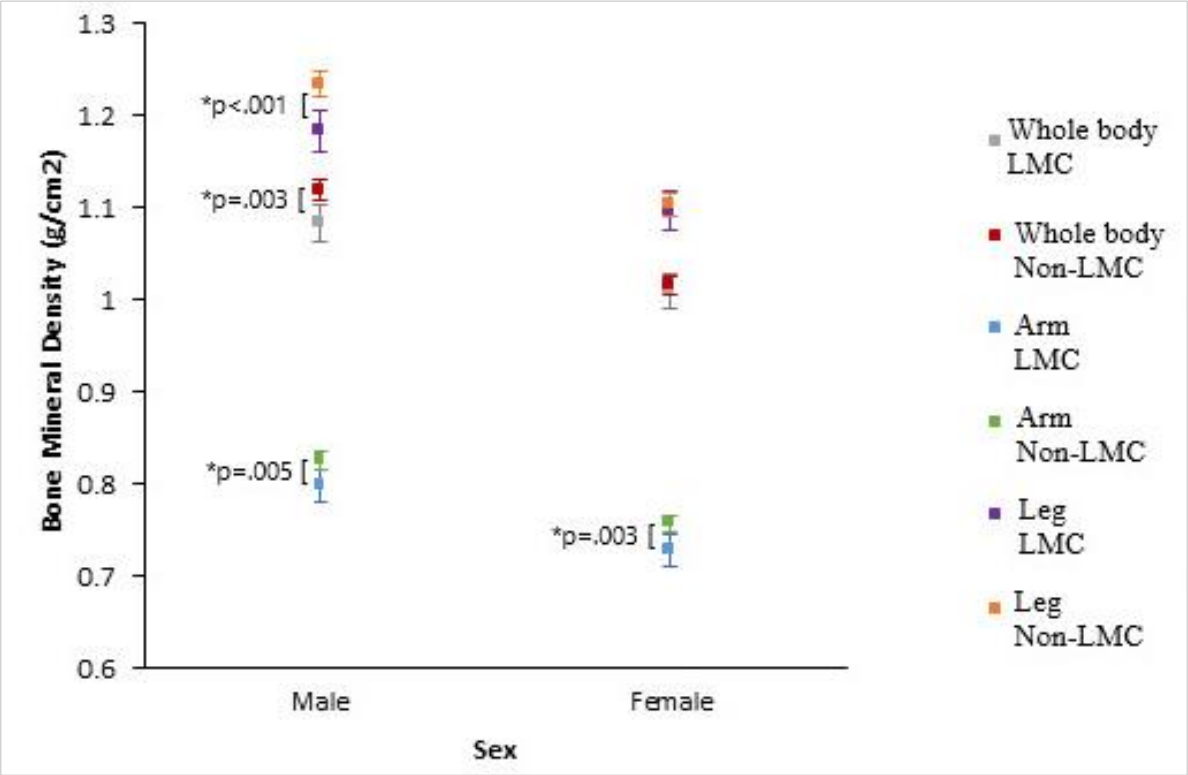
	Male				Female			
	LMC (n=166) *M (SD)* *[Md] {IQR}*	**Non-LMC (n=393)** *M (SD)* *[Md] {IQR}*	**U**	**P**	**LMC (n=106)** *M (SD)* *[Md] {IQR}*	**Non-LMC (n=378)** *M (SD)* *[Md] {IQR}*	**U**	**P**
Bone mineral density (g/cm2)								
Total body	1.0987 (0.112) [1.090] {1.009 to 1.159}	1.126 (0.102) [1.123] {1.056 to 1.192}	-3.29	**.001**	1.008 (0.071) [1.004] {0.964 to 1.058}	1.015 (0.08) [1.013] {0.961 to 1.068}	-0.746	.455
Head	1.756 (0.218) [1.788] {1.629 to 1.922}	1.795 (0.216) [1.768] {1.643 to 1.939}	-0.01	.995	1.798 (0.230) [1.750] {1.626 to 1.974}	1.784 (0.205) [1.772] {1.639 to 1.909}	-0.143	.887
Pelvis	1.191 (0.165) [1.181] {1.089 to 1.291}	1.235 (0.158) [1.226] {1.127 to 1.335}	-3.04	**.002**	1.063 (0.131) [1.070] {1.000 to 1.158}	1.078 (0.119) [1.067] {1.008 to 1.156}	-0.535	.592
Preferred leg	1.194 (0.150) [1.191] {1.096 to 1.282}	1.237 (0.131) [1.237] {1.148 to 1.331}	-3.22	**.001**	1.098 (0.102) [1.090] {1.025 to 1.168}	1.102 (0.100) [1.099] {1.035 to 1.159}	-0.622	.534
Non-preferred leg	1.200 (0.145) [1.210] {1.100 to 1.290}	1.241 (0.134) [1.240] {1.140 to 1.330}	-3.04	**.002**	1.106 (0.097) [1.090] {1.028 to 1.160}	1.099 (0.099) [1.100] {1.030 to 1.160}	-0.205	.837
Preferred arm	0.807 (0.113) [0.817] {0.728 to 0.881}	0.837 (0.095) [0.830] {0.771 to 0.899}	-2.44	**.015**	0.733 (0.069) [0.734] {0.686 to 0.777}	0.754 (0.076) [0.755] {0.709 to 0.798}	-2.326	**.020**
Non-preferred arm	0.791 (0.106) [0.800] {0.715 to 0.865}	0.816 (0.091) [0.820] {0.750 to 0.880}	-2.30	**.021**	0.737 (0.063) [0.740] {0.690 to 0.780}	0.747 (0.075) [0.750] {0.700 to 0.790}	-1.399	.162
Bone mineral density (g/cm2)								
Total body	1.0987 (0.112) [1.090] {1.009 to 1.159}	1.126 (0.102) [1.123] {1.056 to 1.192}	-3.29	**.001**	1.008 (0.071) [1.004] {0.964 to 1.058}	1.015 (0.08) [1.013] {0.961 to 1.068}	-0.746	.455
Head	1.756 (0.218) [1.788] {1.629 to 1.922}	1.795 (0.216) [1.768] {1.643 to 1.939}	-0.01	.995	1.798 (0.230) [1.750] {1.626 to 1.974}	1.784 (0.205) [1.772] {1.639 to 1.909}	-0.143	.887

NOTE: LMC = Low Motor Competence. M=Mean, SD=Standard Deviation, Md=Median, U=Mann-Whitney U standardised score. Whole group characteristics are described in Supp 6B, Appendix C, Table D1.

Models including a LMC by sex interaction showed a significant estimate of effect for the LMC by sex interaction in the models for the legs only (Supp 6B, Appendix C, Table B5). Examination of estimated marginal means indicate that differences in scores by LMC status were confined to males. This effect was particularly noticeable in BMD for the whole body, pelvis, and both legs (Figure 6.2). This relationship was not seen for the non-bone loading site of the head. Analysis where models were split by sex showed that LMC had a significant estimate of effect in males for whole body BMD ($p = .003$), pelvis BMD ($p = .005$), preferred ($p < .001$) and non-preferred leg BMD ($p < .001$), and preferred ($p = .005$) and non-preferred arm BMD ($p = .015$) similar to what was demonstrated in the whole group model (Supp 6C, Appendix C, Table C1). However, this was not demonstrated in the models for females (Supp 6C, Appendix C, Table C2). Using the male only model, the deficit in whole-body BMD in LMC males is equivalent to a 0.033 g/cm^2 deficit when compared to typically developing males. For females, the only model in which LMC showed a significant estimate of effect was for the right arm ($p = .003$). Puberty status did not affect these results (Supp 6C, Appendix C, Tables C3 and C4). Models controlling for lean mass, however, showed a significant effect for DCD status on BMD was confined to the pelvis and leg models (Supp 6C, Appendix C, Tables C5 and C6).

Figure 6.2

Estimated Marginal Means for Bone Mineral Density by Sex and Motor Competence Status



LMC= Low Motor Competence. Covariates appearing in the model are fixed at: BMI=23.77, age=19.95 years, loading score=153.96 ELR/wk, serum 25-hydroxyvitamin D=74.33 nmol/L. Leg and arm are preferred side measurements. Interaction effect is non-significant, except for leg (p = .026). Differences are significant for whole body for males (p = .003), leg for males (p < .001), arm for males (p = .005) and females (p = .003).

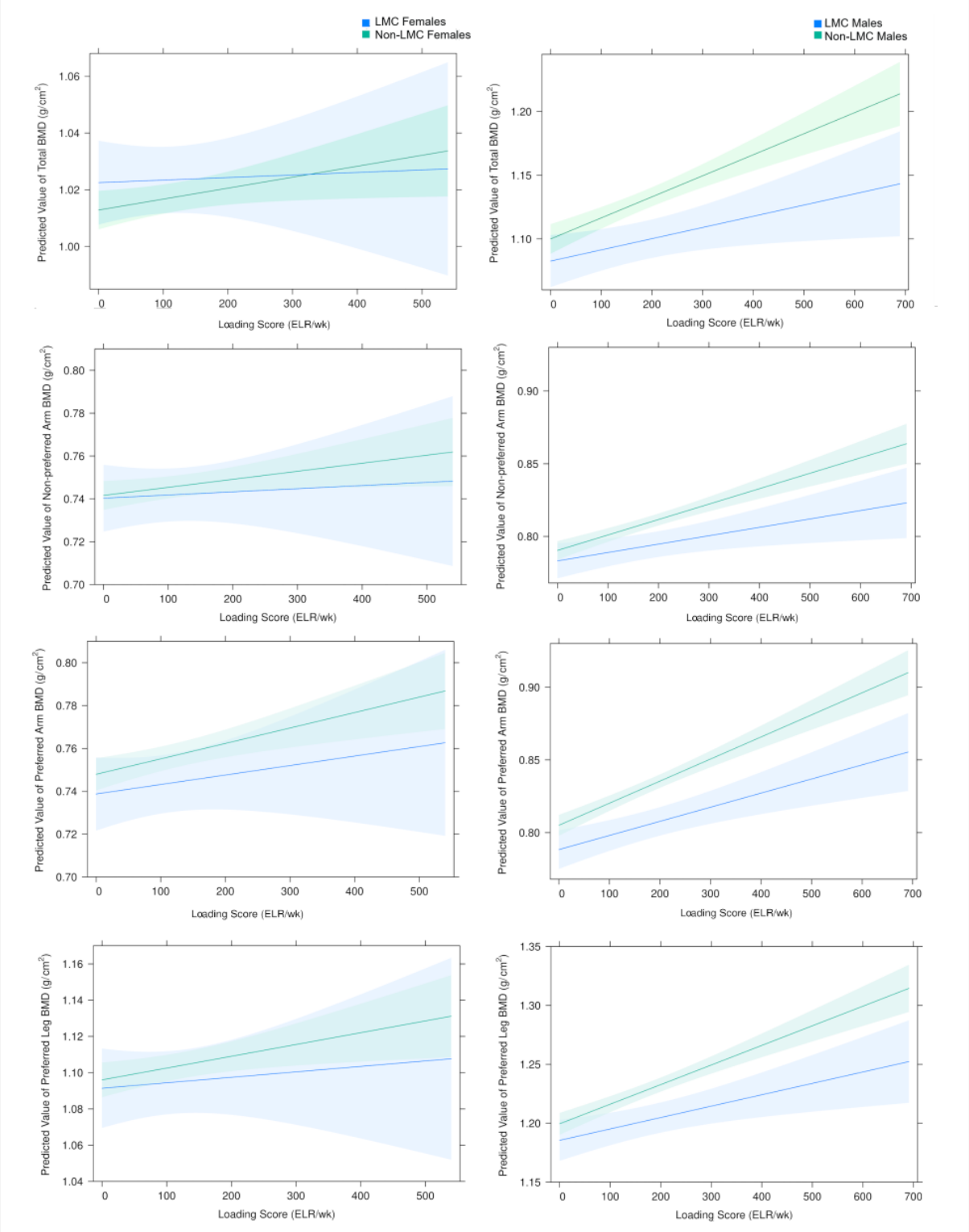
6.3.3 Association Between Physical Activity and BMD

Loading score showed a significant estimate of effect within the models for total BMD (p = .001), pelvis BMD (p < .001), and BMD at the preferred (p = .002) and non-preferred legs (p < .001), and preferred (p < .001) and non-preferred arms (p = .008). This relationship was such that a LMC female with mean characteristics but a loading score at the 25th percentile would have a whole body BMD 0.020 g/cm^2 lower than would be seen in a female with the same characteristics but a loading score at the 75th percentile. Models for sedentary behaviour (Supp 6B, Appendix C, Tables B6, B7 and B8) did not show a significant estimate of effect for sedentary behaviour for the whole group, however β coefficients for LMC status were similar to that seen in the loading models.

The models for BMD in the whole body, pelvis, legs, and arms show an increase in BMD as loading levels increase for all groups, except for females with LMC, who show no increase in the pelvis and a decrease with increased loading in the arms. Graphs depicting the impact of loading on BMD outcomes, detailed in Figure 6.3, showed a differing effect by LMC status and sex. More variability can be seen in females as a group compared to males. More variability is also present for males with LMC than typically developing males. In spite of differences by loading scores, males without LMC had significantly higher BMD than those with LMC, a difference which was not seen in females. Although a sharper increase in BMD with increased loading can be seen for the non-LMC group of both sexes than is seen in the LMC group, the difference based on LMC status is smaller than if observed by sex. Models designed to verify these results by including a LMC by loading interaction effect found no significant contribution from this variable (Supp 6B, Appendix C, Table B9) with gender specific models in Supp 6C, Appendix C, Tables C7 and C8.

Figure 6.3

Relationship Between Bone Loading Score and Bone Mineral Density (BMD) by Gender and Developmental Coordination Disorder (DCD) Status



Models are adjusted for age, BMI, and vitamin D status. All relationships are of a linear nature (p for non-linearity >.050). For visual simplicity the x-axis for each group was truncated at 3 standard deviations. The shaded area represents 95% confidence intervals. BMD=Bone mineral density.

Furthermore, although the models for males showed a significant estimate of effect for loading for BMD for the whole body (p = .011), pelvis (p = .005), preferred (p = .015) and non-preferred leg (p = .012), and preferred (p < .001) and non-preferred arm (p = .039), loading did not show an estimate of effect for females. In models where lean mass was controlled for loading scores were no longer significant for the nonpreferred arm. Models for sedentary behaviour showed a significant estimate of effect in the preferred arm for males (p = .001) (Supp 6C, Appendix C, Table C9), and pelvis for females (p = .027) (Supp 6C, Appendix C, Table C10) which was unaffected by puberty (Supp 6C, Appendix C, Tables C11 and C12) and lean mass (Supp 6C, Appendix C, Tables C13 and C14). These effects were such that BMD decreased in males with increasing sedentary time but increased for females.

6.4 Discussion

Our results indicated LMC status was associated with decreased BMD in load-bearing bone sites for males only, possibly due to differences in physical activity engagement between the sexes through-out childhood and adolescence. This was even beyond the physical activity contribution in late adolescence that was adjusted for in analyses (Chivers et al., 2019; Jenkins et al., 2018). Nevertheless, these differences continued to be present after adjustment for BMI, vitamin D status, physical activity levels and puberty status at age 17. For females, an association between LMC and BMD was only shown in the preferred arm. Physical activity's impact was also sex dependent, with a stronger influence from increased loading found in males than females and a larger difference present based on LMC status for males.

6.4.1 Bone Health Differences

Our findings of a gender difference in the association between bone and loading support the findings of Chivers et al. (2019) in adolescents (n=39, M_{age}=14.4) showing bone deficits by peripheral quantitative computed tomography (pQCT) were isolated to males. As the Chivers et al. (2019) study indicated, differences in bone quality were unable to be determined by the current study, therefore the combined findings of these studies indicate that LMC status is not associated with bone health in females but impedes multiple areas of bone health in males. By contrast, Ireland et al. (2016) reported a deficit in hip BMD for females with LMC compared to their non-LMC counterparts, although smaller than the deficit seen in males. Ireland et al. (2016)

also reported a decreased level of bone loading based upon LMC status, not demonstrated in the current study, which may have impacted upon bone health levels. Additionally, a potential reason for this discrepancy is environmental differences between the United Kingdom and Australia (Kimlin et al., 2007) which may have affected bone health, via physical activity engagement and vitamin D levels with about 20% less participants having sufficient vitamin D in the Ireland et al. (2016) study cohort than in the current study (Holick, 2007; Tolppanen, Fraser, Fraser, & Lawlor, 2012). Most importantly however, participants in the current study were approximately two years older than the participants in Ireland et al. (2016)'s study and additional bone mass is likely to have been attained over this time (Matkovic et al., 1994). Participants in the current cohort ranged in age from 19.1 to 21.8 years and were likely to be at or very close to peak bone mass with little additional bone mass accumulation expected. As such, this finding indicates that although females no longer show bone health deficits when peak bone mass is accrued, males show a continued deficit with potential for future health implications, particularly fractures.

Males with LMC may be at increased risk of fracture given their lower bone density, the higher occurrence of fractures in males (Alswat, 2017; Jenkins et al., 2018), and potentially a higher risk of injury due to their poor motor skills (Hands, Chivers, et al., 2015). A systematic review has indicated the potential for an increased fracture rate (odds ratio 3.1 to 8.3 for lifetime fracture risk) in adolescents with LMC but sex-specific fracture risks are not known (J Tan, Murphy, et al., 2022). The current study, however, found that there was not a higher frequency of fracture or other injuries for the LMC group than non-LMC. Differences in fracture rates could be due to the form or intensity of physical activity being engaged in, as higher levels of physical activity engagement have been reported to increase fracture risk (D Ma et al., 2004; Weaver et al., 2016). Although similar levels of physical activity were reported for the LMC and non-LMC group, participants with LMC were less likely to be participating in competitive sports which may have reduced their fracture risk. An altered physical activity pattern has been reported in other studies on LMC populations with lower intensity in activity participation (Scott-Roberts & Purcell, 2018; Tsang et al., 2012), and reduced diversity (Jarus et al., 2011). Adults with LMC have also reported adjusting their behaviour in order to reduce exposure to injury risks, such as avoiding slopes and stairs (Scott-Roberts & Purcell, 2018). The presence of similar behaviour

in this cohort might explain vitamin D and lean mass differences between the groups, for example less activity in outdoor spaces due to the presence of natural hazards (Drenowatz, 2021). Although differences remained for males after serum 25OHD was controlled for, vitamin D ceased to be significant in many models when lean mass was controlled for. This may indicate differences in activity are beyond the effects of vitamin D differences. Such differences in behaviour if present in this cohort may have reduced the risk of fracture and require further examination.

6.4.2 Physical Activity Differences and Relationship to Bone Health

The presence of differences in the relationship between loading and bone were demonstrated by sex and LMC status, with only males showing increases in BMD with loading in all regions (barring the head). This supports the findings of Chivers et al. (2019) that showed a sex by LMC status effect for upper body muscle density and subcutaneous fat, likely reflecting physical activity engagement. Although, a differing relationship between physical activity and bone outcomes by sex has been reported (Bland et al., 2020), differences in the response to loading by sex and LMC status indicate that differences in the type or form of physical activity participated in may also be a factor. Bone is most responsive to dynamic loads, of at least moderate magnitude, short duration, differing load direction, and which are applied quickly (Weaver et al., 2016). Individuals with LMC have slow, inefficient movements of reduced quality (Blank et al., 2012) and as such, activities may not provide enough stimulus to trigger bone adaptation (Beck & Snow, 2003; Hart et al., 2020; Hart, Nimphius, et al., 2017), resulting in a reduced bone response to loading activities. The significant difference in lean mass between groups as well as the loss of significant estimate of effect for the impact of loading when lean mass was accounted for may reflect on these physical activity differences. Differences in movement quality have previously been suggested as a potential reason for reduced bone benefit from an exercise intervention as motor impairment increased (J Tan et al., 2020). Unpublished data have also shown that improvements in physical fitness measures as a result of an exercise intervention (Hands et al., 2018) were strongly influenced by motor impairment levels indicating a quality of movement effect. Further support for the role of movement quality on bone outcomes may be seen via the differing change rate in health markers to physical activity in individuals with LMC. For example, BMI in

young adults with LMC changes at a much slower rate with increasing activity than is seen in young adults who do not have LMC (J Tan, Ylä-Kojola, et al., 2022) .

An examination of sedentary behaviour indicated a potential explanation for some of the previously unaccounted for bone variation in females. Sedentary behaviour has been previously shown to have an independent role on bone, outside of that seen from loading, thereby reinforcing the importance of other measures of physical activity than bone loading on bone health differences in a LMC population. These findings indicate that further research is needed as to the cause for bone health differences in individuals with LMC.

6.4.3 Strengths and Limitations

Strengths of this study include the use of longitudinal data from the Raine Study, a large cohort study allowing for the effects of multiple different factors upon bone to be examined. As bone reflects activity throughout life, the use of longitudinal measures strengthens the ability to determine the effects of LMC on bone as there has been sufficient time for the bone to respond to physical activity variation. The consideration of a number of established factors capable of affecting BMD further strengthens the study. The use of self-reported physical activity assessment via self-report rather than device assessment had the potential to overestimate activity levels (Baerg et al., 2011), however device assessment on group differences in physical activity indicates this is not the case. The findings of the study are limited to the particulars of the population being measured and may not be generalisable to other populations. In particular, the rate of LMC detected in this population is much higher than general population rates. A low motor competence score and associated increased rate of LMC has been previously established in this cohort (Hands et al., 2013) and may be a reflection of population differences between a Western Australian population and that of North America where the test was devised in 1982. It is noted that this test has not been validated in an Australian population. Furthermore, differences in puberty rates may have impacted upon MAND results given that lower motor competence scores are known to be associated with a slower rate of biological maturity (Drenowatz & Greier, 2019). The use of motor competence measurements from early in the lifespan prior to when pubertal effects are present helps to counter this concern with the majority of participants having their motor competence assessed at the age of 10 years.

6.4.4 Conclusion

Our study demonstrates that bone health differences in children and adolescents with LMC are present in males with LMC in early adulthood. Differences in the effect of habitual bone loading upon BMD impacts upon these sex-specific associations, however, an independent role of LMC above that from loading in late adolescence can be seen to be present. This indicates other potential causations and may indicate that movement quality is a potential cause for bone health deficits in individuals with LMC. The continuance of bone health differences into young adulthood, indicates that such bone deficits are likely to be lifelong and this population may be at increased risk of osteoporosis and osteoporotic fractures. Further research is required into potential implications as well as the effects of movement quality and execution and other physical activity variables on bone health in this group.

Chapter 7

Discussion and Conclusion

This chapter provides a synthesis of the research presented in this thesis. The summary of findings outlines the key contributions from each study as related to the overarching research aims, objectives, and hypothesis and then discussed using the LCHD Framework with emerging themes presented. Finally, the strengths and limitations of the overall research project are summarised.

7.1 Summary of Findings

7.1.1 Research Objective 1

To examine bone development into early adulthood in individuals with DCD, to determine whether a bone deficit exists.

Research Question 1:
Does DCD Status Impact Upon Bone Health in Adolescence and Adulthood?

Bone deficits were present in individuals with DCD until at least the time of peak bone mass. As deficits observed at the time of peak bone mass are likely to continue throughout adulthood and bone deficits have been reported in multiple DCD populations into at least late adolescence (Chapter 2, (J Tan, Murphy, et al., 2022)), a lifetime deficit in bone health can be considered likely to be present in individuals with DCD. This deficit may be limited to males, with females having similar bone mass to their typically developing peers.

Hypothesis

H1: Bone detriments will be present in individuals with DCD and LMC up until at least the time of peak bone mass. *Partially accepted.*

H2: The nature of bone detriments in individuals with DCD and LMC will reflect a lower level of engagement in physical activity. *Accepted*

H3: Individuals with DCD who engage in a structured exercise intervention will show improvements in bone health. *Accepted*

Research Question 1.1.
What is the Current Evidence on the Relationship Between Bone Health and DCD?

A systematic review indicated individuals with DCD present with a bone deficit that is one to two standard deviations below that of a typically developing group or normative data for the population (Chapter 2, (J Tan, Murphy, et al., 2022)). This assessment had low confidence due to the level of evidence available, particularly the small sample size, and heterogeneity in methods of bone measurements and DCD assessment. Studies on bone health in DCD are largely cross-sectional and given that motor competence can vary over time the direction of effect was unable to be determined. Evidence from several studies in childhood showed delays in skeletal age and a deficit in bone mineral content compared to typical development. Studies in adolescence demonstrated deficits on multiple measures of bone architecture and density for the DCD group compared to population norms and typical development. However, studies in adolescence were limited to only two cohorts. There was only one study providing evidence of bone health detriments in adulthood, using a small cross-sectional design which captured bone health in middle adulthood. Combined, the evidence indicates the presence of a detriment throughout childhood and adolescence which may continue into adulthood. As studies have been performed on both density and architecture measures, a complete picture can be seen as to bone vulnerability in this population. Although it appears these detriments continue into adulthood, there is no evidence as to bone health detriments at the time of peak bone mass (Chapter 2, (J Tan, Murphy, et al., 2022)). This review confirmed our hypothesis that current evidence was limited to early in the lifespan with a need for additional information at the time of peak bone mass.

Research Question 1.2.
What is the Incidence of Impaired Bone Health in a Population with DCD?

The systematic review confirmed evidence for an increased incidence of impaired bone health in a population with DCD. However, rates of bone impairment were unable to be determined due to heterogeneity between studies (Chapter 2,(J Tan, Murphy, et al., 2022)). Individual studies in a childhood population reported a bone health detriment in between 50 to 66% of DCD participants. There was also an increased risk of fracture, with a risk ratio from adolescent studies in the whole body

of between 3.1 (95% CI 1.2 to 7.9) (Hands, Chivers, et al., 2015) and 8.3 (95% CI 1.0 to 70.5) (Hellgren et al., 1993). The presence of an impairment in bone health was verified to be present in 75% of reported studies, with the remaining studies having neutral findings. Bone health detriments compared to a typical population were present in all age groups reported: 75% of childhood studies; 80% of adolescent studies; and in the only adult population study. As such, the hypothesis of an increased incidence of impaired bone health in a DCD population was confirmed, although it was not possible to determine incidence rates.

Research Question 1.3.
What is the Extent of Impairment in Bone Health in a Population with DCD?

The systematic review (Chapter 2, (J Tan, Murphy, et al., 2022)) indicated that when present, bone health impairments for the DCD group were between one and two standard deviations below comparator groups or age appropriate norms. Impairments in architecture in the form of deficits in cortical area and stress strain index of 1.7 and 0.7 standard deviations below population norms were further confirmed in an adolescent sample (Chapter 5, (J Tan et al., 2020)). Such a deficit is at the level of osteopenia but not at a level that would be considered clinically osteoporotic (World Health Organization, 1994). The study in young adults however found significant deficits were confined to males and were smaller than deficits reported in childhood and adolescence, with the deficit being less than one standard deviation below that of typically developing individuals (Chapter 6). As such, the hypothesis of an osteopenic level of bone health impairment is confirmed in childhood and adolescence but not in adulthood. Bone health impairments in adulthood may be at a subclinical level, although any deficit in bone health on a population level is associated with an early onset of osteoporosis and osteoporotic fracture.

Research Question 1.4.
What Bone Material, Structure, and Strength Adaptations (Measured by Peripheral Quantitative Computed Tomography) Occur in Adolescents with DCD Participating in a Supervised Exercise Program?

Adolescents with DCD participating in a 13 week exercise program showed improvements in their tibial bone parameters compared to baseline measures (Chapter 5, (J Tan et al., 2020)). These improvements indicated a shift from a detrimental bone

phenotype at baseline, towards a healthier bone phenotype following the intervention. Changes in bone phenotype were through bone material and bone structural changes with bone mass and cortical area increasing prior to statistical adjustment for fitness improvements. Participants who were engaging in the intervention for the first time also showed significant gains in bone strength with improvements in the stress strain index and fracture load across anterior-posterior and mediolateral loading axes when controlling for other variables affecting bone health. Improvements in fitness positively impacted upon the amount of improvement shown on these variables as well as other bone health measures such as cortical density and bone area. Hence adolescents bone measures can be improved by participating in an exercise intervention program.

Research Question 1.5.
Do Young Adults with DCD Show an Impairment in Bone Health at the Time of Peak Bone Mass Compared to their Typically Developing Peers?

Investigation of bone health in young adults with DCD compared to typically developing young adults showed that bone health impairments, as represented by BMD at the time of peak bone mass, were present only in males. Females with DCD showed no detriment at the time of peak bone mass compared to typically developing females. Accordingly, the hypothesis of a continued detriment in bone was confirmed only in males.

Research Question 1.6.
Is There a Relationship Between Engagement in Physical Activity and Bone Health Impairments in Individuals with DCD Compared to their Typically Developing Peers?

The location of bone deficits in individuals with DCD were indictive of reduced loading from changes in physical activity. At the time of peak bone mass, bone deficits for males with DCD were present at all weight bearing sites but were not present at the non-weight bearing site of the head (Chapter 6). This finding is reinforced by the systematic review where more deficits were present at weight bearing sites, particularly the tibia and hip, than in non-weight bearing sites, such as the fibula and ulna (Chapter 2, (J Tan, Murphy, et al., 2022)). Additionally, studies that used bone architecture evaluations found more deficits in bone traits responsive to loading, such as cortical area. As such, the location of deficits is indicative of bone impairments being at least partially due to loading from physical activity.

Furthermore, the findings from the Raine Cohort Study (Chapter 6, (J Tan et al., In press)) indicate a relationship between physical activity engagement and bone health impairments by motor competence status which was sex specific. In this study, a differing estimate of effect from loading from physical activity at the age of 17 years upon bone at 20 years by motor competence status was seen only for males (Chapter 6, (J Tan et al., In press)). Graphs of the relationship between loading and BMD showed males with LMC had a smaller BMD increase with increasing loading than was seen in males without LMC. An additional role for other aspects of physical activity such as sedentary behaviour and movement quality should also be considered as differences in bone health in individuals with LMC indicate a role for physical activity beyond that of loading (Chapter 6, (J Tan et al., In press)). As such, the hypothesis that there would be a relationship between physical activity and bone health impairments was confirmed but requires further investigation.

7.1.2 Research Objective 2

To examine the role of motor competence, as well as specific motor impairments on highly osteogenic physical activity to disentangle the role of physical activity on bone deficits in individuals with DCD.

Research Question 2:
What is the Relationship Between DCD and Osteogenic Physical Activity?

This thesis determined that DCD risk status was associated with deficits in physical activity across the lifespan from childhood through to early adulthood compared to typically developing individuals. The lower physical activity associated with DCD was also found to be influenced by other factors such as individual motor skills (Chapter 3), degree of motor impairment (Chapter 5 (J Tan et al., 2020)), and visuomotor impairment (Chapter 4 (J Tan, Ylä-Kojola, et al., 2022)). Findings however indicate the presence of a role of physical activity upon bone health differences beyond that of specifically osteogenic activity (Chapter 6, (J Tan et al., In press)).

Hypothesis.

H1: Engagement in specific highly osteogenic physical activity will be lower in individuals with DCD. These differences will be present from childhood through to early adulthood. *Rejected***.**

H2: Reduced osteogenic physical activity will be dependent upon individual factors, including the extent of motor impairment, the nature of motor impairment (i.e., the skills that are impaired) and the presence of other conditions. *Accepted***.**

Research Question 2.1.
Is There a Reduction in Osteogenic Physical Activity in Children with DCD Compared to Their Typically Developing Peers?

Children with DCD did not show a reduction in osteogenic physical activity at a mean age of 8.9 years, or on any physical activity variable compared to typically developing children (Chapter 3). Although it did not reach statistical significance, a lower number of medium and high impact peaks for boys at risk of DCD was seen compared to typically developing boys (Chapter 3). Differences in MVPA may be present in adolescence with a lower frequency of sports club membership and engagement in MVPA compared to typically developing peers (Chapter 6, (J Tan et al., In press)). However, these differences are not necessary specifically osteogenic (Chapter 6, (J Tan et al., In press)). As such, although there are some indicators of physical activity differences which warrant further investigation, the hypothesis of a reduction in osteogenic physical activity was not confirmed by this research work.

Research Question 2.2.
Is There a Reduction in Physical Activity in Adults with DCD Compared to Their Typically Developing Peers?

Adults with DCD from Finnish and Australian populations showed physical activity differences when compared to typically developing individuals (Chapter 4 (J Tan, Ylä-Kojola, et al., 2022), and Chapter 6, (J Tan et al., In press)). Australian adults with DCD reported lower frequency of participation in moderate physical activity at 20 years of age compared to typically developing adults (Chapter 6, J Tan et al. (In press)). A lower number of steps and lower sedentary light physical activity, as well as a lower vigorous physical activity via an interaction between DCD status and BMI, was also observed in accelerometry of Finnish adults with DCD compared to adults without DCD (Chapter 4, (J Tan, Ylä-Kojola, et al., 2022)). Combined these findings indicate a negative physical activity pattern in individuals with DCD and confirms the hypothesis of a reduction in physical activity in adults with DCD.

Research Question 2.3.
Are Physical Activity Differences in Individuals with DCD, Seen When Compared to Their Typically Developing Peers, Impacted by the Presence of Specific Motor Skill Impairments or the Presence of VMI Impairment?

This thesis suggests the effect of DCD on physical activity is likely to be influenced by co-occurrent impairments, including specific motor skill impairment. Impairment in locomotor and/or balance skills continued to show an estimate of effect of lower osteogenic physical activity even after controlling for DCD risk (Chapter 3). Accounting for variation in motor skills in children did not affect the role of DCD status, however, controlling for DCD status did reduce the role of some motor skills upon physical activity levels (Chapter 3). These findings indicate that overall motor impairment and planning issues impact upon physical activity such that the effect of reduced performance on individual motor skills is not seen. This may indicate that individuals with DCD with impaired locomotor or balance skills are particularly vulnerable to lower osteogenic activity. Additionally, individuals with DCD had a varying response to an exercise intervention depending on the degree of motor impairment, with higher bone gains seen for those who were experienced in performing the exercises within the program (Chapter 5, (J Tan et al., 2020)). Combined with the small change in muscle seen in this group (Chapter 5, (J Tan et al., 2020)) this may indicate a reduced impact on bone from exercise interventions than would be seen in a typically developing population. Such a reduction is potentially due to reduced movement quality as evidenced by lower bone health gains in individuals with high motor impairment and higher bone gains as individuals become more experienced in performing the intervention exercises. Evidence in adults showed that VMI impairment increased the role of DCD on physical activity detriments for sedentary light activity, moderate activity and MVPA (Chapter 4, (J Tan, Ylä-Kojola, et al., 2022)). As such individuals with DCD physical activity levels can be seen to be impacted by heterogeneity in degree of motor impairment, specific motor skill impairment and VMI impairment.

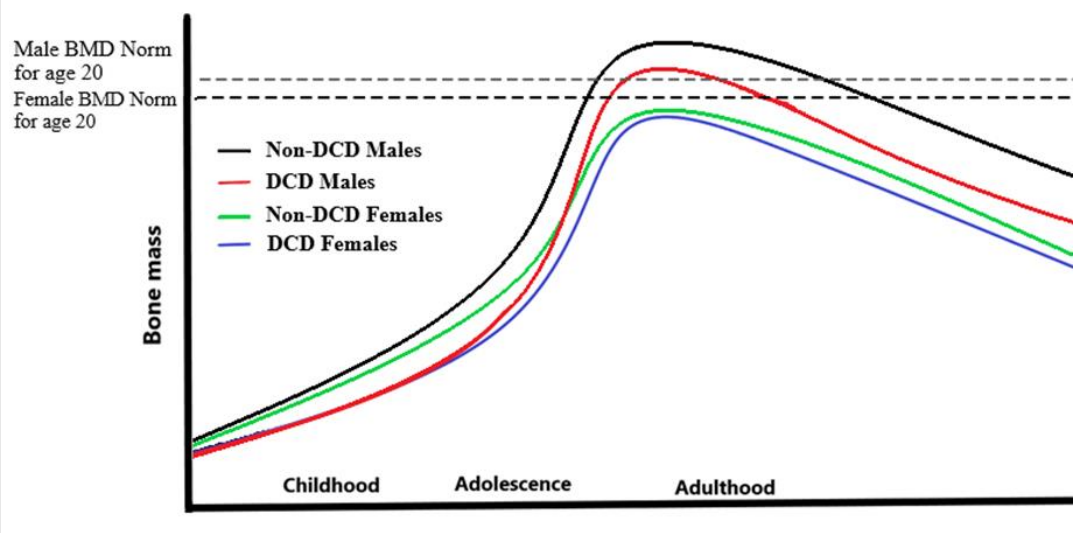
7.2 Discussion

This thesis aimed to determine the presence of bone health deficits in individuals with DCD from childhood through to early adulthood. Additionally, it aimed to determine whether lower physical activity engagement in individuals in DCD contributed to any identified bone deficits. The LCHD framework was used to shape this research project. In keeping with this framework, bone health and physical activity were viewed as continuous health entities which could be either moving towards or away from a healthier phenotype in response to environmental factors.

The outcomes of this thesis showed that bone deficits are present in individuals with DCD throughout childhood and adolescence, established for both sexes in several different populations. However, the systematic review in this thesis (Chapter 2, (J Tan, Murphy, et al., 2022)) indicated an absence of information at the time of peak bone mass. When examining Australian adults at the time of peak bone mass, it was determined that a deficit compared to typically developing peers was only present in males (Chapter 6, (J Tan et al., In press)). A sex specific difference was also identified in the systematic review in adolescence (Chapter 2, (J Tan, Murphy, et al., 2022)). Combined this indicated that the sex specific difference in bone health is reflective of changes occurring over the adolescent period. The adolescent period is a critical time for bone development, in keeping with the LCHD framework of sensitive time points. During the adolescent period, hormonal and developmental changes result in bone mineral being accrued rapidly. These changes also result in bone gains in response to physical activity loading being enhanced (Bass et al., 2002; Farr et al., 2014). However, according to the LCHD framework, social and environment factors also impact upon health and as such the potential for adolescence to also be a critical time period for physical activity engagement must be considered. The environmental change of entering secondary school has physical and social changes related to physical activity engagement including an increased autonomy over the level and type of physical activity undertaken (Fraguela-Vale, Varela-Garrote, Carretero-García, & Peralbo-Rubio, 2020). Social and cognitive changes also occur that relate to physical activity engagement, specifically an increased valuing of independence and peer relationships. Combined these may result in an alteration in an individual's physical activity trajectory (Fraguela-Vale et al., 2020). Such changes may be positive via increased active transportation and organised competitive sports, or negative via changed leisure preferences to more sedentary activities.

Figure 7.1

Proposed Model for Bone Development Trajectory Based Upon Data from Chapters 2, 5 and 6



Note: Figure is not to scale.

The time frame for the separation of male and female bone deficits compared to typically developing individuals indicates that these changes are likely due to a change in physical activity trajectories over these times. It is important to note however that although males with DCD had a deficit in bone health in comparison to typically developing males, overall males had a healthier bone phenotype than was seen in females. Both groups of females, DCD and typically developing, had bone health deficits according to Z-scores from age and sex matched normative ranges (Chapter 6, (J Tan et al., In press)). This indicates that the findings of this thesis are not that females with DCD do not have the pre-disease status of impaired bone health but rather that their bone health is concordant with the bone impairments seen in typically developing females. The physical activity patterns reported in studies in this thesis do not show evidence of a positive change in trajectory for physical activity in females with DCD, but rather a negative shift in activity patterns for the typically developing females. These findings are in keeping with a known reduction in physical activity in girls increasing over adolescence particularly related to organised and informal sport engagement (Dumith et al., 2011; Rinta-Antila et al., 2022). For example, physical activity pattern detriments in male adolescents with DCD compared to typically developing males are smaller than the detriments in physical activity seen between typically developing males and females (Green et al., 2011). This pattern was also

shown in the study of Australian adults where greater differences were seen in physical activity levels and the effects of bone loading upon BMD based on gender than was seen based upon DCD status (Chapter 6, (J Tan et al., In press)). The finding, whereby a typically developing female had a lower loading effect upon bone than was seen by males with DCD was in keeping with BMD findings of a deficit in males with DCD compared to typically developing males but higher BMD than typically developing females (Chapter 6, (J Tan et al., In press)).

The presence of detriments in physical activity by sex is further supported by the study in Finnish children. In this study, girls showed a different physical activity pattern than boys, with fewer and shorter bouts of moderate physical activity and longer time spent in sedentary breaks (Chapter 3). Such a physical activity pattern is likely to result in reduced stamina and endurance compared to individuals without such a pattern. This is likely to result in a flow on negative effect to physical activity patterns throughout childhood (King-Dowling et al., 2019). A childhood of low physical activity patterns may then exacerbate the decline in physical activity during adolescence. This decline in late childhood and adolescence has been demonstrated to occur in Finland and to be greater in individuals with cognitive and psychological disabilities than the general population (Kämppi, Asunta, & Tammelin, 2022). As females and males decrease physical activity by early adulthood, sex differences in physical activity may not be as visible in adulthood. For example, the study in the Finnish adults showed that although typically developing females tended to have lower physical activity than typically developing males, these activity levels were usually above that of males with DCD (Chapter 4, (J Tan, Ylä-Kojola, et al., 2022)). However, bone detriments due to low levels of physical activity in adolescence are likely to be long lasting. Additionally, physical activity differences may still be present in aspects not well reflected by the cardiovascular based physical activity assessment of conventional accelerometry impacting upon bone development. For example, the sort of activity engaged in will have an important impact on bone gains (Weidauer, Eilers, Binkley, Vukovich, & Specker, 2012). Females are known to reduce engagement in competitive sports over adolescence. Reduced sports engagement reduces bone stimulation due to reduced high magnitude loading and the variety of strain experienced by the bone. Strains on the bone experienced from competitive sports have been shown to increase bone benefits from physical activity beyond the level that

is seen in individuals that are active and engaging in physical activity at least three times a week (Nikander, Kannus, et al., 2010). Therefore, adolescent females may continue to be physically active but by reducing their engagement in sports and higher impact activity have reduced bone benefit from physical activity. Importantly, a meta-analysis on physical activity levels over adolescence indicates that physical activity decreased earlier in the lifespan in females (nine to 12 years) than males (13 to 16 years) (Dumith et al., 2011). The decrease in physical activity in females coincides with the beginning of the adolescent pubertal period (Kail & Cavanaugh, 2010), a critical period for bone growth where bone gains from physical activity are accentuated. Such a reduction will result in compromised bone development over this critical adolescent period. As physical activity reduction occurs later in the pubertal period for males, the impact of reduced physical activity upon bone is likely smaller. As organised sports participation supports physical activity levels into adulthood, lower levels of sports participation in females may also have ramifications for bone health maintenance in adulthood (Rinta-Antila et al., 2022).

Outside of sex effects, physical activity differences throughout the lifespan are a likely cause of bone deficits in individuals with DCD. The systematic review showed changes in bone architecture were indicative of decreased loading from reduced physical activity levels. Additionally, bone mass deficits compared to typical development were more frequently observed in locations that received more mechanical loading from physical activity (Chapter 2, (J Tan, Murphy, et al., 2022)) and confirmed in a study of Western Australian adults (Chapter 6, (J Tan et al., In press)). For example, in the Raine cohort a larger deficit was seen in the legs than the arm, and in the preferred arm compared to the non-preferred arm (Chapter 6, (J Tan et al., In press)). Such findings indicate that bone deficits due to DCD status are likely the result of altered bone loading from physical activity. However, the study in the Raine cohort indicated a role for DCD status above that accounted for by loading during the late adolescent period which was partly mediated in models including lean mass. This indicates that bone differences may reflect on physical activity differences that occurred earlier in the lifespan, such as those demonstrated in Chapter 3. These differences may also indicate the impact of other aspects of physical activity such as movement quality rather than the loading that can be expected to occur from physical activity.

Individuals with DCD tend to have a low quality of movement, with movements being slow and inefficient (Blank et al., 2019). Due to this poorer execution of movement, the actual stimulation received on the bone may be lower than calculated from self-reported or accelerometry data and as such bone adaptions may be smaller than expected (Beck & Snow, 2003; Hart et al., 2020; Hart, Nimphius, et al., 2017). Slow movement in weightlifting, for example, results in lower muscle-contraction induced strain which may be the cause of lower bone adaption in weightlifters than is anticipated from the weight load (Nikander, Sievänen, Uusi-Rasi, Heinonen, & Kannus, 2006). The bone changes demonstrated in this thesis occurred following engagement in an exercise program, indicated the presence of a reduced response to bone from loading in individuals with DCD (Chapter 5, (J Tan et al., 2020)). Furthermore, in the exercise program (J Tan et al., 2020), it was shown that this response appeared to be further decreased with increasing motor impairment. That is bone gains from exercise reduced as impairment increased. This suggests that motor competence level impaired the ability to execute motor skills in such a way that an osteogenic response was optimally stimulated (Chapter 5, (J Tan et al., 2020)). For example, individuals with DCD may perform activities more slowly so reducing strain rates, they may use incorrect technique moving the strain received to other non-targeted muscles, or they may be slower to increase loading than would be normally anticipated hence limiting the potential for the bone to adapt. Other evidence from the study, of smaller gains in muscle than would be normally anticipated from an exercise regime in this age group and a greater improvement in bone health as adolescents gained experience in the intervention provides supporting evidence of a reduction in gains in bone health due to motor impairment (Chapter 5, (J Tan et al., 2020)). As resistance training is known to improve coordination and neuromuscular learning in typically developing individuals (Faigenbaum, 2007), continued experience in the program may have improved movement quality leading to an increased osteogenic response to exercise.

Inefficient and poor executed movements are also likely to reduce osteogenic response to other activities including activities of daily living and social activities. Individuals with DCD have impairments in performing activities of daily living (American Psychiatric Association, 2013) which may affect their bone development. For example, children with DCD often have difficulty in opening food containers

(Moraal-van der Linde et al., 2015), which may result in a slower opening process in opening a container than the usual rapid movement, they may use two hands or use tools for assistance so reducing the strain received by the muscle and as such the stimulus received by the bone. Furthermore, children with DCD participate less in activities of daily living than typically developing peers, with engagement decreasing as their performance ability decreases (Moraal-van der Linde et al., 2015) so reducing the average daily loading received by bone. Such, a reduction in engagement in activities of daily living may explain the bone deficit demonstrated in the preferred arm for adult females with DCD when compared to their typically developing peers (Chapter 6, (J Tan et al., In press)). This was the only bone location to demonstrate a deficit in females with DCD and may reflect on the large role this limb plays in everyday activity engagement rather than specific physical activity. The difference in bone density between preferred and nonpreferred arm is proportionally larger than that seen between the preferred and nonpreferred leg reflecting on the increased use of the preferred limb in everyday activities that does not occur in legs. As such, a reduction in engagement and movement quality in everyday activities is most likely to be reflected in the preferred arm.

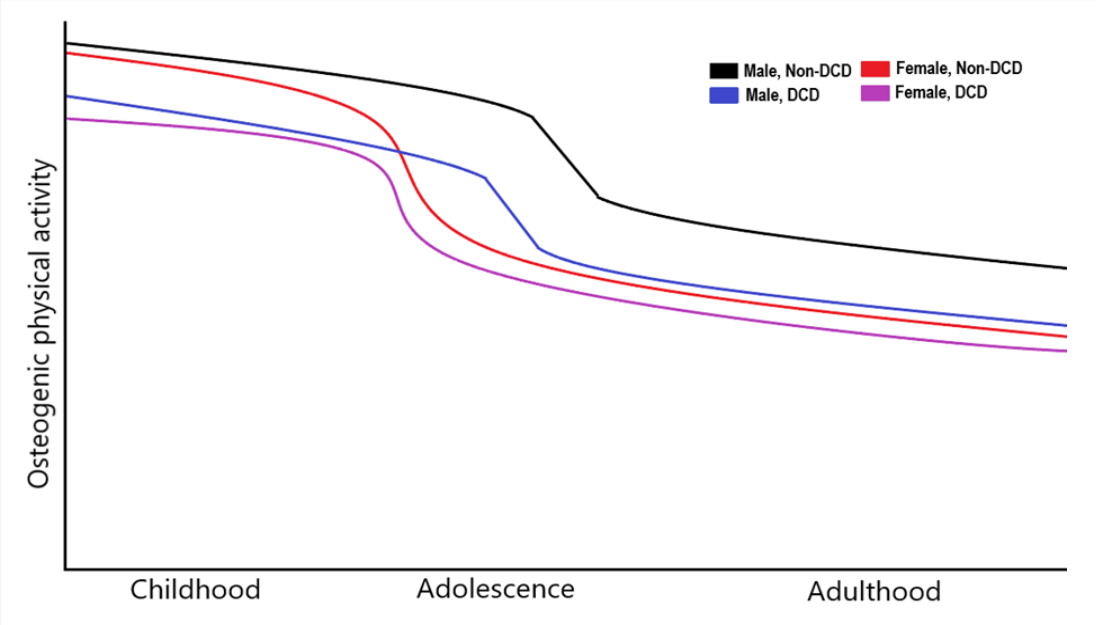
This difference in movement quality may be the reason why no distinct effect on osteogenic physical activity from DCD could be proven in either childhood or adulthood (Chapter 3, 4 (J Tan, Ylä-Kojola, et al., 2022) and 6 (J Tan et al., In press)). However, combining the findings of these studies indicates a pattern of less-than-optimal physical activity in individuals with DCD throughout their lifespan. A conference presentation of preliminary results from a study of Australian adults, conducted as part of this thesis[1] and using a bone-specific self-report measure of physical activity found lower intensity and diversity in physical activity for adults with DCD (J Tan, Rantalainen, Hart, & Chivers, 2022) (Appendix A). Lower levels of overall physical activity may also have been present in the Australian study (Chapter 6, (J Tan et al., In press)) compared to the Finnish study (Chapter 4, (J Tan, Ylä-Kojola, et al., 2022)) given known differences in physical activity between these populations (Aubert et al., 2022). Additionally, the findings of a non-significant difference in estimated marginal means on osteogenic physical activity for Finnish boys with DCD

[1] Data collection was put on hold due to COVID 19 pandemic and region specific restrictions.

is suggestive of low level differences in osteogenic activity in childhood that may continue through the lifespan resulting in a lifetime reduction in bone gains (Chapter 3). Lifetime differences in osteogenic physical activity, as illustrated in Figure 7.2, provides a potential explanation for the role of DCD above the effect of bone loading physical activity in Australian adults (Chapter 6, (J Tan et al., In press)). It also provides an explanation for the sex difference in bone deficits given the higher engagement in osteogenic activity shown in males in childhood. Higher scores on the osteogenic index are known to be predictive of bone changes in adolescence (Deere et al., 2012b) and as such this slight difference in osteogenic engagement may impact on overall bone mass in later life.

Figure 7.2

A Conceptual Model for Differences in Physical Activity Patterns Over Time by Sex and DCD Status



Note: This model is based upon data from Finnish children, Finnish adults and Australian adults.

The pattern of less than optimal lifetime physical activity demonstrated through this thesis to be present in individuals with DCD may be the cause for identified bone deficits, rather than an isolated reduction in one measure of physical activity. One example of such an activity pattern is that of sedentary behaviour across studies. A non-significant trend of increased sedentary behaviour was observed in early childhood compared to typically developing peers, as children with DCD appeared to have more sedentary breaks and longer sedentary bouts. Other physical activity domains had lower

levels of physical activity for individuals with DCD compared to typical development with physical activity performed in fewer bouts of shorter length than those of their typical developing peers (Chapter 3). Such a pattern may reduce endurance such that engagement in MVPA is more difficult hence providing a potential explanation for the lower levels of MVPA engagement in adolescence (Chapter 6, J Tan et al. (In press)) and higher levels of sedentary light activity in adulthood when compared to typically developing peers (Chapter 4, J Tan, Ylä-Kojola, et al. (2022)). The interrelationship between these differing aspects of physical activity is necessary to consider in order to have a complete understanding of physical activity across the lifespan and its relationship to health outcomes (Bland et al., 2020; Burchartz et al., 2020; Salinas-Rodríguez, Manrique-Espinoza, Palazuelos-González, Rivera-Almaraz, & Jáuregui, 2022). For example, accelerometry analysis on the intensity of physical activity may need to be supplemented with information as to the spread of physical activity throughout the day and the variety and type of activities engaged to fully capture osteogenic physical activity (Bland et al., 2020). Similarly, MET information derived from accelerometry can be combined with intensity measurements to provide important information upon physical activity patterns.

Dis-engagement in organised sports was identified as part of a detrimental physical activity pattern in individuals with DCD. A study of Finnish children indicated a potential for reduced engagement in organised sports for children with DCD via the removal of a role of object control skills (i.e., overhand throw) upon physical activity outcomes when controlling for DCD status (Chapter 3). An Australian population also demonstrated lower engagement in organised sports clubs for adolescents with DCD compared to typically developing peers (Chapter 6, (J Tan et al., In press)). Organised sports participation is a driver of physical activity throughout adolescence and adulthood (Rinta-Antila et al., 2022) and has been noted by a number of studies to be reduced in children with DCD (Cairney, Hay, Faught, Wade, et al., 2005; Magalhães et al., 2011; Rivilis et al., 2011). Aside from being an overall predictor of physical activity, high school and early adulthood sports engagement has been found to be an independent predictor of bone health in adulthood with BMD increasing with long term sustainment of engagement (Minett et al., 2018). Engaging in team sports exposes individuals to high intensity impacts as well as a variety of different strains including from novel directions, these strains are referred

to as odd impacts (Nikander, Kannus, et al., 2010; Weidauer et al., 2012). Bone is highly responsive to strain magnitude, rate, and gradient such that loading coming from a novel direction, as might occur in a team sport, has an increased osteogenic effect than would be predicted based upon loading alone (Weidauer et al., 2014). Nikander et al. (2006)'s study demonstrated an increased benefit on many aspects of bone health from team sports and high impact activities, with the degree likely to be underestimated due to the comparison group being active individuals while the study group were athletes for whom the strains were likely less novel and had a relatively reduced bone response. Another study (Weidauer et al., 2012) using college athletes with a lower level of physical activity than Nikander et al. (2006) showed increased cortical thickness in soccer players than was seen in a control group who engaged in less than two physical activity sessions a week, with an increase in cortical area and thickness being seen over the course of a sports season not demonstrated in moderate and high impact sports that did not have these odd impacts (Weidauer et al., 2014). As such, team sports participation in adolescents at a club level is likely to result in considerable bone gains due to exposure to odd impacts and so increase their bone health above that of the solo physical activities usually preferred by individuals with DCD (Blank et al., 2019). Other potentially important osteogenic parameters, such as the presence of additional strains, were not investigated via accelerometry analysis but are an important area for further investigation.

Engagement in organised sports may also provide an explanation for why controlling for VMI levels resulted in an increased estimate of effect for DCD status upon models for moderate physical activity and MVPA in adults with DCD (Chapter 4, (J Tan, Ylä-Kojola, et al., 2022)). VMI impairment reduces the coordination skills necessary for team sport engagement (Armando & Rahman, 2020; Lust et al., 2022). As such, individuals with DCD but normal levels of VMI may have better hand-eye coordination skills and have a higher engagement in team sports than an individual with DCD and VMI impairment. Such individuals may be more similar in activity levels to an individual without DCD whose engagement in team sports is reduced due to VMI impairment. This interacting effect of differing impairment levels, for which VMI impairment is but one subtype (Lust et al., 2022), is likely to cause an underestimation of the effect of DCD on osteogenic physical activity and so bone estimates for some individuals. That is individuals with co-occurring conditions such

as DCD and VMI impairment will have a greater reduction in physical activity and likely a greater deficit in bone than is seen in individuals without these co-occurrences. A similar effect is seen from the role of individual motor impairments upon physical activity in children. Individuals with DCD do not have a consistent phenotype regarding the motor skill affected, although some impairments occur more frequently (Kaplan, Crawford, Cantell, Kooistra, & Dewey, 2006).

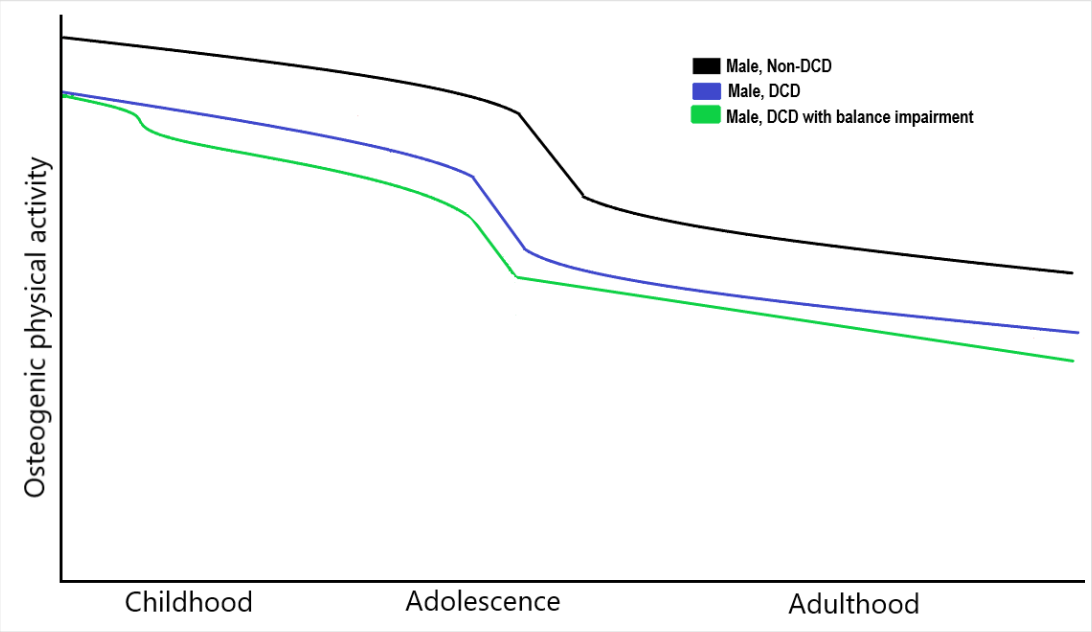
Investigating the effect of motor skills on physical activity showed that locomotor and balance skills, in the form of hopping, and to a lesser extent sideways jumping showed an estimate of effect on high osteogenic impact peaks, with a likely increase in bone strength (Chapter 3). This finding indicates that an individual with DCD and low locomotor and balance skills is likely to have a lower level of physical activity in childhood and so lower bone strength than an individual with DCD and higher locomotor and balance skills (Chapter 3). As hopping and locomotor skills are important for social physical activities in childhood such as jump rope or hopscotch, and are a common part of school physical education, children with poorer skills in these areas may disengage from physical activity (Robinson et al., 2015). This may result in a trajectory of lower physical activity due to a perceived low ability for physical activity performance even past the timepoint where these skills are valuable for the engagement of physical activity (Robinson et al., 2015). This relationship is known to exist for other motor skills and may be exacerbated in this population.

Furthermore, individuals who have impairments in other motor skills may show more impairment in physical activity later in life. For example, object control skills may reduce physical activity in later childhood and adolescence as ball sports become dominant (Robinson et al., 2015). Due to the varying effects of individual motor skills and co-occurrent conditions demonstrated in this thesis and the heterogeneity of DCD as a condition each individual's physical activity trajectory must be seen separately in keeping with the LCHD framework. Theoretical trajectories are depicted in Figure 7.3, however the combined effect of multiple variables must also be considered. For example, an individual with DCD may have an overall negative physical activity trajectory, further decreased in childhood by VMI impairment but partially offset by increased locomotor skills compared to other individuals with DCD. As such, to fully comprehend the impact of DCD on an individual's bone health the effect of individual variability on several skills should be considered.

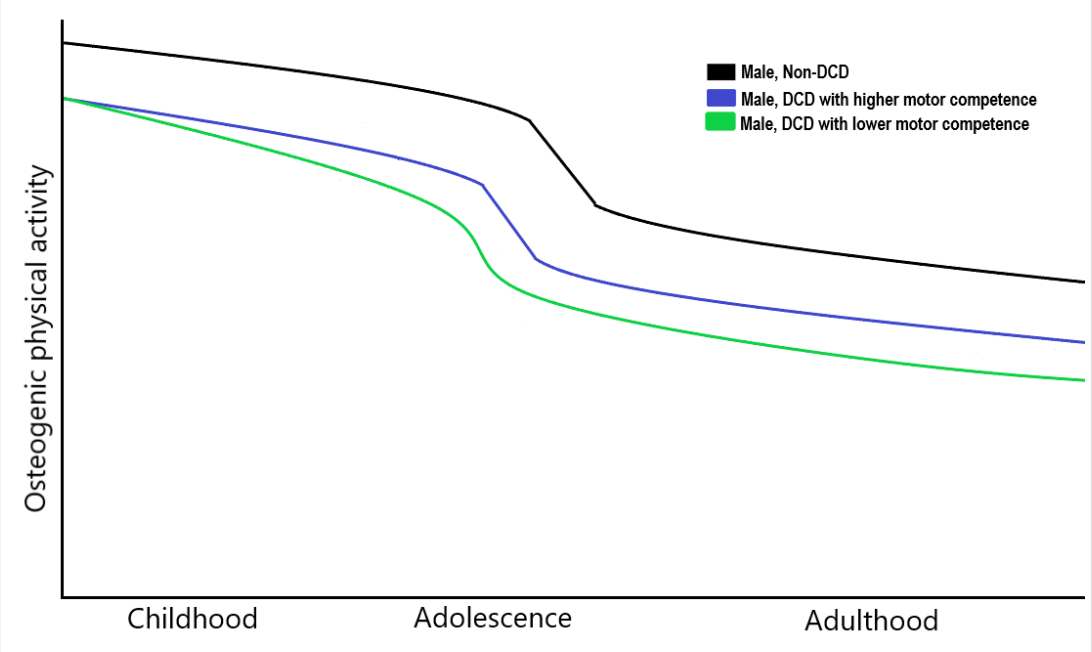
Figure 7.3

Theoretical Trajectories of Osteogenic Physical Activity Based Upon Study Findings at Individual Time Points

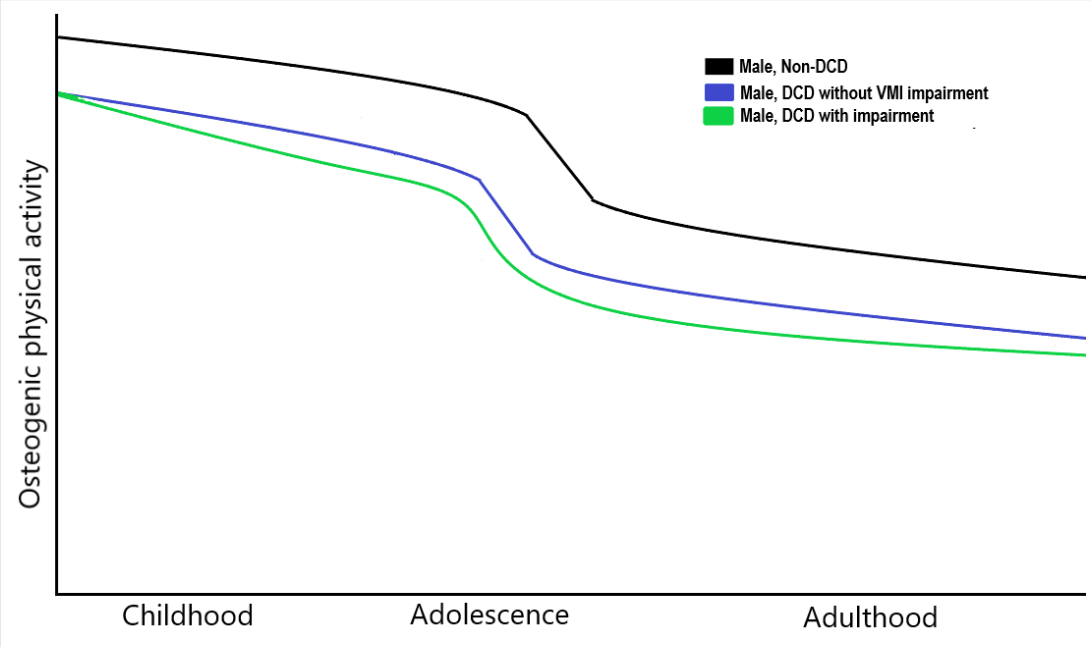
a) Impact of Balance Impairments on Osteogenic Physical Activity in Males



b) Impact of Motor Competence Levels on Osteogenic Physical Activity in Males



c) Impact of Visuo-Motor Impairment on Osteogenic Physical Activity in Males



Notes:

a) Impact of balance skills in early childhood impacting physical activity throughout life. Balance skills are considered likely to continue to reduce physical activity into adulthood due to its impact on all aspects of physical activity

b) Impact of higher and lower motor competence in a DCD population based on effect established in adolescents. This relationship is considered likely to persist throughout life as although measured physical activity may be similar, the osteogenic effect is reduced due to movement issues.

c) Impact of the presence of VMI impairment based on the enhancement of effects from DCD in adulthood. The relationship is pictured as starting in childhood, when VMI differences were detected but physical activity not measured, due to VMI's known impact on object skills which are known to impact on physical activity in childhood.

7.3 Implications for Future Research

Further Research Area #1
Role of Motor Competence Levels and Individual Motor Skills Upon Fracture and Other Injury Rates

The presence of poor bone health through to the time of peak bone mass in individuals with DCD is an important finding for this thesis, especially as peak bone mass is predictive of bone health in later adulthood and the age at which osteoporosis will onset (Hernandez et al., 2003). This thesis reinforces the vulnerability of all females to osteoporosis and further identifies that males with DCD are likely to have osteoporosis onset at an earlier age than their typically developing peers. However, the clinical and health impact of osteoporosis and osteoporotic fracture in a DCD population needs further confirmation. This is especially important as males tend to have a later onset of osteoporosis relative to females (NIH Consensus Development Panel on Osteoporosis Prevention Diagnosis and Therapy, 2001; Orwoll, Vanderschueren, & Boonen, 2013). Additionally, the concept of a double disadvantage from osteoporosis and an increased risk of injury due to poor motor skills in individuals with DCD requires further investigation, as there is no current research on injury rates in DCD outside of a sports setting, nor the impact of age-related falls in the DCD population.

Further Research Area #2
Standardised Measures of Physical Activity to Determine Osteogenic Impact, Particularly in Adolescence and Adulthood.

This thesis has identified the need for further investigation on the effect of DCD upon physical activity. By using device assessment and osteogenic specific analysis of physical activity, this thesis has found physical activity variations not previously reported. These findings highlight the importance of using device assessments, particularly osteogenic specific measures, for physical activity measurements in a DCD population. Such measures are rare in the standard assessment of physical activity in DCD, particularly in adolescence and adulthood. Given that adolescence is a critical time for bone development the use of standardised measurements in adolescence is particularly vital.

Further Research Area #3
Use of Alternative Measures of Accelerometry Assessment to Determine Osteogenic Effect of Physical Activity in a DCD Population

Similarly, the identification of an effect from physical activity upon bone health in DCD beyond that of physical activity engagement is an important area for further investigation. Horizontal (mediolateral and anterior-posterior) measurements from accelerometry, in conjunction with the traditional vertical measures, will allow for the determination of the impact of non-efficient movements upon activity. Inefficiency of movements may also be captured via analysing METs as a continuous variable rather than categorisation. Such assessments would be particularly valuable in conjunction with bone assessment such that the osteogenic impact of non-efficient movements may be considered. There is also a need to validate tools such as OI within DCD and paediatric populations.

Further Research Area #4
Identification of the Impact of Non-Efficient Movements on Bone Gains from Exercise

Although this thesis has identified a role for physical activity upon bone health in a DCD population, the findings of this thesis indicate a reduction in changes in bone from physical activity. As such further information is needed on the impact of non-efficient movements and movement quality upon the osteogenic impact of exercise in a DCD population. The intensity of physical activity in the DCD population from an osteogenic point of view has not been established. Given the known leisure preferences of individuals with DCD assessment of accelerometry data for intensity via peaks and OI would be particularly useful. This could be determined by examining bone changes from adolescents with and without DCD engaging in physical activity with different loading modalities. Additionally, the tracking of bone improvements over an extended period of engagement in an exercise intervention may also provide important insights on the impact of quality of movement compared to a typical trajectory. Accelerometry assessment of individuals with DCD while engaging in exercise (e.g. by assessing MET measures) may also provide important insights on the level of activity being engaged in.

Further Research Area #5
Identification of Methods for Bone Improvement via Intervention

Finally, this thesis identified that adolescents with DCD may improve bone health via a targeted exercise intervention. Further research is needed to determine the best method of exercise delivery and whether engaging adolescents in structured exercise interventions may return them to a healthy bone development trajectory. Accelerometry measurements to assess intensity along with bone scans may provide important insights into this area. Within this context the impact of individual factors, such as individual motor skills or VMI impairment, upon an individual's bone gains may also need investigation in order to determine if there is a subgroup that may most benefit from intervention. Additionally, as this thesis identified bone impairments in females in the Western Australian population at the time of peak bone mass, wider population level interventions should be considered.

7.4 Implications for Practice

This thesis has important implications for the health and clinical management of individuals with DCD. Firstly, the presence of bone deficits into early adulthood in males with DCD indicates that this population is likely at increased risk of osteoporosis over a typically developing male population with associated potential health implications. The identification of bone deficits as well as a less healthy body compensation associated with lifelong levels of physical activity indicates the need for lifestyle interventions in this group. Additionally, this thesis identified important knowledge gaps regarding the role of contributing factors which are important for informing future treatment options and strategies in managing individuals with DCD.

Key Recommendation #1
Motor Competence Status Should be Considered as a Key Factor Within a Risk-Based Approach When Determining if Bone Density Assessments are Necessary

The identification of males with DCD as having a poorer bone phenotype than typically developing males indicates an increased risk of developing osteoporosis at an earlier time point compared to typically developing males. The greatest health risk from osteoporosis presents in the form of osteoporotic fracture, which is associated with lengthy hospitalization and disability, as well as high morbidity (Cauley, 2013; McLeod, Brodie, Fahey, & Gray, 2005). This effect is increased in male cases of

osteoporotic fracture as they tend to be younger with higher mortality than females with osteoporotic fracture (Alswat, 2017). This disadvantage is increased by bone density underscreening and undertreatment of osteoporosis in males, increasing the risk of osteoporotic fracture (Alswat, 2017). Although, males in this thesis, had a higher bone mineral density than females, male osteoporotic fractures occur at a higher bone mineral density than females (Alswat, 2017). As such, males with DCD should be considered for bone density screening alongside females.

Additionally, all individuals with DCD have an additional potential for osteoporotic fracture in the setting of low bone density due to the contribution of poor motor skills to falls (Fujimoto et al., 2015). This may be particularly enhanced for males, given the increase in fall rate in males in early adulthood (Weidauer et al., 2015). Although fracture rates in older adults with DCD has not been investigated, falls are a known major contributor to fractures (Beck & Snow, 2003; Blain et al., 2014). The identification of a potential increased risk of fracture is important for the continued health care and support for individuals with DCD, particularly in an aging society. Although further research is needed prior to recommending bone density screening for males with DCD, health care providers should be aware of the potential for bone vulnerability in this population. . Additionally, given the relationship between bone loading and low bone health an awareness of an individual's lifetime physical activity history should be considered as part of deciding on bone density assessment in adulthood for both sexes.

Key Recommendation #2
Engagement of Individuals with DCD in Exercise and Physical Activity Interventions Should be a Priority

This thesis indicated lifetime physical activity differences in individuals with DCD. However, it also importantly indicated that that engaging of adolescents with DCD in a targeted exercise intervention improved their bone health. As such, engaging individuals with DCD in an exercise intervention at any point in their life is likely to be beneficial. Given that bone deficits are recognized to be sustained in this group into early adulthood, the adolescent period is a critical time period for such an exercise intervention. Therapists working with adolescents presenting with DCD should encourage them to engage in highly osteogenic physical activity

interventions, particularly over the period of peak bone gain. Given that the findings emphasised the importance of a prolonged period of engagement to achieve maximum benefit it is important to encourage engagement for at least 12 months to give time for motor skill mastery needed to effectively perform the exercises. Additionally, although physical activity differences were shown to be present in the DCD population as a whole, this thesis identified a susceptible group, with children with poor dynamic balance and adults with VMI impairments as having particularly low osteogenic physical activity. As such, individuals with DCD who also show these deficits should be particularly targeted for support in improving engagement in physical activity throughout their lifespan.

Individuals of all motor competence levels should be encouraged to participate in physical activity as individuals with high motor competence within a DCD population show the greatest improvements in bone from engagement in an exercise intervention. However, it should be recognised that those individuals with greater motor impairment will need a longer period of engagement to show a benefit upon their bone and this should be communicated to the adolescent and their families. Given the identification of an impairment in bone health in individuals with DCD at the time of peak bone mass and the associated implications, as well as the finding of improvement in bone over the adolescent period, this thesis indicates a need for re-engagement of allied health professionals with individuals with DCD during adolescence to improve their overall physical activity and consequently bone health. Consideration should also be given to engaging adolescents with DCD via other means, such as via school-based programs.

Key Recommendation #3
Improvement of Physical Activity at a Population Level

Finally, while this thesis was focused on a clinical population, the findings of bone health impairments related to low physical activity engagement also apply to the general population. As such the need to increase high impact physical activity over the vital adolescent period is important for the general population, particularly for females given the declining rates of physical activity and less than optimal bone in early adulthood. Increasing engagement in physical activity at a population level, particularly peak bone mass, is likely to result in a decrease in future osteoporosis rates.

7.5 Limitations

Findings from this thesis, aside from the systematic review, are limited to the geographic regions from which the populations were derived and may not be generalisable to other countries and their society related habitual physical activity behaviours. This limitation is somewhat overcome by Finland and Australia being regions with distinct geographic, cultural and climate features (Kämppi et al., 2022), allowing for some generalisability of findings confirmed in both populations. Studies explicitly assessing bone health were limited to Western Australia, and as such unique features of the Western Australian climate and culture must be considered in interpreting these findings. In particular, compared to the rest of Australia, Western Australia has high sun hours a day (Bureau of Meteorology, 2022), low levels of active transportation (Australian Goverment, 2022), and physical activity focused on organised sports (Aubert et al., 2022; Hesketh et al., 2023). Additionally, the majority of participants in the Western Australian bone studies were Caucasian and the importance of ethnicity on bone should be considered in result interpretation (Dvornyk et al., 2005). However, the systematic review included studies across multiple different geographic regions with similar results indicating this does not seem to have an effect on bone differences in this population.

Additionally, findings are limited to the time in the lifespan at which they were measured. Although the findings on bone health show a trajectory through which other time frames can be inferred, it is important to consider that one of the adolescent timepoints has a modest sample size and does not have a control group for typical development. The findings on physical activity are similarly limited to the time in the lifespan in which they were measured. Time points for measurement were in early childhood prior to the age at which physical self-beliefs begin to affect activity (Babic et al., 2014; Ruiz-Montero, Chiva-Bartoll, Baena-Extremera, & Hortigüela-Alcalá, 2020) and during late adolescence and adulthood where sedentary behaviour has increased (Janssen et al., 2016). As such, a more pronounced difference in osteogenic activity may have been present during the unmeasured time points of middle childhood and early adolescence where activity levels are higher but impacted by physical activity beliefs. The lack of validation of tools to measure physical activity in a DCD population should also be considered in the interpretation of any results.

Classification for participants as having DCD was based upon researcher classification based on scores on motor competence tests and limited to the constraints of these tests that differed across the studies (i.e., KTK (Kiphard & Schilling, 1974), MAND (McCarron, 1997), Zurich neuromotor assessment (Largo et al., 2001)). As such participants cannot be considered a clinical sample. Attempts were made to overcome this limitation via the application of DSM-V diagnostic criteria (American Psychiatric Association, 2013) to participants where possible, including the exclusion of participants for whom other factors may have affected their motor score and the use of motor skill assessments from early in life. Despite this, it is possible that some participants had low motor competence rather than a clinical case of DCD. As such it is recognised that a clinical DCD group may show deficits not detected in these samples. This limitation however has the advantage of widening the applicability of the studies to be indicative of overall low motor competence, which may be particularly important given population declines in motor competence (Bardid, Rudd, Lenoir, Polman, & Barnett, 2015).

7.6 Key Findings

- Bone health deficits of one to two standard deviations were present through the lifespan in individuals with DCD when compared to typically developing reference ranges, as assessed by DXA and pQCT.
- Bone health deficits were present in early adulthood for DCD and typically developing females, and for DCD males indicating an increased bone health risk in these groups throughout the lifespan. The location of bone health deficits indicated an influence from loading via physical activity.
- Physical activity differences were determined to be present at multiple timepoints through the lifespan.
- The impact of DCD upon physical activity was influenced by individual variation in motor skills as well as co-occurrent conditions such as VMI impairment.
- Sex specific differences were identified in loading from physical activity upon bone with DCD status influencing loading effects for males only.
- The effect of DCD status on bone was above that that can be seen to be present due to loading and indicates the role of other aspects of physical activity.

- Bone health in individuals with DCD can be improved via exercise, however this may be slower than seen in typically developing individuals.

7.7 Conclusion

Using a life course health development model this thesis examined the presence of bone health deficits in individuals with DCD across distinct periods of growth and adolescence into early adulthood. It was shown that a deficit was present throughout childhood and adolescence, but that by early adulthood, where peak bone mass occurs, bone deficits were no longer present for females compared to typically developing individuals. A deficit was seen to be present in peak bone mass for males placing them at a potentially higher risk of osteoporotic fracture than typically developing males.

Cross-sectional examination of physical activity patterns throughout the lifespan showed a potential causation for these differences, although further investigation is needed to disentangle the complex interplay of factors. The overall findings of this study indicated a negative activity pattern from childhood through to adulthood, with a differing effect of loading on bone for males with DCD. Improvements in bone measurements were shown to be possible via engagement in an exercise intervention and may provide an opportunity for clinical focus although further evaluation is needed.

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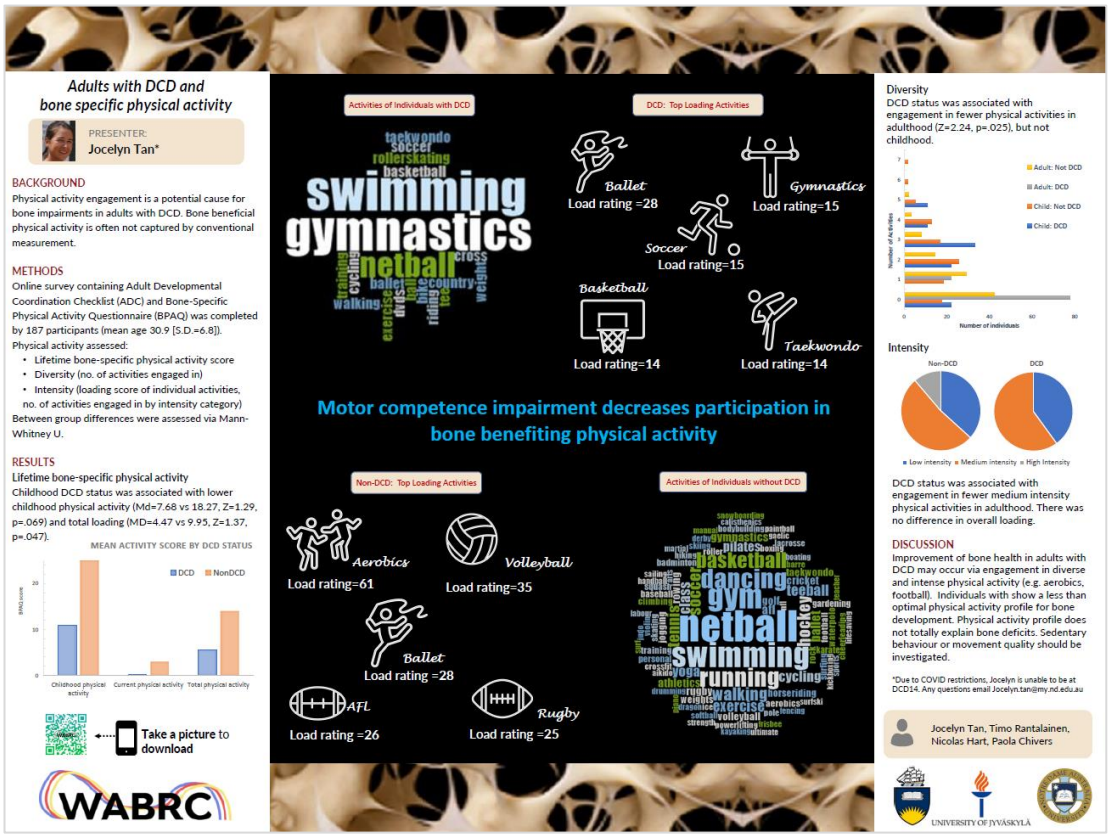
APPENDICES

Appendix A

Adult DCD Study



Appendix B

Published Papers

B.1 Biological Basis of Bone Strength: Anatomy, Physiology and Measurement

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Journal of Musculoskeletal and Neuronal Interactions JMNI

Review Article

Biological basis of bone strength: anatomy, physiology and measurement

Nicolas H. Hart[1,2,3,4], Robert U. Newton[1,4], Jocelyn Tan[2,3,5], Timo Rantalainen[1,2,3,4,6], Paola Chivers[1,2,3,4], Aris Siafarikas[1,2,3,7,8], Sophia Nimphius[3,4]

[1]Exercise Medicine Research Institute, Edith Cowan University, Perth, W.A., Australia; [2]Institute of Health Research, The University of Notre Dame Australia, Fremantle, W.A., Australia; [3]Western Australian Bone Research Collaboration, Perth, W.A., Australia; [4]School of Medical and Health Sciences, Edith Cowan University, Perth, W.A., Australia; [5]School of Health Sciences, The University of Notre Dame Australia, Perth, W.A., Australia; [6]Gerontology Research Center, University of Jyväskylä, Jyväskylä, Finland; [7]Department of Endocrinology and Diabetes, Perth Childrens Hospital, Perth, W.A., Australia; [8]School of Paediatrics and Child Health, University of Western Australia, Perth, W.A., Australia

Abstract

Understanding how bones are innately designed, robustly developed and delicately maintained through intricate anatomical features and physiological processes across the lifespan is vital to inform our assessment of normal bone health, and essential to aid our interpretation of adverse clinical outcomes affecting bone through primary or secondary causes. Accordingly this review serves to introduce new researchers and clinicians engaging with bone and mineral metabolism, and provide a contemporary update for established researchers or clinicians. Specifically, we describe the mechanical and non-mechanical functions of the skeleton; its multidimensional and hierarchical anatomy (macroscopic, microscopic, organic, inorganic, woven and lamellar features); its cellular and hormonal physiology (deterministic and homeostatic processes that govern and regulate bone); and processes of mechanotransduction, modelling, remodelling and degradation that underpin bone adaptation or maladaptation. In addition, we also explore commonly used methods for measuring bone metabolic activity or material features (imaging or biochemical markers) together with their limitations.

Keywords: Cortical, Imaging, Modelling, Remodelling, Trabecular

Introduction

Bone is a remarkable and exquisite biomaterial. It is highly adaptive, structurally dynamic and metabolically active, and is superior to all other biomaterials in terms of strength and toughness[1-4]. In particular, bone structure, size and strength are reliant upon and responsive to the routine physiological and mechanical demands placed upon it[5-12]. Mechanical stimuli thus initiate or inhibit bone modelling and remodelling processes in response to variations in internal or external forces or as a consequence of immobilisation[13-17]. More specifically, bone continuously modifies and regenerates itself in the presence or absence of mechanical loading, which subsequently leads to the accrual (formation), maintenance (homeostasis) or degradation (resorption) of bone mass[18-24]. This is achieved through a sophisticated process involving the careful cellular regulation and coordination of osteoblasts (bone matrix deposit) and osteoclasts (bone matrix resorption) in order to remove damaged or extraneous bone material and subsequently replace it with new robust material[19-21,25-30]. As bone remodelling is a continuous process, even a slight perturbation or imbalance in either of these regulatory cells can lead to osteopenia or osteoporosis; such is the importance of bone health to load tolerance capabilities[29-35]. In particular, the mechanical integrity and performance of bone under various loading conditions is directly affected by its mechanical properties and geometric characteristics[1,7,12,13,18,36] which are both

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Corresponding author: Dr. Nicolas H. Hart – PhD, AES, CSCS, ESSAM, Senior Research Fellow, Edith Cowan University, 270 Joondalup Drive, JOONDALUP, Perth, WA, Australia, 6027

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indicators of bone health and underpin bone strength.

The ability of bone to withstand forces and moments (mechanical loads) differs substantially across the loading spectrum under various loading conditions, specific to the mode, magnitude, direction, rate and frequency of load applied[3,12,16,17,37-39]. As bone is anisotropic in nature, it has different thresholds of load tolerability across different planes of action[2,18,40,41]. Indeed, habitual human behaviours routinely expose bones to various, often unpredictable loading patterns spanning from cyclical low-grade forces when walking or running, to sudden high-grade forces when jumping, landing or changing direction. As a result, compressive, torsional, transverse and tensile loads in combination and isolation are routinely applied to bone, exposing the skeleton to stimuli that can lead to positive bone-specific and site-specific adaptations[16,42-49], or in the absence of suitable conditioning, recovery and nutrition, an increased likelihood of injury[50-57].

Despite the complex and multidimensional relationship between various loading schemes and bone mechanical properties (beyond the scope of this review, and published earlier[12]), bone strength and stiffness are greatest in the direction by which loads are most commonly expressed[13,44,49,58]. The prevaling bone structure reflects an appropriate adaptation to mechanical loading highlighting a specificity of adaptation (site-specific) as force transmission regulates osteogenic (anabolic) bone formation outcomes concomitantly with other stochastic (spatially non-specific) adaptations[2,16,20,21,59]. In particular, the regulation and co-ordination of bone to physically adapt to loading demands is initiated and managed at the cellular level by osteocytes through mechanotransduction[59-62]. Proportionate to mechanical stimulation, osteocytes biochemically promote osteogenesis by coordinating osteoblast and osteoclast activity so that overall bone morphology and bone shape positively adapts in favour of greater bone strength[63-65]. Within this process, older osteoblasts make way for new osteoblasts by transforming into osteocytes which become embedded into the bone-matrix. As osteocytes form 95% of bone-matrix composition, this increase in osteocyte concentration leads to an increase in bone mass while maintaining regulatory osteoblast-to-osteoclast homeostasis[7,19-21,66,67].

As reviewed below, bone loss and bone accrual are not necessarily co-located and occur in a targeted or site-specific manner around bone circumference and along its length, additional to observable coadaptive bone morphological traits. A thorough understanding of these cellular and physiologic processes and their contribution to determining and maintaining bone strength will facilitate clinical diagnostics, designing appropriate interventions, and evaluating clinical musculoskeletal outcomes of pharmacological and non-pharmacological interventions[68]. Accordingly, this review aims to provide a comprehensive update of current scientific literature and our understanding of these processes for clinicians and researchers, in companionship with the mechanical basis of bone strength[12] published earlier.

Bone strength

Bone strength explicitly refers to the ability of bone to withstand force prior to catastrophic failure[1,24,69-72], and is inextricably linked with fatigue resistance to repetitive loads[73-78]. Given the complex and multidimensional nature of bone, its strength is ultimately determined by the interaction and adjustment of its material and structural properties evident at macroscopic, microscopic and nanoscopic levels[1,70,72,79-82]. At the material level, the collagenous extracellular matrix of bone provides resistance to tension, whereas the mineral inorganic phase of bone provides resistance to compression. Indeed, variations in collagen (such as osteogenesis imperfecta) or mineralisation (such as anti-resorptive drugs) can weaken or strengthen bone. Microscopically, the trabeculae in trabecular meshwork have implications on bone stuctural strength, and macroscopically, varying the shape of the bone will increase or decrease the amount of bending and torsion a bone can withstand given a particular amount of total mineral mass.

The adaptability, modulation and regulation of bone to mechanical and non-mechanical stimuli provides practitioners with the ability to directly influence and target bone strength through numerous interdependent mechanisms. Specifically, deterministic site-specific bone strength adaptations are driven by habitual mechanical loading, whereas general and non-specific bone strength adaptations are predominantly driven through endocrinological variations, responsive to physical, pharmacological and nutritional interventions[1,32,33,83-86]. As all forms of bone adaptation collaboratively determine structural integrity and mechanical competency, it is desirable to optimise and preserve bone strength during growth, development, maturity and advanced age through multi-disciplinary and holistic approaches which importantly address all bone strength determinants. The biological basis of bone strength is determined by its structure and function through its anatomy and physiology.

Bone anatomy

Skeletal function

Our skeletons are responsible for several important mechanical and non-mechanical functions[22,36,87]. Mechanically, they provide a structural framework and stable foundation for human movement and locomotion to occur, generating mechanical rigidity and kinematic connectivity within the body[22,36,88-90]. It specifically achieves this by providing skeletal muscle with attachment sites to use as leverage points and platforms with which to act, contract and produce force, and serves to protect the brain, spinal cord and internal organs[2,18,26,36,91,92]. Non-mechanically, bone provides a reservoir for mineral deposition and blood regulation of calcium and phosphorous, supports haematopoiesis, defends against acidosis, and absorbs or captures potentially toxic minerals[22,26,36,91,93]. In order to fulfil these many functions

simultaneously, bone has unique structural, morphological and mechanical properties that are highly dynamic, metabolically active and physiologically adaptive to the environment in which they're exposed[21,23,88,94]. Bone is also highly vascular, facilitating the perfusion of oxygenated blood to enable the removal of metabolites and provision of nutrient availability required by bone to constantly model (form new bone) and remodel (recycle damaged bone) in response to routinely imposed mechanical demands, subsequently altering its configuration and material properties to preserve or increase strength in order to meet its functional requirements[18,19,24,79,89].

In its adult form, the human skeleton consists of approximately 200 distinguishable bones, with 74 located in the axial skeleton, and 126 located in the appendicular skeleton[22,95]. Long bones, however, are the most commonly loaded structures and therefore strongest load-bearing bones in the body, predominantly in the appendicular skeleton. They comprise of a hollow cylindrical shaft known as the diaphysis, a cone-shaped proximal and distal metaphysis, and rounded proximal and distal epiphysis[22,96-98], each portion has different architectural features which are organised and configured to withstand and manage different physical loads during regular activities of daily living[79,80,88,99].

Macroscopic architecture

Bone is a structurally complex and sophisticated biomaterial[1,2,4,33]. It must be rigid and stiff to withstand forces and accommodate loading, yet be flexible and elastic to deform and absorb energy[24,80,100,101]. It must shorten and widen under compression, yet lengthen and narrow under tension, whilst also withstanding torsional and shear forces in isolation and in combination without experiencing catastrophic failure[24,79]. In order to manage these contradictory and paradoxical requirements, the skeleton contains two macroscopic osseous tissues (trabecular and cortical bone) which are architecturally and functionally different[33,81,102-105]. In its entirety, skeletal mass consists of approximately 20% trabecular tissue and 80% cortical tissue, which co-exists at various proportions in all bones through-out the body in accordance with the functional and regional demands of each individual bone[18,22,79,80,105,106]. The structural intricacies and interactions between these two osseous tissues, enable long bones to be remarkably light yet durable and strong in order to facilitate locomotion[24,79,82,107,108].

Trabecular bone

Trabecular bone, also known as cancellous bone, is encapsulated beneath cortical bone. It is most prominently found in weight-bearing skeletal structures, specifically the proximal and distal ends of long-bones (epiphyseal and metaphyseal regions), the carpals and tarsals of the extremities, and vertebrae[22,79,81,109,110]. Texturally, trabecular tissue presents as a meshwork of bone (trabeculae) with many interconnecting spaces through-out which contain red bone marrow[88,102,111-114]. The three-dimensional lattice-like structure of trabecular bone is primarily organised in the direction from which the greatest stresses are most commonly experienced, a design best suited for the mechanical loading of bone[7,89,101,109,114-116]. The spongy and porous architecture of trabecular bone enables it to store large amounts of energy prior to yielding[18,23,105,117,118], thus allowing it to routinely tolerate cyclical low-grade forces.

Cortical bone

Cortical bone, also known as compact bone, forms the thin superficial layer of all bones, though is most prominently found in the thick central cortex (diaphysis) of long bones through-out the appendicular skeleton[2,22,95,119]. Cortical bone encapsulates trabecular bone, however the relative co-existence and composition of each tissue varies between bones through-out the skeleton[1,18,99,102]. In long bones, cortical tissue is arranged in a cylindrical fashion with concentric layers across two primary surfaces: the periosteum (a dense fibrous membrane forming the outside layer) and endosteum (a thin membrane forming the inner layer) of the diaphyseal shaft[79,95,97,111,119-122]. Both surfaces contain important cells (osteoclasts, osteoblasts and osteocytes) responsible for modelling and remodelling processes essential to bone adaptation and osteogenesis[17,24,25,97,123]. The endosteum additionally lines the central cavity with yellow marrow[88,95,111,112,122]. Structurally, cortical bone is highly organised, densely packed, rigid, and texturally smooth[18,23,111,120], with mineralized lamellar bone and collagen fibre matrix most prominently arranged in the direction of routine mechanical stress[69,101,119,120,124,125]. This provides cortical bone with an increased capability to tolerate sudden, high impact forces i.e. a sample of cortical bone is ~25% stronger than a sample of trabecular bone[1,18,23, 119,126].

Microscopic architecture

Bone also has microscopic and sub-microscopic levels which, together with the macroscopic level, form a multidimensional architectural biomaterial with a deliberate mass (size, geometry and density) aimed at achieving optimal structural strength[1,33,70,73,80]. Microscopically, bone presents in the form of woven and lamellar bone at the tissue level[81,98,127-129], and consists of organic and inorganic components at the material level[26,33,59,130-132].

Tissue level

Bone presents in the form of immature (woven) and mature (lamellar) tissue at different stages of the modelling and re-modelling processes at the microscopic level[22,100,127,129,133-135]. Woven tissue is an immature form of bone characterised by a random and spontaneous collagen arrangement, a large volume of cells, and relatively low tissue density[100,104]. It is formed rapidly, producing a highly unorganised and porous structure[22,127,128]. Woven bone features primarily through-out development, exclusively forming the entire skeleton at

birth prior to a gradual transformation into mature lamellar bone during growth and physical maturation[22,98,100,136]. At any other time, woven bone formation occurs only following an injury or extreme structural overload which is thought to be a rapid, protective and restorative response to significantly damaged or weakened hard tissue structures[2,127,137-139]. It is therefore considered a premature and provisional material. Lamellar tissue, however, is a mature form of bone, which eventually replaces woven tissue in the form of trabecular or cortical bone formations. Lamellar tissue is characterised by a precise and deliberate parallel and concentric arrangement of lamellae sheets produced slowly due to a low turnover rate[2,81,98,134]. Lamellae sheets are formed in alternating directions that vary in rotational position and thickness in order to optimally withstand mechanical loads, in particular torsional stress[1,81,95,128,134]. Lamellar bone is therefore denser and stronger than woven bone[22,100,101,140].

Material level

Bone is a specialised, bi-phasic connective tissue consisting of extracellular organic material coupled with a uniquely high content of mineralised inorganic material[1,18,33,124,130,141]. The organic portion provides bone with one-third of its mass and two-thirds of its volume; whereas the inorganic portion provides bone with the remaining two-thirds of its mass and one-third of its volume[59,70,132]. The extracellular organic component is mostly collagenous, conferring flexibility and resilience to bone by solidifying in tension as a protection against stretching, twisting and torsion[142-146]. Conversely, the mineralised inorganic component is primarily calcium and phosphate in the form of an insoluble salt known as hydroxyapatite[130,147-152], giving bone its hardness and rigidity, particularly in compression[153-155]. As a result, the overall structural strength of bone relies upon the joint contribution and inter-play of these organic and inorganic material properties[1,2,24,148,153], such that variations of inorganic mineral density will potentially adjust stiffness and flexibility arrangements in bone[24,130,156], the optimal balance of which remains largely unknown. That is, highly mineralised bone can become brittle (e.g. atypical femoral fractures), whereas less mineralised bone will be tougher yet less stiff (e.g. greenstick fracture). Fortunately, this can be somewhat examined as elements held within the mineralised (inorganic) portion of bone provide considerable resistance to X-ray beams, forming the theoretical basis underpinning the use of bone densitometry devices.

Bone physiology

Historically, bone has been regarded as the domain of anatomical study. However mechanically receptive, biologically adaptive and metabolically active features of bone have since solidified it as a biomaterial well-suited for physiological and biomechanical investigation[2,12,69,89,157]. In particular, the skeleton is able to construct (model) and reconstruct (remodel) itself through cellular processes in response to developmental and mechanical loading demands through tightly controlled cellular activities[20,21,24,25,91,93,158].

Cellular mechanisms

Bone is generated, regulated and maintained by an interaction of four key cells: osteoblasts, osteoclasts, osteocytes and extra-cellular lining cells[13,19,26-28,159]. Osteoblasts are anabolic in nature, producing new bone material by synthesizing and calcifying newly generated collagen[2,21,23,141]. Osteoblasts are uniquely adaptable and compatible, transforming into bone lining cells (surrounding the extra-cellular matrix) and osteocytes (embedded within the bone matrix) during the osteogenic process[25,160-162]. Conversely, osteoclasts are a catabolic cell which degrades, dissolves and resorbs bone material, often as a response to material damage or disuse[21,29,123,163]. Osteoclasts have a limited lifespan, undergoing apoptosis (programmed cell death) within 2 to 4 weeks of osteoclastogenesis[25,123,164]. Osteoblasts and osteoclasts work independently during bone creation and formation (modelling), and co-operatively via a basic multi-cellular unit (BMU) during bone maintenance and homeostasis (remodelling).

Osteocytes are central to bone development and renewal as the most abundant residential cell in bone, accounting for approximately 90% to 95% of all bone cells[66,141,162,165,166]. Specifically, osteocytes are descendants of osteoblasts produced during osteogenesis, which subsequently become entombed within the mineralised collagen matrix[25,27,66,109,162]. Osteocytes form a well-connected network of sensory channels to detect environmental alterations and communicate reactionary processes to osteoblasts, bone lining cells and fellow osteocytes[13,136,165,167,168]. This network is explicitly formed by dendritic connections (~60 to 80 per osteocyte) which proliferate through canaliculated passages to provide a functional and mechanosensitive platform integral to the detection of mechanical load and associated microdamage[13,66,158,165,167]. This mechanically sensitive function, known as mechanotransduction, enables bone to physiologically detect and convert mechanical energy into proportionate biochemical signals in order to promote growth and repair processes[59,60,65,158,168]. The process of mechanotransduction, including how bones sense mechanical changes, are described further under the Bone Adaptation section of this review.

Hormonal mechanisms

Bone growth, development and preservation is largely reliant upon hormonal regulation, globally controlling skeletal homeostasis somewhat independently of mechanical loads through-out the lifespan in order to facilitate non-mechanical functions of bone[33,169-173]. Specifically, the endocrine system serves to maintain bone mineral deposition and homeostatic cellular balance through continual, non-mechanically induced generation and regeneration of bone during biological growth and maturation[24,174-177]. While the endocrine system does

Table 1. Endocrine regulation of bone metabolism.

Hormones	General Description	Bone Metabolism
Growth Regulators		
hGH	Peptide hormone secreted from the anterior pituitary; influences muscle, liver, kidney and bone; promotes longitudinal growth of bone.	Stimulates Formation
IGF-1	Polypeptide with an essential role in growth and development; primarily circulated by liver; also paracrine delivered by non-hepatic tissues.	Stimulates Formation
Glucocorticoids	Produced by adrenal glands, inhibits synthesis of IGF-1, supresses BMP-2 and calcium absorption.	Inhibits Formation Stimulates Resorption
Ghrelin	Gut-derived peptide hormone; secretagogue of growth hormone; modulates energy homeostasis.	Stimulates Formation Inhibits Resorption
Leptin	Adipocyte peptide hormone; proportional to fat stores; modulates energy homeostasis.	Inhibits Formation Stimulates Resorption
Thyroxin (T_3 and T_4)	Tyrosine-based hormones produced by thyroid gland; regulates energy metabolism through thyroid stimulation hormone (TSH) activity.	Stimulates Formation Stimulates Resorption Net Effect: Homeostatic
ACTH	Peptide hormone secreted from the anterior pituitary; stimulates cortisol production; dose- dependent proliferation of osteoblast activity.	Stimulates Formation Stimulates Resorption Net Effect: Homeostatic
Oxytocin	Peptide hormone secreted from the posterior pituitary; modulated by estrogen; autocrine- paracrine osteoblast regulator of formation.	Stimulates Formation Stimulates Resorption Net Effect: Homeostatic
Gonadal Regulators		
Androgens	Sex steroid secreted from testes (men) and adrenals (men and women); also converts to estrogen; acts in presence of hGH.	Stimulates Formation
Estrogen	Synthesised from androgens in ovaries (women) and extra-glandular tissue (men and women); dominant role in bone metabolism.	Permits Formation Inhibits Resorption
Calcitropic Regulators		
PTH	Polypeptide secreted by parathyroid gland, tightly controls calcium and phosphate; acts to maintain bone mineral homeostasis.	Stimulates Formation Stimulates Resorption Net Effect: Formation
Calcitonin	Secreted by thyroid gland when plasma calcium is elevated; lowers plasma calcium; deposits into bone; relatively weak in comparison to PTH.	Stimulates Formation Inhibits Resorption
Vitamin D_3	Activated in the liver and kidney; essential for intestinal absorption of calcium and phosphate; deficiency results in bone demineralisation.	Permits Formation Stimulates Resorption

not explicitly strive to optimise bone strength, endocrine status can have a profound, indirect and negative impact on structural integrity and mechanical competency when irregular hormonal environments arise[172,173,178-183]. Endocrine activity therefore forms a central component of a complex biological system that mediates calcium-phosphate balance, energy metabolism and bone mineralisation in response to dynamic and volatile physiological requirements[179,184-190]. In this regard, endocrine function majorly influences bone health and metabolism, ascending into domination through adulthood and advanced ageing[169,175,178,182,183,191,192].

Endocrinological regulation of bone metabolism is highly influenced and tightly controlled by sub-categories of growth, gonadal and calcitropic hormones (Table 1), with varying levels of contribution and relative dominance through-out life[170,174,175,178,187-206]. Specifically, growth hormones exert formative effects; gonadal hormones exert formative and anti-resorptive effects; and calcitropic hormones exert homeostatic effects; co-operatively acting to promote bone mass accrual during growth and maturation[171,178,179,183-186,189,192,207-213]. However, hormonal activity begins to decline following the establishment of peak bone mass, as bone formation and resorption shifts from net formation during ontogeny, to equilibrium during early-to-middle adulthood, and net resorption during advanced and older age[24,34,71,173,214]. This imbalance in bone metabolism is primarily driven by altered endocrine-paracrine activity, and confounded by multi-dimensional, synergistic and antagonistic hormonal interactions necessary to achieve and maintain metabolic homeostasis[21,23,123,191,215]. As a result, hormonal imbalances and environmental irregularities underpinning deficient endocrine function form the nutritional and pharmacological basis of bone preservation strategies[34,214,216-218], utilising natural and artificial suppression and stimulation of bone

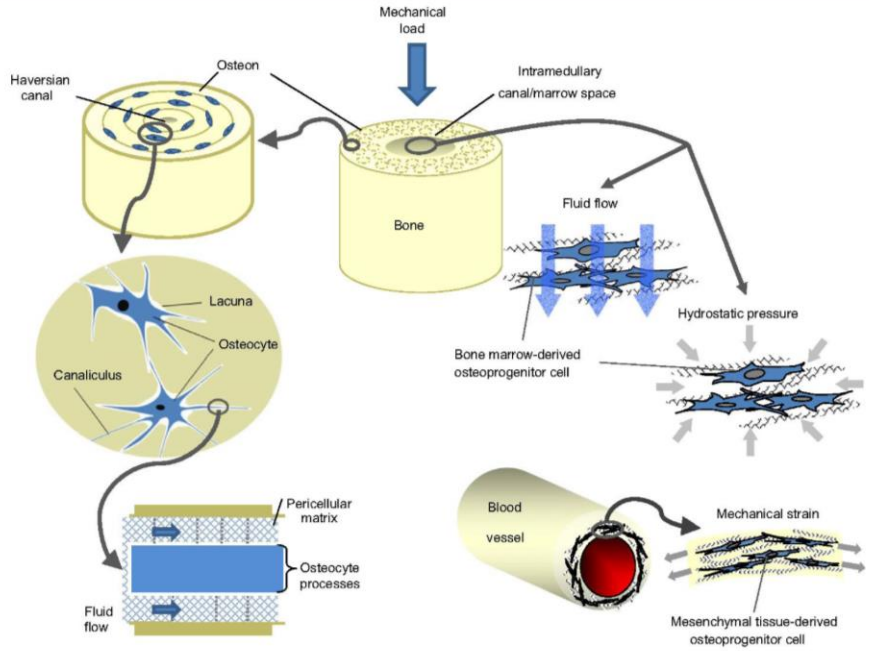

Figure 1. Mechanotransduction (adapted from [14,15]): illustrating the hierarchical structure of bone and the organizational structure of osteocytes within (left); and the mechanically induced fluid flow from hydrostatic pressure and osteoprogenitors through which biochemical signals proliferate (right).

resorption and formation to prevent and manage pathogenic conditions through-out the life-span.

Bone adaptation

Mechanotransduction

Bone modelling and remodelling paradigms pioneered by Julius Wolff, improved by Wilhelm Roux (Wolff's Law), and expanded upon by Harold Frost (Mechanostat Theory), remain the central focus of emerging and contemporary research[11,89,219-233]. Their meritorious work collectively describes the ability of bone to alter its mass and structure in response to routine mechanical loads[15,69,92,106,234-238]. However, scientific understanding of this mechanobiological relationship remains elusive and poorly understood. The conceptual basis of mechanical events stimulating and mediating bone formation, adaptation, maintenance and repair is widely accepted[2,15,61,141,239]. However, the cellular mechanisms and structural framework which underpins this observed phenomenon is not yet fully understood and forms the basis of current-day research[15,59,62,67,240,241].

In principle, mechanotransduction (Figure 1) refers to the conversion of biophysical forces (mechanical load) into cellular responses which drive morphological change at the tissue level, a functional adaptation of bone which purposely improves structural integrity and strength[13,63-65,158,242,243]. This biologic detection of mechanical force and their conferred cellular responses primarily involve four key activities: 1) mechanical coupling, 2) biochemical coupling, 3) signal transmission, and 4) effector response[60,63,98,133,244]. Specifically, forces which lead to bone deformation create interstitial fluid movement within canaliculi, stimulating biochemical activity via mechanosensory cells[64,245-251]. Piezoelectric signals are then transmitted through comprehensive lacuno-canalicular networks of osteocytes, lining cells and osteoblasts to determine the format and magnitude of cellular response relative to the perceived dose of mechanical load[59,65,98,113,141,252-255]. This fundamental dose-response relationship between mechanical load and structural bone adaptation provides the foundation of bone modelling and re-modelling theory[63-65,158,240,243,256].

Modelling

Modelling is a dynamic and constructive process which adjusts the size, shape and strength of bone in order to

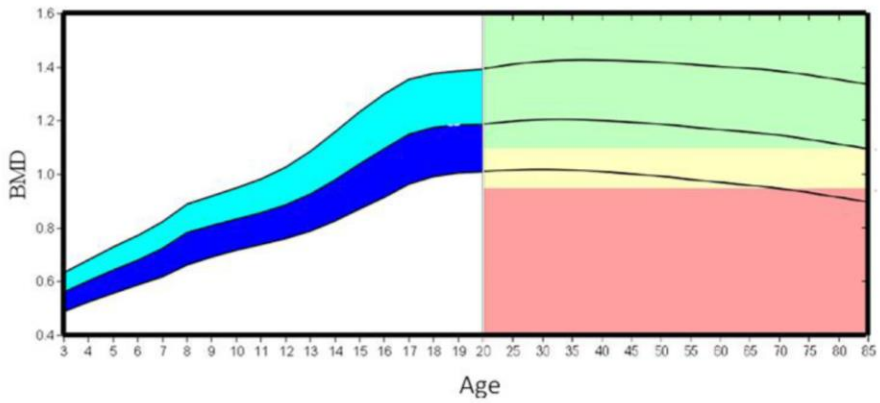

Figure 2. Bone mineral density accrual, maintenance and loss through-out the life-span as indication of bone mass alterations; with approximately 50–60% of total adult bone mass gained during adolescent years preceding peak bone mass and skeletal maturity at ~30 years of age. Bone mass deteriorates gradually following peak bone mass into older age to within normal (green), osteopaenic (yellow) or osteoporotic (red) bone density ranges.

achieve its structural potential during ontogeny, specifically in response to physiological and mechanical influences through-out physical maturation[22,79,111,122,257-259]. It comprises of a complex and multifarious array of cellular and material activity which interact to position and configure cells and matrices during growth and development[7,69,239]. At the cellular level, osteoblasts work independently from osteoclasts to create an environment where matrix deposition exceeds matrix resorption[11,15,22,111,260,261]. At the tissue level, this is expressed through periosteal apposition and simultaneous yet slower endocortical resorption[22,73,82,97,107,111,122,261,262], leading to the formation of new bone material and partial preservation of old bone material to deliver a net increase in bone mass[15,24,79,243,263,264].

Longitudinal and radial growth are developmental features of depositional modelling during ontogeny. In particular, collagen is synthesised and deposited onto the extracellular matrix in order to elongate, thicken and widen the periosteum, while endocortical resorption expands the marrow cavity to concurrently increase the diameter of the endosteum together with the periosteum[22,69,79,82,97,107,122,265]. These morphological alterations structurally enhance bone strength through two key mechanisms: 1) increasing the bony (i.e. excluding any cavities) cross-sectional area, and 2) by placing the material farther from the centre of the bone, which increases the polar moment of inertia[1,22,69,73,82,258]. Increasing the amount of bone material in a given cross-section improves bone strength in compression and tension, whereas distributing bone material farther from the centre of the bone improves strength in bending and torsion. For further details on bone mechanics, refer to our companion review[12]. Ultimately, these morphological alterations keep stresses and strains of applied mechanical loads within a desired range by distributing compressive forces over a larger area, while also resisting bending and twisting forces at the mid-shaft[69,72,73,107,266-268].

Bone formation is presently thought to be limited to the first three-decades of human life, achieving maturity at this time to establish peak bone mass[269-271]. The potential of bone to develop during growth is influenced by a range of non-modifiable (gender, ethnicity, genetics) and modifiable (nutrition, hormones, lifestyle, physical activity) factors which ultimately determine skeletal development[73,82,97,257,262,267,272-277]. However, the accrual of bone is not a linear process, with bone developing most rapidly in adolescent years, acquiring ~50 to 60% of total adult bone mass within this short and critical period of time[216,278-282]. Given the heightened sensitivity and responsiveness of bone during its premature stage of life, a considerable opportunity (window of adaptation) is provided to improve skeletal robustness and resilience through maximising bone mass during early-stage development[83,267,283-290]. Despite this apparent ceiling of bone mass augmentation (Figure 2), bone strength is able to increase through other spatially relevant mechanisms in maturity using a regulatory process known as re-modelling[33,73,79,91,269,291,292].

Remodelling

Remodelling is an on-going, homeostatic and restorative process which replaces old and damaged bone with new and healthy material (Figure 3) to maintain and improve structural integrity and mechanical competency[19-21,23,26,29,82,107,159,293]. The regulatory nature of

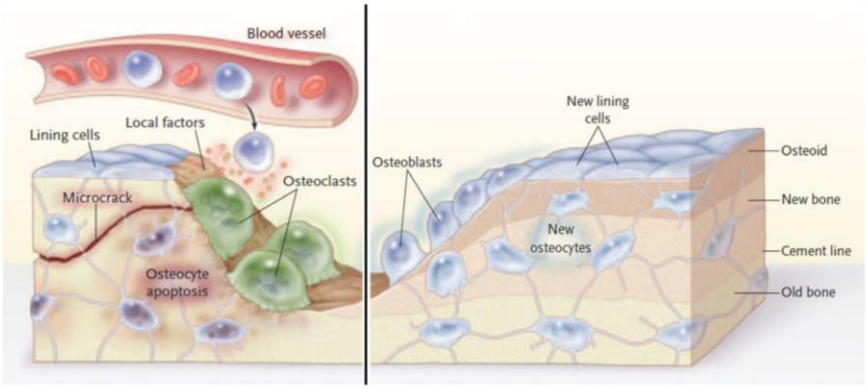

Figure 3. A graphical representation of the remodelling cycle (adapted from [24]). Bone resorption (left) is stimulated by a micro-crack which severs canaliculi channels between osteocytes leading to osteocytic apoptosis. Lining cells and osteocytes release signals attracting cells from blood and marrow reservoirs into the damaged area leading to osteoclastogenesis. Bone formation (right) commences with successive streams of osteoblastic activity depositing new lamellar bone. Osteoblasts then transform into new lining cells (extra-cellular layer) or osteocytes (embedded in osteoid and bone matrix).

Table 2. Adult bone remodelling (adapted from [96,109,110,123]).

• Lifespan of BMU: **~6-9 months**
• Duration of remodelling: **~4-6 months**
• Speed of remodelling: **~25 µm/day**
• Bone volume replaced by a single BMU: **~0.025 mm^3**
• Lifespan of osteoclasts: **~2 weeks**
• Lifespan of osteoblasts (active): **~3 months**
• Interval between successive remodelling events at the same location: **~2-5 years.**
• Rate of turnover of whole skeleton: **~10% per year** [a]
[a] 10% per year approximation assumes 4% turnover per year of cortical bone (75% of the skeleton), and 28% turnover per year of trabecular bone (25% of the skeleton): Calculated as [0.75 x 4] + [0.25 x 28] = 10%; BMU = basic multicellular unit.

re-modelling relies upon integrated sensory signals in order to provide a feedback-controlled modulation of skeletal structure; a mechanism designed to sustain current and future functional requirements[20-24,79,80,91,111]. This complex and multidimensional process is essential to ensure bone structure remains balanced between excessive bone mass and excessive bone fragility (a continuum of robustness to slenderness) in order to optimise bone strength without sacrificing mobility; one of many paradoxical expressions of bone adaptation[17,25,29,82,107,123].

Remodelling occurs through stochastic and deterministic mechanisms[19,20,59,80,91,294]. Stochastic remodelling describes randomly delivered and spatially non-specific forms of regeneration via the endocrine system, whereas deterministic remodelling forms the morphological and mechanosensitive basis of bone strength adaptation through-out the lifespan[15,17,123,293,295]. Specifically, deterministic remodelling represents a precisely assigned, targeted and site-specific form of remediation to repair damaged bone or initiated as a consequence of mechanical behaviour[2,19,237,292,293,296,297]. In particular, bone acutely and accumulatively incurs microdamage in response to mechanical loading (gravitational and muscular forces), requiring coordinated cellular-level and tissue-level activity in order to manage and prevent structural failure and bone fracture[21,59,79,80,297]. As a result, bone is resorbed in regionally and temporally distinct locations, detected and driven at the cellular level by osteocytes through mechanotransduction in order to target, repair and replace damaged material at the tissue-level[19,20,24,29,79,293,296].

Unlike modelling, remodelling requires a coordinated, tightly coupled and sequentially activated cellular response between osteoclasts and osteoblasts in order to resorb damaged bone and deposit healthy bone without sacrificing mechanical competency[19,29,33,111,159,242]. This response is effectuated by basic multicellular units (BMU's), temporary structures composed of grouped osteoclasts and osteoblasts in the presence of blood supply and connective tissue[11,21,26,82,110,219,298,299]. Biologically, these multicellular units are similar between cortical and trabecular bone, following a standard activation-resorption-formation sequence via osteocyte-osteoclast-osteoblast integration[23,25,123,242,294,299,300]. However, owing to their differences in organisation, morphology and vascular supply, cortical bone remodels using a tunnel-like resorptive cavity (2000 µm long; 200 µm wide), with a low surface-to-volume ratio and slow turnover rate; whereas trabecular bone remodels using a superficial trench-like resorptive cavity (60 µm deep), with a high surface-to-volume ratio and faster turnover rate[7,17,20,23,242]. As a proportion of total skeletal mass, approximately 3 to 5% of cortical bone and 25 to 28% of trabecular bone is remodeled each year, completely regenerating the adult skeleton approximately every 10 years[23,27,110,123].

Degradation

Degradation is a gradual deconstructive process whereby bone material and structure begin to decline and decay through catabolic cellular activity such that resorption exceeds deposition overtime, subsequently compromising the mechanical competency and ultimate strength of bone[17,296,301-304]. This occurs through non-mechanical and mechanical mechanisms in isolation and combination. Non-mechanical degradation represents bone loss during advanced biological ageing and associated pathological conditions such as osteopenia, osteoporosis and other disease-states[26,33,34,79,84,305-308]; whereas mechanical degradation refers to environments of disuse (immobilisation and microgravity) or overuse (repetitive loading) which are preventable and reversible[17,309-315]. As the cellular governance of bone generation, regeneration and repair is mainly responsive to mechanical load[11,17,24,157,277,296,304,306,316], the absence or overload stimulus can lead to net-resorptive activity and subsequent bone degradation[26,303,307,312, 317-319].

Removal of mechanical loads through microgravity (space travel), disuse (immobilisation) or spinal cord injury (partial or complete paralysis) results in rapid loss of bone mass[303,309,312,315,320-332]. Specifically, bone density decreases by ~2% each month through microgravity, partial paralysis or immobilisation without injury, and ~7% each month following complete paralysis or immobilisation with associated musculoskeletal injury[17,26,303,319,321,322,333-338]. However, actual strength loss is likely greater, as concurrent reductions in cross-sectional area and mineral content are concealed by bone density measures, yet have dramatic consequences on bone strength[1,36,70,73,80,103,316,339]. Nevertheless, bone loss is incremental and progressive with time and occurs more rapidly in trabecular bone than cortical bone, owing to their different rates of responsiveness to muscular and gravitational osteogenic stimuli[17,26,103,115,307,308]. In reversible situations, the time-course and magnitude of recovery is markedly slower and more gradual than loss[17,309,315,319,326,327,340,341].

Bone loss is also uniquely layer specific within the skeleton, eloquently demonstrated in ageing and spinal cord injury cohorts[303,342]. Specifically, through aging or following spinal cord injury, bone cross-sectional area observably loses material from the endosteal border and intra-cortically, with no clear evidence at the periosteal level[102,343,344]. For example, individuals with traumatic paralyisis prior to growth cessation develop smaller periosteal circumferences relative to non-paralysed referents, however individuals paralysed after growth cessation have similar periosteal circumferences to non-paralysed referents[303,342,345-347]. Conversely, bone accretion can occur at the endosteal and periosteal surfaces[348-350], however whether or not age-related endosteal and intracortical bone resorption can be reduced or prevented with skeletal loading is currently unclear[351,352]. In contrast to deterministic mechanical loading effects, antiresorptive and proformative drugs exert their effects systemtically (stochastically) through-out bone material[353-355]. Taken together, while cellular proceses are tighly coupled, whole organ bone resorption and accretion may be situated at different locations within and along the bone, and that particular surfaces may be preferentially affected. This complex inter-play of bone loss and bone accretion across bone cross-sectional areas and along bone lengths requires dutiful consideration when designing and evaluating mechanical, dietary or pharmacological interventions.

Excessive mechanical loads supplied through repetitive and cyclical activity may also yield net-resorptive and degradative effects on bone[38,52,74,75,356]. In the absence of appropriate recovery, bone fatigue leads to the accumulation of microdamage and coalescence of microcracks, subsequently increasing the total magnitude and rate of remodelling activity at any given time[51,75,296,357-359]. Given that bone reparation requires damaged tissue to be removed (~1 month) and then replaced (~3 months) at various bone sites simultaneously; excessive magnitudes and rates of remodelling have considerable microstructural consequences, progressively weakening bone through loss of stiffness and strength until eventual failure in the form of stress reactions, stress fractures, or heightened susceptibility to traumatic fracture[38,51,52,74,91,356,358]. In this regard, weakened bone acquires damage at lower relative strain magnitudes; thus fatigued bone creates a progressive and positive feed-back loop between mechanical load and damage accumulation[57,76,157,301,304,317,358-360]. Increasing bone strength reduces fatigability to customary loads, providing greater protection against exercise-induced degeneration, however, more importantly, rest and recovery periods are imperative to ensure structural integrity and mechanical competency remain[1,17,70,157,306,361].

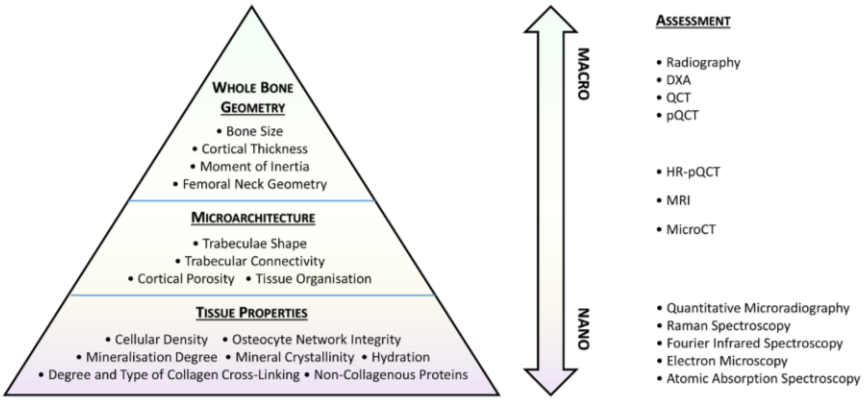

Figure 4. Material and structural determinants of bone strength or fragility (left) with associated technologies required to examine bone properties (right); along the macroscopic, microscopic and nanoscopic continuum [top to bottom], (adapted from [1]).

Measuring bone strength

Bone material, structure and strength must be quantifiable in order to examine, diagnose, monitor and manage skeletal health and bone quality cross-sectionally and longitudinally as a mechanism to establish interventional efficacy of programs designed to enhance or preserve bone strength[1,24,36,362,363]. However the accessibility of bone in-vivo remains a constant barrier to scientists. While cadavers are often used to investigate historical events and lasting transactions in bone[76,78,364-366], understanding the volatile and evolving adaptations of living and responsive hard-tissue remains elusive[24,367,368]. Modern-day advancements have attempted to overcome such limitations by developing a multitude of technologies (Figure 4) aimed at non-invasively measuring bone density, structure and strength of various depths, scales and resolutions[1,369-372]. Owing to their relative cost, availability and levels of radiation exposure, DXA and pQCT are commonly used bone densitometry devices in clinical and research environments[372-377], often supported by the collection of biochemical markers through serological and urianalytical samples as surrogate measures of bone metabolism[87,378,379].

Dual-energy X-ray absorptiometry

Dual-energy X-ray Absorptiometry (DXA) is a low-resolution, uniplanar, two-dimensional bone densitometry imaging device which measures full-body and segmental projections of mass quantities and densities in-vivo using low-level radiation through x-ray technology[374,380]. Specifically, DXA emits two distinct photon energies (140 KeV/70 KeV) via collimated pencil, fan or narrow beams which pass through the individual; the attenuation coefficients and ratios of which differentiate hard tissue from soft tissue, and fat mass from lean mass in an expedient and effective manner[380-382]. Importantly, DXA quantifies areal bone mineral density (aBMD) and its derivatives (bone area and bone mineral content) in order to examine bone quality[383-385], while also measuring body composition, specifically quantifying soft tissue (fat mass and lean mass) simultaneous with hard tissue (bone mass) in order to concurrently measure materials which co-adapt with each other[381,386-388]. While DXA produces valid and reliable, scan-rescan measures of whole-body bone mass characteristics and body composition components, numerous standardised nutritional, procedural and analytical controls are required to ensure longitudinal integrity of measures when examining interventional efficacy[386,389-394].

Bone health and skeletal fragility diagnoses of bone disorders are clinically defined by the World Health Organisation using DXA-derived aBMD T-scores from population-based reference values, highlighting its established and reputed position as the gold standard in clinical environments[384,395-397]. However, clinical examinations using DXA technology are inherently flawed, as bone material (architecture) and structure (size and shape) cannot be measured[374,383,398,399]. Specifically, DXA's uniplanar, low-resolution images restrict clinicians to descriptions of whole bone mass, which only partially explains bone strength variation[24,398,400-402]. Inaccurate diagnoses of osteoporosis therefore prevail, with many fragility fractures prevalent in categorically low-to-moderate risk individuals, classified within normal or osteopenic regions[72,275,373,397,403], further confounded by regional disparities and T-score variations between measurable sites within a given individual. Indeed, denser bone isn't always stronger, and low density isn't

Table 3. Available biochemical markers used to examine formative, resorptive and rate of bone metabolism through serological and urianalytical mechanisms[87,431].

Biochemical Marker	Abbreviation	Sample	Bone Metabolism
Bone Alkaline Phosphate	BAP / BALP	Serum	Formation
Osteocalcin	OC / BGP	Serum	Formation
Carboxyterminal, Type I Collagen	PICP	Serum	Formation
Aminoterminal, Type I Collagen	PINP	Serum	Formation
Pyridinoline	PYR	Serum & Urine	Resorption
Deoxypiridoline	DPD / D-PYR	Serum & Urine	Resorption
Carboxyterminal Crosslink, Procollagen I	ITCP	Serum	Resorption
Carboxyterminal Crosslink, Type I Collagen	CTx	Urine	Resorption
Aminoterminal Cross-link, Type I Collagen	NTx	Urine	Resorption
Tartrate-resistant Acid Phosphate	TRAP5	Serum	Resorption
Parathyroid Hormone	PTH	Serum	Turnover Rate
Note: Information adapted from [69,431].			

always osteoporotic[383,384,403,404], thus no identifiable total body or site-specific BMD threshold abruptly or disproportionately increases fracture risk. Instead, BMD is continuously variable with fracture risk, such that lower BMD equates to higher fracture risk, however does not explicitly predict it[373,384,401,404]. Therefore, more refined and detailed analyses of bone material and structure are required for more appropriate and predictive diagnoses, potentially deliverable with other technologies[24,383,385,399,405,406].

peripheral Quantitative Computed Tomography

Quantitative Computed Tomography (QCT, axial; pQCT, peripheral) is a multi-planar, three-dimensional bone densitometry imaging device which measures the material and structural properties of bone at macroscopic depth, providing clinicians with more accurate descriptions of bone shape, size and quality[399,407,408]. Specifically, pQCT transmits targeted collimated beams at selected sites along the length of a given long bone, reconstructing rotational and contiguous two-dimensional samples at each site to deliver a three-dimensional cross-sectional tomographic image of bone, muscle and fat[409-411]. As a result, pQCT devices are able to provide unobstructed circumferential measures of hard- and soft- tissue masses, generating volumetric measures of area, content and density for trabecular bone, cortical bone, marrow, muscle and fat compartments; bone strength indices and fracture loads; periosteal and endosteal size; cortical thickness; and bone mass[410-414]. Diagnostically, this enables pQCT to address many limitations previously experienced through DXA examinations which provide precise, stable and reliable measures of bone and muscle components[333,376,383,399,407,411,412,415].

Bone quality and skeletal fragility examinations using pQCT are superior to those provided by DXA[373,408,414,416]. Importantly, applications of mechanical assumptions to quantified material and structural properties across numerous cross-sections allow indices of bone strength to be established, providing better predictive accuracy of fracture risk beyond generic aBMD and vBMD measures[383,408,412-415,417,418]. Despite the advantageous diagnostic power afforded to clinicians using pQCT, complexity arises as normative and comparative data for general, specific and special populations scarcely exist at present, owing to its emerging status as an alternate imaging device in clinical and research environments[373,399,419-422]. Supplementing DXA measures with pQCT measures has been suggested as a potential solution for a detailed insight of bone strength adaptation and fracture risk with clinically relevant reference values[423]. Some forms of pQCT are limited to macroscopic depth, however the emerging use of micro-scanners (HR-pQCT) provides higher resolution images that are capable of detecting critically important microarchitectural features including trabecular thickness, connectivity and number; cortical porosity; volume fraction; and arterial calcification[127,369,417,418]. HR-pQCT is still gaining ascendency in clinical and research settings due to its relative infancy in development, high associated cost, and limited ability to access an array of peripheral skeletal sites. HR-pQCT is likely to increase in popularity given the diagnostic importance and catastrophic consequence of microarchitectural deterioration in disease-states and advanced ageing, particularly as its technology and capabilities evolve[80,127,275,403,424].

Biochemical markers

Serological and urianalytical provisions of biochemical markers provide clinicians with a useful methodology to examine physiological alterations in bone metabolism, specifically the prevalence of formative and resorptive activity within the skeleton[425-428]. Bone mass accrual, maintenance and degradation are explicitly determined by counteracting

metabolic processes (formation and resorption) responsive to endogenous (hormones, cytokines, growth factors) and exogenous (mechanical loading) factors[318,378,429,430].

Biomarkers become clinically useful to examine bone turnover rates underpinning bone health or skeletal disease (Table 3) and importantly quantify acute and chronic metabolic alterations to experienced stimulus and targeted interventions[87,368,379,425-427,432]. While biochemical samples are easily collected and analysed, do not involve harmful radiation, and have high sensitivity to change; their diagnostic capabilities in isolation are limited[87,368,433,434]. In particular, biomarker concentrations and behavioural profiles are highly variable between individuals, and indiscriminately represent global anabolic or catabolic activity of the entire skeleton, such that biomarker analyses cannot provide targeted and localised examinations of formative and resorptive behaviour[368,433,434]. However, owing to its sensitivity to measure dynamic early onset alterations, biochemical markers can be complementary to other bone quality and skeletal fragility examinations, performed in conjunction with static morphological measures provided by radiographic and densitometric devices[87,378,427,435,436].

Conclusion and future research

Bone is impressive in its design, architecture and maintenance as a living biomaterial with distinct porosities (trabecular and cortical), tissues (woven and lamellar) and materials (organic and inorganic) that, together, form a robust multidimensional structure (macroscopic to nanoscopic) with a deliberate mass (size, geometry and density) aimed at achieving optimal mechanical strength to support locomotion and activities of daily living. Growth, development and homeostasis is eloquently achieved through tightly coupled cellular processes (osteoblasts, osteoclasts, osteocytes and bone lining cells) which underpin bone quality and the continual generation and regeneration of bone in response to mechanical loading and damage acquisition through mechanotransduction.

Although, broadly speaking, bone resorption and formation are tightly coupled, the balance between these two processes can tilt to favour one or the other resulting in net gain or net loss. Key reasons for shifts in otherwise homeostatic balance can be due to the presence or absence of mechanical loading, metabolism (for example, withdrawal of female reproductive hormones through menopause), or pathology. Moreover during growth and development, formation and resorption are not necessarily co-localised in bone (for example, transformative morphological narrowing of long bone metaphyses to become diaphyseal). In addition to understanding the net effect, it is important to realise that the timing and duration of bone resportion and formation do not necessarily happen concurrently. Rather, bone resorption takes less time than formation and typically precedes formation. Additionally, bone formation occurs across essentially two phases: 1) laying down the collagen meshwork, and 2) subsequent mineralisation (explained further in our companion review paper[12]). In terms of the gross bone morpohology, it bears repeating that responses to mechanical loads are site-sepcific. That is, it is entirely possible to have strong lower limb skeletal structures yet weak upper limb skeletal structures as is the case in endurance runners for example. Moreover, even within a long bone, at a particular site-specific location along the length of the bone, it is possible to lay new bone material in particular directions, while the direction at a right angle remains unmodified by loads, and similarly, the diaphysis may adapt while no changes are observed in the epiphysis.

This review highlights the complexity of evolving bone morphology, specific to bone anatomy and physiology, underpinning the biological basis of bone strength, and the many cooperative or competing processes required to delicately maintain bone health. Taking the above together, we assert the need for clinicians and researchers to understand and thus consider the underlying physiology and technical limiations of assessing bone as paramount in devising appropriate clinical measurement and active monitoring strategies to allow timely yet accurate assessments which capture the properties of interest. For example, attempting to capture bone formation with x-ray-based, bone densometric methods will fail unless sufficient time for mineralisation is allowed as only the mineral incorporated into the bone contributes meaningfully to absorbing the radiation used to assess the bone. To this end, for clinical or research interventions aiming to evaluate observed x-ray based, densiometric changes in such properties, a minimum of 6 to 12 months would be our recommendation. Similarly, in-vivo and non-invasive methodologies to assess the quality and properties of type 1 collagen at given bone sites or skeletal regions is a potentially necessary yet presently absent assessment, relying solely on systemic biomarkers (from serum or urine) or bone biopsy, thus limiting the accessibility and our understanding of the organic matrix of bone. Owing to the dynamic nature of bone biology, and its complex and routine interaction and communication between bone cells and other bodily organs, a deeper recognition and understanding of the governance and subservience of various processes and organs within the human body, such as muscle-bone interactions (described in our companion review[12]), will continue to produce new knowledge and assist clinicians and researchers in the development new therapeutic approaches to bone diseases, and management of bone health across the lifespan.

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B.2 Association Between Developmental Coordination Disorder or Low Motor Competence and Risk of Impaired Bone Health Across the Lifespan: Protocol for a Systematic Review and Meta-analysis

SYSTEMATIC REVIEW PROTOCOL

Association between developmental coordination disorder or low motor competence, and risk of impaired bone health across the lifespan: protocol for a systematic review and meta-analysis

Jocelyn Tan[1,2] • Nicolas H. Hart[2,3,4,5] • Timo Rantalainen[2,3,4,5,6] • Paola Chivers[1,2,3,4,5]

[1]School of Health Sciences, University of Notre Dame Australia, Fremantle, WA, Australia, [2]Western Australian Bone Research Collaboration, Perth, WA, Australia, [3]Exercise Medicine Research Institute, Edith Cowan University, Joondalup, WA, Australia, [4]Institute for Health Research, University of Notre Dame Australia, Fremantle, WA, Australia, [5]School of Medical and Health Science, Edith Cowan University, Joondalup, Perth, WA, Australia, and [6]Gerontology Research Center, University of Jyväskylä, Jyväskylä, Finland

ABSTRACT

Objective: This systematic review will assess the association between developmental coordination disorder and low motor competence, and impairments in bone health across the lifespan.

Introduction: Individuals with developmental coordination disorder tend to have a pattern of physical activity associated with bone health impairments. Preliminary studies have found impairments in bone health measures, including fractures, throughout the lifespan with potential public health ramifications. As studies in this area are of small samples across wide age ranges no comprehensive picture of bone health in this group has been formed, hindering action. A systematic review is needed to determine the potential risk of bone impairment in this population.

Inclusion criteria: Studies that assess the relationship between developmental coordination disorder/low motor competence and bone health, regardless of measures used, will be included in the review. There will be no exclusions based on region, study design, or participant demographic characteristics.

Methods: Published studies and gray literature will be searched, with no limits on publication date or language. Assessment of studies for inclusion, as well as data extraction, will be performed by two reviewers, with data cross checked for accuracy. Studies will be appraised using the appropriate JBI tool for the study design. Data to be extracted include unadjusted results and effect sizes for bone health measures. A narrative synthesis will be performed and if there is a sufficient number of studies, a meta-analysis using the same outcome measures will be performed on odds ratios of abnormal bone phenotype and fracture in this population.

Systematic review registration number: PROSPERO CRD42020167301

Keywords bone density; bone strength; developmental disabilities; motor control; movement coordination

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Introduction

Developmental coordination disorder (DCD) is a neurodevelopmental disorder involving deficits in the acquisition and performance of coordinated motor skills throughout the lifespan.[1] The condition is estimated to affect 5% of the population worldwide, with diagnosis more common in males.[2] According to the Diagnostic and Statistical Manual of Mental Disorders, 5th edition,[1] the diagnostic criteria for DCD specify that acquisition and execution of motor skills are significantly below what is expected given the individual's age and skill learning opportunities (criterion A), which consequently have an ongoing significant impact on age-appropriate daily living activities, leisure, education, or employment (criterion B).[1] As impairments with motor skills can occur due to inactivity and medical

Corresponding: Jocelyn Tan, jocelyn.tan@my.nd.edu.au
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conditions, the diagnostic criteria specify that motor deficits must present early in development (criterion C) and be beyond what can be explained by conditions affecting motor skills such as intellectual disability, visual impairment, or neurological conditions affecting movement (eg, cerebral palsy) (criterion D).[1] Due to low diagnosis rates, research on DCD often includes researcher assessment of a participant's ability to meet diagnostic criteria, with low motor competence (LMC)—a more general term for motor skill difficulty[3]—being used when the full diagnostic criteria have not been assessed.[4]

Due to their motor skill deficits, individuals with DCD tend to have low levels of physical activity from a very early age continuing throughout the lifespan.[2] This is particularly applicable for diverse and high-intensity physical activity.[2,5,6] This pattern of physical activity has been linked to impairments in bone health development in other populations.[7-9] Bone health is a dynamic system impacted by a number of factors such as genetics, hormones, and nutrition, alongside physical activity.[8] Some of these conditions occur more commonly in individuals reported to have DCD, either due to a common causative pathway, such as prematurity and low birth weight,[10] or due to classification of other intrinsic movement difficulties as DCD.[2] Preliminary studies in this area have found an impairment in bone health in individuals with DCD on a variety of bone health measures across age groups.[11-15] Studies in the pediatric population have found impairments in overall bone health, measured indirectly via skeletal age[14] and directly via bone mineral density.[15] Extended cohort studies in an adolescent population have consistently found decreased bone health measures by peripheral quantitative computed tomography,[11-13] and the only known study in the adult population found decreased bone mineral density in the hip,[16] indicating that this continues through the lifespan. However, current research in this area has contained small samples, broad age ranges, and mixed definitions of DCD and LMC, making it difficult to draw a comprehensive picture.

A comprehensive understanding of impaired bone health in this population is necessary, as there is potential for profound ramifications for health. Individuals with DCD have a high fall occurrence,[13,17] which, combined with impaired bone health, substantially increases the risk of osteoporotic fracture. Studies in adolescent DCD populations have found an increased fracture rate compared to population norms,[13] which could be reasonably projected to continue into adulthood. Given the high prevlance of DCD in this population, there are public health ramifications if a higher rate of bone health impairment is found in this group. As such, this review may be useful for creating clinical guidelines for bone density screening. It is likely, however, that the greatest interest will be in association with treatment priorities in pediatric groups, particularly for allied health professionals. Evidence collected by the identification of key gaps in empirical evidence will assist in focusing future research.

The objective of this review is to assess the association between DCD, and more generally LMC, and bone health measures across the lifespan. It aims to do this by determining if the incidence and extent of impaired bone health among DCD and LMC subgroups is greater than seen in the general population. A prelimary search for previous systematic reviews on the topic in PROSPERO, Cochrane Library, and *JBI Database of Systematic Reviews and Implementation Reports* determined that no other systematic reviews on this topic have been performed.

Review question

What is the association between developmental coordination disorder/low motor competence and impairment of bone health across the lifespan?

Inclusion criteria

Participants

All human studies that include a bone health outcome in a DCD/LMC population will be considered, with no restriction based on sample region, age, or sex. Due to the impact of movement limitations on bone health, studies that predominantly include a population with a condition that could be predicted to substantially limit movement, such as cerebral palsy, arthritis, or intellectual disabilities (eg, Rett syndrome), will be excluded from analysis unless movement levels are specified to be within normal ranges. Similarly, studies will be excluded if they predominantly include a population with health conditions that have a documented direct effect on bone. Examples of bone-affecting conditions include genetic conditions (eg, osteogenesis imperfecta), hormonal conditions (eg, premature menopause), and conditions affecting nutrient absorption (eg,

celiac disease, inflammatory bowel disease). If the effect of the condition on bone is unclear, the opinions of two bone experts will be sought, with a third bone expert to arbitrate if consensus is not reached. Anti-osteoporotic medication is the only medication whose use is exclusionary.

Exposure

The presence of DCD may be identified via a clinical diagnosis or an assessment of the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition, diagnostic criteria.[1] Using the recommendations of Geuze *et al.*[18], studies will be assessed to determine if they contain a DCD or LMC population, with those that meet all diagnostic criteria being classified as DCD and those that do not meet criterion C or D as LMC. Studies that do not demonstrate an impairment in age-appropriate motor skills that impacts daily living, as per criterion A and B,[1] will be excluded. If it is not clear from the study whether the diagnostic criteria are fulfilled, the study's authors will be contacted. If authors are uncontactable or non-responsive, the classification of the group will be determined in consultation with two known experts in DCD. Where consensus is not reached, a third DCD expert will adjudicate.

Outcome

Studies including a measurement known to be an indicator of bone health will be included in the review. This will include direct measurement via dual-energy X-ray absorptiometry, peripheral quantitative computed tomography, quantitative ultrasound, and skeletal or bone age, as well as indirect measurements, such as bone biomarkers and fracture incidence rates.

Types of studies

Study designs to be included, based on Guyatt *et al.*[19] and JBI methodology,[20] are cohort series (prospective and retrospective), case-control studies, cross-sectional studies, case series, and case reports. Experimental study designs, such as randomized controlled trials, will be included for baseline measurements only. Cross-sectional studies will be included regardless of the presence of a comparator population, as measurements may be compared to population norms. Similarly, experimental study designs will be included regardless of whether they include a non-DCD/LMC comparator group. Information about the presence and type of comparator population will be recorded and sensitivity analyses performed, if appropriate.

Methods

The protocol will be performed in accordance with JBI methodology for systematic reviews of etiology and risk.[20] This protocol has been registered with PROSPERO (CRD42020167301).

Search strategy

The search strategy is designed to locate published and unpublished studies. An initial search of PubMed and ScienceDirect was undertaken to identify articles on the topic. Search terms were derived using keywords from titles and abstracts of located articles and index terms to create a search strategy. This will be adapted to each database, and initial limited searches were run to identify any further additional keywords. An example search conducted in PubMed is presented in Appendix I. Reference lists of included studies will be examined to identify additional studies. Authors of major studies will be contacted for unpublished studies. Forward citation searching will be conducted using Scopus. If necessary, after a review of search results and study reference lists, search terms will be updated.

The following databases will be searched from inception until present: PubMed (Ovid), Embase (Ovid), Cochrane Central Register of Controlled Trials (Cochrane Library), Informit Health Collection (Informit Online), and ScienceDirect.

Gray literature will be examined for unpublished data via Google Scholar and WorldWideScience as well as searching the following electronic databases: OpenGrey, Trove, Digital Commons Network, Networked Digital Library of Theses and Dissertations, WorldCat (restricted to theses), DART-Europe E-theses portal, EThOS, and Scopus. In addition, the following conference websites will be searched: American Society for Bone and Mineral Research, International Conference on Children's Bone Health, National Conference on Developmental Coordination Disorder (UK), and the International Conference on Developmental Coordination Disorder.

There is no limitation based on language or publication date; databases will be searched from inception until present. Studies in languages other than English will be translated as required.

Study selection

Following the search, duplicates will be removed using EndNote X9 (Clarivate Analytics, PA, USA) and all remaining articles will be uploaded to Rayyan (Qatar Computing Research Institute, Doha, Qatar)[21] for screening. Two reviewers will independently examine the titles and abstracts for reference to motor competence and bone measurements, which will be sufficient to justify full-text screening. The full texts of the relevant articles will be reviewed independently for fulfilment of inclusion criteria, and non-qualifying studies removed. Disagreements as to the inclusion of articles will be resolved via discussion and then by third author arbitration. Exclusion reasons for full-text articles will be documented and reported in the review. The process of study selection will be detailed in a flow diagram as per Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.[22]

Assessment of methodological quality

Bias will be assessed for each study at the study level using the appropriate JBI critical appraisal checklist for each study design by two independent reviewers, with third author arbitration for disputes.[20] Any identified bias that may reflect the cumulative evidence will be reported in the results. Critical appraisal results will be reported in a table for all studies highlighting the strengths and weaknesses of each study and how this affects the validity of the study's findings. Given the expected small number of studies in this area, studies will not be excluded from analysis based on study quality; however, the decision to perform meta-analysis will include consideration of level of bias. Meta-analysis will not be conducted if most of the studies show a high level of bias (eg, bias on more than half of measures, bias not justifiable based on study design). Subgroup and sensitivity analyses will be performed to explore the impact of the level of study bias. If there are more than 10 studies included in the meta-analysis, publication and selective reporting bias will be formally tested using funnel plot asymmetry.

Data extraction

Data will be extracted by two reviewers following a prescribed data extraction form in Appendix II. This has been modified from the JBI data extraction form for systematic reviews of etiology and risk[20] to include motor competence measures and individual outcomes, as effect measures were considered unlikely to be in all studies. Data will be extracted into MS Excel (Redmond, Washington, USA) and cross-checked. Discrepancies will be discussed and referred to a third party should disagreement remain.

Items extracted will include the diagnostic assessment method, motor impairment measures, measures of bone health, and those required for sensitivity analysis (eg, medication use). Unadjusted results will be extracted as will effect size, if present. Study authors will be contacted to obtain any missing information.

Given the small number of research projects in this area, care will be taken to avoid multiple reports from the same study cohort being included. To assist in this, data will be extracted on the authors, institution, dates of data collection, and ethical approval details. If it is considered likely that reports are from the same study, the study author will be contacted. Multiple reports by the same study group will be linked for inclusion in the study. Data extraction will otherwise be performed as per the Cochrane Handbook for Systematic Reviews of Interventions[23] and JBI methodology.[20]

Data synthesis

A narrative synthesis will be performed as per JBI methodology for etiology and risk,[20] and reported in accordance with PRISMA reporting guidelines. This will include a description of the clinical and methodological characteristics of the studies, including evidence of bias and the plausible impact of any other outcomes reported (eg, physical activity levels). Patterns across studies will be explained, including any heterogeneity between studies, particularly between DCD and LMC populations and for age-based differences. Quantitative data, including point and interval estimates, with effect sizes presented as counts for dichotomous data and mean differences for continuous data, will be included in the narrative summary and graphs used for study comparison.

If two or more studies are identified of having low bias with the same outcome measure, a meta-analysis will be performed. Odds ratios of abnormal bone phenotype and fracture will be pooled for meta-analyses. If odds ratios are not presented in the text, they will be calculated where possible. Incidence of abnormal bone phenotype will be calculated when absent using the methodology described in

Bekkering *et al.*[24] Abnormal bone phenotype will be considered present when results are more than one standard deviation below reference scores for the relevant tool and population, in keeping with World Health Organization recommendations.[25] Heterogeneity will be assessed visually and using the I^2 statistic. Both the Mantel-Haenszel fixed effects method and the DerSimonian and Laird random effects method will be used for meta-analyses, with the random effects model being reported if there are sufficient events and funnel plot shows no asymmetry.[23] If events are considered rare, the Maentel-Haneszel model will be used.[23] If considerable heterogeneity is present, only a narrative synthesis will be presented.

Subgroup analyses will be done via stratification on a DCD versus a LMC population, and by age group. For age analyses, studies will be classified based on the primary age group present, as defined by the mean and 95% confidence interval, based on established trajectories of bone health parameters[26,27] into a pediatric (primary age group up to age 12 years), adolescent (12 to 25 years) and adult (older than 25 years). If possible, adults will be further classified as being between 25 to 40 years of age and older than 40 years. Sensitivity analyses will be performed as required, for example, to examine the effects of excluding studies based on sample size or to compare between fixed- and random-effects models.

If there are insufficient studies for meta-analysis, vote counting will be used to determine evidence of an effect and its direction. Statistical significance and size of effect will not be considered. The impact will be visualized using harvest plots, with studies weighted using the inverse-variance method.

Assessing certainty in the findings

Quality of evidence will be assessed using a modified Grading of Recommendation, Assessment, Development and Evaluation (GRADE) approach for prognostic studies as defined by Huguet *et al.*[28] and a Summary of findings created using GRADEpro GDT (McMaster University, ON, Canada). The Summary of Findings will include the absolute risk for DCD/LMC populations, relative risk estimate, and a ranking of the quality of the evidence. Assessment of bias and quality will be done by two assessors working independently who will meet to discuss the results for final appraisal. If agreement cannot be reached, a decision will be referred to an independent third party. A narrative summary will be provided of the overall methodological quality of the included studies.

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This review will contribute towards a PhD for JT.

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Appendix I: Search strategy

PubMed (National Library of Medicine). Search conducted on 23 June 2020.

Search	Query	Records retrieved
#1	"Bone and Bones"[mh:exp] OR "bone density"[MeSH Terms] OR "fractures, bone"[MeSH Terms] OR ("osteoporosis, postmenopausal"[MeSH Terms] OR "osteoporosis"[MeSH Terms]) OR "age determination by skeleton"[MeSH Terms] OR "tomography, x-ray computed"[MeSH Terms] OR "Bone health"[tw] OR "osteoporosis"[tw] OR ("bone"[tw] AND "density"[tw]) OR ("bone"[tw] AND "mineral"[tw] AND "content"[tw]) OR ("fractures"[tw] AND "bone"[tw]) OR ("bone"[tw] AND "fracture"[tw]) OR "age determination by skeleton"[MeSH Terms] OR ("age"[tw] AND "skeleton"[tw]) OR "age determination by skeleton"[tw] OR "bone mineral density"[tw] OR (Skeletal[tw] AND "growth"[tw] AND "development"[tw])	1,192,153
#2	"motor skills disorders"[MeSH Terms:exp] OR "apraxias"[MeSH Terms] OR "movement disorders"[MeSH Terms:exp] OR "developmental disabilities"[MeSH Terms:exp] OR "learning disabilities"[MeSH Terms:exp] OR "psychomotor disorders"[MeSH Terms] OR "motor skills"[MeSH Terms:exp] OR "motor activity/physiopathology"[Mesh Terms] OR ("motor"[tw] AND "skills"[tw] AND "disorders"[tw]) OR ("developmental"[tw] AND "coordination"[tw] AND "disorder"[tw]) OR "motor competence"[tw] OR Clumsiness[tw] OR "apraxias"[tw] OR "dyspraxia"[tw] OR (Motor[tw] AND difficulties[tw]) OR ("learning"[tw]) AND difficulties[tw]) OR "physical awkwardness"[tw] OR "ataxia"[MeSH Terms] OR "ataxia"[tw] OR ("coordination"[tw] AND "disorder"[tw]) OR ("coordination"[tw] AND "impairment"[tw]) OR "specific developmental disorder of motor function"[tw] OR (motorically[tw] AND awkward[tw]) OR "minimal cerebral dysfunction"[tw] OR ("minimal"[tw] AND "brain"[tw] AND "dysfunction"[tw]) OR ("motor"[tw] AND "control"[tw])	229,982
#3	#1 AND #2	5900
Limited to humans		5661

Appendix II: Data extraction table

Study details	Variable
Reviewer	
Study ID/record number	
Date	
Study title	
Authors	
Year	
Journal	
Institution name	
Aim of the study	
Methods	
Motor competence terminology	
Setting (eg, clinical, general population, rural, urban)	
Location	
Study design	
Date of data collection	
Duration of data collection	
Ethical approval	
Method of data analysis	
Participants	
Recruitment procedure used	
Tool used to measure DSM-5 criterion A (impairment of motor skills)	
Tool used to measure DSM-5 criterion B (impact on daily living)	
Tool used to assess DSM-5 criterion C (onset in early development)	
Tool used to assess DSM-5 criterion D (not better explained by comorbidities)	
Total number of participants	
Age characteristics	
Sex characteristics	
Pubertal stage (if applicable)	
Motor skill measure (mean, standard deviation, 95% confidence interval)	
Mean score on daily living measure (mean, standard deviation, 95% confidence interval)	
Comorbidities	
Comparison group	
Presence	
Criteria	

(*Continued*)	
Study details	**Variable**
Age characteristics	
Sex characteristics	
Pubertal stage (if applicable)	
Outcomes	
Tool used for measurement of bone health	
Body area assessed	
Primary outcome measures	
Secondary outcome measures	
Unit of measurement	
Other factors measured (include tool used and units of measurement)	
Results	
Risk ratio/relative risk/odds ratio of impaired bone health *P* value and 95% confidence interval	
Individual outcome measures • Estimate of effect with confidence interval • Standard error of effect • *P* value	
Other outcome measure (eg, physical activity levels, body mass index, muscle density, muscle size, cardiorespiratory fitness measures) • Estimate of effect with confidence interval • Standard error of effect • Pvalue	
Effect measures (risk ratio, relative risk ratio, odds ratio)	
Results of any subgroup analysis	
Bias	
Presence of incomplete outcome data	
Selective outcome reporting	
Any other bias concerns, such as funding	
Miscellaneous	
Key conclusion of study authors	
Miscellaneous comments from the study authors	
Any other information necessary for analysis of the quality of the study	
Any other comments	

DSM-5, Diagnostic and Statistical Manual of Mental Disorders, 5th edition

B.3 Osteogenic Potential of Physical Activities and their Associations with Bone Mass in Young Adults: The Raine Study

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ORIGINAL ARTICLE

Physical activity estimated by osteogenic potential and energy expenditure has differing associations with bone mass in young adults: the raine study

Carrie-Anne Ng[1] · David Scott[1,2] · Marc Sim[3,4,5] · Kun Zhu[4,6] · Aris Siafarikas[4,5,7,8,9,10] · Nicolas H. Hart[5,7,10,11,12] · Jocelyn Tan[5,13] · Paola Chivers[5,7,10]

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Abstract

Summary Ground impacts during physical activity may be important for peak bone mass. We found differences in how energy expenditure and impact scores estimated from a physical activity questionnaire related to bone health in young adults. Using both estimate types can improve our understanding of the skeletal benefits of physical activity.

Purpose It is unclear whether mechanical loading during physical activity, estimated from physical activity questionnaires which assess metabolic equivalents of task (METs), is associated with skeletal health. This longitudinal study investigated how physical activity loading scores, assessed at ages 17 and 20 years, (a) compares with physical activity measured in METs, and (b) is associated with bone mass at age 20 years.

Methods A total of 826 participants from the Raine Study Gen2 were assessed for physical activity energy expenditure via the International Physical Activity Questionnaire (IPAQ) at age 17 and 20 years. Loading scores (the product of peak force and application rate) per week were subsequently estimated from the IPAQ. Whole-body and appendicular bone mineral density (BMD) at age 20 years were assessed by dual-energy X-ray absorptiometry.

Results Bland–Altman minimal detectable difference for physical activity Z-scores at age 17 and 20 years were 1.59 standard deviations (SDs) and 1.33 SDs, respectively, greater than the a priori minimal clinically important change of 0.5 SDs. Loading score, but not IPAQ score, had significant positive associations with whole-body and leg BMD after adjustment for covariates ($\beta = 0.008$ and 0.012 g/cm^2, respectively, for age 17 and 20 years loading scores). IPAQ score at age 20 years, but not loading score, had a significant positive association with arm BMD ($\beta = 0.007$ g/cm^2).

Conclusion This study revealed disagreement in associations of self-reported METs and loading score estimates with bone health in young adults. Coupling traditional energy expenditure questionnaire outcomes with bone-loading estimates may improve understanding of the location-specific skeletal benefits of physical activity in young adults.

Keywords Physical activity · Bone mineral density · DXA · Peak bone mass · Population study

Introduction

Maximising peak bone mass attainment by young adulthood is important for long-term skeletal health. Specifically, peak bone mass is estimated to be six times more influential on the development of osteoporosis than other well-established risk factors, including age of menopause or rate of bone loss [1]. Optimising bone accrual during the critical peri-adolescent growth period may thus be of greatest significance in preventing fractures as we age [2, 3]. The positive influence of physical activity on peak bone mass is well recognised, but recommendations on the optimal type, dose, and frequency of activity remain unclear [3, 4].

Physical activities with a combination of high and rapid impact, multi-directional loading, and weight-bearing have the most significant physiological effects on bone structure [5]. Targeted high-impact exercise in randomised controlled trials results in increased bone mineral density (BMD) and bone strength during the prepubertal and peripubertal stages [6, 7]. However, in determining the skeletal benefits of habitual physical activity, observational studies have

✉ Carrie-Anne Ng
carrie.ng@monash.edu

Extended author information available on the last page of the article

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commonly utilised traditional physical activity questionnaires with calculations based on metabolic equivalents of task (METs), such as the International Physical Activity Questionnaire (IPAQ) [4, 8]. Such methodologies fail to capture key characteristics of osteogenesis during specific physical activities, specifically mechanical load magnitude and application rate.

To better understand associations between physical activity and bone health, activities should be quantified by the intensity and application rate of ground reaction forces generated, based on underlying principles of the *osteogenic index* [9, 10]. Taking such principles into account, the Bone-specific Physical Activity Questionnaire (BPAQ) was developed. The BPAQ utilises measured effective load ratings for a range of physical activities based on the intensity and application rate of ground reaction forces exerted on the lower limb [10]. Cross-sectional studies using the BPAQ have since demonstrated that osteogenic physical activity has location-specific benefits for tibial shaft microarchitecture in children and young adults [11, 12].

However, there is limited evidence favouring such bone loading questionnaires over METs estimates when assessing bone outcomes. In older men, bone loading scores (derived from METs-based questionnaires), but not METs estimates themselves, were associated with greater maintenance of BMD over several years [13] and also with higher bone quality compared to total time spent in physical activity [14]. Similar adaptations of METs-based questionnaires have been undertaken in younger adults which likewise revealed positive associations between higher loading and bone mass and microarchitecture [15–18]. However, in these studies, few direct comparisons with energy estimates from the original questionnaire were made and as such it is unclear whether calculating bone loading scores provides additional insights into the effects of physical activity on bone health.

Effects of higher-impact physical activity in young adults who are in the maintenance phase of peak bone mass, estimated to occur after age 20 years [19], are also unclear. Of the few interventional studies conducted in this age group, improvements in bone mass from high-impact exercise were less marked compared to younger participants [3]. Furthermore, detraining in young adulthood may lead to a loss of skeletal benefits from physical activity due to bone remodelling [20]. Thus, the aims of this study were to: (a) compare energy expenditure and loading intensity estimated from a self-administered physical activity questionnaire and (b) determine whether participation in physical activity with higher loading intensities and rates assessed at ages 17 and 20 years are associated with bone mass at age 20 years.

Materials and methods

Study design

This study included data of the offspring (Gen2) of the Raine Study Gen1 participants. Pregnant women (n = 2900) were initially recruited from antenatal clinics at King Edward Memorial Hospital for Women in Perth, Western Australia, between 1989 and 1991. The resulting 2868 live born children underwent follow-up assessments at ages 1, 2, 3, 5, 8, 10, 14, 17, 20, and 22 years and were broadly representative of the Western Australian population [21]. The Raine Study Gen2 design has been described in detail elsewhere [21]. Written informed consent was obtained at each follow-up from parents or participants as appropriate for age. The original study and follow-ups were approved by the institutional ethics committees of King Edward Memorial Hospital, Princess Margaret Hospital for Children, the University of Western Australia, and Curtin University. This study was approved by The University of Notre Dame Australia (2020-094F), Edith Cowan University (2020–01705-SIM), and Monash University (25205) institutional human research ethics committees.

The Raine Study Gen2–20-year follow-up methodology has been previously described according to investigations with the IPAQ [22], dual-energy X-ray absorptiometry (DXA), and vitamin D status [23, 24]. 1348 participants attended the physical assessment component at the Gen2–20-year follow-up. Of these, 73 participants did not undergo a DXA scan and a further 92 did not have a valid DXA scan due to the presence of artefacts in the region of interest or because participants could not fit in the scanning area. Of the participants who had a valid DXA scan, further complete data for body mass index (BMI), smoking habits, alcohol consumption, dietary calcium intake, and serum 25-hydroxyvitamin D (25(OH)D) were available for 826 participants (Fig. 1). These participants also completed the IPAQ at either the Gen2–17- or Gen2–20-year follow-ups, with 629 completing the questionnaire at both time points. Compared to the Raine study participants who attended the Gen2–20-year follow-up but were excluded (39%), the participants in the present study did not differ significantly by physical activity or bone parameters, except for arm bone mineral content (BMC) and BMD which were significantly lower among those included (Supplementary Table 1).

Physical activity

Physical activity in the past 7 days was assessed via the IPAQ, previously validated with objective measures of

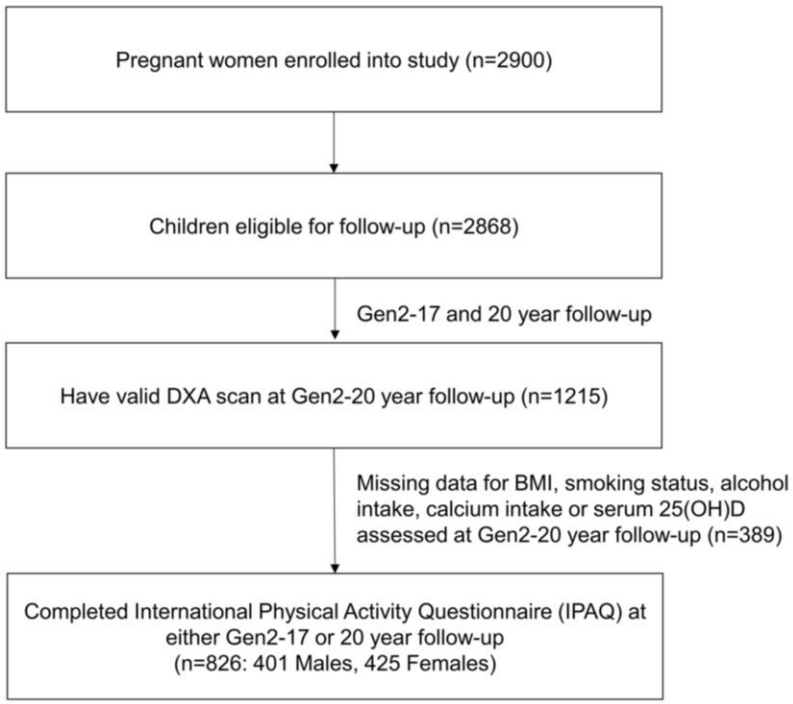

Fig. 1 Raine study Gen2 participation flow diagram

physical activity [25]. The long IPAQ form was self-administered at the Raine Study Gen2–17-year follow-up while the short form was self-administered at the Gen2–20-year follow-up. This was likely due to a qualitative preference of the short form, and no observed differences in the reliability and validity of both forms [26]. In the short version, participants reported the frequency, in days, and duration, in hours and minutes per day, of walking, moderate activity, and vigorous activity. The long form further assessed the frequency and duration of these activity intensities within five subdomains: occupational activity, leisure activity, active transport, housework, and yard work (Supplementary Table 2). Data cleaning, processing and the categorising of low, moderate and high activity participation were performed according to guidelines by the IPAQ research committee [26]. The resulting IPAQ scores (MET-min/wk) were calculated as frequency × duration × MET estimate, summed across physical activity domains for the short form, or subdomains for the long form (Supplementary Table 2).

To assess the osteogenic potential of physical activity, effective load ratings (ELRs) were used instead of MET estimates (Supplementary Table 2), similar to previous work [13]. ELRs were previously determined following the principles of estimating intensity and application rate of ground reaction forces used in the BPAQ [10]. Briefly, the BPAQ estimates peak vertical ground reaction force and the rate of force application of the fundamental actions of an activity using a force platform. The ELR of a physical activity is the product of the peak force and application rate of the fundamental actions composing the activity, and aggregate values for impact intensity categories were used [27]. Loading scores (ELR/wk) were calculated as frequency × ELR, also summed across physical activity domains and subdomains. Days of physical activity per week, rather than minutes, were used in this equation as osteogenesis is reported to be enhanced by number of sessions rather than the duration of individual sessions [9].

To allow for comparability between short and long forms between the two time points, an adapted calculation was applied to the long form where physical activity subdomains were assigned the same MET estimate or ELR as its associated domain (Supplementary Table 2).

Whole-body DXA

Whole-body DXA scans were performed at the Raine Study Gen2–20-year follow-up visit using the Norland XR-36 densitometer (Norland Medical Systems, Inc., Fort Atkinson, WI, USA) according to manufacturer-recommended

procedures [23, 24]. Scan analysis using the built-in machine software (version 4.3.0) provided estimates of BMC (g) and areal BMD (g/cm^2) for the whole body (including head), legs and arms. Whole-body fat percentage (%) and lean mass (kg) were also assessed from whole-body scans. All analyses were checked for consistency by the same researcher. Daily calibration was performed prior to each scanning session, and the interscan coefficient of variation (CV) was less than 2.0% at standard speed.

Anthropometric, sociodemographic, and lifestyle measures

At the Raine Study Gen2–20-year follow-up visit, height was measured to the nearest 0.1 cm with a stadiometer (Seca 202, Hanover, MD) and weight was measured to the nearest 0.1 kg using an automatic electronic scale (Personal Precision scales UC-321; A&D Company). Participants wore light clothing without shoes during measurements. BMI was calculated as body mass (kg)/ squared height (m^2). Usual dietary intake was assessed by the Dietary Questionnaire for Epidemiological Studies (DQES V2), a validated 74-item semi-quantitative food frequency questionnaire developed by the Cancer Council of Victoria [28]. The data collected by DQES v2 were used to calculate dietary calcium intake (mg/day) and presence of alcohol beverage intake (never or "sometimes"). Smoking was assessed by a questionnaire via the question "Do you currently smoke cigarettes/ cigars?" and participants were categorised as smokers or non-smokers.

25(OH)D

Fasting venous blood samples were collected at the Raine Study Gen2–20-year follow-up and stored at -80 °C until analysed. Serum 25(OH)D_2 and 25(OH)D_3 concentrations were measured by RMIT Drug Discovery Technologies using isotope dilution liquid chromatography–tandem mass spectrometry (LC–MS/MS). As blood samples were collected year round, the seasonal component was removed from serum 25(OH)D concentrations according to published formulae [29]. Total serum 25(OH)D was the summation of deseasonalised 25(OH)D_2 and 25(OH)D_3. The CVs for 25(OH)D_3 were 5.8% at 28 nmol/l, 5.2% at 80 nmol/l and 9.2% at 188 nmol/l, and the CVs for 25(OH)D_2 were 7.9% at 25 nmol/l, 6.6% at 75 nmol/l and 10.4% at 185 nmol/l.

Statistical analyses

Characteristics of participants were summarised with descriptive statistics and compared across groups based on tertile cut points of loading score at the Raine Study Gen2–20-year follow-up, using one-way ANOVA or Kruskal–Wallis tests for continuous variables and Chi-square tests for categorical variables. Normality of continuous variables was assessed via histograms. Bonferroni post hoc tests or Dunn's post-test were performed for these analyses. Wilcoxon signed-rank tests compared IPAQ and loading scores from the Gen2–17- to Gen2–20-year follow-ups.

Spearman's correlation assessed the relationship between IPAQ scores and ELRs at each follow-up time point. While correlation can describe the strength of linear relationships, it does not necessarily suggest comparability or agreement [30]. Hence, to estimate agreement between the physical activity measures, Bland–Altman plots were constructed separately at Gen2–17- and Gen2–20-year follow-ups, where differences between Z-score transformed IPAQ and loading scores were plotted against their averages. The 95% confidence interval (CI) limits of agreement were calculated as mean bias ± 1.96 standard deviation (SD) of the differences and represent 95% of the difference between the two scores. The minimal detectable change (MDC) was then obtained, defined as one-half the limit of agreement width, and is the smallest change between IPAQ and loading scores independent of measurement error. A MDC greater than an a priori minimal clinically important change (MCIC) of 0.5 SDs [31] would indicate clinically important disagreement between IPAQ and loading scores. To detect proportional bias, which may occur when the differences in Z-IPAQ and loading scores change in proportion to their average, linear regression was additionally performed.

To examine potential non-linearity, a likelihood ratio test was first used to compare nested models with and without the nonlinear terms for IPAQ and loading scores. For linear associations, generalised linear models compared bone and body composition parameters with standardised IPAQ and loading scores at the Raine Study Gen2–17- and Gen2–20-year follow-ups, and standardised change in IPAQ and loading scores between the two time points. Models were presented as: Model 1 which adjusted for sex and BMI at Gen2–20-year follow-up and Model 2 which included Model 1 + smoking status, alcohol consumption, dietary calcium intake and serum 25(OH)D at Gen2–20-year follow-up. Self-rated health and well-being assessed via the 12-item health survey was not a significant predictor of outcome variables in any model and was not included as a covariate. A predictive equation was generated to estimate whole-body BMD for the maximum loading score able to be detected by the questionnaire at age 20 years. To compare the goodness of fit of Models 1 and 2, the Akaike Information Criterion (AIC) was used, where the model with the smaller AIC values was considered a better fit [32].

For analyses between physical activity assessed at the Gen2–17-year follow-up and bone parameters, the original long-form physical activity scores were used for comprehensiveness. For analyses of change in physical activity, the

adapted long-to-short form of scores assessed at Gen2–17-year follow-up was used to allow for comparability between the time points. Further analysis examining interaction terms for sex was conducted to determine if associations differed between males and females. For significant observed interactions, subsequent analyses were performed separately for each gender to investigate where differences lay. To examine if observed associations were independent of intensity levels or loading scores of physical activity, analyses were performed where IPAQ score was added as a covariate in loading score analyses, and vice versa. For this analysis, collinearity between IPAQ and loading scores was assessed in using the variance inflation factor (VIF), with a value of >4 to be evidence of collinearity [33].

Statistical analyses were performed with SPSS IBM software (version 25; IBM, Chicago, IL, USA), and graphs were generated in R (version 4.0.3; R Foundation for Statistical Computing). Statistical significance was defined as $p < 0.05$ (2-tailed).

Results

Descriptive variables of included participants at the Raine Study Gen2–20-year follow-up visit are presented in Table 1. Participants within the highest tertile of loading score were more likely to be male and had higher daily dietary calcium intake and serum 25(OH)D levels compared to those in the lowest tertile. Lean mass, arm BMC, whole-body, and leg BMC and BMD were also significantly higher among participants in the highest tertile compared to the middle and lowest tertile, with the converse observed for total fat percentage.

Table 1 Characteristics of the raine study participants at Gen2–20-year follow-up according to tertiles of loading score

			Tertiles of loading score at Gen2–20-year follow-up (N = 823)					
	Included into analysis		Lowest <70.1 ELR/wk		Middle 70.1–220.7 ELR/wk		Highest >220.7 ELR/wk	
N	826		274		274		275	
	Mean or %	SD	Mean or %	SD	Mean or %	SD	Mean or %	SD
Age	19.96	0.44	19.92	0.43	19.97	0.47	19.98	0.41
Sex (% of males)	48.5		32.5 [b,c]		46.4 [a,c]		66.9 [a,b]	
BMI (kg/m^2)	23.88	4.30	23.45	4.30	23.80	4.14	24.31	4.33
Smoker (%)	13.8		14.2		12.8		14.2	
Alcohol consumer (%)	92.9		92.0		92.7		94.2	
Calcium Intake (mg/day)	903.9	409.6	816.9 [c]	376.5	886.7 [c]	395.5	1003.0 [a,b]	427.8
Serum 25(OH)D (nmol/L)	73.68	23.51	69.10 [c]	23.09	71.99 [c]	23.25	79.91 [a,b]	22.74
Whole-body total fat (%)	30.85	12.52	35.20 [b,c]	12.06	31.36 [a,c]	11.54	25.87 [a,b]	12.15
Whole-body lean mass (kg)	46.28	12.16	40.94 [b,c]	9.93	45.41 [a,c]	11.37	52.43 [a,b]	12.12
Whole-body BMC (g)	2938.0	459.2	2804.8 [b,c]	395.4	2896.2 [a,c]	458.3	3110.9 [a,b]	467.4
Whole-body BMD (g/cm^2)	1.072	0.109	1.042 [b,c]	0.994	1.064 [a,c]	0.110	1.110 [a,b]	0.107
Whole-body Z-score	0.14	1.34	-0.29 [b,c]	1.17	-0.08 [a,c]	1.35	0.54 [a,b]	1.35
Arms BMC (g)	374.1	83.5	347.3 [b,c]	71.1	365.7 [a,c]	82.3	409.3 [a,b]	84.3
Arms BMD (g/cm^2)	0.784	0.091	0.765 [c]	0.086	0.775 [c]	0.090	0.811 [a,b]	0.091
Legs BMC (g)	1045.4	197.4	979.1 [b,c]	172.0	1032.0 [a,c]	197.0	1124.7 [a,b]	194.5
Legs BMD (g/cm^2)	1.166	0.134	1.124 [b,c]	0.122	1.157 [a,c]	0.135	1.217[a,b]	0.129
	Median	IQR	Median	IQR	Median	IQR	Median	IQR
IPAQ Score (MET-min/week)	2466.0	838.0 —4920.0	693.0 [b,c]	99.0 —1971.5	2578.0 [a,c]	1440.0 — 4212.0	6000.0 [a,b]	2853.0 — 9390.0
Loading Score (ELR/week)	152.5	43.7 — 274.5	14.8 [b,c]	2.0 — 43.7	152.5 [a,c]	111.2 — 181.4	318.1 [a,b]	263.7 —373.1

[a] Significant difference to tertile 1

[b] Significant difference to tertile 2

[c] Significant difference to tertile 3 (Bonferroni post hoc tests or Dunn's post-test)

Abbreviations: ELR, effective load rating; SD, standard deviation; BMI, body mass index; 25(OH)D, 25-hydroxyvitamin D; BMC, bone mineral content; BMD, bone mineral density; IQR, inter-quartile range; IPAQ, International Physical Activity Questionnaire; MET, metabolic equivalent of task

There were no significant differences in age, BMI, smoking status, or alcohol consumption between tertiles.

From the Gen2–17-year to Gen2–20-year follow-up, median self-reported physical activity scores decreased from 3070 (IQR: 1140.5 – 5602.5) to 2400 (831.3 – 4773.0) MET-min/wk for IPAQ scores ($p<0.001$), with a reduction in moderate and high activity participation from 31.8% and 60.9% to 24.5% and 48.5%, respectively. Loading scores also decreased from 154.1 (IQR: 54.7 – 289.4) to 152.9 (54.9 – 263.7) ELR/wk ($p<0.001$). IPAQ scores were positively correlated with loading score at both Gen2–17-year ($r_s=0.75$, $p<0.001$) and Gen2–20-year follow-ups ($r_s=0.64$, $p<0.001$). Figure 2 presents Bland–Altman plots at both follow-ups. The lower and upper limits of agreement were -1.33 and 1.33, respectively, at Gen2–17-year follow-up, and -1.59 and 1.59, respectively, at Gen2–20-year follow-up. As the average of the standardised scores increased, the dispersion of the differences increased. At each follow-up, the MDC was greater than the a priori MCIC of 0.5, indicating clinically relevant disagreement between the two scores. Linear regression did not reveal proportional bias for both comparisons (both $p=1.000$).

The multivariable-adjusted relationship between whole-body BMC and BMD, and IPAQ and loading scores at

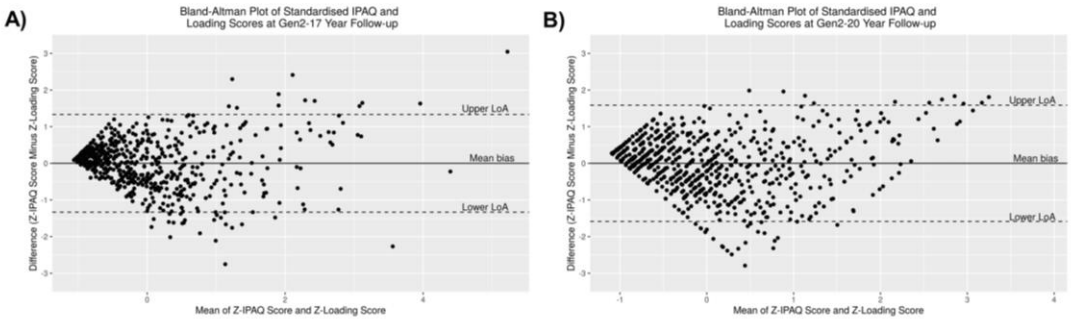

Fig. 2 Bland–Altman plots for standardised IPAQ and loading scores at: **A)** Gen2–17-year and **B)** Gen2–20-year follow-ups. The x-axis displays the mean of Z-score transformed IPAQ and loading scores and y-axis displays the difference of the two estimates. The central line represents the mean bias (intermethod difference), which is 0 as Z-scores were used. The dashed lines indicate the 95% limits of agreement. Abbreviations: IPAQ, International Physical Activity Questionnaire; LoA, limits of agreement

Table 2 Associations between DXA-derived measures at Gen2–20-year follow-up per standard deviation increase in IPAQ and loading scores at Gen2–17-year follow-up

	Model 1		Model 2	
	IPAQ score	Loading score	IPAQ score	Loading score
Whole-body				
BMC (g)	28.94 (-0.89, 58.77)	**41.25*** (9.72, 72.77)	15.88 (-11.92, 43.67)	24.03 (-5.74, 53.80)
BMD (g/cm^2)	**0.010*** (0.002, 0.017)	**0.011**** (0.004, 0.019)	0.007 (0.000, 0.013)	**0.008*** (0.000, 0.015)
Arms				
BMC (g)	**7.25**** (2.17, 12.33)	**8.58**** (3.47, 13.70)	**4.93*** (0.25, 9.60)	**5.89*** (1.05, 10.73)
BMD (g/cm^2)	**0.013**** (0.007, 0.019)	**0.011**** (0.005, 0.017)	**0.011**** (0.005, 0.017)	**0.008**** (0.002, 0.014)
Legs				
BMC (g)	9.55 (-2.58, 21.67)	**19.47**** (6.47, 32.47)	4.95 (-6.78, 16.69)	**13.60*** (1.07, 26.13)
BMD (g/cm^2)	**0.010*** (0.001, 0.019)	**0.017**** (0.007, 0.026)	0.007 (-0.002, 0.015)	**0.012**** (0.004, 0.021)
Total Fat (%)	**-1.03**** (-1.55, -0.52)	**-1.31**** (-1.81, -0.80)	**-0.73**** (-1.20, -0.26)	**-0.97**** (-1.44, -0.50)
Total Lean Mass (kg)	**0.81**** (0.21, 1.40)	**1.18**** (0.62, 1.75)	0.51 (-0.04, 1.05)	**0.79**** (0.26, 1.32)

Data presented as β coefficients (95% confidence interval). Bolded values are significant at $p<0.05$* or $p<0.01$**

Model 1 adjusted for sex and BMI at Gen2–20-year follow-up

Model 2 adjusted for sex, BMI, smoking, alcohol, calcium intake and serum 25(OH)D at Gen2–20-year follow-up

Abbreviations: DXA, dual-energy x-ray absorptiometry; IPAQ, International Physical Activity Questionnaire; BMC, bone mineral content; BMD, bone mineral density; BMI, body mass index; 25(OH)D, 25-hydroxyvitamin D

Table 3 Associations between DXA-derived measures per standard deviation increase in IPAQ and loading scores at Gen2–20-year follow-up

	Model 1		Model 2	
	IPAQ score	Loading score	IPAQ score	Loading score
Whole-body				
BMC (g)	**53.78**** (28.71, 78.86)	**58.65**** (33.72, 83.58)	**34.48**** (10.14, 58.82)	**34.51**** (9.44, 59.58)
BMD (g/cm^2)	**0.009**** (0.003, 0.015)	**0.013**** (0.007, 0.019)	0.005 (-0.001, 0.010)	**0.008*** (0.001, 0.014)
Arms				
BMC (g)	**11.75**** (7.43, 16.08)	**10.24**** (5.96, 14.53)	**8.64**** (4.48, 12.79)	**6.36*** (2.05, 10.67)
BMD (g/cm^2)	**0.010**** (0.004, 0.015)	**0.009**** (0.004, 0.014)	**0.007*** (0.001, 0.012)	0.005 (0.000, 0.011)
Legs				
BMC (g)	**22.04**** (11.62, 32.45)	**27.07**** (16.74, 37.39)	**15.10**** (4.85, 25.36)	**18.74**** (8.25, 29.24)
BMD (g/cm^2)	**0.011**** (0.004, 0.019)	**0.018**** (0.010, 0.025)	0.006 (-0.001, 0.014)	**0.012**** (0.004, 0.020)
Total Fat (%)	**-1.34**** (-1.76, -0.92)	**-1.94**** (-2.36, -1.53)	**-0.91**** (-1.32 -0.49)	**-1.49**** (-1.90, -1.07)
Total Lean Mass (kg)	**1.55**** (1.10, 2.01)	**1.92**** (1.49, 2.34)	**1.09**** (0.66, 1.53)	**1.38**** (0.97, 1.80)

Data presented as β coefficients (95% confidence interval). Bolded values are significant at $p<0.05$* or $p<0.01$**

Model 1 adjusted for sex and BMI at Gen2–20-year follow-up

Model 2 adjusted for sex, BMI, smoking, alcohol, calcium intake and serum 25(OH)D at Gen2–20-year follow-up

Abbreviations: DXA, dual-energy x-ray absorptiometry; IPAQ, International Physical Activity Questionnaire; BMC, bone mineral content; BMD, bone mineral density; BMI, body mass index; 25(OH)D, 25-hydroxyvitamin D

Gen2–17- or Gen2–20-year follow-up, or their change, were of a linear nature (p for non-linearity > 0.054 in Model 2; Supplementary Fig. 1). Thus, generalised linear models determined associations of IPAQ and loading scores at Gen2–17-year (Table 2) and Gen2–20-year follow-ups (Table 3), and their changes between follow-ups (Supplementary Table 3) with DXA-derived bone and body composition parameters at Gen2–20-year follow-up. Loading score at Gen2–17-year follow-up was positively associated with all bone parameters and lean mass, and negatively associated with total fat percentage in Model 1 (all $p \leq 0.010$) and 2 (all $p < 0.039$), except for whole-body BMC which was not significant after adjustment for multiple confounders in Model 2. IPAQ score was positively associated with arms BMC ($p = 0.039$) and BMD ($p < 0.001$) and negatively associated with total fat percentage ($p = 0.002$) in Model 2.

At Gen2–20-year follow-up, IPAQ and loading scores were positively associated with all bone parameters and total lean mass, and negatively associated with total fat percentage in Model 1 (all $p < 0.010$) (Table 3). After further adjustment in Model 2, the association between IPAQ score and whole-body BMD and leg BMD, and between loading score and arm BMD was attenuated. IPAQ score had greater standardised effects with arm BMC and BMD than loading score, while loading score had greater standardised effects with whole-body and leg BMC and BMD, total fat percentage, and lean mass. Loading score was positively associated with whole-body BMD ($p = 0.017$), and the predictive equation was:

$$\begin{aligned} &\textit{Whole-body BMD}\left(g/cm^2\right) \\ &= 0.698 + 0.096\ (\times 1\ \textit{if male}) + 0.011\ (\textit{BMI}) \\ &\quad + 0.004\ (\times 1\ \textit{if non-smoker}) \\ &\quad - 0.035\ (\times 1\ \textit{if no alcohol consumption}) \\ &\quad + 0.001\ (\textit{Serum}\ 25(OH)D)) \\ &\quad + 0.000\ (\textit{Calcium intake}) \\ &\quad + 0.008\ (\textit{Z-score of loading score}) \end{aligned}$$

As an example, for a male non-smoker who does not consume alcohol with mean values for serum 25(OH)D and calcium intake, and who had a maximal loading score (483.14 ELR/wk; Z-score = 2.34) at the Gen2–20-year follow-up, the equation would be:

$$\begin{aligned} &= 0.698 + 0.096 + 0.011(23.88) + 0.004 - 0.035 \\ &\quad + 0.001(73.68) + 0.000(903.9) + 0.008(2.34) \end{aligned}$$

resulting in predicted whole-body BMD of 1.106g/cm^2.

AIC values in Model 2 were lower than observed in Model 1 at both follow-ups for each outcome, indicating a better model fit. There were significant sex and IPAQ score interactions for arm BMD in Models 1 and 2 at Gen2–17-year follow-up, and Model 1 at Gen2–20-year follow-up. Separate analyses revealed significant positive associations between IPAQ score and arm BMD for males ($\beta > 0.012$ g/cm^2) and non-significant associations for females ($\beta < 0.001$ g/cm^2).

When loading score was added as a covariate to Model 2 in IPAQ score analyses, only arm BMD remained significantly positively associated with IPAQ score at Gen2–17-year follow-up (β = 0.010 g/cm^2, 95% CI = 0.002, 0.018), and arm BMC remained significantly positively associated with IPAQ score at Gen2–20-year follow-up (β = 7.71 g, 95% CI = 2.35, 13.08). Conversely, when IPAQ score was added as a covariate, only leg BMC and BMD remained significantly positively associated with loading score at both Gen2–17-year (β = 20.86 g, 95% CI = 4.37, 37.35 for leg BMC and β = 0.016 g/cm^2, 95% CI = 0.004, 0.027 for leg BMD) and Gen2–20-year follow-ups (β = 14.89 g, 95% CI = 1.20, 28.57 for leg BMC and β = 0.013 g/cm^2, 95% CI = 0.004, 0.023 for leg BMD). In this adjustment, VIF values for IPAQ and loading score, respectively, were 2.34 and 2.31 at Gen2–17-year follow-up, and 1.87 and 1.95 at Gen2–20-year follow-up.

Changes in IPAQ and loading score from Gen2–17- to Gen2–20-year follow-ups were not significantly associated with any bone or body composition measures (Supplementary Table 3).

Discussion

This study used a novel approach to estimate bone loading from an energy expenditure-based physical activity questionnaire and investigated its association with bone parameters in young adults. We found clinically important disagreement between loading scores and energy expenditure measured by IPAQ at both Gen2–17- and Gen2–20-year follow-ups. Participation in physical activity with higher loading scores was more strongly associated with greater whole-body and leg bone mass, while energy expenditure was positively associated with arm bone mass. However, there were no observed significant associations between change in loading or IPAQ scores and bone parameters.

Bland–Altman analyses revealed wide limits of agreement greater than the MCIC of 0.5 SD, which is a clinically important threshold in discriminating between self-reported health-related measures [31]. This indicates that loading scores and IPAQ scores cannot be used interchangeably [34] and confirms our hypothesis that METs are insufficient in identifying bone-relevant mechanical loading. However, as neither score reflects objective means of measuring physical activity, we can only make relative comparisons independent of the subjective nature of the questionnaire. Regardless, such differences have previously been demonstrated in young adults whereby a weak, non-significant correlation between METs/week and BPAQ score of the past one year was reported (r = -0.26) [10]. In the current study, the moderate to strong positive correlation between IPAQ and loading scores may have been attributed to reduced variation at smaller magnitudes, observed by a narrower dispersion at lower scores in the plots. Indeed, it may be difficult to differentiate the mechanical loading and cardiometabolic components of physical activity in relatively sedentary individuals. Further generalisability of our findings is limited by a lack of correlation or agreement analyses in studies of bone loading scores [16, 17, 35]. Relevant past findings may also have been confounded by different observed self-report timeframes, such as in a study of young adult females, where energy expenditure over the past week was not correlated with lifetime bone loading scores (r = 0.02) [12].

We observed that loading scores, but not IPAQ scores, at both Gen2–17- and Gen2–20-year follow-ups, were associated with whole-body and leg BMD in the fully adjusted model. The lack of significant associations between physical activity scores and whole-body and leg BMC at Gen2–17-follow-up, compared to that at Gen2–20, may be because taller participants in the Raine Study may not have yet attained peak bone mass [24]. Indeed, adjusting for height rather than BMI in the models resulted in positive significant associations between IPAQ and loading scores and BMC at all sites (data not shown). β values between standardised loading scores and BMC and BMD at these sites were also higher than that of IPAQ scores. These results correspond with findings from a systematic review in young adults, whereby studies assessing weight-bearing physical activities demonstrated more consistent positive associations with bone mass compared to when physical activity was quantified by energy estimates [4]. However, few direct comparisons of these distinct physical activity types in the same population have been made. Notably, in the Amsterdam Growth and Health Longitudinal Study (AGAHLS), the mechanical component of physical activity in young adulthood (ages 21–27 years), but not the metabolic component, was associated with lumbar spine and femoral neck BMD [18, 35]. Interestingly, both components of physical activity during adolescence (ages 13–16 years) in this study were not associated with BMD at either site [18, 36], suggesting that loading during the years of peak bone mass may be more conducive for osteogenesis, or that bone structural changes may have occurred that were undetected by DXA scans.

However, the pre- and peri-pubertal periods, where there is high linear growth of bone, have been well established to be optimally responsive to mechanical loading [7]. Our findings may thus be attributed to maintenance of participation in physical activity of high to moderate impact from adolescence to young adulthood. Indeed, almost half of the Raine Study Gen2 participants were reported to have consistent organised sport participation trajectories, and this group had greater peak BMC than sport dropouts [37]. However, the nature of these sports is unclear as physical activity prior to age 17 years was assessed in the Raine Study by a single

polar (yes/no) question about participation in organised sport outside of school hours. In the current study, no significant association was observed between change in either loading or IPAQ scores and bone mass. This may be because the effects of physical activity at age 17 years on bone may be indistinguishable to that at age 20 years. When IPAQ or loading score at 17 years was included in the models, an increase in IPAQ scores over three years was significantly positively associated with BMC at all sites, while an increase in loading scores was only similarly associated with leg BMC (data not shown). This suggests that while young adults can begin participation in more metabolically intense activities in young adulthood to improve overall bone mass, a more consistent participation in impact physical activity from earlier in life may be required. Longitudinal studies including the AGAHLS have commonly defined specific physical activity time periods such as adolescence or young adulthood when investigating their skeletal effects [16–18, 36]. When trends of physical activity were evaluated, sustained high-impact activity from adolescence to adulthood was associated with BMD at clinically relevant sites in males [17]. As such, the current study's short observatory period of physical activity may have limited us in explaining our findings.

From our predictive equation example, the estimated whole-body BMD of 1.106 g/cm^2 in an average male who achieves a maximal loading score is higher than the mean BMD by 0.31 SD. A previous study in Raine Study Gen2 participants reported a comparable increase of 0.35 SD in whole-body BMD at age 20 years among those with consistently higher vitamin D status trajectory from age 6 years [23], suggesting the importance of lifestyle and physiological factors in influencing peak bone mass. Clinically, a 1 SD increase in peak bone mass can reduce osteoporotic fracture risk in later life by 50% [2]. In the current study, a maximal loading score would be achieved if one performs a combination of walking, and moderate and vigorous physical activity daily for at least 10 min. Participants who achieved this may have had more varied physical activity types with greater diversification of loading favourable for osteogenesis [38].

Location-specific skeletal effects of loading scores were apparent, where positive associations between loading scores and leg BMC and BMD were independent of IPAQ score. Similar findings were reported in the Gothenburg Osteoporosis and Obesity Determinants study, where higher physical activity peak strain score in young adults was associated with significantly greater BMD at the femoral neck and lumbar spine (10.5–14.0% difference with sedentary group) compared to at the radius (3.0% difference) [39]. Calculation of these peak strain scores applied ground reaction force principles like in our current method and placed greater emphasis on activities that involved strain to the lower limb, such as jumping [36]. As such, upward dissipation of forces may result only in observations of associations at the lower limb and axial sites. Indeed, we found that IPAQ scores were positively associated with arm BMC and BMD, with associations tending to remain significant after adjustment with loading score. Our observed associations were driven by males, whose bones may have sustained mechanosensitivity to physical activity after puberty compared to females [8]. In contrast, past studies demonstrate a lack of association between physical activity metabolic intensity and radius bone mass and microarchitecture, instead citing lean mass, body weight, or physical function as stronger predictors [40, 41]. However, the association between IPAQ scores at Gen2–17-year follow-up and arm BMD remained significant following adjustment for lean mass (data not shown), suggesting that the osteogenic effect of physical activity was not a function of local effects. It is possible that males in this study engaged in greater weight-bearing activities at the upper arm such as weightlifting and rugby [42], and perceived the intensity of such activities as moderate, which can disproportionately increase IPAQ scores relative to loading scores.

Despite these positive findings, this study has several limitations. The observational nature of the study prevents us from inferring causality, and the study was not designed to longitudinally observe the skeletal effects of physical activity types. As such, the long and short IPAQ forms were administered at the Gen2–17- and Gen2–20-year follow-ups, respectively. It has been reported that the two forms have poor agreement [43]. Our long-to-short-form adaptation intended to overcome this incompatibility, but this conversion has not been validated, and may have contributed to the lack of observed association between change in physical activity and bone mass. Self-reported physical activity intensity levels are also subject to recall bias, physical function, and individual interpretation. The latter has been a criticism of the IPAQ due to its ambiguous instructions, particularly describing moderate and vigorous physical activity as making one "breathe harder than normal", thus creating difficulties in differentiating between activities of varying intensities [44]. Such IPAQ questions were also designed to assess metabolic intensity, instead of mechanical loading. However, it is probably more unlikely that individuals are able to conceptualise and distinguish between moderate- and high-impact physical activity as these forms of activities are less familiar. Instead, past studies have extracted bone loading scores from physical activities recorded in free-text form [45]. This can be a time-consuming task in large cohorts, especially in a young population where types of physical activity can vary greatly. Our current approach may have simplified this process for ease of loading score calculation, but its accuracy and validity are unknown. We also did not examine bone mass at other clinically relevant skeletal sites, which may have achieved peak bone mass at varying stages

and respond to mechanical loading differently [19], nor did we adjust for maturity due to insufficient data regarding the timing of puberty in our cohort.

Our novel approach may support retrospective re-analyses of existing datasets where peak bone mass is of interest. Coupling traditional energy expenditure questionnaire outcomes with bone-loading estimates may also improve understanding of the location-specific skeletal benefits of physical activity in young adults. In conclusion, our study revealed important disagreements in associations of loading intensity and energy expenditure from a self-administered physical activity questionnaire with peak bone mass in young adults, but limited relationships with change in physical activity measures from age 17 to 20 years.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11657-022-01100-1.

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Declarations

Conflict of interest Carrie-Anne Ng, David Scott, Marc Sim, Kun Zhu, Aris Siafarikas, Nicolas H. Hart, Jocelyn Tan, and Paola Chivers declare that they have no conflict of interest.

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Authors and Affiliations

Carrie-Anne Ng[1] · David Scott[1,2] · Marc Sim[3,4,5] · Kun Zhu[4,6] · Aris Siafarikas[4,5,7,8,9,10] · Nicolas H. Hart[5,7,10,11,12] · Jocelyn Tan[5,13] · Paola Chivers[5,7,10]

1 Department of Medicine, School of Clinical Sciences at Monash Health, Monash University, Clayton, VIC 3168, Australia

2 Institute for Physical Activity and Nutrition, School of Exercise and Nutrition Sciences, Deakin University, Burwood, VIC, Australia

3 Institute for Nutrition Research, School of Medical and Health Sciences, Edith Cowan University, Joondalup, WA, Australia

4 Medical School, The University of Western Australia, Perth, WA, Australia

5 Western Australian Bone Research Collaboration, Perth, WA, Australia

6 Department of Endocrinology and Diabetes, Sir Charles Gairdner Hospital, Perth, WA, Australia

7 School of Medical and Health Sciences, Edith Cowan University, Joondalup, WA, Australia

8 Department of Endocrinology and Diabetes, Perth Children's Hospital, Perth, WA, Australia

9 Telethon Kids Institute for Health Research, Perth, WA, Australia

10 Institute for Health Research, The University of Notre Dame Australia, Fremantle, WA, Australia

11 Caring Futures Institute, College of Nursing and Health Sciences, Flinders University, Adelaide, South Australia, Australia

12 School of Nursing, Faculty of Health, Queensland University of Technology, Brisbane, QLD, Australia

13 School of Nursing, Midwifery, Health Sciences and Physiotherapy, The University of Notre Dame Australia, Fremantle, WA, Australia

Appendix C

Supplementary Material

Supplementary Material for Chapter 2

Supp 2A Systematic Review: Search Strategy

Research Question	What is the association between developmental coordination disorder/low motor competence and impairment of bone health across the lifespan?
Information Sources	Databases: PubMed; Cochrane Central Register of Controlled Trials; Informit Health Collection; ScienceDirect. Unpublished literature: OpenGrey; Trove; Digital Commons Network; Networked Digital Library of Theses and Dissertations; WorldCat; DART-Europe E-these portal; EThOs,; Scopus. Conference websites: American Society for Bone and Mineral Research and International Conference on Children's Bone Health, National Conference on Developmental Coordination Disorder, International Conference on Developmental Coordination Disorder) Google Scholar and WorldWideScience

Source:	Date of search	Search strategy used (keywords & Boolean)	Search Limits or filters (e.g. dates, language)	# results found
Pubmed	2/6/20	("Bone and Bones"[mh:exp] OR "bone density" [MeSH Terms] OR "fractures, bone"[MeSH Terms] OR ("osteoporosis, postmenopausal"[MeSH Terms] OR "osteoporosis"[MeSH Terms]) OR "age determination by skeleton"[MeSH Terms] OR "tomography, x-ray computed"[MeSH Terms] OR "Bone health"[tw] OR "osteoporosis"[tw] OR ("bone"[tw] AND "density"[tw]) OR ("bone"[tw] AND "mineral"[tw] AND "content"[tw]) OR ("fractures"[tw] AND "bone"[tw]) OR ("bone"[tw] AND "fracture"[tw]) OR ("age"[tw] AND "skeleton"[tw]) OR "age determination by skeleton"[tw] OR "bone mineral density"[tw] OR (Skeletal[tw] AND "growth"[tw] AND "development"[tw])) AND ("motor skills disorders"[MeSH Terms:exp] OR "apraxias "[MeSH Terms] OR "movement disorders"[MeSH Terms:exp] OR "developmental disabilities"[MeSH Terms:exp] OR "learning	AND ((Case Reports[ptyp] OR Clinical Conference[ptyp] OR Classical Article[ptyp] OR Clinical Study[ptyp] OR Clinical Trial[ptyp] OR Clinical Trial, Phase I[ptyp] OR Clinical Trial, Phase II[ptyp] OR Clinical Trial, Phase IV[ptyp] OR Clinical Trial, Phase III[ptyp] OR Comparative Study[ptyp] OR Controlled Clinical Trial[ptyp] OR Corrected and Republished Article[sb] OR Journal Article[ptyp] OR Multicenter Study[ptyp] OR Observational Study[ptyp] OR Practice Guideline[ptyp] OR Pragmatic Clinical Trial[ptyp] OR Published Erratum[sb] OR Randomized Controlled Trial[ptyp] OR Retracted Publication[sb] OR Retraction of Publication[sb] OR Review[ptyp] OR systematic[sb] OR Twin Study[ptyp]) AND "humans"[MeSH Terms])	5553

Source:	Date of search	Search strategy used (keywords & Boolean)	Search Limits or filters (e.g. dates, language)	# results found
		disabilities"[MeSH Terms:exp] OR "psychomotor disorders"[MeSH Terms] OR "motor skills"[MeSH Terms:exp] OR "motor activity/physiopathology"[Mesh Terms] OR ("motor"[tw] AND "skills"[tw] AND "disorders"[tw]) OR ("developmental"[tw] AND "coordination"[tw] AND "disorder"[tw]) OR "motor competence"[tw] OR "Clumsiness"[tw] OR "apraxias"[tw] OR "dyspraxia"[tw] OR (Motor[tw] AND difficulties[tw]) OR ("learning"[tw] AND difficulties[tw]) OR "physical awkwardness"[tw] OR ("coordination"[tw] AND "disorder"[tw]) OR ("coordination"[tw] AND "impairment"[tw]) OR "specific developmental disorder of motor function"[tw] OR (motorically[tw] AND awkward[tw]) OR "minimal cerebral dysfunction"[tw] OR ("minimal"[tw] AND "brain"[tw] AND "dysfunction"[tw]) OR ("deficits in attention, motor control and perception"[tw]))		
Pubmed	31/3/21	As above	Limited to 2020-2021	79
Pubmed	24/6/22	As above	Limited to 2021-2022	46
Cochrane central register	10/3/20	("developmental coordination disorder" OR motor competence OR clums* OR dyspraxia OR motor learning difficult* OR awkward* OR coordination disorder OR coordination impairment OR (lack AND coordination) OR motor skill disorder OR "motor skills disorder" OR motor disorder* OR motor difficult* OR minimal neurological dysfunction OR "specific developmental disorder of motor function" OR motorically awkward OR "minimal cerebral		364

Source:	Date of search	Search strategy used (keywords & Boolean)	Search Limits or filters (e.g. dates, language)	# results found
		dysfunction" OR minimal brain dysfunction OR deficits in attention, motor control and perception):ti,ab,kw AND ("bone health" OR osteop* OR bone densit* OR fracture OR bone disease OR bone mineral content OR skeletal development OR PQCT or "DXA scan" OR "DEXA scan"):ti,ab,kw		
Cochrane central register	31/3/21	As above	Cochrane Library publication date in the last year	45
Cochrane central register	24/6/22	As above	Cochrane Library publication date in the last year	47
Informit	10/3/20	(Developmental Coordination Disorder OR motor competence OR clums* OR dyspraxi* OR motor learning difficult* OR physical awkward* OR coordination disorder OR coordination impair* OR lack coordination OR motor skill* disorder OR apraxia OR "motor difficulty" OR "motor difficulties" OR minimal neurological dysfunction OR "specific developmental disorder of motor function" OR motorically awkward OR "minimal cerebral dysfunction' OR minimal brain dysfunction or deficits in attention, motor control and perception) AND ("bone health" OR osteop* or bone densit* OR fracture OR "bone disease" OR bone mineral content OR skeletal %5 development OR pQCT OR DXA OR DEXA)		35
Informit	10/3/21		In the last year	0
Informit	24/6/22	As above	In the last year	0

Source:	Date of search	Search strategy used (keywords & Boolean)	Search Limits or filters (e.g. dates, language)	# results found
ScienceDirect	10/3/20	("Coordination disorder" AND pQCT); (motor AND competence AND pQCT); (clumsy OR clumsiness OR dyspraxia OR dyspraxic AND pQCT); (motor AND learning AND difficulty AND pQCT); (motor AND learning AND difficulties AND pqct); (awkwardness OR awkwardly OR awkward AND pqct; coordination AND impairment AND pQCT); (coordination AND lack AND pQCT); (motor AND skill AND disorder AND pQCT); (apraxia AND pqct); (motor AND difficulty AND pQCT); (motor AND difficulties AND pqct); (Minimal AND neurological AND dysfunction AND pQCT); ("specific developmental disorder of motor function" OR "minimal cerebral dysfunction" AND pQCT); (Motorically AND awkward AND pQCT); (Minimal AND brain AND dysfunction AND pQCT); ("deficits in attention, motor control and perception" AND pQCT); ("Coordination disorder" AND DXA); (motor AND competence AND DXA); (clumsy OR clumsiness OR dyspraxia OR dyspraxic AND DXA); (motor AND learning AND difficulty AND DXA(; (motor AND learning AND difficulties AND DXA); (awkwardness OR awkwardly OR awkward AND DXA); (coordination AND impairment AND DXA); (coordination AND lack AND DXA); (motor AND skill AND disorder AND DXA); (apraxia AND DXA); (motor AND difficulty AND DXA); (motor AND difficulties AND DXA); (Minimal AND neurological AND dysfunction AND DXA); ("specific developmental disorder		2189

Source:	Date of search	Search strategy used (keywords & Boolean)	Search Limits or filters (e.g. dates, language)	# results found
		of motor function" OR "minimal cerebral dysfunction" AND DXA); (Motorically AND awkward AND DXA); (Minimal AND brain AND dysfunction AND DXA); ("deficits in attention, motor control and perception" AND DXA); ("Coordination disorder" AND bone AND density); (motor AND competence AND bone AND density); (clumsy OR clumsiness OR dyspraxia OR dyspraxic AND bone AND density); (motor AND learning AND difficulty AND bone AND density); (motor AND learning AND difficulties AND bone AND density); (awkwardness OR awkwardly OR awkward AND bone AND density); (coordination AND impairment AND bone AND density); (coordination AND lack AND bone AND density); (motor AND skill AND disorder AND bone AND density); (apraxia AND bone AND density); (motor AND difficulty AND bone AND density); (motor AND difficulties AND bone AND density); (Minimal AND neurological AND dysfunction AND bone AND density); ("specific developmental disorder of motor function" OR "minimal cerebral dysfunction" AND bone AND density); (Motorically AND awkward AND bone AND density); (Minimal AND brain AND dysfunction AND bone AND density); ("deficits in attention, motor control and perception" AND bone AND density); ("Coordination disorder" AND bone AND density); (motor AND competence AND bone AND density); (clumsy OR clumsiness OR dyspraxia OR dyspraxic AND bone AND density); (motor AND learning AND difficulty AND bone AND density); (motor AND learning		

Source:	Date of search	Search strategy used (keywords & Boolean)	Search Limits or filters (e.g. dates, language)	# results found
		AND difficulties AND bone AND density); (awkwardness OR awkwardly OR awkward AND bone AND density); (coordination AND impairment AND bone AND density); (coordination AND lack AND bone AND density); (motor AND skill AND disorder AND bone AND density); (apraxia AND bone AND density); (motor AND difficulty AND bone AND density); (motor AND difficulties AND bone AND density); (Minimal AND neurological AND dysfunction AND bone AND density); ("specific developmental disorder of motor function" OR "minimal cerebral dysfunction" AND bone AND density); (Motorically AND awkward AND bone AND density); (Minimal AND brain AND dysfunction AND fracture); ("deficits in attention, motor control and perception" AND fracture); ("Coordination disorder" AND bone AND mineral AND content); (motor AND competence AND bone AND mineral AND content); (clumsy OR clumsiness OR dyspraxia OR dyspraxic AND bone AND mineral AND content); (motor AND learning AND difficulty AND bone AND mineral AND content); (motor AND learning AND difficulties AND bone AND mineral AND content); (awkwardness OR awkwardly OR awkward AND bone AND mineral AND content); (coordination AND impairment AND bone AND mineral AND content); (coordination AND lack AND bone AND mineral AND content); (motor AND skill AND disorder AND bone AND mineral AND content); (apraxia AND bone AND mineral AND content); (motor AND difficulty AND bone		

Source:	Date of search	Search strategy used (keywords & Boolean)	Search Limits or filters (e.g. dates, language)	# results found
		AND mineral AND content) ; (motor AND difficulties AND bone AND mineral AND content); (Minimal AND neurological AND dysfunction AND bone AND mineral AND content); ("specific developmental disorder of motor function" OR "minimal cerebral dysfunction" AND bone AND mineral AND content); (Motorically AND awkward AND bone AND mineral AND content); (Minimal AND brain AND dysfunction AND bone AND mineral AND content); ("deficits in attention, motor control and perception" AND bone AND mineral AND content); ("Coordination disorder" AND skeletal AND development); (motor AND competence AND skeletal AND development); (clumsy OR clumsiness OR dyspraxia OR dyspraxic AND skeletal AND development); (motor AND learning AND difficulty AND skeletal AND development); (motor AND learning AND difficulties AND skeletal AND development); (awkwardness OR awkwardly OR awkward AND skeletal AND development); (coordination AND impairment AND skeletal AND development); (coordination AND lack AND skeletal AND development); (motor AND skill AND disorder AND skeletal AND development); (apraxia AND skeletal AND development); (motor AND difficulty AND skeletal AND development); (motor AND difficulties AND skeletal AND development); (Minimal AND neurological AND dysfunction AND skeletal AND development) ;("specific developmental disorder of motor function" OR "minimal cerebral		

Source:	Date of search	Search strategy used (keywords & Boolean)	Search Limits or filters (e.g. dates, language)	# results found
		dysfunction" AND skeletal AND development); (Motorically AND awkward AND skeletal AND development); (Minimal AND brain AND dysfunction AND skeletal AND development); ("deficits in attention, motor control and perception" AND skeletal AND development); ("Coordination disorder" AND "bone health"); (motor AND competence AND "bone health"); (clumsy OR clumsiness OR dyspraxia OR dyspraxic AND "bone health"); (motor AND learning AND difficulty AND "bone health"); (motor AND learning AND difficulties AND "bone health"); (awkwardness OR awkwardly OR awkward AND "bone health"); (coordination AND impairment AND "bone health"); (coordination AND lack AND "bone health"); (motor AND skill AND disorder AND "bone health"); (apraxia AND "bone health"); (motor AND difficulty AND "bone health"); (motor AND difficulties AND "bone health"); (Minimal AND neurological AND dysfunction AND "bone health"); ("specific developmental disorder of motor function" OR "minimal cerebral dysfunction" AND "bone health"); (Motorically AND awkward AND "bone health"); (Minimal AND brain AND dysfunction AND "bone health"); ("deficits in attention, motor control and perception" AND "bone health"); ("Coordination disorder" AND osteoporosis); (motor AND competence AND osteoporosis); (clumsy OR clumsiness OR dyspraxia OR dyspraxic AND osteoporosis); (motor AND learning AND difficulty AND osteoporosis);		

Source:	Date of search	Search strategy used (keywords & Boolean)	Search Limits or filters (e.g. dates, language)	# results found
		(motor AND learning AND difficulties AND osteoporosis); (awkwardness OR awkwardly OR awkward AND osteoporosis); (coordination AND impairment AND osteoporosis); (coordination AND lack AND osteoporosis); (motor AND skill AND disorder AND osteoporosis); (apraxia AND bone AND density); (motor AND difficulty AND osteoporosis); (motor AND difficulties AND osteoporosis); (Minimal AND neurological AND dysfunction AND osteoporosis); ("specific developmental disorder of motor function" OR "minimal cerebral dysfunction" AND osteoporosis); (Motorically AND awkward AND osteoporosis); (Minimal AND brain AND dysfunction AND osteoporosis); ("deficits in attention, motor control and perception" AND osteoporosis); ("Coordination disorder" AND osteopenia); (motor AND competence AND osteopenia); (clumsy OR clumsiness OR dyspraxia OR dyspraxic AND osteopenia); (motor AND learning AND difficulty AND osteopenia); (motor AND learning AND difficulties AND osteopenia); (awkwardness OR awkwardly OR awkward AND osteopenia); (coordination AND impairment AND osteopenia); (coordination AND lack AND osteopenia); (motor AND skill AND disorder AND osteopenia); (apraxia AND osteopenia); (motor AND difficulty AND osteopenia); (motor AND difficulties AND osteopenia); (Minimal AND neurological AND dysfunction AND osteopenia); ("specific developmental disorder of motor function" OR "minimal		

Source:	Date of search	Search strategy used (keywords & Boolean)	Search Limits or filters (e.g. dates, language)	# results found
		cerebral dysfunction" AND osteopenia); (Motorically AND awkward AND osteopenia); (Minimal AND brain AND dysfunction AND osteopenia); ("deficits in attention, motor control and perception" AND osteopenia)		
Sciencedirect	31/3/21	As above	Year: 2020-2021	640
Sciencedirect	25/6/22	As above	Year 2021-2023	1063
NDLTD Global ETD Search	10/3/20	(developmental coordination disorder OR motor OR clumsy OR clumsiness OR dyspraxia OR learning OR backward OR coordination OR "minimal cerebral dysfunction" OR minimal brain dysfunction OR deficit in attention motor control and perception) AND ("bone" OR osteoporosis OR osteopenia OR fracture OR "bone health" OR osteoporosis OR osteopenia OR bone density OR fracture OR "bone disease" OR bone mineral content OR skeletal development OR pQCT OR DXA OR DEXA)		163
NDLTD Global ETD Search	1/4/21	As above	Year: 2020-2021	58
NDLTD Global ETD Search	26/6/22	As above	Year: 2021 – 2022	40
Worldcat	1/4/21	("developmental coordination disorder OR motor OR clumsy OR clumsiness OR dyspraxia OR learning OR awkward OR coordination OR "minimal cerebral dysfunction" OR minimal brain dysfunction OR deficits in attention, motor control and perception)	Limit to theses	4

Source:	Date of search	Search strategy used (keywords & Boolean)	Search Limits or filters (e.g. dates, language)	# results found
		AND (osteoporosis OR osteopenia OR fracture OR "bone health" OR osteoporosis OR osteopenia OR bone density OR fracture OR "bone disease" OR bone mineral content OR skeletal development OR pqct OR DXA OR DEXA)		
Worldcat	27/6/22	As above	Year 2021 – 2022	4
SCOPUS	2/6/20	("coordination disorder" OR (motor AND competence) OR clumsy OR clumsiness OR clumsily OR dyspraxia OR dyspraxic) AND ("bone health" OR osteoporosis OR osteopenia OR (bone AND density) OR fracture OR "bone disease" OR (bone AND mineral AND content) OR (skeletal AND development))	Limit to Human	59
SCOPUS	31/3/21	As above	Year: 2020-2021	3
SCOPUS	27/6/22	As above	Year 2021 to present	11
ASMBR	15/4/20	coord* OR "motor OR Clums* OR Dysprax* OR learning OR awkward		18
ASMBR	28/6/22	As above	2021	7
ICCBH	15/4/20	coord* OR "motor OR Clums* OR Dysprax* OR learning OR awkward		14
ICCBH	28/6/22	Review of 2022 program		0
National Developmental coordination disorder	15/4/20	"bone" OR "bone health" OR osteoporosis OR osteopenia OR bone density OR fracture OR "bone disease" OR bone mineral content OR skeletal development OR PQCT or DXA OR DEXA		0

Source:	Date of search	Search strategy used (keywords & Boolean)	Search Limits or filters (e.g. dates, language)	# results found
conference (UK)				
International conference on Developmental Coordination disorder	15/4/20	"bone" OR "bone health" OR osteoporosis OR osteopenia OR bone density OR fracture OR "bone disease" OR bone mineral content OR skeletal development OR PQCT or DXA OR DEXA		4
International conference on Developmental Coordination disorder	28/6/22	Review of 2022 program		0
Google Scholar	30/3/20	developmental coordination disorder OR Clumsy OR Dyspraxia AND "bone" OR osteoporosis OR fracture		400
Google Scholar	12/3/21	As above	2020-2021	210
Google Scholar	28/6/22	As above	2021-2022	45
Web of Science	30/3/20	(developmental coordination disorder OR Clumsy OR Dyspraxia) AND ("bone" OR osteoporosis OR fracture)		20
Web of Science	12/3/21	As above	2020-2021	1
DART	30/3/20	"coordination disorder" OR (motor AND competence) OR clumsy OR clumsiness OR clumsily OR dyspraxia OR dyspraxic AND "bone health" OR osteoporosis OR osteopenia OR (bone AND density) OR fracture OR "bone disease" OR (bone AND mineral AND content) OR (skeletal AND development)	Limit to Theses	3
DART	12/3/21	As above	Limit to theses	0
DART	28/6/22	As above	Limit to theses	0

Source:	Date of search	Search strategy used (keywords & Boolean)	Search Limits or filters (e.g. dates, language)	# results found
Ethos	30/3/20	"coordination disorder" OR (motor AND competence) OR clumsy OR clumsiness OR clumsily OR dyspraxia OR dyspraxic AND "bone health" OR osteoporosis OR osteopenia OR (bone AND density) OR fracture OR "bone disease" OR (bone AND mineral AND content) OR (skeletal AND development)		3
Ethos	12/3/21	As above	Sorted by date	
Ethos	28/6/22	As above		0
TROVE	30/3/20	"coordination disorder" OR (motor AND competence) OR clumsy OR clumsiness OR clumsily OR dyspraxia OR dyspraxic AND "bone health" OR osteoporosis OR osteopenia OR (bone AND density) OR fracture OR "bone disease" OR (bone AND mineral AND content) OR (skeletal AND development)		206
TROVE	10/3/21	As above	Date range: 2020-	0
TROVE	28/6/22	As above	Date range: 2021-	0
Digital Commons Network	30/3/20	"coordination disorder" OR (motor AND competence) OR clumsy OR clumsiness OR clumsily OR dyspraxia OR dyspraxic) AND ("bone health" OR osteoporosis OR osteopenia OR (bone AND density) OR fracture OR "bone disease" OR (bone AND mineral AND content) OR (skeletal AND development))		23
Digital Commons Network	10/3/21	As above	2020 – 2021	11
Digital Commons Network	28/6/22	As above	2021-	18

Supp 2B Systematic Review: List of Excluded Studies

Absence of Bone Health Assessment.

1. Connolly, A., Fielding, J., Papadopoulos, N., McGinley, M., Murphy, A., & Rinehart, N.J. (2019). Factors associated with accidental injuries in children with ADHD–combined type: more than a motor problem? *Journal of Attention Disorders*, 23(11):1320-30. https://doi.org/10.1177/1087054716633857.
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1 Duplicate identified as a relevant article in both the 2020 and 2021 search. 2. Only relevant section is an article published elsewhere. 3. Duplicate not picked up in earlier screenings.

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Supp 2C Systematic Review: Duplicate Publications

Authors (date)	Title	Study design	Study population		Motor assessment	Bone assessment	Notes
			N	Mean age/age range (years)			
Paediatric studies							
Schlager (1979)	[Weight-height development and skeletal maturation in children with minimal cerebral dysfunction. (Preliminary communication)]	Case series	60	6-12	Clinical diagnosis of minimal brain dysfunction	Skeletal age (Greulich and Pyle norms)	
Fong, Liu, Fong, Yuen, and Guo (2017)	Adapted taekwondo training for skeletal development and motor proficiency in prepubertal children with developmental coordination disorder: a randomised controlled trial	RCT	145	7.4/7.5	MABC	Ultrasonic skeletal age	Paediatric cohort No baseline data
Fong et al. (2018)	Variety of activity participation influences leg bone mineral content of pre-pubertal children with developmental coordination disorder	Cross- sectional	52	7.5	Not stated	DXA	Paediatric cohort
Adolescent studies							
Ireland et al. (2015)	Early life motor control is positively associated with adolescent bone strength	Longitudinal	3810	17	Denver developmental screening test	DXA/pQCT	Conference presentation
Chivers et al. (2017)	Gender differences in bone health in a cohort of adolescents with developmental coordination disorder	Cross-sectional	39	14.4	Not stated	pQCT	Adolescent cohort Conference presentation

Authors (date)	Title	Study design	Study population		Motor assessment	Bone assessment	Notes
			N	Mean age/age range (years)			
Chivers et al. (2017)	Suboptimal bone status for adolescents with movement difficulties – it's gender specific	Cross-sectional	39	12-18	MAND	pQCT	Adolescent cohort Conference presentation
Chivers et al. (2019)	Disease-specific pathological traits of youth at risk of secondary osteoporosis as determined through peripheral Quantitative Computed Tomography	Cross-sectional	Not stated	Not stated	Not stated	pQCT	Adolescent cohort Conference presentation
Tan, Siafarikas, et al. (2019)	Feasibility of a 13-week targeted exercise intervention on tibial bone mineral density in adolescents with Developmental Coordination Disorder	Case series	28	14.1	Not stated	pQCT	Adolescent cohort Conference presentation
Tan, Hands, et al. (2019)	Impact of a 13-week targeted exercise intervention on Tibial bone mineral density and lower limb fitness measures in adolescents with DCD	Case series	28	14.1	Not stated	pQCT	Adolescent cohort Conference presentation

Authors (date)	Title	Study design	Study population		Motor assessment	Bone assessment	Notes
			N	Mean age/age range (years)			
Jenkins et al. (2019)	Youth with Developmental Coordination Disorder and low motor competence have bone deficits similar to youth with neuromuscular and chronic diseases	Cross-sectional	Not stated	Not stated	Not stated	pQCT	Adolescent cohort Conference presentation

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Chivers, P., Rantalainen, T., McIntyre, F., Hands, B., Weeks, B., Beck, B., Hart, N., & Siafarikas, A. (2017). *Gender differences in bone health in a cohort of adolescents with developmental coordination disorder* [Presentation]. 8th International Conference on Children's Bone Health, Wurzburg, Germany. https://doi.org/10.1530/boneabs.6.p143

Chivers, P., Rantalainen, T., McIntyre, F., Hands, B., Weeks, B., Beck, B., Hart, N., & Siafarikas, A. (2017). *Suboptimal Bone Status for Adolescents with Movement Difficulties – It's Gender Specific* [Presentation], 12th International Conference on Developmental Coordination Disorder, Fremantle, Australia. https://www.researchgate.net/publication/318305896

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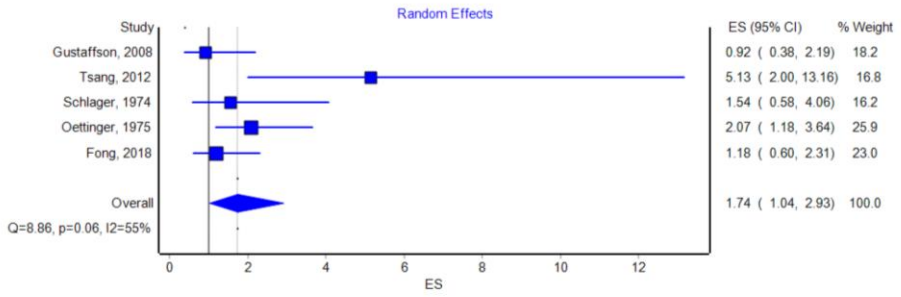
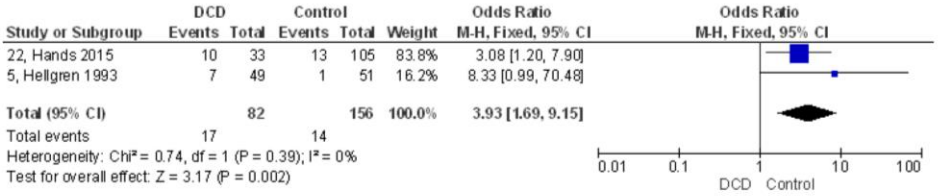
Supp 2D Systematic Review: Metaanalyses Results

Skeletal Age Studies Excluding Linked Studies.



Fracture Rates.



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Iki, M., Kagamimori, S., Kagawa, Y., Matsuzaki, T., Yoneshima, H., & Marumo, F. (2001). Bone mineral density of the spine, hip and distal forearm in representative samples of the Japanese female population: Japanese population-based osteoporosis (JPOS) study. *Osteoporosis International, 12*(7), 529-537. doi:10.1007/s001980170073

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Tan, J., Siafarikas, A., Rantalainen, T., Hart, N. H., McIntyre, F., s, B., & Chivers, P. (2020). Impact of a multimodal exercise program on tibial bone health in adolescents with Development Coordination Disorder: an examination of feasibility and potential efficacy. *Journal of Musculoskeletal & Neuronal Interactions, 20*(4), 445. Retrieved from internal-pdf://1948641664/JMNI-20M-05-081[3084].pdf

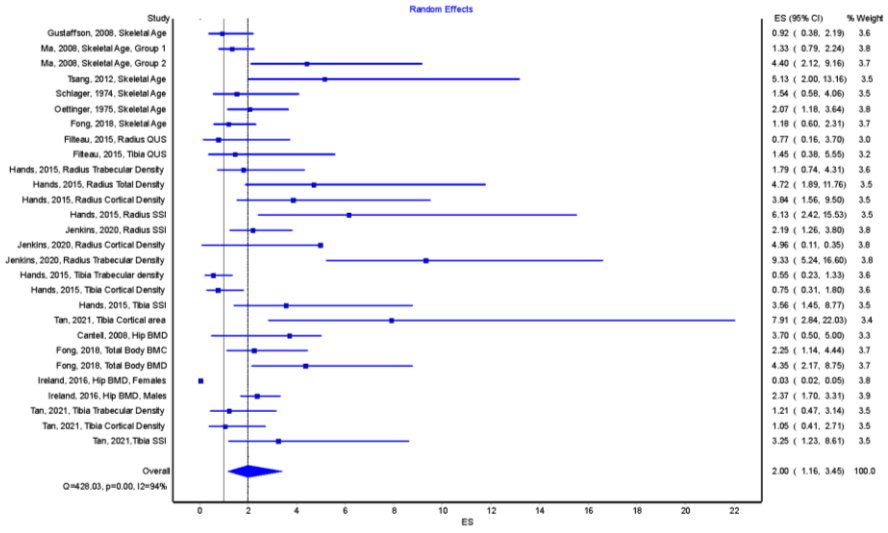
Methods. In text Z-scores were used preferentially when presented (Hands et al., 2015; Tan et al., 2020), otherwise a Z-score was calculated from mean values using a population reference norm (Ashby et al., 2009; Guo, Xu, Gong, Tang, & Xu, 2013; Iki et al., 2001; Mølgaard, Thomsen, Prentice, Cole, & Michaelsen, 1997) when available for the tool and bone analysis site. Population reference norms were only used when appropriate to the age and geographic region of the population. Effect sizes were calculated using the Z-scores and converted to odds ratios. Z-scores were able to be calculated for all studies, however, due to an absence of reference norms (Fonseca, Gordon, & Barr, 2013), only 35 out of 74 outcomes (47.3%) from 24 sites out of the 31(77.4%) sites measured could have odds ratios calculated.

Meta-analysis results were visualised using a forest plot. Fixed effect results are presented for fracture rates due to the rareness of events; random effects are reported for other analysis.

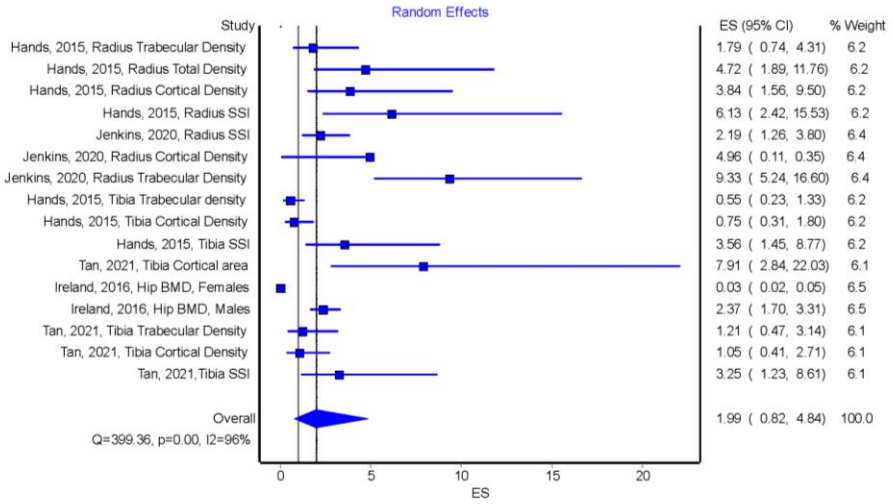
Results.

Impaired Bone Health.

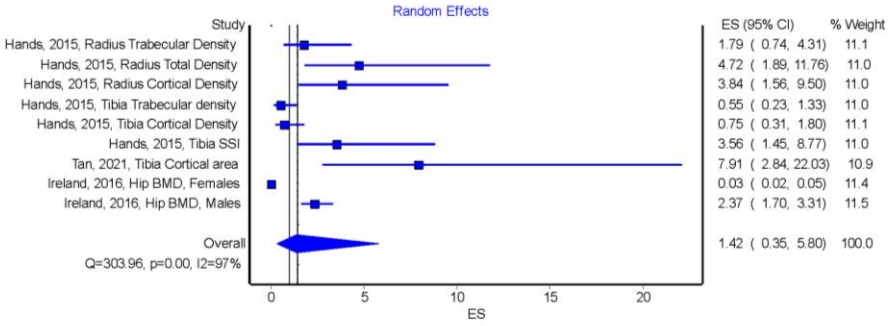
All Results.



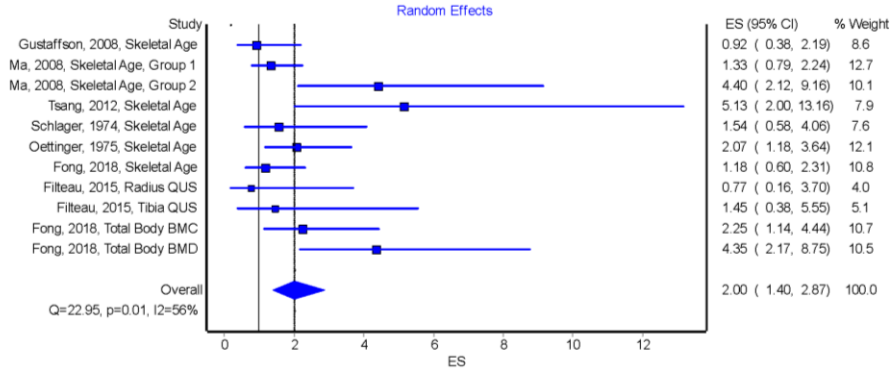
Impaired Bone Health.
Adolescent Studies.



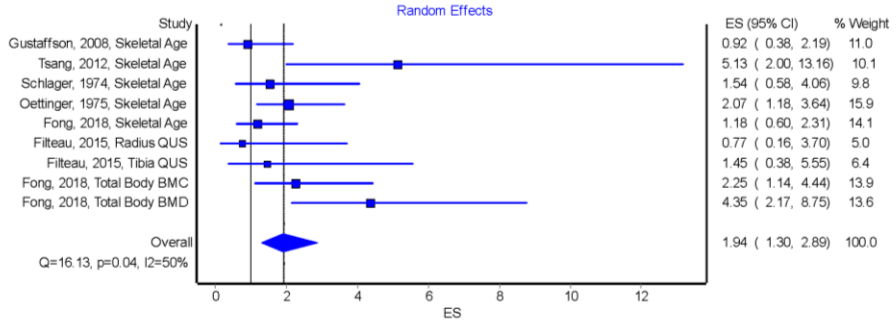
Impaired Bone Health.
Adolescent Studies with Linked Cohorts Removed where Same Outcomes were Reported.



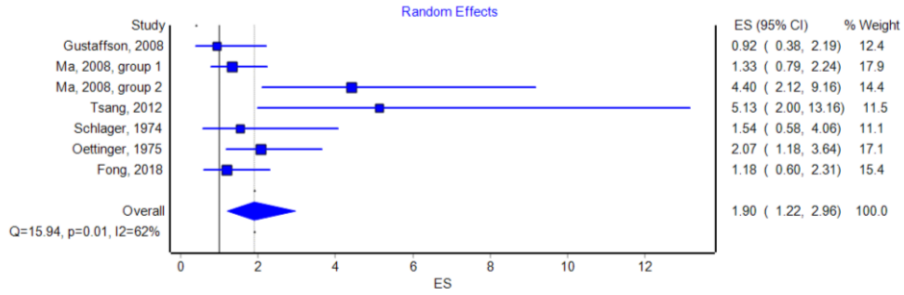
Impaired Bone Health.
Paediatric Studies.



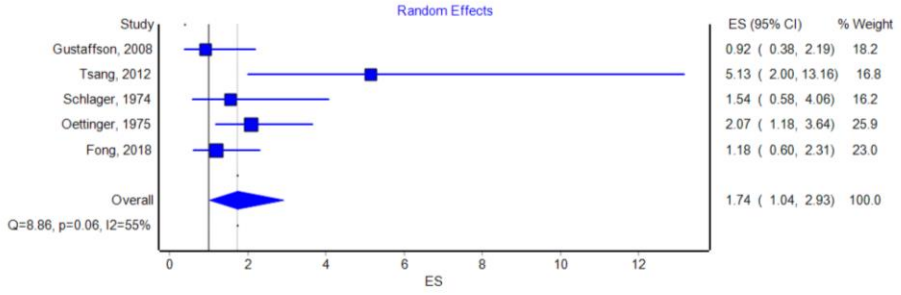
Impaired Bone Health.
Paediatric Studies with Linked Studies Removed for the Same Outcomes.



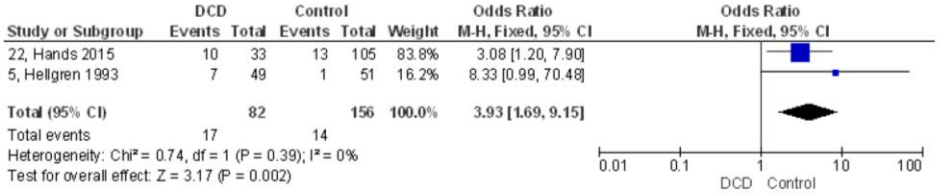
Skeletal Age Studies.



Skeletal Age Studies Excluding Linked Studies.



Fracture Rates.



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Guo, B., Xu, Y., Gong, J., Tang, Y., & Xu, H. (2013). Age trends of bone mineral density and percentile curves in healthy Chinese children and adolescents. *Journal of Bone and Mineral Metabolism, 31*(3), 304-314. doi:10.1007/s00774-012-0401-1

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Supp 2E Systematic Review: GRADE Appraisal for Overall Methodological Quality

GRADE Appraisal Details

GRADE domain	Judgement	Concerns about certainty domains
Fracture Rate		
Risk of bias	Issue of bias noted in both studies is management of confounding factors. One study included individuals with DCD and ADD in the sample, the other sample did not report on the prescence of ADD or other conditions. The contribution of these factors was not noted in analysis. It is noted that one of the studies used a fracture rate for the control population from a different study and so a different population than the study population. One studies used self/parent report as the means of measuring fracture incidence and so risked recall bias, although this would be unlikely for this outcome.	Serious
Indirectness	Hellgreen et al's study includes individuals with ADD which may have increased their risk. It is noted that individuals with motor planning problems and no ADD do not have this increased fracture rate. Hands et al's study does not contain information on comorbidities but is likely to include individuals with ADD. The causality of fractures in a DCD problem (i.e., impaired bone health or a result of falling more etc) is noted.	Serious
Imprecision	Only two studies. Sample sizes are small overall and sample size for one study is below the calculated optimal information criterion (as comparator drawn from another study). Number of events is satisfactory. Confidence intervals of that study is wide and overlaps no effect.	Serious
Inconsistency	Inconsistency I2 test is fine =0.00 but this is likely due to the very wide CI for one study (0.92 to 65). odds ratio varies widely between the studies 3.38 vs 7.78	Serious
Publication bias	Only two studies reported on fracture rates, given the ease of acquiring this information (via parent report), non-publication of results can be considered. Hands et al's sample is of a small sample, with the sample size seeming bigger due to the comparator group which is drawn from another study. It is noted that Hands et al's paper is from a larger cohort study, which has published widely, none of the other studies have reported on fracture rates. Funnel plots are inconclusive as there are only two studies. It is notable that the only papers on this are published, and grey literature has no examples of this.	Strongly suspected
Effect size	Large	Strong association
Plausible confounding/dose response	Confounding by other variables is possible. No assessment of risk of fracture compared to degree of motor impairment	Not assessed as already downgraded, in keeping with GRADE guidelines

Bone Health Outcomes

Risk of bias	Primary issue is that of controlling for confounding factors and statistical management of this. One study used the ASQ which has insufficient specificity and may have resulted in DCD participants being grouped into the control population, older issues used older terms which may result in insufficient specificity. Three studies, from the same cohort, used a comparison population that was from a different population than the study population	Serious
Indirectness	Studies generally assessed DCD/LMC using established tools, one study used a tool with insufficient evidence in establishing DCD, older studies used diagnostic criteria no longer used, two studies used altered MABC so new tool is not established. Lack of identifying or controlling for comorbidities in the participants medical history is a particular concern in assigning causality. Studies were largely focused on paediatric populations, particularly skeletal age, the long-term implications of decreased bone health in this age group are unclear. One study used QUS which may not be an adequate proxy measure. Fracture studies did not report severity of trauma causing the fracture. pQCT and DXA studies often reported variables with significant differences without considering the clinical relevance of those measures vs those which were not different or decreased.	
Imprecision	Total number of participants with potential DCD approximately 601 (with cohorts merged). Effect size was variable between outcomes, but confidence intervals for individual outcomes were generally small likely impacted by individual study size.	Not serious, borderline
Inconsistency	Primary issue is that of controlling for confounding factors and statistical management of this. One study used the ASQ which has insufficient specificity and may have resulted in DCD participants being grouped into the control population, older issues used older terms which may result in insufficient specificity. Three studies, from the same cohort, used a comparison population that was from a different population than the study population	
Publication bias	Studies reported both negative and positive outcomes, although studies were primarily negative some studies did report no effect. The search was comprehensive, and the grey literature did not show a higher rate of positive findings than the published literature	Undetected
Effect size	Small	
Plausible confounding/dose response	Possible confounding factors Dose response was not assessed in any study	Not assessed

Supplementary Material for Chapter 3

Supp 3A Childhood Study: DCD General Linear Model without Motor Competence

GLM (Log Transformed) for DCD, Without Motor Competence Variables

			95% Confidence interval		
	Beta	**S.E.**	**Lower**	**Upper**	**P**
Sedentary behaviour (Ln)					
Intercept	5.500	0.151	5.205	5.795	<.001
Sex†	-0.011	0.025	-0.060	0.038	.656
DCD‡	0.059	0.035	-0.009	0.127	.092
Age	0.052	0.015	0.022	0.082	.001
BMI Z score	0.028	0.011	0.006	0.050	.012
DCD-sex interaction	-0.006	0.050	-0.104	0.093	.907
Light activity (Ln)					
Intercept	6.023	0.153	5.723	6.323	<.001
Sex†	0.049	0.025	-0.001	0.098	.055
DCD‡	-0.035	0.035	-0.104	0.034	.325
Age	-0.074	0.016	-0.104	-0.043	<.001
BMI Z score	-0.010	0.012	-0.033	0.012	.364
DCD-sex interaction	-0.022	0.051	-0.122	0.079	.670
Moderate activity (Ln)					
Intercept	5.603	0.190	5.231	5.975	<.001
Sex†	-0.136	0.032	-0.197	-0.074	<.001
DCD‡	-0.048	0.044	-0.134	0.038	.272
Age	-0.076	0.019	-0.113	-0.038	<.001
BMI Z score	-0.019	0.014	-0.047	0.009	.191
DCD-sex interaction	0.021	0.063	-0.103	0.145	.740
Vigorous activity (Ln)					
Intercept	4.829	0.461	3.925	5.732	<.001
Sex†	-0.308	0.076	-0.458	-0.159	<.001
DCD‡	-0.126	0.106	-0.335	0.083	.236
Age	-0.182	0.047	-0.274	-0.091	<.001
BMI Z score	-0.080	0.035	-0.148	-0.012	.021
DCD-sex interaction	0.082	0.154	-0.220	0.384	.593
MVPA (Ln)					

			95% Confidence interval		
	Beta	**S.E.**	**Lower**	**Upper**	**P**
Intercept	5.894	0.212	5.479	6.309	<.001
Sex†	-0.162	0.035	-0.230	-0.093	<.001
DCD‡	-0.062	0.049	-0.158	0.034	.206
Age	-0.089	0.021	-0.131	-0.047	<.001
BMI Z score	-0.027	0.016	-0.058	0.004	.088
DCD-sex interaction	0.036	0.071	-0.103	0.175	.611
MAD (Ln)					
Intercept	-2.365	0.208	-2.772	-1.958	<.001
Sex†	-0.143	0.034	-0.210	-0.075	<.001
DCD‡	-0.070	0.048	-0.164	0.024	.145
Age	-0.092	0.021	-0.133	-0.051	<.001
BMI Z score	-0.031	0.016	-0.061	0.000	.050
DCD-sex interaction	0.044	0.069	-0.092	0.180	.523
Number of sedentary bouts (Ln)					
Intercept	3.840	0.175	3.496	4.183	<.001
Sex†	-0.025	0.029	-0.082	0.032	.388
DCD‡	0.058	0.040	-0.021	0.137	.151
Age	0.074	0.018	0.039	0.109	<.001
BMI Z score	0.030	0.013	0.004	0.056	.023
DCD-sex interactions	0.016	0.059	-0.099	0.131	.782
Number of light bouts (Ln)					
Intercept	3.355	0.388	2.594	4.116	<.001
Sex†	0.068	0.064	-0.058	0.194	.291
DCD‡	-0.123	0.090	-0.299	0.053	.171
Age	-0.086	0.039	-0.163	-0.009	.029
BMI Z score	0.027	0.029	-0.030	0.085	.346
DCD-sex interaction	0.017	0.130	-0.238	0.271	.897

			95% Confidence interval		
	Beta	**S.E.**	**Lower**	**Upper**	**P**
Number of moderate bouts (Ln)					
Intercept	3.007	0.292	2.435	3.580	<.001
Sex†	-0.252	0.048	-0.347	-0.157	<.001
DCD‡	-0.096	0.067	-0.229	0.036	.153
Age	-0.024	0.030	-0.082	0.034	.416
BMI Z score	0.011	0.022	-0.032	0.054	.604
DCD-sex interaction	0.027	0.098	-0.164	0.219	.780
Sedentary bout duration (Ln)					
Intercept	4.576	0.233	4.118	5.032	<.001
Sex†	-0.037	0.039	-0.113	0.038	.334
DCD‡	0.083	0.054	-0.022	0.189	.121
Age	0.104	0.024	0.058	0.150	<.001
BMI Z score	0.053	0.018	0.019	0.087	.003
DCD-sex interaction	0.000	0.078	-0.152	0.153	.995
Light bout duration (Ln)					
Intercept	4.577	0.582	3.437	5.717	<.001
Sex†	-0.072	0.096	-0.261	0.117	.455
DCD‡	-0.124	0.134	-0.387	0.140	.357
Age	-0.126	0.059	-0.241	-0.011	.032
BMI	0.058	0.044	-0.027	0.144	.180
DCD-sex interaction	0.061	0.194	-0.319	0.442	.752
Moderate bout duration (Ln)					
Intercept	3.348	0.381	2.601	4.094	<.001
Sex†	-0.208	0.063	-0.331	-0.084	.001
DCD‡	-0.056	0.088	-0.228	0.116	.525
Age	-0.010	0.039	-0.085	0.066	.802
BMI Z score	0.015	0.029	-0.041	0.071	.606
DCD-sex interaction	-0.021	0.127	-0.270	0.228	.869

			95% Confidence interval		
	Beta	**S.E.**	**Lower**	**Upper**	**P**
Sedentary breaks (Ln)					
Intercept	6.897	0.145	6.614	7.181	<.001
Sex†	0.057	0.024	0.010	0.104	.018
DCD‡	0.017	0.033	-0.049	0.082	.619
Age	-0.044	0.015	-0.073	-0.016	.002
BMI Z score	-0.022	0.011	-0.043	-0.001	.041
DCD-sex interaction	-0.040	0.048	-0.135	0.055	.406
OI (Ln)					
Intercept	7.196	0.144	6.915	7.478	<.001
Sex†	-0.114	0.024	-0.161	-0.067	<.001
DCD‡	-0.029	0.033	-0.094	0.036	.381
Age	-0.071	0.015	-0.099	-0.042	<.001
BMI Z score	-0.014	0.011	-0.035	0.007	.189
DCD-sex interaction	0.021	0.048	-0.073	0.116	.656
Low impact peaks (Ln)					
Intercept	11.128	0.216	10.705	11.551	<.001
Sex†	-0.200	0.036	-0.270	-0.130	<.001
DCD‡	-0.068	0.050	-0.166	0.029	.171
Age	-0.106	0.022	-0.149	-0.063	<.001
BMI Z score	-0.058	0.016	-0.090	-0.027	<.001
DCD-sex interaction	0.039	0.072	-0.102	0.181	.588
Medium impact peaks (Ln)					
Intercept	10.505	0.340	9.839	11.172	<.001
Sex†	-0.365	0.056	-0.475	-0.254	<.001
DCD‡	-0.118	0.079	-0.272	0.036	.133
Age	-0.202	0.034	-0.269	-0.134	<.001
BMI Z score	-0.089	0.026	-0.139	-0.039	<.001
DCD-sex interaction	0.116	0.114	-0.107	0.338	.309

			95% Confidence interval		
	Beta	**S.E.**	**Lower**	**Upper**	**P**
High impact peaks (Ln)					
Intercept	9.746	0.550	8.668	10.824	<.001
Sex†	-0.485	0.091	-0.664	-0.307	<.001
DCD‡	-0.164	0.127	-0.413	0.085	.196
Age	-0.271	0.056	-0.380	-0.162	<.001
BMI Z score	0.037	0.041	-0.118	0.044	.369
DCD-sex interaction	0.189	0.184	-0.172	0.549	.305

†: Female =1. ‡: DCD=1

Supp 3B Childhood Study: Between Group Differences by Sex

Table

Motor Testing Results by Gender

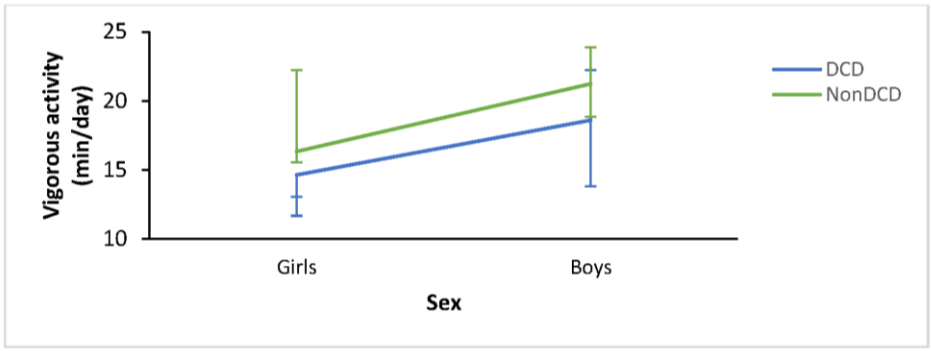
	Girls Mean (Sd) [Md]	Boys Mean (Sd) [Md]	U	d_{cohen}	
T1 testing					
KTK					
Walking backwards	22.12 (11.57) [21.00]	18.21 (13.58) [14.00]	-3.23	-0.31	.
Hopping for height (right)	12.42 (6.89) [13.00]	11.42 (6.93) [11.50]	-1.02	0.15	.
Hopping for height (left)	9.69 (6.41) [10.00]	9.41 (7.23) [8.00]	-0.67	-0.04	.
Hopping for height (total)	22.33 (11.91) [20.00]	20.70 (13.28) [20.00]	-1.09	-0.13	.
Jumping sideways	34.72 (9.49) [33.00]	36.27 (10.48) [36.00]	1.36	0.16	.
Moving sideways	28.80 (6.29) [29.00]	30.03 (7.46) [30.00]	1.35	0.18	.
Total	108.23 (30.19) [105.00]	105.37 (37.03) [106.00]	-0.72	-0.09	.
TGMD3					
Run	6.38 (1.71) [7.00]	6.11 (1.79) [6.00]	-1.79	0.24	.
Gallop	4.75 (1.69) [5.00]	4.48 (1.83) [5.00]	-1.59	-0.15	.
Hop	4.68 (1.92) [5.00]	4.27 (2.21) [4.00]	-2.09	-0.15	.
Skip	3.23 (1.86) [4.00]	2.29 (2.07) [2.00]	-5.10	0.63	*
Hop and Jump	4.82 (2.10) [5.00]	4.71 (2.24) [5.00]	-0.44	0.05	.
Slide	6.18 (2.10) [7.00]	5.80 (2.29) [6.00]	-1.82	0.17	.
Locomotor total	30.01 (7.05) [31.00]	27.74 (7.65) [28.00]	-3.39	0.31	.
2 hand strike	4.98 (2.33) [5.00]	6.47 (2.23) [6.50]	7.10	0.65	*
1 hand strike	1.87 (2.07) [1.00]	3.01 (2.28) [3.00]	5.82	0.52	*
Dribble	1.19 (1.67) [0.00]	1.70 (2.13) [0.00]	2.27	0.27	.
Catch	3.86 (1.41) [4.00]	4.02 (1.42) [4.00]	1.26	0.11	.
Kick	3.09 (1.32) [3.00]	4.18 (1.82) [4.00]	7.00	0.69	*
Overthrow	3.53 (1.81) [3.00]	4.14 (2.18) [4.00]	3.22	0.31	.
Underthrow	4.94 (1.81) [5.00]	5.39 (1.77) [6.00]	2.58	0.25	.
Object control total	23.49 (7.68) [23.00]	28.91 (8.93) [28.00]	6.86	0.65	*
Total	53.53 (12.80) [53.00]	56.65 (14.93) [57.00]	2.62	0.23	.
T2 testing					
Sum of 2 rounds of single leg hopping for distance	5.66 (1.53) [6.00]	5.60 (1.87) [6.00]	0.18	-0.04	.
Sum of 2 rounds of skipping	3.93 (1.54) [4.00]	2.89 (2.05) [4.00]	5.84	-0.58	*
Bouncing a ball	3.24 (1.84) [3.00]	3.89 (1.99) [4.00]	4.23	0.34	*
Overhand throw	4.08 (2.03) [4.00]	5.68 (2.11) [6.00]	8.38	0.77	*
Sideways jumping	51.52 (13.05) [52.00]	52.55 (14.01) [52.00]	0.73	0.08	.

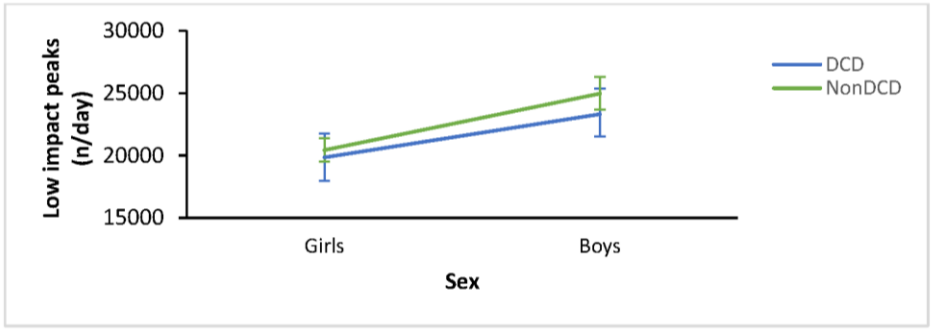
Physical Activity Results

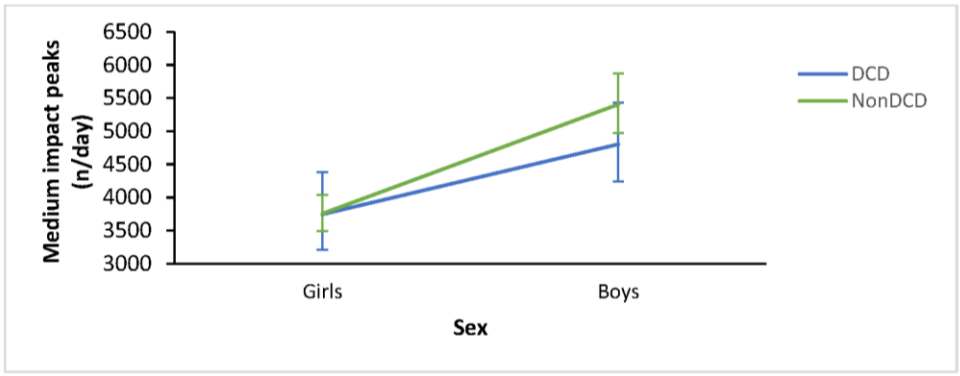
	Girls **Mean (Sd) [Md]**	**Boys** **Mean (Sd) [Md]**	**U**	**d_{cohen}**	**p**
Sedentary behaviour (min/day)	399.67 (66.36) [392.80]	395.37 (68.01) [389.68]	-0.82	-0.09	.413
Light activity (min/day)	221.42 (34.54) [219.44]	211.29 (34.50) [213.79]	-3.13	-0.29	.002
Moderate activity (min/day)	118.05 (24.53) [118.38]	132.74 (27.04) [131.85]	6.16	0.57	<.001
Vigorous activity (min/day)	17.98 (8.54) 16.70]	22.98 (11.16) [21.31]	5.65	0.51	<.001
Very vigorous activity (min/day)	0.51 (0.76) [0.23]	0.50 (0.79) [0.05]	-0.19	-0.01	.847
MVPA (min/day)	136.51 (30.91) [134.64]	156.22 (35.86) [155.65]	6.58	0.59	<.001
MAD	0.04 (0.01) [0.03]	0.04 (0.01) [0.04]	5.64	0.00	<.001
Sedentary bouts (n/day)	92.35 (18.38) [90.57]	92.31 (18.27) [91.88]	0.24	-0.00	.813
Light bouts (n/day)	14.25 (5.39) [13.71]	13.70 (5.13) [13.07]	-1.24	-0.10	.215
Moderate bouts (n/day)	11.58 (4.38) [11.17]	14.38 (5.10) [14.00]	6.55	0.59	<.001
Vigorous bouts (n/day)	1.09 (1.27) [0.71]	1.20 (1.50) [0.71]	0.48	0.08	.634
Sedentary bout length (min/day)	252.54 (65.88) [248.31]	256.91 (71.06) [251.31]	0.50	0.06	.618
Light bout length (min/day)	33.93 (20.45) [27.87]	34.78 (20.92) [31.04]	0.62	0.03	.539
Moderate bout length (min/day)	20.62 (9.51) [19.69]	24.35 (10.13) [23.22]	4.43	0.38	<.001
Vigorous bout length (min/day)	1.75 (2.13) [1.00]	1.96 (2.89) [1.06]	0.37	0.08	.713
Sedentary breaks (n/day)	713.31 (102.78) [712.50]	669.01 (106.01) [667.27]	-4.78	-0.42	<.001
OI	634.81 (92.21) [639.54]	683.96 (98.93) [692.66]	5.99	0.51	<.001
Low impact peaks (n/day)	21406.39 (5150.27) [21095.71]	25487.94 (6517.81) [25255.78]	7.46	0.70	<.001
Medium impact peaks (n/day)	4317.81 (1561.98) [4073.57]	5635.33 (2062.24) [1311.93]	7.76	0.72	<.001
High impact peaks (n/day)	1046.84 (565.89) [951.86]	1463.65 (768.47)	6.92	0.62	<.001

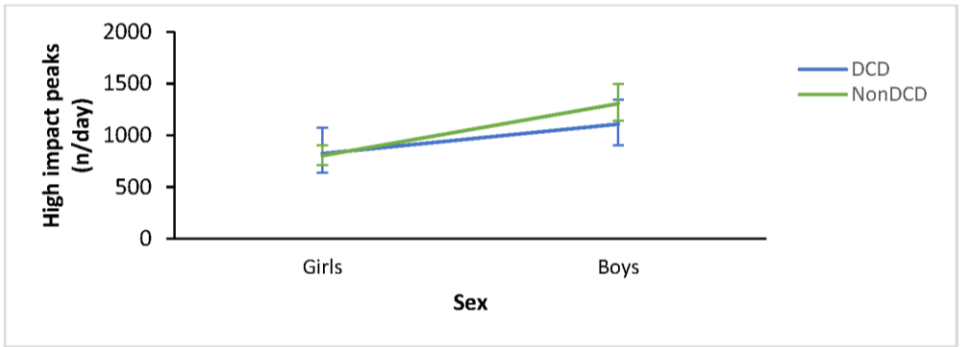
Figure

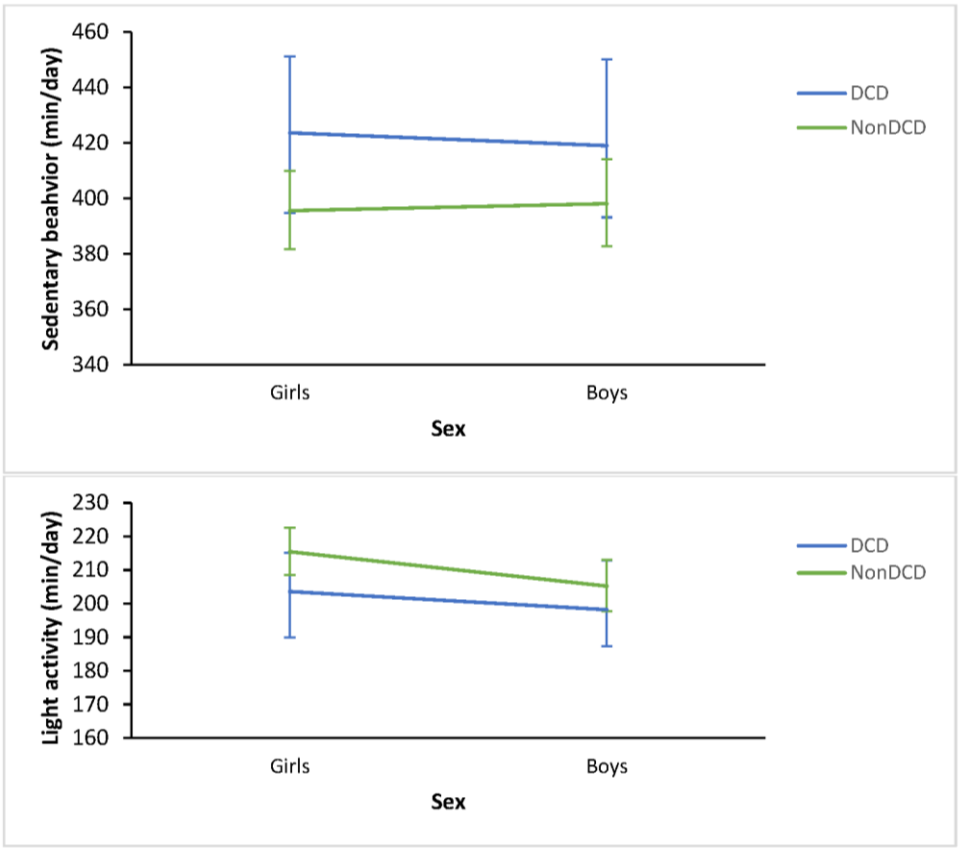
Estimated Marginal Means by DCD Status for Models Including Only Age and BMI Z Score











Age is set at 9.50 and BMI Z score at -0.06

Supp 3C Childhood Study: Mixed Models with Nested Data

General Linear Model for Physical Activity and OI Variables with Nested Variables

			95% Confidence interval		
	β	S.E.	Lower	Upper	P
Sedentary behaviour(Ln)					
Intercept	5.568	0.061	5.448	5.688	<.001
Sex†	0.002	0.016	-0.029	0.032	.032
Age	0.045	0.007	0.030	0.060	<.001
BMI percentile	0.024	0.008	0.008	0.040	.003
Hopping	0.004	0.005	-0.005	0.013	.432
Skipping	0.001	0.004	-0.008	0.009	.829
Bouncing a ball	0.002	0.004	-0.006	0.010	.610
Overhand throw	-0.005	0.003	-0.012	0.002	.148
Sideways jumping	0.000	0.001	-0.001	0.001	.819
Light activity (Ln)					
Intercept	5.735	0.061	5.616	5.855	<.001
Sex†	0.047	0.016	0.016	0.078	.003
Age	-0.048	0.008	-0.063	-0.033	<.001
BMI	0.000	0.008	-0.016	0.015	.975
Hopping	-0.005	0.005	-0.014	0.004	.265
Skipping	-0.005	0.004	-0.014	0.003	.212
Bouncing a ball	0.001	0.004	-0.007	0.009	.865
Overhand throw	0.001	0.003	-0.006	0.007	.855
Sideways jumping	0.001	0.001	0.000	0.003	.038
Moderate activity (Ln)					
Intercept	5.129	0.085	4.961	5.297	<.001
Sex†	-0.094	0.022	-0.138	-0.051	<.001
Age	-0.054	0.011	-0.075	-0.033	<.001
BMI	-0.004	0.011	-0.026	0.017	.698
Hopping	0.001	0.006	-0.011	0.014	.842
Skipping	-0.003	0.006	-0.015	0.008	.600
Bouncing a ball	0.001	0.006	-0.010	0.013	.836
Overhand throw	0.016	0.005	0.007	0.025	.001
Sideways jumping	0.002	0.001	0.001	0.004	.007

			95% Confidence interval		
	β	S.E.	Lower	Upper	P
Vigorous activity (Ln)					
Intercept	3.875	0.172	.3536	4.214	<.001
Sex†	-0.184	0.044	-0.271	-0.097	<.001
Age	-0.160	0.021	-0.202	-0.119	<.001
BMI	-0.046	0.023	-0.090	-0.001	.045
Hopping	0.025	0.013	0.000	0.051	.053
Skipping	-0.015	0.012	-0.039	0.009	.209
Bouncing a ball	0.018	0.012	-0.004	0.041	.114
Overhand throw	0.017	0.010	-0.002	0.036	.082
Sideways jumping	0.007	0.002	0.003	0.011	<.001
MVPA (Ln)					
Intercept	5.421	0.123	5.180	5.663	<.001
Sex†	-0.104	0.023	-0.150	-0.058	<.001
Age	-0.069	0.011	-0.092	-0.047	<.001
BMI	-0.005	0.006	-0.017	0.007	.401
Hopping	0.005	0.007	-0.008	0.019	.419
Skipping	-0.005	0.006	-0.017	0.007	.456
Bouncing a ball	0.003	0.006	-0.009	0.015	.583
Overhand throw	0.017	0.005	0.008	0.027	<.001
Sideways jumping	0.003	0.001	0.001	0.005	<.001
MAD					
Intercept	-2.911	0.084	-3.076	-2.747	<.001
Sex†	-0.085	0.022	-0.128	-0.043	<.001
Age	-0.069	0.010	-0.090	-0.049	<.001
BMI	-0.012	0.011	-0.033	0.010	.287
Hopping	0.007	0.006	-0.005	0.020	.287
Skipping	-0.006	0.006	-0.018	0.005	.269
Bouncing a ball	0.005	0.006	-0.006	0.016	.412
Overhand throw	0.013	0.005	0.004	0.022	.005
Sideways jumping	0.004	0.001	0.002	0.005	<.001

			95% Confidence interval		
	β	S.E.	Lower	Upper	P
Number of sedentary bouts (Ln)					
Intercept	3.821	0.102	3.620	4.021	<.001
Sex†	-0.021	0.019	-0.060	0.017	.269
Age	0.064	0.009	0.045	0.082	<.001
BMI	0.012	0.005	0.003	0.022	.012
Hopping	-0.002	0.006	-0.013	0.009	.751
Skipping	0.004	0.005	-0.006	0.014	.478
Bouncing a ball	-0.002	0.005	-0.013	0.008	.661
Overhand throw	-0.005	0.004	-0.013	0.003	.232
Sideways jumping	-0.001	0.001	-0.002	0.001	.309
Number of light bouts (Ln)					
Intercept	2.501	0.211	2.088	2.914	<.001
Sex†	0.021	0.040	-0.057	0.100	.595
Age	-0.056	0.019	-0.094	-0.018	.004
BMI	0.026	0.010	0.006	0.046	.010
Hopping	-0.016	0.010	-0.038	0.007	.166
Skipping	0.003	0.011	-0.018	0.024	.774
Bouncing a ball	-0.005	0.010	-0.026	0.015	.619
Overhand throw	0.001	0.009	-0.016	0.017	.928
Sideways jumping	0.004	0.002	0.001	0.007	.011
Number of moderate bouts (Ln)					
Intercept	2.127	0.191	1.752	2.502	<.001
Sex†	-0.202	0.036	-0.273	-0.131	<.001
Age	0.020	0.018	-0.014	0.055	.245
BMI	0.010	0.009	-0.008	0.028	.257
Hopping	-0.003	0.010	-0.024	0.017	.763
Skipping	0.017	0.010	-0.001	0.036	.068
Bouncing a ball	-0.013	0.009	-0.032	0.005	.155
Overhand throw	0.020	0.008	0.005	0.035	.009
Sideways jumping	0.002	0.002	-0.001	0.005	.142

			95% Confidence interval		
	β	S.E.	Lower	Upper	P
Sedentary bout duration (Ln)					
Intercept	4.437	0.136	4.170	4.704	<.001
Sex†	-0.035	0.026	-0.085	0.016	.181
Age	0.083	0.013	0.059	0.108	<.001
BMI	0.021	0.007	0.008	0.034	.002
Hopping	0.008	0.007	-0.007	0.022	.295
Skipping	0.007	0.007	-0.006	0.021	.269
Bouncing a ball	0.000	0.007	-0.013	0.013	.977
Overhand throw	-0.006	0.006	-0.017	0.004	.255
Sideways jumping	-0.001	0.001	-0.003	0.001	.553
Light bout duration (Ln)					
Intercept	3.370	0.325	2.733	4.007	<.001
Sex†	-0.105	0.062	-0.226	0.016	.090
Age	-0.084	0.030	-0.142	-0.025	.005
BMI	0.040	0.016	0.009	0.070	.011
Hopping	-0.015	0.018	-0.050	0.019	.390
Skipping	0.026	0.016	-0.005	0.058	.103
Bouncing a ball	-0.014	0.016	-0.045	0.018	.387
Overhand throw	-0.006	0.013	-0.032	0.020	.643
Sideways jumping	0.004	0.003	-0.001	0.009	.096
Moderate bout duration (Ln)					
Intercept	2.512	0.238	2.046	2.979	<.001
Sex†	-0.189	0.045	-0.278	-0.101	<.001
Age	0.028	0.022	-0.015	0.071	.207
BMI	0.014	0.011	-0.009	0.036	.236
Hopping	-0.009	0.013	-0.034	0.017	.495
Skipping	0.024	0.012	0.000	0.047	.046
Bouncing a ball	-0.020	0.012	-0.043	0.003	.094
Overhand throw	0.017	0.010	-0.002	0.036	.076
Sideways jumping	0.003	0.002	-0.001	0.006	.137

			95% Confidence interval		
	β	S.E.	Lower	Upper	P
Sedentary breaks (Ln)					
Intercept	6.902	0.082	6.742	7.063	<.001
Sex†	0.068	0.016	0.037	0.098	<.001
Age	-0.033	0.0-9	-0.048	-0.018	<.001
BMI	-0.006	0.004	-0.014	0.001	.105
Hopping	-0.001	0.005	-0.010	0.008	.790
Skipping	-0.011	0.004	-0.019	-0.003	.008
Bouncing a ball	0.002	0.004	-0.006	0.009	.701
Overhand throw	-0.001	0.003	-0.007	0.006	.803
Sideways jumping	0.000	0.001	-0.001	0.002	.442
OI (Ln)					
Intercept	6.961	0.081	6.802	7.120	<.001
Sex†	-0.065	0.015	-0.095	-0.034	<.001
Age	-0.059	0.008	-0.074	-0.045	<.001
BMI	-0.003	0.004	-0.011	0.005	.429
Hopping	0.004	0.004	-0.004	0.013	.333
Skipping	-0.005	0.004	-0.013	0.003	.209
Bouncing a ball	0.004	0.004	-0.004	0.012	.345
Overhand throw	0.004	0.003	-0.003	0.010	.236
Sideways jumping	0.002	0.001	0.000	0.003	.009
Low impact peaks (Ln)					
Intercept	10.855	0.131	10.598	11.112	<.001
Sex†	-0.145	0.025	-0.194	-0.096	<.001
Age	-0.083	0.012	-0.107	-0.060	<.001
BMI	-0.019	0.006	-0.031	-0.007	.003
Hopping	0.003	0.007	-0.011	0.017	.630
Skipping	0.001	0.007	-0.012	0.013	.928
Bouncing a ball	0.001	0.007	-0.012	0.013	.927
Overhand throw	0.018	0.005	0.007	0.028	.001
Sideways jumping	0.003	0.001	0.002	0.005	.001

			95% Confidence interval		
	β	S.E.	Lower	Upper	P
Moderate impact peaks (Ln)					
Intercept	9.925	0.190	9.554	10.297	<.001
Sex†	-0.236	0.036	-0.307	-0.166	<.001
Age	-0.151	0.017	-0.185	-0.117	<.001
BMI	-0.030	0.009	-0.048	-0.013	.001
Hopping	0.006	0.010	-0.015	0.026	.580
Skipping	-0.003	0.009	-0.022	0.015	.711
Bouncing a ball	0.007	0.009	-0.011	0.026	.440
Overhand throw	0.017	0.008	0.002	0.032	.022
Sideways jumping	0.006	0.002	0.003	0.009	<.001
High impact peaks (Ln)					
Intercept	8.780	0.302	8.189	9.372	<.001
Sex†	-0.294	0.057	-0.406	-0.181	<.001
Age	-0.238	0.028	-0.293	-0.184	<.001
BMI	-0.007	0.015	-0.035	0.022	.634
Hopping	0.022	0.017	-0.010	0.055	.173
Skipping	-0.011	0.015	-0.040	0.019	.483
Bouncing a ball	0.018	0.015	-0.011	0.048	.217
Overhand throw	0.013	0.012	-0.010	0.037	.273
Sideways jumping	0.006	0.002	0.002	0.011	.006

†: Where female is the comparison group and β=1.

Supp 3D Childhood Study: Between Group Differences by DCD

Table

Demographics by Developmental Coordination Disorder (DCD) Risk Status

	DCD (N=54) M (SD) [Md]	Non-DCD (N=170) M (SD) [Md]	U	d_{cohen}	p
Age at T2 (yr)	9.1 (0.8)[9.1]	9.6 (0.7)[9.8]	4.25	0.74	<.001
Body mass at T2 (kg)	33.0 (7.4)[32.5]	36.1(8.5)[34.4]	2.33	0.35	.020
Height at T2 (cm)	135.1 (6.2) [134.5]	140.2 (7.7) [139.9]	4.21	0.69	<.001
Body mass at T1 (kg)	22.5 (4.3) [21.6]	24.2 (4.3) [23.7]	3.08	0.39	.002
BMI	16.5 (2.2) [16.2]	16.4 (1.8) [16.0]	0.02	-0.08	.981
Height at T1 (cm)	116.2 (5.0) [115.9]	121.0 (6.4) [121.0]	4.96	0.79	<.001
Birthweight (g)	3466.6 (549.9) [3520.0]	3502.9 (495.23) [3520.0]	0.14	0.07	.890
Gestation (wks)	39.6 (2.0) [40.0]	39.7 (1.9) [40.0]	0.18	0.05	.857
Age at independent walking (months)	13.2 (2.2) [13.0]	11.8 (1.8) [12.0]	-4.13	-0.74	<.001

Table

Motor Competence Variables by Developmental Coordination Disorder (DCD) Risk Status

	DCD (N=54) M (SD) [Md]	Non-DCD (N=170) M (SD) [Md]	U	d_{cohen}	P
T1 testing					
KTK					
Walking backwards	11.07 (6.45) [9.00]	24.54 (12.25) [23.00]	7.46	1.21	<.001
Hopping for height (right)	6.09 (3.74) [5.50]	14.68 (5.97) [15.00]	8.45	1.37	<.001
Hopping for height (left)	3.40 (2.44) [3.00]	12.28 (6.21) [12.00]	9.01	1.56	<.001
Hopping for height (both legs)	9.43 (4.58) [8.50]	27.02 (10.54) [26.00]	10.04	1.86	<.001
Jumping sideways	27.63 (4.74) [27.00]	39.52 (8.79) [38.50]	8.58	1.48	<.001
Moving sideways	24.87 (4.23) [26.00]	31.97 (5.92) [32.00]	7.50	1.28	<.001
Total score	73.00 (8.57) [73.00]	122.62 (25.21) [116.50]	11.07	2.22	<.001

	DCD (N=54) M (SD) [Md]	Non-DCD (N=170) M (SD) [Md]	U	d_{cohen}	P
TGMD3					
Run	5.89 (2.13) [6.50]	6.45 (1.70) [7.00]	1.54	0.31	.124
Gallop	4.28 (1.82) [4.00]	5.13 (1.55) [5.00]	2.92	0.53	.003
Hop	4.59 (1.68) [4.00]	5.41 (1.52) [6.00]	3.19	0.53	.001
Skip	3.14 (1.83) [4.00]	3.45 (1.84) [4.00]	1.05	0.17	.292
Hop jump	4.31 (2.17) [4.00]	5.78 (1.80) [6.00]	4.25	0.78	<.001
Slide	5.94 (1.96) [6.00]	6.80 (1.79) [8.00]	3.46	0.47	.001
Locomotor total	28.18 (6.99) [30.00]	32.99 (5.18) [34.00]	4.33	0.85	<.001
Strike (2 hand)	6.15 (2.15) [6.50]	6.51 (2.10) [7.00]	0.90	0.17	.366
Strike (1 hand)	2.33 (2.21) [2.00]	3.34 (2.26) [4.00]	2.84	0.45	.005
Dribble	1.27 (1.73) [0.00]	2.39 (2.15) [2.00]	3.40	0.54	.001
Catch	3.98 (1.46) [4.00]	4.57 (1.25) [5.00]	2.54	0.45	.011
Kick	3.27 (1.40) [3.00]	4.33 (1.79) [4.00]	3.99	0.62	<.001
Overthrow	4.14 (1.92) [4.00]	4.26 (1.98) [4.00]	0.44	0.06	.658
Underthrow	5.31 (1.76) [5.50]	5.74 (1.47) [6.00]	1.57	0.28	.116
Object control skills total	26.44 (6.82) [25.50]	31.18 (7.69)[31.00]	3.94	0.63	<.001
Total	54.37 (10.57) [54.00]	64.28 (10.46) [63.00]	5.29	0.95	<.001
T2 testing					
Sideways jumping	47.96(9.29)[48.00]	60.08 (10.86)[59.00]	6.92	1.15	<.001
Sum of 2 rounds of single leg hopping for distance	5.47 (1.87) [6.00]	6.25 (1.47) [6.00]	2.68	0.50	.007
Sum of 2 rounds of skipping	2.51 (1.87) [3.00]	4.09 (1.57) [4.00]	5.43	0.96	<.001
Bouncing a ball	3.22 (2.03) [3.00]	4.29 (1.70) [5.00]	3.41	0.60	.001
Overhand throw	4.35 (2.23) [4.00]	4.86 (2.36) [5.00]	1.49	0.22	.137

Table

Physical Activity Results by Developmental Coordination Disorder (DCD) Risk Status

	DCD (N=54) M (SD) [Md]	Non-DCD (N=170) M (SD) [Md]	U	d_{cohen}	P
Sedentary behaviour (min/day)	420.32 (70.34) [428.89]	405.44 (66.67) [395.57]	-1.74	-0.22	.082
Light activity (min/day)	209.01 (43.56) [207.94]	211.31 (33.65) [211.80]	0.82	0.06	.415
MVPA (min/day)	146.45 (32.92) [145.99]	145.15 (34.88) [143.24]	-0.22	-0.04	.826
Moderate activity (min/day)	125.52 (23.51) [123.86]	124.84 (27.08) [122.70]	-0.24	-0.02	.811
Vigorous (min/day)	20.41 (11.68) [17.35]	19.71 (10.14) [18.95]	0.10	-0.07	.919
Very vigorous (min/day)	0.52 (0.91) [0.14]	0.60 (0.81) [0.28]	1.29	0.10	.196
MAD	0.04 (0.01) [0.04]	0.04 (0.01) [0.04]	0.00	0.00	1.000
Sedentary bouts (n/day)	93.36 (18.44) [100.57]	94.88 (18.21) [92.86]	-1.70	0.08	.089
Light bouts (n/day)	130.09 (5.70) [12.32]	13.95 (5.34) [13.80]	1.26	0.16	2.08
Moderate bouts (n/day)	13.10 (4.13) [12.60]	13.79 (4.81) [13.64]	0.99	0.15	.324
Vigorous bouts (n/day)	1.45 (2.12) [0.29]	1.16 (1.39) [0.71]	-0.02	-0.18	.981
Sedentary bout length (min/day)	279.44 (72.47) [280.95]	266.03 (63.74) [256.25]	-1.50	-0.20	.134
Light bout length (min/day)	34.01 (25.18) [29.23]	32.43 (18.94) [29.27]	0.08	-0.08	.939
Moderate bout length (min/day)	23.27 (9.68) [22.29]	24.11 (9.94) [23.26]	0.77	0.09	.442
Vigorous bout length (min/day)	2.21 (3.22) [1.04]	1.85 (2.31) [1.00]	-0.21	-0.14	.832
Sedentary breaks (n/day)	679.99 (110.96) [675.93]	676.47 (104.38) [671.01]	-0.09	-0.03	.925

Table

Osteogenic Results by Developmental Coordination Disorder (DCD) Risk Status

	DCD		Non-DCD		U	d_{cohen}	P
	M (SD) [Md]		M (SD) [Md]				
OI	660.01 [677.03]	(90.35)	645.65 (102.30) [650.73]		-0.88	-0.14	.382
Low impact peaks (n/day)	23089.36 [2205.31]	(5222.72)	22933.28 [22067.35]	(6130.61)	-0.45	-0.03	.652
0 to 1.50	12014.45 [11786.06]	(2641.95)	11969.70 [11640.51]	(2878.09)	-0.15	-0.02	.879
1.50 to 1.70	5790.82 [5647.89]	(1353.30)	5739.19 [5506.31]	(1634.23)	-0.63	-0.03	.531
1.70 to 1.90	3293.96 [3284.93]	(817.41)	3262.15 [3019.23]	(1050.25)	-0.88	-0.03	.379
1.90 to 2.10	1990.13 [1938.75]	(528.83)	1962.24 [1816.17]	(706.61)	-1.01	-0.04	.315
Medium impact peaks (n/day)	4907.68 [4658.90]	(1641.69)	4732.08 [4348.37]	(2023.50)	-1.29	-0.09	.196
2.10 to 2.30	1298.35 [1251.56]	(377.90)	1258.98 [1171.50]	(491.92)	-1.26	-0.08	.207
2.30 to 2.50	890.07 [846.43]	(277.89)	860.21 (356.10) [805.50]		-1.21	-0.11	.228
2.50 to 2.70	640.99 [607.86]	(215.65)	618.38 (266.92) [565.57]		-1.21	-0.09	.225
2.70 to 2.90	478.51 [446.65]	(171.14)	464.19 (207.02) [417.20]		-1.07	-0.07	.285
2.90 to 3.10	372.56 [354.51]	(137.70)	360.63 (165.57) [325.29]		-1.08	-0.08	.282
3.10 to 3.30	298.04 [282.92]	(114.55)	287.43 (134.88) [256.68]		-1.12	-0.08	.261
3.30 to 3.50	247.11 [244.85]	(97.93)	237.04 (114.58) [208.80]		-1.19	-0.09	.236
3.50 to 3.70	208.68 [198.57]	(83.75)	199.62 (97.64) [181.21]		-1.22	-0.10	.224
3.70 to 3.90	180.02 [178.64]	(74.14)	169.13 (85.29) [152.40]		-1.40	-0.13	.163
3.90 to 4.10	156.29 [154.60]	(67.56)	147.09 (76.10) [133.69]		-1.29	-0.12	.198
4.1 to 4.3	137.07 [132.39]	(59.33)	129.39 (67.79) [116.07]		-1.31	-0.12	.190

	DCD M (SD) [Md]	Non-DCD M (SD) [Md]	U	d_{cohen}	P
High impact peaks	1233.48 (638.97) [1105.50]	1168.82 (688.23) [1068.17]	-0.84	-0.10	.403
4.3 to 4.6	176.92 (79.04) [168.95]	164.92 (87.52) [148.43]	-1.37	-0.14	.171
4.6 to 4.9	149.66 (70.90) [138.81]	139.07 (75.25) [129.43]	1.24	-0.14	.217
4.9 to 5.2	126.21 (61.93) [114.95]	118.08 (64.26) [110.73]	-0.93	-0.13	.350
5.2 to 5.5	107.91 (54.94) [99.12)	100.67 (56.51) [94.71]	-0.98	-0.13	.325
5.5 to 5.8	91.80 (47.36) [82.21]	85.43 (48.50) [79.67]	-0.87	-0.13	.387
5.8 to 6.1	79.20 (40.81) [70.43]	74.05 (43.36) [69.50]	-0.87	-0.12	.384
6.1 to 6.4	67.25 (26.71) [58.67]	63.32 (37.73) [58.07]	-0.73	19.66	.464
6.4 to 6.7	58.73 (32.34) [51.92]	54.96 (33.81) [49.19]	-0.89	-0.11	.376
6.7 to 7.1	64.87 (36.65) [57.42]	60.85 (38.71) [53.79]	-0.87	-0.11	.386
7.1 to 7.5	52.76 (30.52) [49.11]	50.14 (33.02) [44.37]	-0.80	-0.08	.426
7.5 to 7.9	43.74 (26.78) [37.18]	40.98 (28.25) [35.64]	-0.87	-0.10	.385
7.9 to 8.3	35.05 (21.71) [32.44]	33.87 (24.19) [28.50]	-0.74	-0.05	.459
8.3 to 8.8	35.61 (22.80) [30.32]	34.41 (25.62) [27.71]	-0.71	-0.05	.479
8.8 to 9.3	27.82 (17.36) [25.92]	27.33 (21.23) [21.82]	-0.81	-0.02	.421
9.3 to 9.8	22.03 (14.29) [19.44]	21.98 (17.54) [17.19]	-0.59	-0.003	.557
9.8 to 10.30	17.76 (11.77) [15.11]	17.75 (14.72) [13.31]	-0.66	-0.001	.511
10.30 and above	76.16 (52.99) [59.76]	81.03 (69.61) [56.14]	-0.29	0.07	.769

Supplementary Material for Chapter 4

Supp 4A Adult Accelerometry Study: Motor Competence Items and Criteria

Item	Criteria for anormality
Pursing the lips to whistle	Not achieved
Tongue position maintained when stuck out	Not achieved
Imitates tongue movements	Performed with difficulty or not possible
Running	Only possible when pace was slow
Going upstairs	Only achieved with support or performed with even pace
Sideways hopping	Performed less than two jumps
Standing on one leg (right/left)	Performed for less than 5 seconds
Hopping on one leg	Performed for less than five seconds
Forefinger-thumb tapping (right/left)	Could not achieve or achieved only in a jerky fashion
Finger-opposition (right/left)	Not possible
Pegboard (right/left)	Speed of performance in bottom 5% of control population
Hand pro-supination (R/L)	Unable to perform with rhythm
Simultaneous handclapping	Unable to perform with rhythm
Alternate handclapping	Unable to perform with rhythm

Item list derived from Lano (23)

Supp 4B Adult Accelerometry Study: Background Characteristics of Participants According to VMI Status

	VMI <5th percentile	**VMI 5th to 15th percentile**	**VMI >15th percentile**	**Group difference**	
Parental characteristics					
	M (SD) [Md]	*M (SD) [Md]*	*M (SD) [Md]*	*H statistic*	*p*
Mother's age (yrs)	28.9 (5.9) [28.0]	29.1 (4.7) [29.0]	30.2 (4.8) [30.0]	2.4	.308
Father's age (yrs)	31.9 (5.6) [32.0]	32.0 (6.2) [31.0]	32.3 (5.9)[31.0]	0.3	.882
	n (%)	*n (%)*	*n (%)*	χ^2	*p*
Mother's education – primary only	40.9	18.8	17.9	9.8	.132
Mother's education – secondary only	18.2	18.8	20.3		
Mother's education - upper secondary only	27.3	53.1	43.1		
Mother's education – Masters	13.6	9.4	18.8		
Father's education- primary only	40.9	46.9	18.0	29.2	<.001
Father's education – secondary only	45.5	21.9	29.0		
Father's education- upper secondary only	4.5	12.5	27.7		
Father's education- Master's	9.1	18.8	25.3		

	VMI <5th percentile	VMI 5th to 15th percentile	VMI >15th percentile	Group difference	
Pre and perinatal risk factors					
	n (%)	*n (%)*	*n (%)*	χ^2	*p*
Mother severe chronic illness	0.0	3.1	6.4	2.1	.353
Multiple pregnancy	8.7	9.4	4.3	2.5	.284
Pre-eclampsia	8.7	12.5	12.4	0.3	.868
Fetal distress during pregnancy	0.9	6.3	6.9	0.1	.934
Fetal distress during birth	21.7	18.8	16.0	0.7	.714
	M (SD) [Md]	*M (SD) [Md]*	*M (SD) [Md]*	*H statistic*	*p*
Apgar at 5 minutes	9.4 (1.3) [10.0]	9.0 (1.3) [9.0]	9.4 (1.2) [10.0]	8.2	.017
Neonatal characteristics					
Sex (m/f)	16/7	18/14	272/309	5.5	.065
	M (SD) [Md]	*M (SD) [Md]*	*M (SD) [Md]*	*H statistic*	*p*
Gestational age (wks)	38.0 (3.4) [39.0]	38.0 (3.1) [39.0]	38.7 (2.5) [39.0]	2.5	.285
Birth Weight (g)	3370.4 (838.0) [3530.0]	3076.3 (720.7) [3190.0]	3396.5 (721.7) [3490.0]	6.4	.041
	n (%)	*n (%)*	*n (%)*	χ^2	*p*
Small for gestational age (less than 2 SD below mean)	4.3	6.3	6.0	0.1	.943

	VMI <5th percentile	VMI 5th to 15th percentile	VMI >15th percentile	Group difference	
Neonatal risk factors/complications					
	n (%)	*n (%)*	*n (%)*	χ^2	*p*
Hospitalized	60.8	62.5	62.8	0.04	.982
Intubation or ventilator treatment	8.7	15.6	9.1	1.5	.469
Suspicion/verified of septic infection	8.7	3.1	5.7	0.8	.676
Surgical operation	4.3	6.3	1.0	7.4	.025
Severe anemia requiring blood transfusion	8.7	3.1	4.1	1.2	.538
Apnea	8.7	8.3	2.1	9.6	.008
Clinical seizures	4.3	9.4	0.9	17.2	<.001
IVH grade 1-2	8.7	3.1	0.7	14.2	.001
Characteristics at 56 months follow up					
	M (SD) [Md]	*M (SD) [Md]*	*M (SD) [Md]*	*H statistic*	*p*
Age	4.68 (0.02) [4.68]	4.71 (0.04) [4.71]	4.71 (0.04) [4.71]	14.7	.001
Weight	17.9 (2.2) [18.0]	18.4 (3.1) [18.1]	18.2 (2.5) [18.0]	0.2	.912
Height	107.4 (3.5) [108.0]	108.7 (4.6) [108.0]	108.4 (4.5) [108.0]	0.9	.638
BMI	15.4 (1.3) [15.2]	15.5 (1.6) [15.1]	15.5 (1.4) [15.4]	0.6	.727
Motor competence (%) sum score	98.2 (4.0) [100.0]	99.0 (2.3) [100.0]	99.3 (2.5) [100.0]	5.0	.083
Gross motor (Touwen)(% sum score)	94.9 (11.7) [100.0]	93.8 (13.2) [100.0]	95.7 (10.5) [100.0]	0.4	.829
Fine motor (Touwen)(% sum score)	63.8 (30.0) [66.7]	75.0 (26.8) [66.7]	89.4 (18.8) [100.0]	37.1	<.001
VMI score	72.8 (5.1) [75.5]	76.9 (2.8) [75.6]	103.5 (12.2) [103.9]	150.8	<.001
	n (%)	*n (%)*	*n (%)*	χ^2	*p*
Eyesight 0.3-0.6	4.4	15.6	14.0	1.8	.399

	VMI <5th percentile	VMI 5th to 15th percentile	VMI >15th percentile	Group difference	
BMI grouping - underweight	0.0	0.0	1.8	7.1	.308
BMI grouping – healthy weight	72.7	84.4	83.0		
BMI grouping - overweight	27.3	9.4	12.6		
BMI grouping-obese	0.0	6.3	2.7		
Abnormal gross motor	13.0	12.5	6.1	3.6	.165
Abnormal fine motor	34.8	15.6	5.0	36.1	<.001
Unable to ride a bike	0.0	0.0	1.7	1.0	.617
Hardly able to catch a ball	17.4	21.4	16.0	0.6	.740
Only able to run slowly	0.0	3.1	3.8	0.9	.626
Characteristics at 25 year follow up					
	M (SD) [Md]	*M (SD) [Md]*	*M (SD) [Md]*	*H statistic*	*p*
Age	25.3 (0.8) [25.0]	24.8 (0.5) [25.0]	24.8 (0.7) [25.0]	7.4	.025
Weight	79.5 (17.8) [78.5]	71.2 (18.9) [66.7]	72.2 (15.0) [70.3]	5.4	.067
Height	174.6 (9.8) [178.0]	174.1 (8.9) [175.0]	173.0 (9.5) [173.0]	1.8	.415
BMI	26.0 (5.1) [24.9]	23.2 (4.7) [22.7]	24.0 (4.2) [23.2]	6.4	.041
	n (%)	*n (%)*	*n (%)*	χ^2	*p*
BMI grouping-underweight	4.5	12.5	3.1	11.6	.071
BMI grouping – healthy weight	45.5	62.5	64.3		
BMI grouping - overweight	31.8	18.8	23.3		
BMI grouping - obese	18.2	6.3	9.2		

	VMI <5th percentile	VMI 5th to 15th percentile	VMI >15th percentile	Group difference	
Quantified physical activity					
	M (SD) [Md]	*M (SD) [Md]*	*M (SD) [Md]*	*H statistic*	*p*
Sedentary Light	873.1 (91.7) [895.9]	831.8 (101.6) [809.0]	837.9 (106.8) [856.9]	3.0	.227
Moderate	123.5 (61.0) [111.4]	163.9 (80.1) [156.9]	137.8 (79.0) [121.2]	4.5	.105
Vigorous	4.6 (8.6) [1.1]	8.1 (9.6) [6.6]	6.6 (8.1) [3.8]	6.0	.051
Moderate and vigorous	128.1 (67.3) [113.3]	171.9 (84.9) [160.8]	144.4 (82.3) [127.9]	4.6	.098
% sedentary light activity	63.3 (5.6) [63.9]	60.5 (7.0) [59.7]	61.3 (6.5) [61.9]	3.1	.215
% moderate activity	8.9 (4.3) [8.0]	11.9 (5.7) [11.8]	10.1 (5.7) [8.8]	4.5	.104
% vigorous activity	0.3 (0.6) [0.1]	0.6 (0.7) [0.3]	0.5 (0.6) [0.3]	6.0	.049
% moderate and vigorous activity	9.2 (4.8) [8.1]	12.5 (6.1) [12.1]	10.6 (6.0) [9.3]	4.8	.092
Steps	9842.1 (3317.0) [9705.5]	10858.0 (4114.4) [10418.3]	10208.7 (3634.4) [9827.6]	0.7	.707
Mean amplitude deviation	0.99 (0.2) [0.96]	1.1 (0.3) [0.96]	0.98 (0.3) [0.96]	1.2	.541

Supp 4C Adult Accelerometry Study: Accelerometry Complex Models for Physical Activity with DCD as a Probable Risk Factor

			β 95% Confidence interval	
	β	**S.E.**	**Lower**	**Upper**
Sedentary light				
Intercept	6.5	0.03	6.4	6.6
Sex†	-0.01	0.01	-0.03	0.01
Mother's education (secondary)§	-0.01	0.02	-0.04	0.03
Mother's education (upper secondary)¶	-0.003	0.02	-0.04	0.03
Mother's education (Masters)††	0.001	0.01	-0.03	0.03
DCD‡	0.1	0.06	0.02	0.3
BMI	0.01	0.001	0.007	0.01
BMI*DCD interaction effect	-0.01	0.003	-0.01	0.0
Moderate				
Intercept	6.4	0.1	6.2	6.7
Sex†	0.2	0.04	0.1	0.3
Mother's education (secondary)§	0.01	0.1	-0.1	0.1
Mother's education (upper secondary)¶	0.03	0.1	-0.1	0.2
Mother's education (Masters)††	0.05	0.1	-0.1	0.1
DCD‡	-0.5	0.3	-1.1	0.1
BMI	-0.1	0.01	-0.08	-0.06
BMI* DCD interaction effect	0.02	0.01	0.0	0.04
Vigorous				
Intercept	3.5	0.2	3.1	3.9
Sex†	0.1	0.1	-0.03	0.3
Mother's education (secondary)§	-0.2	0.1	-0.4	0.1
Mother's education (upper secondary)¶	-0.1	0.1	-0.3	0.2
Mother's education (Masters)††	0.03	0.1	-0.2	0.2
DCD‡	-0.9	0.5	-1.8	0.04
BMI	-0.1	0.01	-0.1	-0.07
BMI* DCD interaction effect	0.04	0.02	0.001	0.1
MVPA				
Intercept	6.5	0.1	6.3	6.8
Sex†	0.2	0.04	0.1	0.3
Mother's education (secondary)§	0.002	0.1	-0.1	0.1
Mother's education (upper secondary)¶	0.02	0.1	-0.1	0.1
Mother's education (Masters)††	0.04	0.1	-0.1	0.1
DCD‡	-0.5	0.3	-1.1	0.0
BMI	-0.1	0.01	-0.09	-0.06
BMI* DCD	0.02	0.01	-0.002	0.04

			β 95% Confidence interval	
	β	**S.E.**	**Lower**	**Upper**
Steps				
Intercept	9.6	0.1	9.4	9.8
Sex†	-0.1	0.03	-0.2	0.1
Mother's education (secondary)§	-0.01	0.05	-0.1	0.1
Mother's education (upper secondary) ¶	-0.04	0.04	-0.1	0.04
Mother's education (Masters)††	0.03	0.04	-0.1	0.1
DCD‡	-0.2	0.2	-0.6	0.2
BMI	-0.01	0.004	-0.02	-0.01
BMI* DCD interaction effect	0.01	0.007	-0.01	0.02
Mean Amplitude Deviation				
Intercept	0.4	0.1	0.2	0.5
Sex†	-0.004	0.02	-0.04	0.04
Mothers education (secondary)§	0.01	0.03	-0.05	0.1
Mothers education (upper secondary) ¶	0.01	0.03	-0.1	0.1
Mothers education (Masters)††	0.01	0.03	-0.04	0.1
DCD‡	-0.04	0.1	-0.3	0.3
BMI	-0.02	0.003	-0.02	-0.01
BMI* DCD interaction effect	0.001	0.01	-0.01	0.01

† Where male is the comparison group and β=1; ‡ Where DCD is the comparison group and β=1; § Where education is leve
1; ¶ Where education is level 2; †† Where education is level 3

Supp 4D Adult Accelerometry Study: Accelerometry Complex Models for Physical Activity with DCD (DCD5 and DCD15) and VMI as a Continuous Variable

				β 95% Confidence interval		
Model		**β**	**S.E.**	**Lower**	**Upper**	**P**
Sedentary light	Intercept	6.5	0.1	6.4	6.5	<.001
	Sex†	-0.01	0.01	-0.03	0.01	.503
	Mother's education (secondary)§	-0.01	0.02	-0.1	0.03	.633
	Mother's education (upper secondary)¶	-0.001	0.02	-0.03	0.03	.952
	Mother's education (Masters)††	0.004	0.02	-0.03	0.03	.783
	DCD‡	0.2	0.1	0.1	0.3	.007
	VMI score	0.0	0.0004	0.0	0.001	.300
	BMI	0.01	0.001	0.007	0.01	<.001
	BMI* DCD interaction	-0.01	0.003	-0.01	-0.001	.019
Moderate	Intercept	6.7	0.2	6.3	7.04	<.001
	Sex†	0.2	0.04	0.1	0.3	<.001
	Mother's education (secondary)§	0.02	0.1	-0.1	0.1	.714
	Mother's education (upper secondary)¶	0.02	0.1	-0.1	0.1	.708
	Mother's education (Masters)††	0.03	0.1	-0.1	0.1	.548
	DCD‡	-0.6	0.3	-1.2	-0.1	.020
	VMI score	-0.002	0.002	-0.01	0.001	.176
	BMI	-0.1	0.01	-0.08	-0.06	<.001
	BMI* DCD interaction	0.03	0.01	0.0	0.05	.027
Vigorous	Intercept	3.2	0.4	2.5	4.0	<.001
	Sex†	0.1	0.08	-0.01	0.3	.072
	Mother's education (secondary)§	-0.2	0.1	-0.4	0.1	.183
	Mother's education (upper secondary)¶	-0.1	0.1	-0.3	0.2	.615
	Mother's education (Masters)††	0.03	0.1	-0.2	0.2	.775
	DCD‡	-0.8	0.5	-1.7	0.2	.137
	VMI score	0.003	0.003	0.0	0.01	.256
	BMI	-0.1	0.01	-0.1	-0.07	<.001
	BMI* DCD interaction	0.03	0.02	0.0	0.1	.078
MVPA	Intercept	6.7	0.2	6.3	7.1	<.001
	Sex†	0.2	0.04	0.1	0.3	<.001
	Mother's education (secondary)§	0.01	0.1	-0.1	0.1	.835
	Mother's education (upper secondary)¶	0.01	0.1	-0.1	0.1	.835
	Mother's education (Masters)††	0.03	0.1	-0.1	0.1	.580
	DCD‡	-0.7	0.3	-1.2	-0.1	.014
	VMI score	-0.002	0.002	-0.01	0.0	.258
	BMI	-0.08	0.01	-0.09	-0.07	<.001
	BMI*DCD interaction	0.03	0.01	0.0	0.05	.018

Model		β	S.E.	β 95% Confidence interval Lower	Upper	P
Steps	Intercept	9.6	0.1	9.4	9.9	<.001
	Sex†	-0.1	0.03	-0.2	-0.1	<.001
	Mother's education (secondary)§	-0.01	0.05	-0.1	0.1	.800
	Mother's education (upper secondary)¶	-0.05	0.04	-0.1	0.03	.252
	Mother's education (Masters)††	0.02	0.04	-0.1	0.1	.640
	DCD‡	-0.3	0.2	-0.6	0.1	.204
	VMI score	-0.001	0.001	-0.003	0.002	.609
	BMI	-0.02	0.004	-0.02	-0.01	<.001
	BMI*DCD interaction	0.01	0.01	-0.01	0.02	.252
Mean amplitude deviation	Intercept	0.5	0.1	0.3	0.7	<.001
	Sex†	-0.01	0.02	-0.1	0.0	.734
	Mother's education (secondary)§	0.01	0.03	-0.1	0.1	.743
	Mother's education (upper secondary)¶	-0.001	0.03	-0.1	0.1	.970
	Mother's education (Masters)††	0.01	0.03	0.0	0.1	.766
	DCD‡	-0.1	0.2	-0.4	0.2	.718
	VMI score	-0.001	0.001	-0.002	0.001	.315
	BMI	-0.02	0.003	-0.02	-0.01	<.001
	BMI*DCD interaction	0.002	0.01	-0.01	0.01	.748

† Where male is the comparison group and β=1; ‡ Where DCD is the comparison group and β=1; § Where education is level 1; ¶ Where education is level 2; †† Where education is level 3

Supp 4E Adult Accelerometry Study: VMI Between Group Differences and Models

Between group difference tests showed no significant difference in accelerometry measures a the 15th percentile and a significant difference in vigorous physical activity at the 5th percentil (Table 5), with those in the 5th percentile performing significantly less vigorous physica activity than those above the 15th percentile.

Modelling of the bottom 15th percentile of VMI scores did not show significant role for VM risk (Table 6), with BMI being the only statistically significant influencer in all models, witl sex being an influencer for the models for moderate activity, MVPA and steps, and ar interaction effect between BMI and the VMI risk group in the model for mean MAD. Thes are shown in table eleven. This interaction effect was such that mean MAD decreased witl increasing BMI for the VMI risk group only (Figure 3).

Table

Accelerometry Differences Based on VMI Risk Status (5th Percentile)

	Less than 5% **N=23**	**Greater than 15%** **N=581**	**Group difference**		
	M (SD) [Md]	***M (SD) [Md]***	d_{Cohen}	**U-statistic**	**I**
Age	25.3 (0.8) [25.0]	24.8 (0.7) [25.0]	-0.7	2.8 †	.
BMI	26.0 (5.1) [24.9]	24.0 (4.2) [23.2]	0.5	4919.0	.
Sedentary light (min/day)	873.1 (91.7) [895.9]	837.9 (106.8) [856.9]	-0.3	5485.0	.
Moderate (min/day)	123.5 (61.0) [111.4]	137.8 (79.0) [121.2]	0.2	6192.0	.
Vigorous (min/day)	4.6 (8.6) [1.1]	6.6 (8.1) [3.8]	0.2	4780.0	.
Moderate and vigorous (min/day)	128.1 (67.3) [113.3]	144.4 (82.3) [127.9]	0.2	6017.5	.
% sedentary light activity	63.3 (5.6) [63.9]	61.3 (6.4) [61.9]	-0.3	5701.0	.
% moderate activity	8.9 (4.3) [8.0]	10.1 (5.7) [8.8]	0.1	6332.0	.
% vigorous activity	0.3 (0.6) [0.1]	0.5 (0.6) [0.3]	0.2	4997.0	.
% moderate and vigorous activity	9.2 (4.8) [8.1]	10.6 (6.0) [9.3]	0.2	6170.0	.
Steps	9842.1 (3317.0) [9705.5]	10208.7 (3634.4) [9827.6]	0.1	6390.0	.
Mean amplitude deviation	1.0 (0.2) [1.0]	1.0 (0.3) [1.0]	0.0	6555.0	.

	5-15% N=32	Greater than 15% N=581	Group difference		
	M (SD) [Md]	*M (SD) [Md]*	d_{Cohen}	U-statistic	I
Age (yrs)	24.8 (0.5) [25.0]	24.8 (0.7) [25.0]	0.0	-0.1[†]	.
BMI	23.2 (4.7) [22.7]	24.0 (4.2) [23.2]	0.2	8069.0	.
Sedentary light (min/day)	831.8 (101.6) [809.0]	837.9 (106.8) [856.9]	0.2	8435.5	.
Moderate (min/day)	163.9 (80.1) [156.9]	137.8 (79.0) [121.2]	-0.3	7349.0	.
Vigorous (min/day)	8.1 (9.6) [4.4]	6.6 (8.1) [3.8]	-0.2	8610.5	.
Moderate and vigorous (min/day)	171.9 (84.9) [160.8]	144.4 (82.3) [127.9]	-0.3	7385.0	.
% sedentary light activity	60.5 (7.0) [59.7]	61.3 (6.4) [62.0]	0.1	8493.0	.
% moderate activity	11.9 (5.7) [11.8]	10.1 (5.7) [8.8]	-0.3	7391.0	.
% vigorous activity	0.6 (0.7) [0.3]	0.5 (0.6) [0.3]	-0.2	8658.0	.
% moderate and vigorous activity	12.5 (6.1) [12.1]	10.6 (6.0) [9.3]	-0.3	7411.0	.
Steps	10858.0 (4114.4) [10418.3]	10208.7 (3634.4) [9827.6]	-0.2	8577.0	.
Mean amplitude deviation	1.1 (0.3) [1.0]	1.0 (0.3) [1.0]	-0.3	8221.0	.

	Less than 15% **N=55**	**Greater than 15%** **N=581**	**Group difference**		
	M (SD) [Md]	***M (SD) [Md]***	d_{Cohen}	**U**	
Age (yrs)	25.0 (0.7) [25.0]	24.8 (0.7) [25.0]	-0.2	1.8†	.
BMI	24.4 (5.0) [23.5]	24.0 (4.2) [23.2]	-0.1	15442.0	.
Sedentary light (min/day)	849.1 (98.9) [831.5]	837.9 (106.8) [856.9]	-0.1	15641.5	.
Moderate (min/day)	147.0 (74.9) [133.1]	137.8 (79.0) [121.2]	-0.1	14520.0	.
Vigorous (min/day)	6.6 (9.3) [2.7]	6.6 (8.1) [3.8]	-0.002	14761.5	.
Moderate and vigorous (min/day)	153.6 (80.4) [135.9]	144.4 (82.3) [127.9]	-0.1	14730.5	.
% sedentary light activity	61.4 (5.6) [63.9]	61.3 (6.4) [61.9]	-0.04	15514.0	.
% moderate activity	8.9 (4.3) [8.0]	10.1 (5.7) [8.8]	-0.1	14685.0	.
% vigorous activity	0.3 (0.6) [0.1]	0.5 (0.6) [0.3]	0.0	14685.0	.
% moderate and vigorous activity	9.2 (4.8) [8.1]	10.6 (6.0) [9.3]	-0.1	14855.0	.
Steps	10433.2 (3802.2) [9705.5]	10208.7 (3634.4) [9827.6]	-0.1	15550.0	.
Mean amplitude deviation	1.03 (0.3) [0.96]	0.99 (0.3) [0.96]	-0.2	14776.0	.

†=t-test

Table

Accelerometry Complex Models for Physical Activity for VMI Categorised on the 15th Percentile

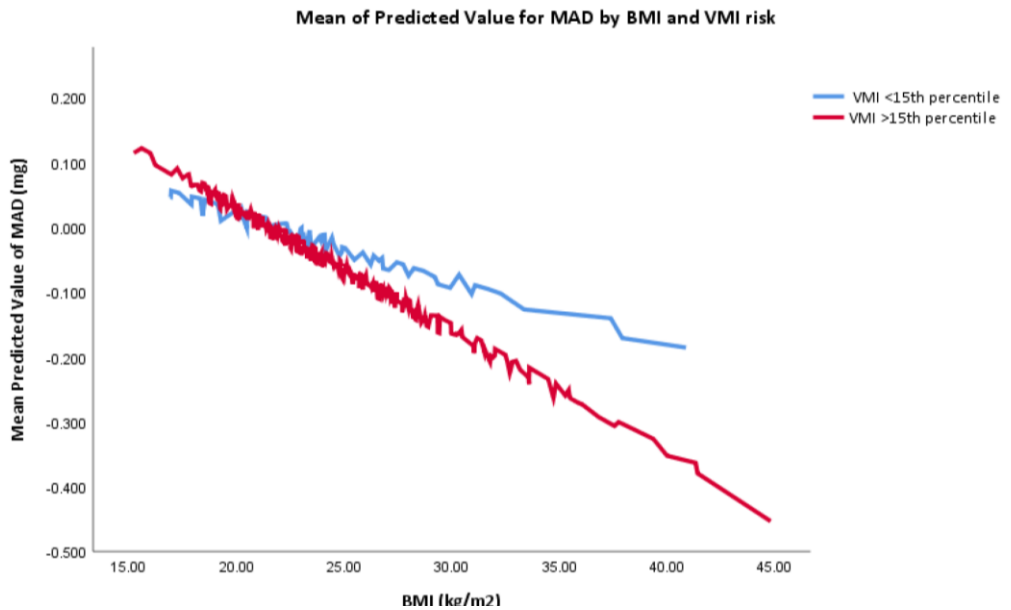
Model		β	S.E.	95% Confidence interval Lower	Upper	P
Sedentary light	Intercept	6.5	0.03	6.5	6.6	<.001
	Sex†	-0.01	0.01	-0.03	0.02	.645
	Mother's education (secondary)§	-0.01	0.02	-0.05	0.03	.562
	Mother's education (upper secondary)¶	-0.002	0.02	-0.04	0.03	.902
	Mother's education (Masters)††	0.004	0.02	-0.03	0.03	.770
	VMI category‡	-0.01	0.1	-0.1	0.1	.882
	BMI	0.01	0.001	0.006	0.01	<.001
	BMI*VMI interaction	0.001	0.003	-0.004	0.01	.713
Moderate	Intercept	6.4	0.1	6.1	6.6	<.001
	Sex†	0.2	0.04	0.1	0.3	<.001
	Mother's education (secondary)§	0.02	0.06	-0.1	0.1	.713
	Mother's education (upper secondary)¶	0.02	0.06	-0.1	0.1	.785
	Mother's education (Masters)††	0.03	0.05	-0.1	0.1	.581
	VMI category‡	-0.3	0.3	-0.8	0.2	.271
	BMI	-0.07	0.01	-0.08	-0.06	<.001
	BMI*VMI interaction	0.02	0.01	-0.01	0.04	.177
Vigorous	Intercept	3.4	0.2	2.9	3.8	<.001
	Sex†	0.1	0.1	-0.01	0.3	.069
	Mother's education (secondary)§	-0.2	0.1	-0.4	0.1	.130
	Mother's education (upper secondary)¶	-0.1	0.1	-0.3	0.2	.474
	Mother's education (Masters)††	0.02	0.1	-0.2	0.2	.882
	VMI category‡	0.2	0.5	-0.9	1.3	.710
	BMI	-0.08	0.01	-0.1	-0.06	<.001
	BMI*VMI interaction	-0.01	0.02	-0.05	0.03	.560
MVPA	Intercept	6.5	0.1	6.2	6.7	<.001
	Sex†	0.2	0.04	0.1	0.3	<.001
	Mothers education (secondary)§	0.01	0.06	-0.1	0.1	.855
	Mothers education (upper secondary)¶	0.01	0.06	-0.1	0.1	.931
	Mothers education (Masters)††	0.03	0.05	-0.1	0.1	.627
	VMI category‡	-0.3	0.3	-0.8	0.3	.310
	BMI	-0.07	0.01	-0.08	-0.06	<.001

Model		β	S.E.	95% Confidence interval Lower	Upper	P
Steps	Intercept	9.6	0.1	9.4	9.8	<.001
	Sex†	-0.1	0.03	-0.2	-0.08	<.001
	Mother's education (secondary)§	-0.01	0.05	-0.1	0.1	.778
	Mother's education (upper secondary)¶	-0.05	0.04	-0.1	0.03	.220
	Mother's education (Masters)††	0.02	0.04	-0.1	0.1	.663
	VMI category‡	-0.3	0.2	-0.7	0.2	.258
	BMI	-0.01	0.004	-0.02	-0.01	<.001
	BMI*VMI interaction	0.01	0.01	-0.01	0.03	.168
Mean amplitude deviation	Intercept	0.4	0.1	0.3	0.5	<.001
	Sex†	-0.01	0.02	-0.05	0.03	.522
	Mother's education (secondary)§	0.01	0.03	-0.1	0.1	.722
	Mother's education (upper secondary)¶	-0.004	0.03	-0.06	0.06	.886
	Mother's education (Masters)††	0.01	0.03	-0.04	0.06	.717
	VMI category‡	0.2	0.2	-0.5	0.05	.104
	BMI	-0.02	0.003	-0.02	-0.01	<.001
	BMI*VMI interaction	0.01	0.01	0.0	0.02	.034

† Where male is the comparison group and β=1; ‡ Where VMI under 15th percentile is the comparison group and β=1; § Where education is level 1; ¶ Where education is level 2; †† Where education is level 3

Figure

Interaction Effect for VMI Models for Mean Amplitude Deviation



Supp 4F Adult Accelerometry Study: Differences in Accelerometry Measures Between Risk Categories, with Sub-analysis by Sex

DCD Risk Groups

Table

Accelerometry Differences Between DCD Risk Groups

	DCD5 *M (SD)*	*DCD15* *M (SD)*	*Not at risk* *M (SD)*	*H statistic*	*P*
Male	*N=23*	*N=43*	*N=250*		
Sedentary Light	842.2 (123.6)	873.0 (91.8)	839.1 (109.1)	3.3	.193
Moderate	124.2 (64.8)	136.0 (67.5)	150.5 (84.4)	2.1	.346
Vigorous	5.7 (6.9)	6.8 (8.4)	7.0 (8.9)	0.3	.852
MVPA	129.9 (67.0)	142.7 (70.5)	157.5 (88.8)	2.0	.366
% sedentary light activity	27.6 (4.8)	27.1 (3.6)	27.1 (4.0)	2.2	.327
% moderate activity	9.1 (4.5)	9.8 (4.8)	11.0 (6.1)	2.3	.317
% vigorous activity	0.4 (0.5)	0.5 (0.6)	0.5 (0.6)	0.3	.862
% MVPA	9.6 (4.6)	10.2 (5.0)	11.5 (6.4)	2.2	.338
Steps	8776.8 (3412.0)	9369.7 (3635.4)	9677.5 (3729.5)	1.4	.493
Mean amplitude deviation	0.97 (0.3)	0.97 (0.3)	0.98 (0.3)	0.2	.918
Female	*N=7*	*N=10*	*N=325*		
Sedentary Light	846.3 (120.7)	868.6 (100.9)	834.6 (102.4)	1.7	.424
Moderate	147.3 (85.7)	107.8 (53.3)	130.3 (73.5)	1.7	.433
Vigorous	4.53 (3.8)	4.7 (4.1)	6.3 (7.7)	0.03	.985
MVPA	151.8 (86.6)	112.5 (54.1)	136.6 (76.3)	1.5	.465
% sedentary light activity	63.2 (7.9)	63.2 (4.1)	61.0 (6.1)	1.6	.447
% moderate activity	10.8 (6.1)	7.8 (3.7)	9.5 (5.4)	1.8	.412
% vigorous activity	0.3 (0.3)	0.3 (0.3)	0.5 (0.6)	0.1	.974
% MVPA	11.2 (6.2)	8.1 (3.7)	10.0 (5.6)	1.7	.433
Steps	10316.7 (2202.5)	9725.6 (2489.4)	10842.1 (3496.2)	0.8	.675
Mean amplitude deviation	0.96 (0.2)	0.93 (0.2)	0.99 (0.2)	0.51	.776

A=T-test

Table

Accelerometry Group Difference Between At Risk of DCD (Under 5th Percentile) and Those Not At Risk

	DCD	Not at risk	Group difference	
	M (SD)	*M (SD)*	d_{Cohen}	U-statistic
Males	*N=23*	*N=250*		
Age (yrs)	24.8 (0.7)	24.8 (0.8)	0.001	0.004†
BMI	25.6 (4.5)	24.5 (4.0)	0.2	2388.5
Sedentary light (mins)	842.2 (123.6)	839.1 (109.1)	0.01	2847.0
Moderate (mins)	121.2 (64.8)	150.5 (84.4)	0.2	2430.0
Vigorous (mins)	5.7 (6.9)	7.0 (8.9)	0.1	2671.5
MVPA (mins)	129.9 (67.0)	157.5 (88.8)	0.1	2445.0
% sedentary light activity	62.8 (5.9)	61.4 (6.9)	0.1	2575.0
% moderate activity	9.1 (4.5)	11.0 (6.1)	0.1	2460.0
% vigorous activity	0.4 (0.5)	0.5 (0.6)	0.1	2679.0
% MVPA	9.6 (4.6)	11.5 (6.4)	0.1	2463.0
Steps	8776.8 (3411.9)	9677.5 (3729.5)	0.1	2458.0
Mean amplitude deviation	0.97 (0.3)	0.98 (0.3)	0.02	2831.0
Females	*N=7*	*N=325*		
Age (yrs)	25.1 (0.9)	24.8 (0.7)	0.3	0.9†
BMI	26.5 (10.1)	23.5 (4.3)	0.02	1092.0
Sedentary light (mins)	846.3 (120.7)	834.6 (102.4)	0.01	1120.0
Moderate (mins)	147.3 (85.7)	130.3 (73.5)	0.1	970.0
Vigorous (mins)	4.5 (3.8)	6.3 (7.7)	0.0	1136.5
MVPA (mins)	151.8 (86.6)	136.6 (76.3)	0.1	982.0
% sedentary light activity	63.2 (7.9)	61.0 (6.1)	0.1	1000.0
% moderate activity	10.8 (6.1)	9.5 (5.4)	0.1	971.0
% vigorous activity	0.3 (0.3)	0.5 (0.6)	0.01	1120.0
% MVPA	11.2 (6.2)	10.0 (5.6)	0.1	994.0
Steps	10316.7 (2202.5)	10842.1 (3496.2)	0.02	1101.0
Mean amplitude deviation	0.96 (0.2)	1.0 (0.2)	0.05	1030.0

†=t-test

Table

Accelerometry Group Difference Between Probably At Risk of DCD (5th to 15th percentile) and Those Not At Risk

	DCD	Not at risk	Group difference	
	M (SD)	*M (SD)*	d_{Cohen}	U-statistic
Males	*N=43*	*N=250*		
Age (yrs)	24.9 (0.6)	24.8 (0.8)	0.1	0.73†
BMI	24.7 (4.4)	24.5 (4.0)	0.001	5372.0
Sedentary light (mins)	873.0 (91.8)	839.1 (109.1)	0.2	4444.0
Moderate (mins)	136.0 (67.5)	150.5 (84.4)	0.1	4904.5
Vigorous (mins)	6.8 (8.4)	7.0 (8.9)	0.01	5342.0
MVPA (mins)	142.7 (70.5)	157.5 (88.8)	0.1	4914.5
% sedentary light activity	62.7 (6.3)	61.4 (6.9)	0.2	4692.0
% moderate activity	9.8 (4.8)	11.0 (6.1)	0.1	4803.00
% vigorous activity	0.5 (0.6)	0.2 (0.6)	0.01	5351.50
% MVPA	10.2 (5.0)	11.5 (6.4)	0.1	4835.0
Steps	9369.7 (3635.4)	9677.5 (3729.5)	0.1	5134.0
Mean amplitude deviation	0.97 (0.3)	0.98 (0.3)	0.1	5162.0
Females	N=10	N=325		
Age (yrs)	24.9 (0.6)	24.8 (0.7)	0.1	0.4†
BMI	24.7 (5.0)	23.5 (4.3)	0.1	1274.5
Sedentary light (mins)	868.6 (100.9)	834.6 (102.4)	0.1	1230.0
Moderate (mins)	107.8 (53.3)	130.3 (73.5)	0.1	1295.0
Vigorous (mins)	4.7 (4.1)	6.3 (7.7)	0.02	1573.0
MVPA (mins)	112.5 (54.1)	136.6 (76.3)	0.1	1304.0
% sedentary light activity	63.2 (4.1)	61.0 (6.1)	0.1	1275.0
% moderate activity	7.8 (3.7)	0.5 (5.4)	0.1	1279.0
% vigorous activity	0.3 (0.3)	0.5 (0.6)	0.02	1559.0
% MVPA	8.1 (3.7)	10.0 (5.6)	0.1	1278.0
Steps	9725.6 (2489.4)	10842.1 (33496.2)	0.1	1362.0
Mean amplitude deviation	0.93 (0.2)	1.00 (0.2)	0.1	1450.0

A=T-test

Table

Accelerometry Group Difference Between DCD Risk Group (DCD5 and 15) and Not At Risk

	DCD	Not at risk	Group difference	
	M (SD)	***M (SD)***	d_{Cohen}	**U-statistic**
Males	*N=66*	*N=250*		
Age (yrs)	24.9 (0.6)	24.8 (0.8)	0.1	0.7†
BMI	25.0 (4.4)	24.5 (4.0)	0.1	7766.5
Sedentary light (mins)	862.3 (104.1)	839.1 (109.1)	0.2	7291.0
Moderate (mins)	131.9 (66.3)	150.5 (84.4)	0.2	7334.5
Vigorous (mins)	6.4 (7.9)	7.0 (8.9)	0.03	8079.5
MVPA (mins)	138.3 (69.1)	157.5 (88.8)	0.2	7359.5
% sedentary light activity	62.7 (6.1)	61.4 (6.9)	0.2	7267.0
% moderate activity	9.5 (4.7)	11.0 (6.1)	0.2	7263.0
% vigorous activity	0.5 (0.6)	0.5 (0.6)	0.04	8030.5
% MVPA	10.0 (4.9)	11.5 (6.4)	0.2	7298.0
Steps	9163.1 (3544.2)	9677.5 (3729.5)	0.1	7592.0
Mean amplitude deviation	0.97 (0.3)	0.98 (0.3)	0.04	7993.0
Females	*N=17*	*N=325*		
Age (yrs)	25.0 (0.7)	24.8 (0.7)	0.2	0.9†
BMI	25.4 (7.3)	23.5 (4.3)	0.1	2457.5
Sedentary light (mins)	859.4 (106.4)	834.6 (102.4)	0.1	2385.0
Moderate (mins)	124.1 (68.9)	130.3 (73.5)	0.04	2600.0
Vigorous (mins)	4.6 (3.9)	6.3 (7.7)	0.01	2709.5
MVPA (mins)	128.7 (69.7)	136.6 (76.3)	0.05	2597.0
% sedentary light activity	63.2 (5.7)	61.0 (6.1)	0.13	2275.0
% moderate activity	9.1 (4.9)	9.5 (5.4)	0.05	2583.0
% vigorous activity	0.3 (0.3)	0.5 (0.6)	0.01	2714.0
% MVPA	9.4 (4.9)	10.0 (5.6)	0.1	2559.0
Steps	9969.0 (2322.7)	10842.1 (3496.2)	0.1	2463.0
Mean amplitude deviation	0.9 (0.2)	1.0 (0.2)	0.1	2480.0

†=T-test

VMI Risk Categories

Table

Accelerometry Group Difference Between Berry Under 5th Percentile and Those Above the 15th Percentile

	<5th percentile	>15th percentile	Group difference	
	M (SD)	***M (SD)***	d_{Cohen}	**U-statistic**
Males	*N=16*	*N=272*		
Age (yrs)	25.3 (0.8)	24.8 (0.7)	0.7	2.6†
BMI	26.5 (4.8)	24.5 (3.9)	0.3	1491.0
Sedentary light (mins)	891.3 (80.2)	838.9 (109.9)	0.2	1588.5
Moderate (mins)	124.1 (64.9)	148.4 (83.0)	0.1	1793.5
Vigorous (mins)	3.1 (7.8)	7.3 (9.0)	0.3	1237.5
MVPA (mins)	127.2 (71.1)	155.7 (87.2)	0.2	1721.5
% sedentary light activity	64.7 (4.4)	61.3 (6.8)	0.2	1519.0
% moderate activity	8.9 (4.5)	10.8 (6.0)	0.2	1764.0
% vigorous activity	0.2 (0.6)	0.5 (0.7)	0.3	1223.5
% MVPA	9.1 (5.0)	11.4 (6.3)	0.2	1691.0
Steps	9355.1 (3727.3)	9638.7 (3730.2)	0.04	2065.0
Mean amplitude deviation	0.94 (0.2)	0.98 (0.3)	0.1	2003.0
Females	*N=7*	*N=309*		
Age (yrs)	25.1 (0.9)	24.8 (0.7)	0.3	0.9†
BMI	24.9 (5.9)	23.7 (4.5)	0.05	973.5
Sedentary light (mins)	831.4 (108.9)	837.1 (104.2)	0.04	992.5
Moderate (mins)	122.3 (55.8)	128.5 (74.1)	0.02	1050.0
Vigorous (mins)	7.9 (10.2)	6.0 (7.2)	0.03	1028.5
MVPA (mins)	130.1 (62.8)	134.5 (76.5)	0.02	1040.5
% sedentary light activity	59.9 (6.9)	61.3 (6.1)	0.07	943.0
% moderate activity	8.9 (4.1)	9.4 (5.4)	0.01	1057.0
% vigorous activity	0.56 (0.73)	0.4 (0.5)	0.02	1030.5
% MVPA	9.4 (4.6)	9.9 (5.6)	0.01	1053.0
Steps	10955.4 (1879.5)	10710.6 (3477.2)	0.1	956.0
Mean amplitude deviation	1.1 (0.2)	1.0 (0.2)	0.2	728.0

†=T-test

Table

Accelerometry Group Difference Between Berry 5th to 15th Percentile and Those Above the 15th Percentile

	5-15th percentile	>15th percentile	Group difference	
	M (SD)	***M (SD)***	d_{Cohen}	**U-statistic**
Males	*N=18*	*N=272*		
Age (yrs)	24.9 (0.6)	24.8 (0.7)	0.1	0.5†
BMI	24.8 (5.5)	24.5 (3.9)	0.02	2379.0
Sedentary light (mins)	850.1 (119.0)	838.9 (109.9)	0.02	2399.5
Moderate (mins)	159.7 (92.5)	148.4 (90.0)	0.05	2304.0
Vigorous (mins)	7.3 (8.1)	7.3 (9.0)	0.01	2430.5
MVPA (mins)	167.1 (95.5)	155.7 (87.2)	0.06	2283.0
% sedentary light activity	61.7 (8.3)	61.3 (6.8)	0.03	2352.0
% moderate activity	11.6 (6.7)	10.8 (6.0)	0.04	2328.0
% vigorous activity	0.5 (0.6)	0.5 (0.7)	0.002	2443.0
% MVPA	12.1 (6.9)	11.4 (6.3)	0.05	2300.0
Steps	9522.8 (4106.1)	9638.7 (3730.2)	0.05	2309.0
Mean amplitude deviation	1.0 (0.3)	0.98 (0.3)	0.04	2329.0
Female	*N=14*	*N=309*		
Age (yrs)	24.7 (0.5)	24.8 (0.7)	0.3	1.0†
BMI	21.3 (2.2)	23.7 (4.5)	0.2	1466.0
Sedentary light (mins)	808.3 (71.0)	837.1 (104.2)	0.2	1662.5
Moderate (mins)	169.2 (63.8)	128.5 (74.1)	0.3	1261.0
Vigorous (mins)	9.1 (11.5)	6.0 (7.2)	0.1	1843.0
MVPA (mins)	178.2 (72.1)	134.5 (76.5)	0.3	1299.5
% sedentary light activity	59.0 (4.8)	61.3 (6.1)	0.2	1573.0
% moderate activity	12.3 (4.5)	9.4 (5.4)	0.3	1268.0
% vigorous activity	0.7 (0.8)	0.4 (0.5)	0.1	1854.5
% MVPA	13.0 (5.1)	9.9 (5.6)	0.3	1314.0
Steps	12574.8 (3560.6)	10710.6 (3477.2)	0.2	1478.0
Mean amplitude deviation	1.11 (0.3)	0.99 (0.2)	0.2	1670.0

†=T-test

Table

Accelerometry Group Difference Between Berry Under 15th Percentile and Those Above the 15th Percentile

	<15th percentile	>15th percentile	Group difference	
	M (SD)	***M (SD)***	d_{Cohen}	**U-statistic**
Males	*N=34*	*N=282*		
Age (yrs)	*25.1 (0.7)*	*24.8 (0.7)*	***0.02***	2.3†
BMI	25.6 (5.2)	24.5 (3.9)	0.2	3870.0
Sedentary light (mins)	869.5 (103.2)	838.9 (109.9)	0.2	3988.0
Moderate (mins)	143.0 (81.5)	148.4 (83.0)	0.1	4385.5
Vigorous (mins)	5.3 (8.1)	6.3 (9.0)	0.2	3703.0
MVPA (mins)	148.3 (86.1)	155.7 (87.2)	0.1	4334.5
% sedentary light activity	63.1 (6.8)	61.3 (6.8)	0.2	3871.0
% moderate activity	10.3 (5.8)	10.8 (6.0)	0.1	4332.0
% vigorous activity	0.4 (0.6)	0.5 (0.7)	1.2	366.5
% MVPA	10.7 (6.2)	11.4 (6.3)	0.1	4287.0
Steps	9443.9 (3874.0)	9638.7 (3730.2)	0.1	4374.0
Mean amplitude deviation	0.98 (0.25)	0.98 (0.28)	0.01	4570.0
Females	*N=21*	*N=309*		
Age (yrs)	24.9 (0.7)	24.8 (0.7)	0.02	0.1†
BMI	22.4 (4.1)	23.7 (4.5)	0.2	2655.5
Sedentary light (mins)	816.0 (83.4)	837.1 (104.2)	0.2	2615.0
Moderate (mins)	153.5 (64.0)	128.5 (74.1)	0.2	2311.0
Vigorous (mins)	8.7 (10.8)	6.0 (7.2)	0.1	2871.5
MVPA (mins)	162.2 (71.4)	134.5 (76.5)	0.2	2340.0
% sedentary light activity	59.3 (5.4)	61.3 (6.1)	0.2	2516.0
% moderate activity	11.2 (4.6)	9.4 (5.4)	0.2	2325.0
% vigorous activity	0.6 (0.8)	0.4 (0.5)	0.1	2885.0
% MVPA	11.8 (5.1)	9.9 (5.6)	0.2	2367.0
Steps	12035.0 (3148.4)	10710.6 (3477.2)	0.2	2434.0
Mean amplitude deviation	1.11 (0.3)	0.99 (0.2)	0.2	2398.0

†=T-test

Supp 4G Adult Accelerometry Study: Sensitivity Analysis Based on Four Days Wear

Table

Accelerometry Group Difference Between DCD (DCD5 and 15) and Not At Risk

	DCD N=80 *M (SD) [Md]*	Not at risk N=570 *M (SD)*	Group difference d_{Cohen}	U-statistic	
Age (yrs)	24.9 (0.6) [25.0]	24.8 (0.7) [25.0]	-0.1	21465.5	.35
BMI	24.9 (5.0) [23.8]	23.9 (4.2) [23.1]	-0.2	19890.5	.06
Sedentary light (mins/day)	860.9 (104.5) [866.2]	837.8 (103.1) [853.9]	-0.2	20087.0	.08
Moderate (mins/day)	130.6 (67.4) [118.8]	139.5 (79.1) [122.4]	0.1	21750.0	.50
Vigorous (mins/day)	5.8 (6.9) [3.6]	6.6 (8.3) [3.6]	0.1	22065.5	.64
MVPA (mins/day)	136.3 (69.8) [124.1]	146.1 (82.6) [129.2]	0.1	21635.5	.45
% Sedentary light activity	62.8 (6.0) [63.8]	61.2 (6.4) [61.8]	-0.3	19352.0	.02
% Moderate activity	9.5 (4.7) [8.6]	10.2 (5.8) [8.9]	0.1	21642.0	.46
% Vigorous activity	0.4 (0.5) [0.3]	0.5 (0.6) [0.3]	0.2	22008.0	.61
% MVPA	9.9 (4.9) [8.9]	10.7 (6.0) [9.4]	0.1	21516.0	.41
Steps	9213.7 (3247.9) [9035.0]	10362.7 (3637.7) [9958.0]	0.3	18774.0	.01
Mean amplitude deviation	0.96 (0.3) [0.92]	0.97 (0.3)[0.96]	0.03	21064.0	.27

Table

Accelerometry Complex Models for Physical Activity with DCD as a Probable Risk Factor

Model		β	S.E.	β 95% Confidence interval Lower	Upper	P
Sedentary light	Intercept	6.5	0.03	6.4	6.6	<.001
	Sex†	-0.01	0.01	-0.03	0.01	.328
	Mother's education (secondary)§	-0.01	0.02	-0.04	0.02	.518
	Mother's education (upper secondary)¶	-0.01	0.02	-0.04	0.02	.477
	Mother's education (Masters)††	-0.01	0.01	-0.03	0.02	.637
	DCD‡	0.2	0.1	0.02	0.3	.022
	BMI	0.01	0.001	0.007	0.01	<.001
	BMI*DCD interaction effect	-0.01	0.003	-0.01	0.0	.048
Moderate	Intercept	6.4	0.1	6.2	6.7	<.001
	Sex†	0.2	0.04	0.1	0.3	<.001
	Mother's education (secondary)§	0.01	0.1	-0.1	0.1	.855
	Mother's education (upper secondary)¶	0.04	0.1	-0.1	0.2	.515
	Mother's education (Masters)††	0.05	0.05	-0.1	0.1	.351
	DCD‡	-0.5	0.3	-1.1	0.1	.130
	BMI	-0.1	0.01	-0.08	-0.06	<.001
	BMI* DCD interaction effect	0.02	0.01	-0.01	0.04	.187
Vigorous	Intercept	3.5	0.2	3.1	3.9	<.001
	Sex†	0.1	0.1	-0.04	0.3	.143
	Mother's education (secondary)§	-0.2	0.1	-0.4	0.1	.184
	Mother's education (upper secondary)¶	-0.1	0.1	-0.3	0.2	.529
	Mother's education (Masters)††	0.01	0.1	-0.2	0.2	.892
	DCD‡	-0.9	0.5	-1.9	0.05	.062
	BMI	-0.1	0.01	-0.1	-0.06	<.001
	BMI* DCD interaction effect	0.04	0.02	-0.002	0.07	.063
MVPA	Intercept	6.5	0.1	6.3	6.8	<.001
	Sex†	0.2	0.04	0.1	0.3	<.001
	Mother's education (secondary)§	0.0	0.1	-0.1	0.1	.965
	Mother's education (upper secondary)¶	0.03	0.1	-0.1	0.1	.643
	Mother's education (Masters)††	0.04	0.1	-0.1	0.1	.393
	DCD‡	-0.5	0.3	-1.1	0.1	.098
	BMI	-0.1	0.01	-0.1	-0.07	<.001
	BMI* DCD	0.02	0.01	-0.01	0.04	.147

Model		β	S.E.	β 95% Confidence interval Lower	Upper	P
Steps	Intercept	9.6	0.1	9.4	9.8	<.001
	Sex†	-0.1	0.03	-0.2	-0.1	<.001
	Mother's education (secondary)§	-0.01	0.1	-0.1	0.01	.784
	Mother's education (upper secondary)¶	-0.04	0.04	-0.1	0.04	.347
	Mother's education (Masters)††	0.03	0.04	-0.05	0.1	.470
	DCD‡	-0.2	0.02	-0.6	0.2	.261
	BMI	-0.01	0.004	-0.02	-0.01	<.001
	BMI* DCD interaction effect	0.01	0.01	-0.01	0.02	.419
Mean amplitude deviation	Intercept	0.4	0.1	0.2	0.5	<.001
	Sex†	-0.01	0.02	-0.1	0.04	.827
	Mother's education (secondary)§	0.01	0.03	-0.1	0.1	.660
	Mother's education (upper secondary)¶	0.01	0.03	-0.1	0.1	.787
	Mother's education (Masters)††	0.01	0.03	-0.04	0.1	.601
	DCD‡	-0.02	0.2	-0.3	0.3	.876
	BMI	-0.02	0.003	-0.02	-0.01	<.001
	BMI* DCD interaction effect	0.0	0.01	-0.01	0.01	.972

† Where male is the comparison group and β=1; ‡ Where DCD is the comparison group and β=1; § Where education is level 1; ¶ Where education is level 2; †† Where education is level 3

Table

Accelerometry Differences Based on VMI Risk Status (15th Percentile)

	Less than 15% N=54 *M (SD) [Md]*	Greater than 15% N=574 *M (SD) [Md]*	Group difference d_{Cohen}	U statistic	
Age (yrs)	25.0 (0.7) [25.0]	24.8 (0.7) [25.0]	-0.3	13304.5	.
BMI	24.1 (4.7) [23.4]	24.0 (4.3) [23.2]	-0.02	15247.5	.
Sedentary light (min/day)	846.8 (98.4) [828.6]	839.2 (104.8) [856.9]	-0.1	13504.0	.
Moderate (min/day)	148.2 (75.1) [134.4]	138.2 (79.2) [121.8]	-0.1	13955.0	.
Vigorous (min/day)	6.7 (9.3) [2.8]	6.6 (8.1) [3.8]	-0.01	14411.0	.
Moderate and vigorous (min/day)	154.9 (80.6) [138.9]	144.8 (82.6) [128.0]	-0.1	14153.5	.
% sedentary light activity	61.5 (6.5) [62.4]	61.3 (6.5) [62.0]	-0.03	15285.0	.
% moderate activity	10.7 (5.4) [9.6]	10.1 (5.7) [8.8]	-0.1	14068.0	.
% vigorous activity	0.5 (0.7) [0.2]	0.5 (0.6) [0.3]	0.0	14350.0	.
% moderate and vigorous activity	11.2 (5.8) [9.9]	10.6 (6.0) [9.3]	-0.1	14239.0	.
Steps	10492.1 (3812.5) [9931.9]	10217.9 (3623.8) [9488.9]	-0.1	14939.0	.
Mean amplitude deviation	1.03 (0.3) [1.0]	1.0 (0.3) [1.0]	-0.1	14196.0	.

†=t-test

Table

Accelerometry Complex Models for Physical Activity for VMI Categorised on the 15th Percentile

Model		β	S.E.	95% Confidence interval Lower	Upper	P
Sedentary light	Intercept	6.5	0.03	6.5	6.6	<.00
	Sex†	-0.01	0.01	-0.03	0.01	.411
	Mother's education (secondary)§	-0.01	0.02	-0.1	0.02	.443
	Mother's education (upper secondary)¶	-0.01	0.02	-0.04	0.02	.543
	Mother's education (Masters)††	0.0	0.01	-0.03	0.02	.813
	VMI category‡	-0.01	0.1	-0.2	0.1	.897
	BMI	0.01	0.001	0.006	0.01	<.00
	BMI*VMI interaction	0.001	0.003	-0.01	0.01	.764
Moderate	Intercept	6.4	0.1	6.1	6.6	<.00
	Sex†	0.2	0.04	0.1	0.2	<.00
	Mother's education (secondary)§	0.03	0.1	-0.1	0.1	.690
	Mother's education (upper secondary)¶	0.02	0.1	-0.1	0.1	.695
	Mother's education (Masters)††	0.03	0.05	-0.1	0.1	.558
	VMI category‡	-0.2	0.3	-0.8	0.4	.419
	BMI	-0.1	0.01	-0.1	-0.06	<.00
	BMI*VMI interaction	0.01	0.01	-0.01	0.04	.320
Vigorous	Intercept	3.4	0.2	3.0	3.8	<.00
	Sex†	0.1	0.1	-0.03	0.3	.112
	Mother's education (secondary)§	-0.2	0.1	-0.5	0.04	.105
	Mother's education (upper secondary)¶	-0.1	0.1	-0.3	0.1	.444
	Mother's education (Masters)††	0.0	0.1	-0.2	0.2	1.00
	VMI category‡	0.3	0.6	-0.8	1.4	.622
	BMI	-0.1	0.01	-0.1	-0.06	<.00
	BMI*VMI interaction	-0.02	0.02	-0.1	0.03	.483
MVPA	Intercept	6.5	0.1	6.2	6.7	<.00
	Sex†	0.2	0.04	0.1	0.2	<.00
	Mother's education (secondary)§	0.01	0.1	-0.1	0.1	.838
	Mother's education (upper secondary)¶	0.01	0.1	-0.1	0.1	.843
	Mother's education (Masters)††	0.03	0.1	-0.08	0.1	.618
	VMI category‡	-0.2	0.3	-0.8	0.4	.465
	BMI	-0.1	0.01	-0.1	-0.06	<.00
	BMI*VMI interaction	0.01	0.01	-0.01	0.04	.371

Model		β	S.E.	95% Confidence interval Lower	Upper	P
Steps	Intercept	9.6	0.1	9.4	9.8	<.00
	Sex†	-0.1	0.03	-0.2	-0.1	<.00
	Mother's education (secondary)§	-0.01	0.05	-0.1	0.01	.798
	Mother's education (upper secondary)¶	-0.05	0.04	-0.1	0.04	.267
	Mother's education (Masters)††	0.02	0.04	-0.1	0.1	.666
	VMI category‡	-0.3	0.2	-0.8	0.2	.200
	BMI	-0.02	0.004	-0.02	-0.01	<.00
	BMI*VMI interaction	0.02	0.01	-0.01	0.04	.137
Mean amplitude deviation	Intercept	0.4	0.1	0.3	0.5	<.00
	Sex†	-0.02	0.02	-0.1	0.03	.478
	Mother's education (secondary)§	0.01	0.03	-0.1	0.1	.704
	Mother's education (upper secondary)¶	-0.002	0.03	-0.1	0.1	.957
	Mother's education (Masters)††	0.01	0.03	-0.04	0.1	.697
	VMI category‡	-0.3	0.2	-0.6	0.1	.099
	BMI	-0.02	0.003	-0.02	-0.01	<.00
	BMI*VMI interaction	0.01	0.01	0.001	0.03	.039

† Where male is the comparison group and β=1; ‡ Where VMI under 15th percentile is the comparison group an β=1; § Where education is level 1; ¶ Where education is level 2; †† Where education is level 3

Supplementary Material for Chapter 5

Supp 5A Adolescent Exercise Study: GEE Modelling Showing Relationships Between Changes in Bone Health and Potential Mediators

	β	SE	β 95% Confidence interval	p
T4 Mass				
Pre/Post[a]	0.04	0.09	-0.14 to 0.22	0.636
Sex[b]	0.15	0.14	-0.13 to 0.42	0.291
Puberty score	-0.20	0.06	-0.33 to -0.07	*0.002
Age	5.54	1.33	2.94 to 8.14	*<0.001
Age^2	-0.19	0.05	-0.28 to -0.10	*<0.001
Height	0.00	0.01	-0.01 to 0.02	0.726
Weight	0.03	0.01	0.01 to 0.05	*0.003
1 RM leg press	0.00	0.002	0.00 to 0.01	0.250
Vertical jump	0.03	0.01	0.00 to 0.05	*0.018
Standing broad jump	0.00	0.01	-0.02 to 0.02	0.933
NDI	0.00	0.004	-0.01 to 0.004	0.414
T4 Total area				
Pre/Post[a]	-24.39	21.88	-67.28 to 18.50	0.265
Sex[b]	98.91	38.27	23.90 to 173.91	*0.010
Puberty score	-42.11	12.66	-66.92 to -17.30	0.001
Age	1212.31	225.24	770.85 to 1653.76	<0.005
Age^2	-40.32	7.01	-54.06 to -26.59	<0.005
Height	3.89	2.62	-1.25 to 9.02	0.138
Weight	0.58	2.04	-3.42 to 4.58	0.776
1RM leg press	-0.66	0.74	-2.10 to 0.79	0.372
Vertical jump	6.96	3.30	0.48 to 13.43	***0.035**
Standing broad jump	-3.42	3.55	-10.38 to 3.55	0.336
NDI	2.02	1.04	-0.02 to 4.06	0.052
T4 Total density				
Pre/Post[a]	8.76	6.30	-3.58 to 21.10	0.164
Sex[b]	-12.81	6.46	-25.46 to -0.15	*0.047
Puberty score	-5.24	3.08	-11.28 to 0.81	0.089
Age	174.66	89.32	-0.42 to 349.73	0.051
Age^2	-6.16	3.07	-12.18 to -0.15	*0.045
Height	-0.52	0.41	-1.32 to 0.28	0.201
Weight	2.17	0.46	1.26 to 3.07	*<0.001
1 RM leg press	0.30	0.19	-0.07 to 0.66	0.110
Vertical jump	0.37	0.59	-0.78 to 1.53	0.527
Standing broad jump	0.90	0.43	0.06 to 1.74	***0.036**
NDI	-0.68	0.31	-1.30 to -0.06	***0.031**

	β	SE	β 95% Confidence interval	p
T4 Trabecular density				
Pre/Post[a]	10.55	8.86	-6.82 to 27.91	0.234
Sex[b]	3.63	8.96	-13.94 to 21.19	0.686
Puberty score	-7.87	4.11	-15.94 to 0.19	0.056
Age	180.77	111.25	-37.28 to 398.82	0.104
Age^2	-6.64	3.73	-13.96 to 0.68	0.075
Height	0.21	0.57	-0.91 to 1.33	0.709
Weight	1.76	0.53	0.72 to 2.79	*0.001
1RM leg press	0.52	0.21	0.11 to 0.94	***0.014**
Vertical jump	0.94	0.82	-0.67 to 2.55	0.253
Standing broad jump	0.06	0.66	-1.23 to 1.35	0.930
NDI	-0.74	0.32	-1.37 to -0.11	***0.021**
T4 Trabecular density Z score				
Pre/Post[a]	0.91	0.82	-0.70 to 2.52	0.268
Puberty score	-0.40	0.24	-0.86 to 0.07	0.094
Age	6.66	4.08	-1.33 to 14.66	0.102
Age^2	-0.26	0.14	-0.53 to 0.01	0.060
Weight	0.06	0.02	0.02 to 0.10	*0.003
1RM leg press	0.03	0.02	0.00 to 0.07	0.057
Vertical jump	0.07	0.06	-0.0 to 0.19	0.288
Standing broad jump	0.01	0.03	-0.05 to 0.07	0.822
NDI	-0.04	0.02	-0.08 to 0.00	***0.034**
T66 Mass				
Pre/Post[a]	0.10	0.08	-0.07 to 0.26	0.243
Sex[b]	-0.48	0.13	-0.72 to -0.22	*<0.001
Puberty score	-0.08	0.06	-0.20 to 0.04	0.184
Age	5.45	0.89	3.70 to 7.19	<0.001
Age^2	-0.17	0.03	-0.22 to -0.11	<0.001
Height	-0.02	0.01	-0.04 to 0.01	0.007
Weight	0.02	0.01	0.00 to 0.03	0.048
1 RM leg press	0.00	0.003	-0.01 to 0.003	0.243
Vertical jump	0.01	0.01	-0.01 to 0.03	0.355
Standing broad jump	-0.01	0.01	-0.02 to 0.01	0.507
NDI	0.01	0.004	0.00 to 0.02	**0.036**

	β	SE	β 95% Confidence interval	p
T66 SSI				
Pre/Post[a]	170.88	66.81	39.94 to 301.83	*0.011
Sex[b]	-216.73	124.13	-460.02 to 26.57	0.081
Puberty score	-29.96	48.34	-121.71 to 67.79	0.577
Age	2541.25	982.46	615.66 to 4466.84	*0.010
Age^2	-81.38	31.96	-144.02 to -18.75	*0.011
Height	-4.01	9.44	-22.51 to 14.49	0.671
Weight	13.22	6.41	0.66 to 25.78	*0.039
1RM leg press	-2.41	3.21	-8.70 to 3.88	0.454
Vertical jump	10.68	12.43	-13.69 to 35.05	0.390
Standing broad jump	2.31	8.47	-14.30 to 18.92	0.786
NDI	2.20	3.77	-5.19 to 9.59	0.559
T66 SSI Z score				
Pre/Post[a]	0.27	0.23	-0.19 to 0.72	0.255
Puberty score	0.05	0.21	-0.36 to 0.46	0.814
Age	-1.03	4.53	-9.91 to 7.85	0.820
Age^2	0.02	0.15	-0.28 to 0.32	0.877
Weight	0.02	0.02	-0.02 to 0.06	0.341
1RM leg press	0.00	0.01	-0.02 to 0.02	0.837
Vertical jump	0.03	0.03	-0.03 to 0.09	0.292
Standing broad jump	0.00	0.02	-0.05 to 0.04	0.976
NDI	0.00	0.02	-0.03 to 0.04	0.899
T66 Total area				
Pre/Post[a]	47.28	36.08	-23.44 to 118.00	0.190
Sex[b]	1.61	46.52	-89.56 to 92.78	0.972
Puberty score	-13.39	18.20	-49.05 to 22.28	0.462
Age	461.60	306.75	-139.62 to 1062.82	0.132
Age^2	-13.88	10.39	-34.23 to 6.48	0.181
Height	-3.88	2.16	-8.10 to 0.35	0.072
Weight	3.86	3.07	-2.15 to 9.87	0.208
1RM leg press	-0.70	0.84	-2.34 to 0.95	0.409
Vertical jump	-1.76	3.30	-8.23 to 4.71	0.594
Standing broad jump	-0.09	2.38	-4.75 to 4.58	0.971
NDI	1.39	1.66	-1.88 to 4.65	0.405

	β	SE	β 95% Confidence interval	p
T66 Cortical density				
Pre/Post[a]	0.77	11.02	-20.83 to 22.37	0.944
Sex[b]	-41.92	9.50	-60.54 to -23.29	*<0.001
Puberty score	-4.06	4.84	-13.55 to 5.43	0.401
Age	152.09	79.73	-4.17 to 308.35	0.056
Age^2	-4.69	2.74	-10.06 to 0.67	0.086
Height	-0.58	0.42	-1.41 to 0.25	0.171
Weight	0.30	0.67	-1.02 to 1.62	0.655
1RM leg press	0.61	0.23	0.15 to 1.07	***0.010**
Vertical jump	1.74	1.22	-0.65 to 4.12	0.153
Standing broad jump	-0.01	0.67	-1.32 to 1.30	0.987
NDI	-0.58	0.48	-1.51 to 0.35	0.222
T66 Cortical density Z score				
Pre/Post[a]	-0.04	0.29	-0.61 to 0.53	0.893
Puberty score	0.01	0.16	-0.29 to 0.32	0.930
Age	0.72	2.45	-4.08 to 5.51	0.770
Age^2	-0.02	0.08	-0.18 to 0.14	0.784
Weight	-0.02	0.02	-0.06 to 0.02	0.364
1RM leg press	0.02	0.01	0.001 to 0.03	**0.034**
Vertical jump	0.03	0.04	-0.04 to 0.10	0.380
Standing broad jump	0.01	0.02	-0.03 to 0.06	0.621
NDI	-0.02	0.01	-0.04 to 0.01	0.232
T66 Cortical area				
Pre/Post[a]	8.46	8.95	-9.07 to 26.00	0.344
Sex[b]	-34.40	12.77	-59.43 to -9.37	*0.007
Puberty score	-9.86	6.79	-23.17 to 3.45	0.147
Age	510.67	123.36	268.90 to 752.45	<0.001
Age^2	-16.12	4.23	-24.41 to -7.82	<0.001
Height	-0.37	0.80	-1.94 to 1.21	0.648
Weight	1.38	0.82	-0.23 to 2.99	0.093
1RM leg press	-0.04	0.32	-0.66 to 0.59	0.911
Vertical jump	2.11	0.99	0.17 to 4.05	***0.033**
Standing broad jump	-0.42	0.79	-1.98 to 1.13	0.593
NDI	0.42	0.56	-0.68 to 1.53	0.450

	β	SE	β 95% Confidence interval	p
T66 Cortical area Z-score				
Pre/Post[a]	-0.01	0.32	-0.64 to 0.61	0.969
Puberty Score	-0.17	0.28	-0.71 to 0.38	0.549
Age	5.97	6.14	-6.07 to 18.01	0.331
Age^2	-0.20	0.21	-0.61 to 0.21	0.340
Weight	0.02	0.03	-0.05 to 0.09	0.515
1 RM leg press	0.01	0.01	-0.02 to 0.03	0.463
Vertical jump	0.07	0.04	0.00 to 0.14	0.065
Standing broad jump	-0.02	0.03	-0.07 to 0.04	0.595
NDI	0.00	0.02	-0.04 to 0.05	0.833
T66 Fracture load X3N				
Pre/Post[a]	372.85	131.02	116.04 to 629.65	0.004
Sex[b]	-913.33	266.30	-1435.27 to -391.39	*0.001
Puberty score	-223.51	107.92	-435.04 to -11.99	*0.038
Age	1-204.22	2129.87	6119.76 to 14468.68	<0.001
Age^2	-327.68	68.88	-462.67 to -192.68	<0.001
Height	-23.86	19.92	-62.90 to 15.19	0.231
Weight	41.35	14.03	13.86 to 68.84	0.003
1RM leg press	-4.40	6.93	-17.98 to 9.18	0.525
Vertical jump	35.11	25.48	-14.83 to 85.05	0.168
Standing broad jump	12.45	16.27	-19.44 to 44.34	0.444
NDI	2.73	7.84	-12.63 to 18.09	0.728
T66 Fracture load Y3N				
Pre/Post[a]	304.03	184.08	-56.77 to 664.83	0.099
Sex[b]	-189.64	239.69	-659.42 to 280.15	0.429
Puberty score	73.68	105.01	-132.13 to 279.49	0.483
Age	2880.67	22225.56	-1481.34 to 7242.68	0.196
Age^2	-86.61	75.07	-233.75 to 60.53	0.249
Height	-6.20	16.06	-37.69 to 25.28	0.699
Weight	17.90	12.12	-5.86 to 41.66	0.140
1RM leg press	-12.58	6.47	-25.26 to 0.11	0.052
Vertical jump	4.77	24.19	-42.64 to 52.18	0.844
Standing broad jump	5.04	16.55	-27.39 to 37.47	0.761
NDI	9.94	8.70	-7.12 to 26.99	0.254

a Where pre-intervention is the comparison group and ϐ=1; b Where male is the comparison group and ϐ=1

Supp 5B Adolescent Exercise Study: GEE Modelling Showing Relationships Between Changes in Bone Health and Potential Mediators with Age2 Included

	β	SE	β 95% Confidence interval	p
T4 Mass				
Pre/Post[a]	0.04	0.09	-0.14 to 0.22	0.636
Sex[b]	0.15	0.14	-0.13 to 0.42	0.291
Puberty score	-0.20	0.06	-0.33 to -0.07	*0.002
Age	5.54	1.33	2.94 to 8.14	*<0.001
Age^2	-0.19	0.05	-0.28 to -0.10	*<0.001
Height	0.00	0.01	-0.01 to 0.02	0.726
Weight	0.03	0.01	0.01 to 0.05	*0.003
1 RM leg press	0.00	0.002	0.00 to 0.01	0.250
Vertical jump	0.03	0.01	0.00 to 0.05	*0.018
Standing broad jump	0.00	0.01	-0.02 to 0.02	0.933
NDI	0.00	0.004	-0.01 to 0.004	0.414
T4 Total area				
Pre/Post[a]	-24.39	21.88	-67.28 to 18.50	0.265
Sex[b]	98.91	38.27	23.90 to 173.91	*0.010
Puberty score	-42.11	12.66	-66.92 to -17.30	0.001
Age	1212.31	225.24	770.85 to 1653.76	<0.005
Age^2	-40.32	7.01	-54.06 to -26.59	<0.005
Height	3.89	2.62	-1.25 to 9.02	0.138
Weight	0.58	2.04	-3.42 to 4.58	0.776
1RM leg press	-0.66	0.74	-2.10 to 0.79	0.372
Vertical jump	6.96	3.30	0.48 to 13.43	***0.035**
Standing broad jump	-3.42	3.55	-10.38 to 3.55	0.336
NDI	2.02	1.04	-0.02 to 4.06	0.052
T4 Total density				
Pre/Post[a]	8.76	6.30	-3.58 to 21.10	0.164
Sex[b]	-12.81	6.46	-25.46 to -0.15	*0.047
Puberty score	-5.24	3.08	-11.28 to 0.81	0.089
Age	174.66	89.32	-0.42 to 349.73	0.051
Age^2	-6.16	3.07	-12.18 to -0.15	*0.045
Height	-0.52	0.41	-1.32 to 0.28	0.201
Weight	2.17	0.46	1.26 to 3.07	*<0.001
1 RM leg press	0.30	0.19	-0.07 to 0.66	0.110
Vertical jump	0.37	0.59	-0.78 to 1.53	0.527
Standing broad jump	0.90	0.43	0.06 to 1.74	***0.036**
NDI	-0.68	0.31	-1.30 to -0.06	***0.031**

	β	SE	β 95% Confidence interval	p
T4 Trabecular density				
Pre/Post[a]	10.55	8.86	-6.82 to 27.91	0.234
Sex[b]	3.63	8.96	-13.94 to 21.19	0.686
Puberty score	-7.87	4.11	-15.94 to 0.19	0.056
Age	180.77	111.25	-37.28 to 398.82	0.104
Age^2	-6.64	3.73	-13.96 to 0.68	0.075
Height	0.21	0.57	-0.91 to 1.33	0.709
Weight	1.76	0.53	0.72 to 2.79	*0.001
1RM leg press	0.52	0.21	0.11 to 0.94	***0.014**
Vertical jump	0.94	0.82	-0.67 to 2.55	0.253
Standing broad jump	0.06	0.66	-1.23 to 1.35	0.930
NDI	-0.74	0.32	-1.37 to -0.11	***0.021**
T4 Trabecular density Z score				
Pre/Post[a]	0.91	0.82	-0.70 to 2.52	0.268
Puberty score	-0.40	0.24	-0.86 to 0.07	0.094
Age	6.66	4.08	-1.33 to 14.66	0.102
Age^2	-0.26	0.14	-0.53 to 0.01	0.060
Weight	0.06	0.02	0.02 to 0.10	*0.003
1RM leg press	0.03	0.02	0.00 to 0.07	0.057
Vertical jump	0.07	0.06	-0.0 to 0.19	0.288
Standing broad jump	0.01	0.03	-0.05 to 0.07	0.822
NDI	-0.04	0.02	-0.08 to 0.00	***0.034**
T66 Mass				
Pre/Post[a]	0.10	0.08	-0.07 to 0.26	0.243
Sex[b]	-0.48	0.13	-0.72 to -0.22	*<0.001
Puberty score	-0.08	0.06	-0.20 to 0.04	0.184
Age	5.45	0.89	3.70 to 7.19	<0.001
Age^2	-0.17	0.03	-0.22 to -0.11	<0.001
Height	-0.02	0.01	-0.04 to 0.01	0.007
Weight	0.02	0.01	0.00 to 0.03	0.048
1 RM leg press	0.00	0.003	-0.01 to 0.003	0.243
Vertical jump	0.01	0.01	-0.01 to 0.03	0.355
Standing broad jump	-0.01	0.01	-0.02 to 0.01	0.507
NDI	0.01	0.004	0.00 to 0.02	**0.036**

	β	SE	β 95% Confidence interval	p
T66 SSI				
Pre/Post[a]	170.88	66.81	39.94 to 301.83	*0.011
Sex[b]	-216.73	124.13	-460.02 to 26.57	0.081
Puberty score	-29.96	48.34	-121.71 to 67.79	0.577
Age	2541.25	982.46	615.66 to 4466.84	*0.010
Age^2	-81.38	31.96	-144.02 to -18.75	*0.011
Height	-4.01	9.44	-22.51 to 14.49	0.671
Weight	13.22	6.41	0.66 to 25.78	*0.039
1RM leg press	-2.41	3.21	-8.70 to 3.88	0.454
Vertical jump	10.68	12.43	-13.69 to 35.05	0.390
Standing broad jump	2.31	8.47	-14.30 to 18.92	0.786
NDI	2.20	3.77	-5.19 to 9.59	0.559
T66 SSI Z score				
Pre/Post[a]	0.27	0.23	-0.19 to 0.72	0.255
Puberty score	0.05	0.21	-0.36 to 0.46	0.814
Age	-1.03	4.53	-9.91 to 7.85	0.820
Age^2	0.02	0.15	-0.28 to 0.32	0.877
Weight	0.02	0.02	-0.02 to 0.06	0.341
1RM leg press	0.00	0.01	-0.02 to 0.02	0.837
Vertical jump	0.03	0.03	-0.03 to 0.09	0.292
Standing broad jump	0.00	0.02	-0.05 to 0.04	0.976
NDI	0.00	0.02	-0.03 to 0.04	0.899
T66 Total area				
Pre/Post[a]	47.28	36.08	-23.44 to 118.00	0.190
Sex[b]	1.61	46.52	-89.56 to 92.78	0.972
Puberty score	-13.39	18.20	-49.05 to 22.28	0.462
Age	461.60	306.75	-139.62 to 1062.82	0.132
Age^2	-13.88	10.39	-34.23 to 6.48	0.181
Height	-3.88	2.16	-8.10 to 0.35	0.072
Weight	3.86	3.07	-2.15 to 9.87	0.208
1RM leg press	-0.70	0.84	-2.34 to 0.95	0.409
Vertical jump	-1.76	3.30	-8.23 to 4.71	0.594
Standing broad jump	-0.09	2.38	-4.75 to 4.58	0.971
NDI	1.39	1.66	-1.88 to 4.65	0.405

	β	SE	β 95% Confidence interval	p
T66 Cortical density				
Pre/Post[a]	0.77	11.02	-20.83 to 22.37	0.944
Sex[b]	-41.92	9.50	-60.54 to -23.29	*<0.001
Puberty score	-4.06	4.84	-13.55 to 5.43	0.401
Age	152.09	79.73	-4.17 to 308.35	0.056
Age^2	-4.69	2.74	-10.06 to 0.67	0.086
Height	-0.58	0.42	-1.41 to 0.25	0.171
Weight	0.30	0.67	-1.02 to 1.62	0.655
1RM leg press	0.61	0.23	0.15 to 1.07	***0.010**
Vertical jump	1.74	1.22	-0.65 to 4.12	0.153
Standing broad jump	-0.01	0.67	-1.32 to 1.30	0.987
NDI	-0.58	0.48	-1.51 to 0.35	0.222
T66 Cortical density Z score				
Pre/Post[a]	-0.04	0.29	-0.61 to 0.53	0.893
Puberty score	0.01	0.16	-0.29 to 0.32	0.930
Age	0.72	2.45	-4.08 to 5.51	0.770
Age^2	-0.02	0.08	-0.18 to 0.14	0.784
Weight	-0.02	0.02	-0.06 to 0.02	0.364
1RM leg press	0.02	0.01	0.001 to 0.03	**0.034**
Vertical jump	0.03	0.04	-0.04 to 0.10	0.380
Standing broad jump	0.01	0.02	-0.03 to 0.06	0.621
NDI	-0.02	0.01	-0.04 to 0.01	0.232
T66 Cortical area				
Pre/Post[a]	8.46	8.95	-9.07 to 26.00	0.344
Sex[b]	-34.40	12.77	-59.43 to -9.37	*0.007
Puberty score	-9.86	6.79	-23.17 to 3.45	0.147
Age	510.67	123.36	268.90 to 752.45	<0.001
Age^2	-16.12	4.23	-24.41 to -7.82	<0.001
Height	-0.37	0.80	-1.94 to 1.21	0.648
Weight	1.38	0.82	-0.23 to 2.99	0.093
1RM leg press	-0.04	0.32	-0.66 to 0.59	0.911
Vertical jump	2.11	0.99	0.17 to 4.05	***0.033**
Standing broad jump	-0.42	0.79	-1.98 to 1.13	0.593
NDI	0.42	0.56	-0.68 to 1.53	0.450

	β	SE	β 95% Confidence interval	p
T66 Cortical area Z-score				
Pre/Post[a]	-0.01	0.32	-0.64 to 0.61	0.969
Puberty Score	-0.17	0.28	-0.71 to 0.38	0.549
Age	5.97	6.14	-6.07 to 18.01	0.331
Age^2	-0.20	0.21	-0.61 to 0.21	0.340
Weight	0.02	0.03	-0.05 to 0.09	0.515
1 RM leg press	0.01	0.01	-0.02 to 0.03	0.463
Vertical jump	0.07	0.04	0.00 to 0.14	0.065
Standing broad jump	-0.02	0.03	-0.07 to 0.04	0.595
NDI	0.00	0.02	-0.04 to 0.05	0.833
T66 Fracture load X3N				
Pre/Post[a]	372.85	131.02	116.04 to 629.65	0.004
Sex[b]	-913.33	266.30	-1435.27 to -391.39	*0.001
Puberty score	-223.51	107.92	-435.04 to -11.99	*0.038
Age	1-204.22	2129.87	6119.76 to 14468.68	<0.001
Age^2	-327.68	68.88	-462.67 to -192.68	<0.001
Height	-23.86	19.92	-62.90 to 15.19	0.231
Weight	41.35	14.03	13.86 to 68.84	0.003
1RM leg press	-4.40	6.93	-17.98 to 9.18	0.525
Vertical jump	35.11	25.48	-14.83 to 85.05	0.168
Standing broad jump	12.45	16.27	-19.44 to 44.34	0.444
NDI	2.73	7.84	-12.63 to 18.09	0.728
T66 Fracture load Y3N				
Pre/Post[a]	304.03	184.08	-56.77 to 664.83	0.099
Sex[b]	-189.64	239.69	-659.42 to 280.15	0.429
Puberty score	73.68	105.01	-132.13 to 279.49	0.483
Age	2880.67	22225.56	-1481.34 to 7242.68	0.196
Age^2	-86.61	75.07	-233.75 to 60.53	0.249
Height	-6.20	16.06	-37.69 to 25.28	0.699
Weight	17.90	12.12	-5.86 to 41.66	0.140
1RM leg press	-12.58	6.47	-25.26 to 0.11	0.052
Vertical jump	4.77	24.19	-42.64 to 52.18	0.844
Standing broad jump	5.04	16.55	-27.39 to 37.47	0.761
NDI	9.94	8.70	-7.12 to 26.99	0.254

a Where pre-intervention is the comparison group and θ=1; b Where male is the comparison group and θ=1

Supp 5C Adolescent Exercise Study: GEE modelling showing relationships between changes in bone health and potential mediators for intervention-naive participants only

	β	SE	β 95% Confidence interval	p
T4 Mass				
Pre/Post[a]	-0.08	0.17	-0.41 to 0.36	0.653
Sex[b]	-0.07	0.01	-0.27 to 0.12	0.461
Puberty score	-0.23	0.09	-0.41 to 0.05	*0.011
Age	0.29	0.20	-0.10 to 0.68	0.141
Height	0.00	0.01	-0.02 to 0.01	0.683
Weight	0.04	0.01	0.02 to 0.06	*<0.001
1 RM leg press	0.00	0.004	-0.01 to 0.01	0.571
Vertical jump	0.03	0.01	0.01 to 0.06	*0.002
Standing broad jump	0.00	0.08	-0.02 to 0.02	0.941
NDI	-0.01	0.004	-0.01 to 0.00	0.060
T4 Total area				
Pre/Post[a]	-62.18	43.93	-148.29 to 23.92	0.157
Sex[b]	57.40	39.04	-19.12 to 133.93	0.141
Puberty score	-39.77	17.27	-73.63 to -5.91	*0.021
Age	72.35	68.03	-60.99 to 205.69	0.288
Height	2.96	2.90	-2.73 to 8.66	0.308
Weight	2.74	2.48	-2.12 to 7.60	0.269
1RM leg press	-2.28	1.10	-4.43 to -0.12	*0.038
Vertical jump	9.46	3.87	1.87 to 17.04	*0.015
Standing broad jump	-3.35	3.70	-10.69 to 3.91	0.366
NDI	1.40	1.32	-1.18 to 3.98	0.289
T4 Total density				
Pre/Post[a]	-0.28	6.56	-13.13 to 12.57	0.966
Sex[b]	-21.66	7.53	-36.42 to -6.91	*0.004
Puberty score	-6.79	4.56	-15.73 to 2.15	0.137
Age	-4.64	17.02	-37.99 to 28.72	0.785
Height	-0.73	0.58	-1.86 to 0.41	0.211
Weight	2.88	0.41	2.08 to 3.68	*<0.001
1 RM leg press	0.07	0.28	-0.48 to 0.61	0.811
Vertical jump	0.76	0.56	-0.35 to 1.87	0.178
Standing broad jump	1.04	0.49	0.09 to 1.99	*0.033
NDI	-0.91	0.22	-1.33 to -0.48	*<0.001

	β	SE	β 95% Confidence interval	p
T4 Trabecular density				
Pre/Post[a]	6.58	13.67	-20.21 to 33.37	0.630
Sex[b]	-11.91	11.39	-34.25 to 10.42	0.296
Puberty score	-11.64	5.93	-23.26 to -0.03	*0.050
Age	0.20	19.83	-38.67 to 39.07	0.992
Height	-0.32	0.70	-1.70 to 1.06	0.648
Weight	2.62	0.55	1.54 to 3.70	*<0.001
1RM leg press	0.34	0.37	-0.39 to 1.07	0.360
Vertical jump	1.77	0.82	0.17 to 3.37	*0.030
Standing broad jump	-0.09	0.74	-1.55 to 1.36	0.900
NDI	-1.04	0.31	-1.65 to -0.42	*0.001
T4 Trabecular density Z score				
Pre/Post[a]	0.92	1.25	-1.54 to 3.38	0.463
Puberty score	-0.38	0.30	-0.96 to 0.20	0.201
Age	-1.01	0.75	-2.48 to 0.47	0.181
Weight	0.08	0.03	0.04 to 0.13	*<0.001
1RM leg press	0.04	0.03	-0.02 to 0.09	0.171
Vertical jump	0.09	0.07	-0.03 to 0.22	0.151
Standing broad jump	-0.01	0.04	-0.09 to 0.06	0.781
NDI	-0.05	0.02	-0.09 to -0.01	*0.010
T66 Mass				
Pre/Post[a]	-0.07	2.73	-9.61 to 1.09	0.119
Sex[b]	-0.42	0.15	-0.72 to -0.12	*0.005
Puberty score	-0.04	0.07	-0.18 to 0.10	0.579
Age	0.67	0.29	0.09 to 1.24	*0.022
Height	-0.02	0.01	- 0.03 to 0.00	0.090
Weight	0.02	0.01	0.002 to 0.03	*0.022
1 RM leg press	-0.01	0.01	-0.02 to 0.00	0.130
Vertical jump	0.01	0.01	-0.02 to 0.03	0.588
Standing broad jump	0.00	0.01	-0.02 to 0.02	0.864
NDI	0.01	0.05	0.00 to 0.02	0.079

	β	SE	β 95% Confidence interval	p
T66 SSI				
Pre/Post[a]	164.65	79.93	22.72 to 307.59	*0.024
Sex[b]	63.19	144.82	-220.65 to 347.02	0.663
Puberty score	32.82	46.83	-58.97 to 124.60	0.483
Age	27.16	239.47	-442.20 to 496.51	0.910
Height	9.96	8.20	-6.12 to 26.04	0.225
Weight	4.79	5.01	-5.02 to 14.60	0.339
1RM leg press	2.76	3.40	-3.91 to 9.42	0.418
Vertical jump	-1.28	10.36	-21.59 to 19.03	0.902
Standing broad jump	2.19	9.27	-15.97 to 20.35	0.813
NDI	5.08	4.18	-3.11 to 13.27	0.224
T66 SSI Z score				
Pre/Post[a]	0.39	0.21	-0.02 to 0.80	0.061
Puberty score	0.28	0.11	0.05 to 0.50	*0.015
Age	-0.66	0.35	-1.35 to 0.02	0.057
Weight	-0.01	0.02	-0.04 to 0.02	0.541
1RM leg press	0.01	0.01	-0.01 to 0.03	0.188
Vertical jump	-0.01	0.02	-0.06 to 0.03	0.547
Standing broad jump	0.00	0.02	-0.05 to 0.04	0.961
NDI	0.02	0.01	-0.01 to 0.05	0.148
T66 Total area				
Pre/Post[a]	168.54	67.93	35.40 to 301.69	*0.013
Sex[b]	70.55	36.58	-1.15 to 142.25	0.054
Puberty score	-14.01	23.37	-59.82 to 31.81	0.549
Age	136.09	53.60	31.04 to 241.14	*0.011
Height	-0.77	1.31	-3.34 to 1.80	0.555
Weight	-0.51	1.87	-4.18 to 3.16	0.785
1RM leg press	2.70	1.07	0.61 to 4.79	*0.011
Vertical jump	-9.43	2.30	-15.31 to -3.56	*0.002
Standing broad jump	-0.94	1.45	-3.78 to 1.90	0.516
NDI	3.39	0.80	1.82 to 4.95	*<0.001

	β	SE	β 95% Confidence interval	p
T66 Cortical density				
Pre/Post[a]	-15.60	19.94	-54.69 to 23.48	0.434
Sex[b]	-48.27	12.69	-73.14 to -23.40	*<0.001
Puberty score	-3.83	7.65	-18.83 to 11.18	0.617
Age	15.79	23.52	-30.31 to 61.89	0.502
Height	-0.81	0.61	-2.00 to 0.38	0.183
Weight	0.67	0.70	-0.71 to 2.05	0.342
1RM leg press	0.24	0.27	-0.28 to 0.77	0.360
Vertical jump	2.89	1.57	-0.20 to 5.97	0.067
Standing broad jump	0.20	0.65	-1.06 to 1.47	0.753
NDI	-1.03	0.45	-1.92 to -0.14	*0.023
T66 Cortical density Z score				
Pre/Post[a]	-0.48	0.53	-1.52 to 0.56	0.366
Puberty score	0.11	0.23	-0.33 to 0.56	0.616
Age	-0.41	0.61	-1.60 to 0.79	0.506
Weight	-0.01	0.02	-0.05 to 0.03	0.476
1RM leg press	0.01	0.01	-0.01 to 0.03	0.339
Vertical jump	0.06	0.04	-0.03 to 0.14	0.174
Standing broad jump	0.02	0.02	-0.03 to 0.06	0.500
NDI	-0.03	0.01	-0.05 to -0.001	*0.038
T66 Cortical area				
Pre/Post[a]	-27.02	19.80	-65.84 to 15.96	0.799
Sex[b]	-26.41	14.30	-54.43 to 1.62	0.065
Puberty score	-2.39	9.36	-20.73 to 15.96	0.799
Age	16.62	32.85	-47.76 to 81.00	0.613
Height	0.38	0.99	-1.56 to 2.32	0.699
Weight	1.79	0.71	0.39 to 3.18	*0.012
1RM leg press	-0.61	0.56	-1.70 to 0.48	0.274
Vertical jump	2.80	1.03	0.79 to 4.81	*0.006
Standing broad jump	0.12	0.80	-1.37 to 1.62	0.874
NDI	0.57	0.50	-0.93 to 1.04	0.910

	β	SE	β 95% Confidence interval	p
T66 Cortical area Z score				
Pre/Post[a]	-1.02	0.75	-2.48 to 0.44	0.172
Puberty score	0.29	0.31	-0.33 to 0.90	0.360
Age	-1.21	0.86	-2.91 to 0.48	0.161
Weight	0.02	0.03	-0.04 to 0.07	0.609
1RM leg press	0.00	0.02	-0.05 to 0.04	0.865
Vertical jump	0.07	0.03	0.01 to 0.13	*0.034
Standing broad jump	0.00	0.03	-0.06 to 0.05	0.934
NDI	0.01	0.02	-0.03 to 0.05	0.735
T66 Fracture load X3N				
Pre/Post[a]	369.08	164.29	47.09 to 691.08	*0.025
Sex[b]	-270.67	312.20	-882.57 to 341.23	0.386
Puberty score	-81.70	96.43	-270.70 to 107.31	0.397
Age	690.74	513.25	-315.22 to 1696.69	0.178
Height	10.60	17.24	-23.19 to 44.39	0.539
Weight	17.84	10.38	-2.51 to 38.19	0.086
1RM leg press	7.99	7.54	-6.79 to 22.77	0.289
Vertical jump	5.14	17.79	-29.72 to 39.99	0.773
Standing broad jump	13.72	16.98	-19.56 to 47.01	0.419
NDI	8.40	9.24	-9.71 to 26.50	0.363
T66 Fracture load Y3N				
Pre/Post[a]	590.86	258.79	83.65 to 1098.07	*0.022
Sex[b]	-224.60	292.11	-347.94 to 797.13	0.442
Puberty score	123.73	124.84	-120.95 to 368.41	0.322
Age	409.16	521.97	-613.88 to 1432.20	0.433
Height	12.97	17.80	-21.92 to 47.85	0.466
Weight	0.52	13.19	-25.33 to 26.38	0.968
1RM leg press	-0.32	6.63	-13.32 to 12.68	0.962
Vertical jump	-20.33	26.03	-71.35 to 30.68	0.435
Standing broad jump	6.06	18.08	-29.38 to 41.49	0.738
NDI	14.31	10.53	-6.33 to 34.94	0.174

a Where pre-intervention is the comparison group and ϐ=1; b Where male is the comparison group and ϐ=1

Supplementary Material for Chapter 6

Supp 6A Young Adult Study: Demographic and Physical Activity Factors

Table A1

Participant Characteristics including Physical Activity Factors for the Whole Group

	13 years old				17 years old				20 years old			
	LMC M (SD) [Md] {IQR}	**Not LMC M (SD) [Md] {IQR}**	**Z**	**P**	**LMC M (SD) [Md] {IQR}**	**Not LMC M (SD) [Md] {IQR}**	**Z**	**P**	**LMC M (SD) [Md] {IQR}**	**Not LMC M (SD) [Md] {IQR}**	**Z**	**P**
Waist girth (cm)	76.6 (11.1) [74.4] {68.5 to 81.9}	73.9 (9.2) [72.0] {67.5 to 78.5}	-3.33	.001	79.1 (11.1) [77.5] {72.0 to 84.0}	77.9 (9.5) [76.2] {71.5 to 82.2}	-1.54	.123	81.5 (13.0) [79.0] {72.1 to 87.5}	78.9 (11.2) [77.3] {71.2 to 84.3}	-2.56	.010
Height (cm)	164.2 (0.1) [164.0] {159.0 to 170.0}	164.8 (7.5) [164.0] {160.0 to 170.0}	-0.69	.492	172.1 (8.7) [172.0] {166.4 to 178.0}	172.7 (8.9) [172.2] {165.8 to 178.9}	-0.61	.542	173.3 (9.0) [173.0] {167.0 to 180.0}	172.7 (9.4) [172.5] {165.4 to 179.7}	-1.00	.315
Vitamin levels												
25 (OH)D3 concentration (nmol/L)					72.3 (28.3) [69.4] {54.0 to 85.3}	75.4 (27.3) [71.2] {57.7 to 90.3}	-1.60	.109	69.0 (25.5) [66.6] {53.8 to 83.0}	72.9 (24.8) [70.9] {56.8 to 86.8}	-2.31	.021
25 (OH) D2 concentration (nmol/L)									0.1 (0.6) [0.0] {0.0 to 0.0}	0.1 (0.6) [0.0] {0.0 to 0.0}	-0.26	.794
Total vitamin D (nmol/L)					73.1 (26.1) [71.5] {55.4 to 86.3}	75.8 (24.8) [73.6] {58.7 to 89.3}	-1.62	.105	70.2 (24.6) [68.7] {54.6 to 83.0}	74.7 (23.2) [72.8] {58.7 to 88.7}	-2.88	.994

Table A1

Participant Characteristics including Physical Activity Factors for the Whole Group

	13 years old				17 years old				20 years old			
	LMC **M (SD) [Md] {IQR}**	**Not LMC** **M (SD) [Md] {IQR}**	**Z**	**P**	**LMC** **M (SD) [Md] {IQR}**	**Not LMC** **M (SD) [Md] {IQR}**	**Z**	**P**	**LMC** **M (SD) [Md] {IQR}**	**Not LMC** **M (SD) [Md] {IQR}**	**Z**	**P**
Waist girth (cm)	76.6 (11.1) [74.4] {68.5 to 81.9}	73.9 (9.2) [72.0] {67.5 to 78.5}	-3.33	.001	79.1 (11.1) [77.5] {72.0 to 84.0}	77.9 (9.5) [76.2] {71.5 to 82.2}	-1.54	.123	81.5 (13.0) [79.0] {72.1 to 87.5}	78.9 (11.2) [77.3] {71.2 to 84.3}	-2.56	.010
Height (cm)	164.2 (0.1) [164.0] {159.0 to 170.0}	164.8 (7.5) [164.0] {160.0 to 170.0}	-0.69	.492	172.1 (8.7) [172.0] {166.4 to 178.0}	172.7 (8.9) [172.2] {165.8 to 178.9}	-0.61	.542	173.3 (9.0) [173.0] {167.0 to 180.0}	172.7 (9.4) [172.5] {165.4 to 179.7}	-1.00	.315
Vitamin levels												
25 (OH)D3 concentration (nmol/L)					72.3 (28.3) [69.4] {54.0 to 85.3}	75.4 (27.3) [71.2] {57.7 to 90.3}	-1.60	.109	69.0 (25.5) [66.6] {53.8 to 83.0}	72.9 (24.8) [70.9] {56.8 to 86.8}	-2.31	.021
25 (OH) D2 concentration (nmol/L)									0.1 (0.6) [0.0] {0.0 to 0.0}	0.1 (0.6) [0.0] {0.0 to 0.0}	-0.26	.794
Total vitamin D (nmol/L)					73.1 (26.1) [71.5] {55.4 to 86.3}	75.8 (24.8) [73.6] {58.7 to 89.3}	-1.62	.105	70.2 (24.6) [68.7] {54.6 to 83.0}	74.7 (23.2) [72.8] {58.7 to 88.7}	-2.88	.994

	13 years old				17 years old				20 years old			
	LMC M (SD) [Md] {IQR}	**Not LMC M (SD) [Md] {IQR}**	**Z**	**P**	**LMC M (SD) [Md] {IQR}**	**Not LMC M (SD) [Md] {IQR}**	**Z**	**P**	**LMC M (SD) [Md] {IQR}**	**Not LMC M (SD) [Md] {IQR}**	**Z**	**P**
Dietary intake												
Magnesium (mg/day)									289.2 (168.5) [255.4] {192.0 to 332.0}	288.7 (135.9) [264.7] {200.8 to 343.3}	-1.06	.289
Phosphorus (mg/day)									1674.7 (1085.0) [1449.6] {1095.6 to 1990.5}	1638.2 (797.6) [1496.4] {1105.6 to 1496.4}	-0.69	.488
Potassium (mg/day)									2901.2 (1564.0) [2549.1] {1939.4 to 3307.7}	2858.8 (1264.8) [2651.9] {2000.4 to 3355.9}	-0.48	.631
Zinc (mg/day)									13.9 (11.6) [11.7] {8.7 to 15.5}	13.4 (7.8) [12.0] {8.5 to 16.1}	-0.44	.661

	13 years old				17 years old				20 years old			
	LMC M (SD) [Md] {IQR}	**Not LMC M (SD) [Md] {IQR}**	**Z**	**P**	**LMC M (SD) [Md] {IQR}**	**Not LMC M (SD) [Md] {IQR}**	**Z**	**P**	**LMC M (SD) [Md] {IQR}**	**Not LMC M (SD) [Md] {IQR}**	**Z**	**P**
Physical fitness												
Pedometer												
Weekday (steps/day)					10280.9 (3542.2) [9948.6] {7530.1 to 12494.8}	10163.8 (5782.3) [9515.3] {7262.8 to 11858.6}	-0.87	.382				
Weekend (Steps/day)					8315.9 (4129.2) [7896.0] {5451.3 to 11358.8}	9352.0 (5109.7) [8921.0] {5780.2 to 11736.0}	-1.46	.144				
IPAQ scores												
Walking (min/day)					65.5 (69.8) [30.0] {0.0 to 120.0}	60.0 (63.1) [30.0] {10.0 to 120.0}	-0.28	.782	83.4 (68.6) [60.0] {25.0 to 180.0}	73.8 (62.3) [60.0] {30.0 to 120.0}	-1.13	.257
Moderate activity (min/day)					44.3 (60.2) [15.0] {0.0 to 60.0}	53.3 (64.3) [30.0] {0.0 to 87.5}	-2.03	.042	50.6 (61.9) [20.0] {0.0 to 75.0}	60.2 (65.2) [30.0] {0.0 to 120.0}	-2.02	.044
Vigorous activity (min/day)					53.4 (64.1) [30.0] {0.0 to 90.0}	58.6 (60.6) [45.0] {0.0 to 90.0}	-1.71	.088	59.7 (64.9) [42.5] {0.0 to 120.0}	62.4 (60.6) [60.0] {0.0 to 90.0}	-1.02	.306

	13 years old				17 years old				20 years old			
	LMC M (SD) [Md] {IQR}	**Not LMC M (SD) [Md] {IQR}**	**Z**	**P**	**LMC M (SD) [Md] {IQR}**	**Not LMC M (SD) [Md] {IQR}**	**Z**	**P**	**LMC M (SD) [Md] {IQR}**	**Not LMC M (SD) [Md] {IQR}**	**Z**	**P**
Australian Fitness Education Award												
Curl ups (n)	17.4 (15.5) [15.0] {6.0 to 24.0}	24.7 (18.0) [20.0] {12.0 to 32.0}	-5.93	<.001	17.8 (16.0) [15.0] {5.0 to 26.0}	23.8 (17.8) [21.0] {10.5 to 32.0}	-4.37	<.001				
Sit and reach distance (cm)	20.3 (9.3) [19.5] {14.5 to 27.0}	24.7 (8.7) [24.5] {18.0 to 31.0}	-6.20	<.001	20.1 (10.2) [20.3] {14.0 to 28.0}	24.9 (10.3) [25.5] {19.0 to 32.0}	-5.96	<.001				
Basketball throw distance (m)	5.0 (0.9) [4.9] {4.4 to 5.6}	5.4 (0.9) [5.2] {4.7 to 6.0}	-4.89	<.001	5.9 (1.3) [5.8] {4.8 to 6.8}	6.2 (1.4) [6.1] {5.1 to 6.2}	-3.00	.003				
Physical work capacity	110.0 (27.9) [103.7] {90.5 to 103.7}	112.7 (30.4) [107.0] {92.3 to 127.0}	-1.10	.273	126.9 (42.7) [120.9] {92.3 to 158.2}	130.1 (44.3) [121.2] {105.8 to 157.1}	-0.78	.435				
Health												
Physical health composite score					54.1 (7.4) [56.4] {51.1 to 58.9}	55.0 (43.3) [56.7] {51.7 to 59.1}	-1.00	.317				
Age started smoking (yrs)									16.7 (1.8) [17.0] {16.0 to 18.0}	17.0 (1.9) [17.0] {16.0 to 18.0}	-0.74	.458

	%	%	X^2	P	%	%	X^2	P	%	%	X^2	P
Current smoker									14.1	14.6	0.03	.867
Currently live with a smoker									34.0	27.6	3.08	.079
Joints that bend or sprain easily	45.9	44.0	0.58	.747								
Bruise easily	19.5	24.7	2.51	.286								
Medical help for joint or back injury	40.2	35.2	2.03	.363								
Diagnosis												
Anxiety					5.2	4.5	2.33	.507	7.5	6.7	1.01	.798
Behavioural problems					6.2	2.7	5.30	.071	4.7	3.3	1.58	.663
Chronic respiratory problems					0.5	1.0	2.33	.312	1.9	1.3	1.14	.565
Coordination problems					3.3	0.2	17.46	<.001	5.6	1.3	20.72	<.001
Depression					6.6	3.1	0.84	.840	7.0	7.4	2.22	.529
Eating disorder					0.0	1.4	2.97	.226	3.3	1.5	2.00	.573

Table A2

Participant Characteristics Including Physical Activity Factors for Males Only

	13 years old				17 years old				20 years old			
	LMC **M (SD) [Md] {IQR}**	**Not LMC** **M (SD) [Md] {IQR}**	**Z**	**P**	**LMC** **M (SD) [Md] {IQR}**	**Not LMC** **M (SD) [Md] {IQR}**	**Z**	**P**	**LMC** **M (SD) [Md] {IQR}**	**Not LMC** **M (SD) [Md] {IQR}**	**Z**	**P**
Waist girth (cm)	76.7 (11.7) [74.1] {68.3 to 82.6}	75.0 (9.6) [72.8] {68.5 to 79.6}	-1.31	.191	79.9 (10.4) [77.5] {73.4 to 84.0}	79.3 (9.2) [77.5] {73.5 to 83.0}	-0.39	.695	83.1 (12.7) [81.0] {74.1 to 88.2}	82.1 (10.3) [80.0] {75.8 to 86.8}	-0.15	.881
Height (cm)	165.1 (8.9) [165.0] {159.0 to 171.8}	167.1 (8.2) [167.5] {161.0 to 173.0}	-2.18	.029	176.4 (7.2) [176.0] {171.4 to 182.1}	179.3 (7.1) [179.5] {174.1 to 184.5}	-2.32	.020	178.1 (7.4) [177.9} {173.5 to 183.1}	179.2 (7.1) [178.8] {175.0 to 184.0}	-1.58	.114
BMI	21.1 (4.1) [20.3] {18.2 to 23.0}	20.7 (3.4) [19.7] {18.4 to 22.2}	-0.83	.409	22.4 (4.0) [21.6] {19.8 to 24.2}	22.2 (3.5) [21.6] {19.9 to 23.7}	-0.04	.972	24.4 (4.7) [23.6] {21.3 to 26.2}	24.1 (3.9) [23.5] {21.3 to 25.9}	-0.30	.766
Vitamin levels												
Deseasonalised 25(OH)D3 (nmol/L)					73.3 (25.1) [71.6] {55.6 to 86.2}	75.9 (25.8) [73.0] {58.9 to 89.6}	-1.13	.258	67.5 (21.5) [69.3] {52.3 to 82.7}	73.5 (22.4) [73.2] {58.5 to 86.3}	-2.44	.015

	13 years old				17 years old				20 years old			
	LMC	**Not LMC**	**Z**	**P**	**LMC**	**Not LMC**	**Z**	**P**	**LMC**	**Not LMC**	**Z**	**P**
	M (SD) [Md] {IQR}	**M (SD) [Md] {IQR}**			**M (SD) [Md] {IQR}**	**M (SD) [Md] {IQR}**			**M (SD) [Md] {IQR}**	**M (SD) [Md] {IQR}**		
Dietary intake												
Protein (g/day)									117.2 (80.5) [103.2] {77.9 to 131.4}	125.0 (62.4) [110.7] {87.8 to 149.8}	-2.29	.022
Calcium (mg/day)									1013.6 (495.0) [908.2] {673.7 to 1312.9}	1008.7 (401.1) [961.5] {719.0 to 1196.3}	-0.56	.575
Alcohol (g/day)									17.2 (20.9) [8.6] {1.9 to 25.4}	22.4 (22.2) [16.5] {4.4 to 34.4}	-3.06	.002
Magnesium (mg/day)									313.8 (157.4) [284.8] {213.6 to 380.5}	332.3 (147.8) [305.3] {233.7 to 389.7}	-1.82	.068
Phosphorus (mg/day)									1828.6 (1040.6) [1623.8] {1259.4 to 2117.8}	1907.8 (827.6) [1748.4] {1392.4 to 2294.0}	-1.88	.060
Potassium (mg/day)									3141.7 (1525.5) [2865.2] {2187.3 to 3714.7}	3269.8 (1380.1) [3007.0] {2330.0 to 3833.3}	-1.33	.185
Zinc (mg/day)									15.5 (11.9) [13.1] {10.6 to 17.0}	16.3 (8.5) [14.1] {11.0 to 19.9}	-2.09	.037

	13 years old				17 years old				20 years old			
	LMC	**Not LMC**	**Z**	**P**	**LMC**	**Not LMC**	**Z**	**P**	**LMC**	**Not LMC**	**Z**	**P**
	M (SD) [Md] {IQR}	**M (SD) [Md] {IQR}**			**M (SD) [Md] {IQR}**	**M (SD) [Md] {IQR}**			**M (SD) [Md] {IQR}**	**M (SD) [Md] {IQR}**		
Physical fitness												
Pedometer												
Weekday (Steps/day)					11194.6 (3639.4) [11065.8] {8474.5 to 14101.1}	10941.3 (7409.3) [10058.3] {7741.7 to 12999.9}	-1.36	.175				
Weekend (Steps/day)					9213.1 (3819.4) [8937.0] {5798.0 to 12307.0}	10372.3 (6231.2) [9305.0] {5950.5 to 13016.5}	-0.53	.595				
Total (Steps/day)					10336.1 (3134.0) [10344.6] {8335.3 to 13000.8}	10337.8 (4061.4) [10121.4] {8130.1 to 11860.0}	-0.53	.599				
IPAQ scores												
IPAQ total score (METS/wk)					5008.5 (4776.5) [3745.0] {1305.8 to 7100.0}	5047.7 (4494.8) [3805.5] {1906.0 to 6418.5}	-0.64	.524	4709.9 (4826.7) [3210.0] {1095.0 to 7572.0}	4713.0 (4358.4) [3493.0] {1200.0 to 7200.0}	-0.46	.646

	13 years old				17 years old				20 years old			
	LMC	**Not LMC**	**Z**	**P**	**LMC**	**Not LMC**	**Z**	**P**	**LMC**	**Not LMC**	**Z**	**P**
	M (SD) [Md] {IQR}	**M (SD) [Md] {IQR}**			**M (SD) [Md] {IQR}**	**M (SD) [Md] {IQR}**			**M (SD) [Md] {IQR}**	**M (SD) [Md] {IQR}**		
Loading score (ELR/wk)					230.3 (220.8) [152.3] {42.9 to 379.5}	237.5 (173.1) [221.1] {96.5 to 346.2}	1.23	.217	208.5 (144.2) [208.7] {71.0 to 318.1}	213.4 (138.9) [207.9] {91.3 to 344.1}	-0.35	.725
Sedentary behaviour (minutes/day)					1730.5 (369.9) [1710.0] {1470.0 to 2010.0}	1810.7 (313.0) [1800.0] {1590.0 to 2040.0}	-1.95	.052				
Australian Fitness Education Award												
Curl ups (n)	19.5 (16.1) [17.0] {8.0 to 27.0}	29.6 (19.1) [24.0] {15.0 to 44.8}	-5.65	<.001	22.6 (16.4) [20.0] {11.3 to 30.0}	30.5 (18.5) [28.0] {17.0 to 43.0}	-4.06	<.001				
Sit and reach distance (cm)	17.5 (8.6) [17.5] {13.0 to 23.0}	21.4 (7.5) [21.0] {16.0 to 26.1}	-4.57	<.001	18.1 (10.2) [17.5] {13.0 to 24.5}	21.7 (10.3) [22.0] {15.1 to 28.0}	-3.56	<.001				
Basketball throw distance (m)	5.3 (1.0) [5.3] {4.6 to 5.9}	5.9 (0.9) [5.9] {5.3 to 6.5}	-4.83	<.001	6.6 (1.1) [6.6] {5.9 to 7.4}	7.3 (1.1) [7.2] {6.5 to 8.0}	-6.34	<.001				
Physical work capacity	119.7 (29.1) [115.2] {98.4 to 136.6}	126.7 (33.0) [120.3] {104.8 to 147.8}	-2.13	.034	148.8 (39.1) [147.8] {115.2 to 171.4}	155.9 (42.7) [152.3] {126.8 to 185.2}	-1.38	.167				

	%	%	X^2	P	%	%	X^2	P	%	%	X^2	P
Performed moderate activity for leisure									37.1	46.5	2.77	.096
Performed vigorous activity for leisure									47.6	37.2	7.40	.007
Sports club membership	20.0	32.4	4.08	.043								
Exercise club membership	10.7	15.9	1.23	.267								
Outdoor recreation club membership	10.7	10.6	0.00	.993								

Table A3

Participant Characteristics Including Physical Activity Factors for Females Only

	13 years old				17 years old				20 years old			
	LMC M (SD) [Md] {IQR}	Not LMC M (SD) [Md] {IQR}	Z	P	LMC M (SD) [Md] {IQR}	Not LMC M (SD) [Md] {IQR}	Z	P	LMC M (SD) [Md] {IQR}	Not LMC M (SD) [Md] {IQR}	Z	P
Waist girth (cm)	76.4 (10.2) [74.4] {69.4 to 79.5}	72.7 (8.5) [71.2] {66.5 to 76.3}	-3.41	.001	78.0 (12.0) [77.3] {69.4 to 84.4}	76.5 (9.6) [74.3] {69.6 to 81.2}	-1.12	.263	78.9 (13.1) [76.1] {69.9 to 86.3}	75.5 (11.0) [73.0] {68.0 to 80.0}	-2.41	.016
Height (cm)	162.9 (6.1) [163.0] {159.0 to 167.0}	162.5 (6.0) [162.0] {159.0 to 166.0}	-0.84	.401	165.9 (6.7) [166.5] {161.5 to 170.2}	166.5 (6.1) [166.2] {162.3 to 170.5}	-2.41	.016	165.8 (6.4) [166.5] {161.0 to 170.0}	166.0 (6.3) [166.0] {161.7 to 170.0}	-0.09	.925
BMI	22.0 (4.3) [21.3] {18.9 to 23.8}	20.9 (3.5) [20.3] {18.6 to 22.5}	-2.17	.030	23.3 (4.9) [22.4] {20.0 to 25.2}	22.6 (3.8) [21.7] {20.0 to 24.2}	-0.90	.366	24.8 (5.5) [23.4] {21.1 to 27.7}	23.7 (4.7) [22.6] {20.7 to 25.4}	-1.72	.086
Vitamin levels												
Deseasonalised 25(OH)D3 (nmol/L)					72.6 (27.8) [70.3] {54.3 to 87.6}	75.6 (23.7) [73.9] {58.7 to 89.1}	-1.22	.221	74.2 (28.5) [67.4] {56.5 to 85.0}	75.8 (24.1) [72.5] {58.9 to 90.9}	-1.45	.147

	13 years old				17 years old				20 years old			
	LMC M (SD) [Md] {IQR}	Not LMC M (SD) [Md] {IQR}	Z	P	LMC M (SD) [Md] {IQR}	Not LMC M (SD) [Md] {IQR}	Z	P	LMC M (SD) [Md] {IQR}	Not LMC M (SD) [Md] {IQR}	Z	P
Dietary intake												
Protein (g/day)									90.3 (79.8) [77.2] {56.8 to 97.8}	81.6 (46.3) [73.4] {57.1 to 97.4}	-0.34	.735
Calcium (mg/day)									853.6 (464.5) [759.5] {589.2 to 916.2}	812.8 (365.6) [775.3] {577.5 to 993.8}	-0.11	.914
Alcohol (g/day)									13.1 (17.9) [5.1] {1.2 to 17.7}	12.9 (13.7) [8.1] {3.3 to 18.6}	-1.85	.064
Magnesium (mg/day)									255.3 (178.1) [225.1] {178.2 to 274.5}	244.1 (105.4) [226.5] {177.8 to 293.2}	-0.77	.509
Phosphorus (mg/day)									1458.1 (1113.9) [1222.1] {989.3 to 1575.3}	1361.9 (661.0) [1283.2] {999.8 to 1620.2}	-0.32	.751
Potassium (mg/day)									2562.6 (1562.0) [2270.0] {1838.2 to 2859.4}	2437.7 (969.5) [2326.6] {1842.8 to 2872.7}	-0.42	.676
Zinc (mg/day)									11.7 (11.0) [9.8] {7.2 to 12.2}	10.5 (5.7) [9.6] {7.4 to 12.7}	-0.01	.993

	13 years old				17 years old				20 years old			
	LMC M (SD) [Md] {IQR}	Not LMC M (SD) [Md] {IQR}	Z	P	LMC M (SD) [Md] {IQR}	Not LMC M (SD) [Md] {IQR}	Z	P	LMC M (SD) [Md] {IQR}	Not LMC M (SD) [Md] {IQR}	Z	P
Physical fitness												
Pedometer												
Weekday (Steps/day)					8935.3 (3154.5) [8603.1] {6795.2 to 10484.8}	9498.4 (4013.0) [8934.6] {6603.3 to 11217.4}	-0.69	.494				
Weekend (Steps/day)					7640.8 (4318.5) [6785.3] {4711.0 to 9759.4}	8459.7 (3726.0) [8596.5] {5724.6 to 10760.1}	-1.53	.126				
Total (Steps/day)					8555.3 (3137.8) [8275.7] {6500.9 to 9945.6}	9309.9 (4066.8) [9099.0] {6892.8 to 10825.6}	-1.12	.262				
IPAQ scores												
Walking (min/day)									80.7 (69.1) [60.0] {20.0 to 180.0}	73.0 (60.2) [60.0] {30.0 to 120.0}	-0.26	.797
Moderate activity (min/day)									34.2 (52.2) [0.0] {0.0 to 60.0}	44.4 (54.9) [30.0] {0.0 to 60.0}	-2.10	.036

	13 years old				17 years old				20 years old			
	LMC M (SD) [Md] {IQR}	Not LMC M (SD) [Md] {IQR}	Z	P	LMC M (SD) [Md] {IQR}	Not LMC M (SD) [Md] {IQR}	Z	P	LMC M (SD) [Md] {IQR}	Not LMC M (SD) [Md] {IQR}	Z	P
Vigorous activity (min/day)									31.1 (45.3) [0.0] {0.0 to 60.0}	45.2 (50.7) [40.0] {0.0 to 60.0}	-2.66	.008
IPAQ total score (METS/wk)					3232.5 (3671.5) [1566.0] {788.0 to 4302.8}	3499.4 (3222.3) [2481.9] {1407.4 to 4744.5}	-2.35	.019	2019.6 (2525.9) [1157.0] {240.0 to 2792.3}	2691.8 (2450.8) [2131.5] {789.0 to 4051.5}	-3.17	.002
Loading score (ELR/wk)					145.4 (160.9) [76.5] {29.2 to 225.8}	162.0 (154.8) [112.2] {42.8 to 235.6}	-1.48	.140	96.6 (107.5) [56.1] {2.4 to 180.2}	132.2 (116.4) [111.5] {29.2 to 207.6}	-3.04	.002
Sedentary behaviour (minutes/day)					1842.2 (397.4) [1860.0] {1605.0 to 2100.0}	1830.7 (419.3) [1800.0] {1620.0 to 2040.0}	-0.72	.471				
Australian Fitness Education Award												
Curl ups (n)	14.0 (13.8) [11.0] {3.8 to 20.0}	19.7 (15.3) [17.0] {10.0 to 25.0}	-3.79	<.001	10.8 (12.6) [9.0] {0.0 to 17.0}	16.7 (13.8) [15.0] {5.0 to 24.0}	-3.92	<.001				
Sit and reach distance (cm)	24.6 (8.8) [25.0] {17.3 to 31.0}	28.0 (8.6) [28.0] {22.0 to 34.0}	-3.41	.001	23.0 (9.6) [23.5] {16.0 to 31.0}	28.2 (9.2) [29.5] {22.0 to 34.5}	-4.42	<.001				

	13 years old				17 years old				20 years old			
	LMC M (SD) [Md] {IQR}	Not LMC M (SD) [Md] {IQR}	Z	P	LMC M (SD) [Md] {IQR}	Not LMC M (SD) [Md] {IQR}	Z	P	LMC M (SD) [Md] {IQR}	Not LMC M (SD) [Md] {IQR}	Z	P
Basketball throw distance (m)	4.6 (0.6) [4.6] {4.2 to 4.9}	4.8 (0.6) [4.8] {4.4 to 5.2}	-3.59	<.001	4.8 (0.8) [4.8] {4.2 to 5.3}	5.2 (0.8) [5.1] {4.7 to 5.6}	-4.07	<.001				
Physical work capacity	93.7 (15.5) [93.5] {85.5 to 102.1}	98.1 (18.3) [97.2] {87.0 to 108.8}	-2.11	.035	95.8 (24.5) [89.2] {78.8 to 107.3}	101.9 (24.5) [97.2] {87.0 to 108.8}	-2.39	.017				

	%	%	X^2	P	%	%	X^2	P	%	%	X^2	P
Performed moderate activity for leisure									29.1	37.8	2.19	.139
Performed vigorous activity for leisure									36.0	45.0	2.21	.138
Sports club membership	23.1	28.2	0.54	.462								
Exercise club membership	17.3	15.1	0.16	.688								
Outdoor recreation club membership	19.2	15.1	0.54	.461								

Supp 6B Young Adult Study: General Linear Model

Table B1

General Linear Models Accounting for LMC Status and Loading Score

			95% Confidence interval		
	β	**S.E.**	**Lower**	**Upper**	**p**
Total BMD (Ln)					
Intercept	-0.46682	0.15089	-0.76256	-0.17109	.002
LMC	-0.02042	0.0074	-0.03494	-0.00591	**.006**
Sex	0.08971	0.0065	0.07703	0.10239	<.001
BMI	0.01150	0.00089	0.00976	0.01324	<.001
Age	0.00872	0.00747	-0.00592	0.02337	.243
Loading score	0.00007	0.00002	0.00003	0.00011	**.001**
Vitamin D	0.00046	0.00013	0.00020	0.00072	.001
Head BMD (Ln)					
Intercept	0.08438	0.20850	-0.32427	0.49303	.686
LMC	0.00508	0.01014	-0.01480	0.02496	.617
Sex	0.01505	0.00896	-0.00250	0.03261	.093
BMI	0.00574	0.00100	0.00379	0.00770	<.001
Age	0.01668	0.01035	-0.00361	0.03697	.107
Loading score	-0.00003	0.00003	-0.00008	0.00003	.306
Vitamin D	0.00021	0.00019	-0.00016	0.00058	.257
Pelvis BMD (Ln)					
Intercept	-0.39126	0.19062	-0.76487	-0.01765	.040
LMC	-0.02097	0.00905	-0.03871	-0.00323	**.020**
Sex	0.12401	0.00799	0.10834	0.13968	<.001
BMI	0.01529	0.00092	0.01350	0.01709	<.001
Age	0.00163	0.00942	-0.01683	0.02009	.863
Loading score	0.00010	0.00003	0.00005	0.00015	**<.001**
Vitamin D	0.00078	0.00017	0.00045	0.00111	<.001
Nonpreferred leg BMD (Ln)					
Intercept	-0.41713	0.16698	-0.74445	-0.08983	.012
LMC	-0.02879	0.00813	-0.04472	-0.01286	**<.001**
Sex	0.10415	0.00723	0.08998	0.11831	<.001
BMI	0.01200	0.00081	0.01041	0.01360	<.001
Age	0.00922	0.00828	-0.00700	0.02545	.265
Loading score	0.00007	0.00002	0.00003	0.00012	**.001**
Vitamin D	0.00052	0.00015	0.00023	0.00082	.001

	β	S.E.	95% Confidence interval Lower	Upper	p
Preferred leg BMD (Ln)					
Intercept	-0.36946	0.16520	-0.69324	-0.04568	.025
LMC	-0.02515	0.00808	-0.04098	-0.00932	**.002**
Sex	0.10298	0.00715	0.08897	0.11699	<.001
BMI	0.01144	0.00081	0.00986	0.01302	<.001
Age	0.00776	0.00819	-0.00829	0.02381	.343
Loading score	0.00007	0.00002	0.00026	0.00012	.002
Vitamin D	0.00046	0.00015	0.00017	0.00075	.002
Non-preferred arm BMD (Ln)					
Intercept	-0.83142	0.18411	-1.11923	-0.47056	<.001
LMC	-0.02345	0.00884	-0.04078	-0.00612	**.008**
Sex	0.07688	0.00776	0.06167	0.09209	<.001
BMI	0.01190	0.00098	0.00998	0.01381	<.001
Age	0.01077	0.00912	-0.00711	0.02864	.238
Loading score	0.00006	0.00002	0.00002	0.00011	**.010**
Vitamin D	0.00047	0.00016	0.00015	0.00079	.004
Preferred arm BMD (Ln)					
Intercept	-0.86180	0.18665	-1.18379	-0.45212	<.001
LMC	-0.03655	0.00901	-0.05421	-0.01890	**<.001**
Sex	0.08581	0.00792	0.07258	0.10363	<.001
BMI	0.01304	0.00101	0.01105	0.01502	<.001
Age	0.00908	0.00923	-0.00901	0.02717	.325
Loading score	0.00011	0.00003	0.00006	0.00016	**<.001**
Vitamin D	0.00049	0.00017	0.00016	0.00081	.003

Note. β beta coefficient; S.E. standard error; p p-value; LMC Low motor competence

Table B2

Simple General Linear Accounting Only for LMC Status

	β	S.E.	95% Confidence interval Lower	Upper	p
Total BMD (Ln)					
Intercept	-0.46201	0.12000	-0.69721	-0.22681	<.001
LMC	-0.02544	0.00607	-0.03735	-0.01354	**<.001**
Sex	0.09049	0.00528	0.08014	0.10084	<.001
BMI	0.01159	0.00073	0.01016	0.01303	<.001
Age	0.01051	0.00596	-0.00115	0.02217	.077
Head BMD (Ln)					
Intercept	0.23326	0.15974	-0.07981	0.54634	.144
LMC	-0.00341	0.00817	-0.01943	0.01261	.676
Sex	0.00082	0.00722	-0.01334	0.01497	.910
BMI	0.00559	0.00079	0.00403	0.00714	<.001
Age	0.01042	0.00797	-0.00520	0.02604	.191
Pelvis BMD (Ln)					
Intercept	-0.43468	0.15149	-0.73160	-0.13776	.004
LMC	-0.02593	0.00757	-0.04076	-0.01109	**.001**
Sex	0.11979	0.00670	0.10666	0.13291	<.001
BMI	0.01458	0.00077	0.01307	0.01609	<.001
Age	0.00816	0.00751	-0.00657	0.02289	.278
Nonpreferred leg BMD (Ln)					
Intercept	-0.50261	0.13072	-0.75882	-0.24640	<.001
LMC	-0.02613	0.00664	-0.03915	-0.01311	**<.001**
Sex	0.10638	0.00586	0.09490	0.11785	<.001
BMI	0.01155	0.00067	0.01024	0.01285	<.001
Age	0.01629	0.00651	0.00354	0.02904	.012
Preferred leg BMD (Ln)					
Intercept	-0.35323	0.13361	-0.61511	-0.09136	.025
LMC	-0.03165	0.00679	-0.04496	-0.01835	**<.001**
Sex	0.10372	0.00598	0.09154	0.11500	<.001
BMI	0.01124	0.00068	0.00991	0.01258	<.001
Age	0.00925	0.00665	-0.00379	0.02228	.164

	β	S.E.	95% Confidence interval Lower	Upper	p
Non-preferred arm BMD (Ln)					
Intercept	-0.77036	0.14751	-1.05948	-0.48124	<.001
LMC	-0.02820	0.00746	-0.04281	-0.01359	**<.001**
Sex	0.07615	0.00652	0.06336	0.08893	<.001
BMI	0.01190	0.00098	0.00998	0.01381	<.001
Age	0.01228	0.00082	0.01067	0.01389	<.001
Preferred arm BMD (Ln)					
Intercept	-0.90588	0.15221	-1.20420	-0.60756	<.001
LMC	-0.03922	0.00763	-0.05419	-0.02426	**<.001**
Sex	0.09504	0.00673	0.08185	0.10822	<.001
BMI	0.01347	0.00089	0.01174	0.01521	<.001
Age	0.01541	0.00754	0.00064	0.03018	.041

Note. β beta coefficient; S.E. standard error; p p-value; LMC Low motor competence

Table B3

General Linear Model Accounting for LMC Status, Loading Score, and Lean Mass

	Beta	S.E.	95% Confidence interval Lower	Upper	p
Total BMD (Ln)					
Intercept	-0.48233	0.12992	-0.73698	-0.22769	<.001
LMC	-0.00402	0.00648	-0.01672	0.00867	.534
Sex	-0.04721	0.01103	-0.06882	-0.02559	<.001
BMI	0.00581	0.0086	0.00412	0.00750	<.001
Age	0.00458	0.00644	-0.00804	0.01720	.477
Loading score	0.00003	0.00002	-0.00000	0.00007	.077
Vitamin D	0.00002	0.00012	-0.00022	0.00025	.893
Lean mass	0.00001	0.00001	0.00001	0.00001	<.001

			95% Confidence interval		
	Beta	**S.E.**	**Lower**	**Upper**	**p**
Head BMD (Ln)					
Intercept	0.12841	0.20320	-0.26985	0.52667	.527
LMC	0.01302	0.01000	-0.00658	0.03262	.193
Sex	-0.04870	0.01340	-0.07495	-0.02244	<.001
BMI	0.00738	0.00100	0.00541	0.00935	<.001
Age	0.00573	0.01023	-0.01432	0.02577	.576
Loading score	-0.00005	0.00003	-0.00010	0.00001	.098
Vitamin D	0.00001	0.00019	-0.00030	0.00043	.716
Lean mass	0.00006	0.00001	0.00004	0.00008	<.001
Pelvis BMD (Ln)					
Intercept	-0.42943	0.17886	-0.77998	-0.07888	.016
LMC	-0.01018	0.00856	-0.02696	0.00660	.234
Sex	0.03410	0.01190	0.01077	0.05743	.004
BMI	0.00985	0.00103	0.00784	0.01186	<.001
Age	-0.00064	0.00884	-0.01797	0.01668	.942
Loading score	0.00007	0.00002	0.00002	0.00011	**.005**
Vitamin D	0.00049	0.00016	0.00017	0.00080	.002
Lean mass	0.00004	0.00000	0.00003	0.00004	<.001
Non-preferred leg BMD (Ln)					
Intercept	-0.46248	0.14929	-0.75509	-0.16988	.002
LMC	-0.01451	0.00737	-0.02896	-0.00006	**.049**
Sex	-0.00002	0.01036	-0.02032	0.02027	.998
BMI	0.00544	0.00089	0.00370	0.00718	<.001
Age	0.00760	0.00740	-0.00690	0.02210	.304
Loading score	0.00005	0.00002	0.00001	0.00009	**.013**
Vitamin D	0.00014	0.00014	-0.00013	0.00041	.319
Lean mass	0.00003	0.00000	0.00003	0.00004	<.001

			95% Confidence interval		
	Beta	**S.E.**	**Lower**	**Upper**	**p**
Preferred leg BMD (Ln)					
Intercept	-0.34244	0.14764	-0.63180	-0.05308	.020
LMC	-0.01414	0.00727	-0.02839	0.00010	.052
Sex	-0.00041	0.01026	-0.02052	0.01971	.968
BMI	0.00451	0.00090	0.00275	0.00627	<.001
Age	0.00318	0.00732	-0.01118	0.01753	.665
Loading score	0.00005	0.00002	0.00001	0.00009	**.020**
Vitamin D	0.00008	0.00014	-0.00018	0.00035	.547
Lean mass	0.00004	0.00000	0.00003	0.00004	<.001
Non-preferred arm BMD (Ln)					
Intercept	-0.71131	0.17150	-1.04745	-0.37517	<.001
LMC	-0.00825	0.00835	-0.02462	0.00811	.323
Sex	-0.04506	0.01385	-0.07220	-0.01791	.001
BMI	0.00816	0.00098	0.00624	0.1007	<.001
Age	0.00369	0.00850	-0.01298	0.02036	.664
Loading score	0.00004	0.00002	0.00001	0.00008	.108
Vitamin D	0.00009	0.00015	-0.00021	0.00039	.568
Lean mass	0.00007	0.00001	0.00006	0.00008	<.001
Preferred arm BMD (Ln)					
Intercept	-0.74460	0.17071	-1.107918	-0.41002	<.001
LMC	-0.02019	0.00836	-0.03657	-0.00380	**.016**
Sex	-0.04944	0.01424	-0.07734	-0.02154	.001
BMI	0.00873	0.00100	0.00677	0.01070	<.001
Age	0.00426	0.00845	-0.01229	0.02082	.614
Loading score	0.00007	0.00002	0.00003	0.00012	**.002**
Vitamin D	0.00012	0.00015	-0.00018	0.00042	.444
Lean mass	0.00008	0.00001	0.00007	0.00010	<.001

Note. β beta coefficient; S.E. standard error; p p-value; LMC low motor competence

Table B4

General Linear Model Accounting for LMC Status, Loading Score, and Puberty Category

	β	S.E.	95% Confidence interval Lower	Upper	p
Total BMD (Ln)					
Intercept	-0.42038	0.15340	-0.721033	-0.1193	.006
LMC	-0.01872	0.00754	-0.03349	-0.00395	**.013**
Sex	0.08921	0.00706	0.07537	0.10306	<.001
BMI	0.01142	0.00091	0.00964	0.01319	<.001
Age	0.00670	0.00761	-0.00821	0.02162	.379
Loading	0.00007	0.00002	0.00003	0.00011	.001
Vitamin D	0.00043	0.00013	0.00017	0.00069	.001
Puberty category 3	-0.05218	0.02109	-0.09352	-0.01084	.013
Puberty category 4	-0.00239	0.00766	-0.01740	-0.01262	.755
Head BMD (Ln)					
Intercept	0.11855	0.21363	-0.30015	0.53726	.579
LMC	0.00268	0.01046	-0.01782	0.02317	.798
Sex	0.01078	0.00997	-0.00877	0.03033	.280
BMI	0.00552	0.00103	0.00351	0.00753	<.001
Age	0.01592	0.01064	-0.00493	0.03677	.134
Loading	-0.00003	0.00003	-0.00009	0.00003	.289
Vitamin D	0.00016	0.00019	-0.00021	0.00054	.389
Puberty category 3	-0.05942	0.03091	-0.12000	0.00116	.055
Puberty category 4	-0.01835	0.01092	-0.03975	0.00305	.093
Pelvis BMD (Ln)					
Intercept	-0.27817	0.19365	-0.65772	0.10139	.151
LMC	-0.02000	0.00924	-0.03812	-0.00189	**.030**
Sex	0.12524	0.00881	0.10797	0.14251	<.001
BMI	0.01499	0.00094	0.01315	0.01682	<.001
Age	-0.00367	0.00959	-0.02246	0.01512	.702
Loading score	0.00010	0.00003	0.00005	0.00015	**<.001**
Vitamin D	0.00077	0.00017	0.00044	0.00110	<.001
Puberty category 3	-0.05986	0.02726	-0.11329	-0.00643	.028
Puberty category 4	0.00288	0.00969	-0.01611	0.02188	.766

	β	S.E.	95% Confidence interval Lower	Upper	p
Nonpreferred leg BMD (Ln)					
Intercept	-0.37358	0.17052	-0.70779	-0.03937	.028
LMC	-0.02529	0.00839	-0.04173	-0.00885	**.003**
Sex	0.10582	0.00800	0.09014	0.12150	<.001
BMI	0.01175	0.00083	0.01012	0.01338	<.001
Age	0.00740	0.00847	-0.00919	0.02400	.382
Loading score	0.00007	0.00002	0.00003	0.00012	**.002**
Vitamin D	0.00050	0.00015	0.00020	0.00080	.001
Puberty category 3	-0.06544	0.02413	-0.11273	-0.01814	.007
Puberty category 4	0.00093	0.00865	-0.01603	0.01789	.914
Preferred leg BMD (Ln)					
Intercept	-0.29706	0.16903	-0.62836	0.03423	.079
LMC	-0.02317	0.00832	-0.03947	-0.00687	**.005**
Sex	0.10503	0.00793	0.08949	0.12058	<.001
BMI	0.01111	0.00082	0.00950	0.01273	<.001
Age	0.00455	0.00839	-0.01190	0.02100	.588
Loading score	0.00007	0.00002	0.00002	0.00011	**.004**
Vitamin D	0.00045	0.00015	0.00015	0.00075	.003
Puberty category 3	-0.06264	0.02392	-0.10952	-0.01575	.009
Puberty category 4	0.00172	0.00858	-0.01510	0.01853	.841
Non-preferred arm BMD (Ln)					
Intercept	-0.76967	0.18967	-1.14151	-0.39804	<.001
LMC	-0.02259	0.00911	-0.04045	-0.00473	**.013**
Sex	0.07995	0.00863	0.06303	0.09686	<.001
BMI	0.01165	0.00100	0.00968	0.01361	<.001
Age	0.00794	0.00941	-0.01050	0.02638	.399
Loading score	0.00006	0.00003	0.00001	0.00011	**.027**
Vitamin D	0.00046	0.00016	0.00014	0.00078	.005
Puberty category 3	-0.06413	0.02639	-0.11585	-0.01240	.015
Puberty category 4	0.00619	0.00947	-0.01237	0.02476	.513

	β	S.E.	95% Confidence interval Lower	Upper	p
Preferred arm BMD (Ln)					
Intercept	-0.81302	0.19306	-1.19141	-0.43462	<.001
LMC	-0.03588	0.00933	-0.05417	-0.01758	**<.001**
Sex	0.08979	0.00886	0.07242	0.10716	<.001
BMI	0.01287	0.00105	0.01082	0.01492	<.001
Age	0.00900	0.00957	-0.00974	0.02775	.347
Loading score	0.00010	0.00003	0.00005	0.00016	**<.001**
Vitamin D	0.00048	0.00017	0.00015	0.00081	.005
Puberty category 3	-0.03668	0.02738	-0.09034	0.01698	.180
Puberty category 4	0.00516	0.00971	-0.01386	0.02419	.595

Note. β beta coefficient; S.E. standard error; p p-value; LMC Low motor competence

Table B5

General Linear Model Including LMC Status, Loading Score, and LMC by Sex Interaction Effect

	β	S.E.	95% Confidence interval Lower	Upper	p
Total BMD (Ln)					
Intercept	-0.47211	0.15054	-0.76717	-0.17706	.002
LMC	-0.00628	0.01102	-0.02787	0.01531	.569
Sex	0.09538	0.00724	0.08120	0.10957	<.001
BMI	0.01142	0.00089	0.00968	0.01316	<.001
Age	0.00897	0.00745	-0.00564	0.02357	.229
Loading score	0.00007	0.00002	0.00003	0.00011	**.001**
Vitamin D	0.00045	0.00013	0.00019	0.00071	.001
LMC by sex	-0.02564	0.01482	-0.05467	0.00340	.084
Head BMD (Ln)					
Intercept	0.08399	0.20849	-0.32464	0.49262	.687
LMC	0.00162	0.01520	-0.02817	0.03141	.915
Sex	0.01358	0.01017	-0.00634	0.03351	.181
BMI	0.00576	0.00100	0.00380	0.00772	<.001
Age	0.01671	0.01035	-0.00358	0.03700	.107
Loading score	-0.00003	0.00003	-0.00009	0.00003	.303
Vitamin D	0.00021	0.00019	-0.00015	0.00058	.253
LMC by sex	0.00620	0.02028	-0.03356	0.04595	.760

	β	S.E.	95% Confidence interval Lower	Upper	p
Pelvis BMD (Ln)					
Intercept	-0.39414	0.19025	-0.76703	-0.02126	.038
LMC	-0.00417	0.01356	-0.3074	0.02240	.758
Sex	0.13109	0.00904	0.11336	0.14881	<.001
BMI	0.01522	0.00091	0.01343	0.01702	<.001
Age	0.00170	0.00940	-0.01673	0.02012	.857
Loading score	0.00010	0.00003	0.00005	0.00015	**<.001**
Vitamin D	0.00077	0.00017	0.00044	.00110	<.001
LMC by sex	-0.03002	0.01807	-0.06543	0.00539	.097
Nonpreferred leg BMD (Ln)					
Intercept	-0.41894	0.16618	-0.74465	-0.09323	.012
LMC	-0.00572	0.01194	-0.02912	0.01767	.632
Sex	0.11400	0.00817	0.09799	0.13001	<.001
BMI	0.01186	0.00081	0.01027	0.01345	<.001
Age	0.00926	0.00824	-0.00688	0.02540	.261
Loading score	0.00008	0.00002	0.00003	0.00012	**.001**
Vitamin D	0.00514	0.00150	0.00022	0.00807	.001
LMC by sex	-0.04119	0.01617	-0.07289	0.00949	**.011**
Preferred leg BMD (Ln)					
Intercept	-0.37101	0.16458	-0.69359	-0.04844	.024
LMC	-0.00591	0.01182	-0.02908	0.01726	.617
Sex	0.11149	0.00809	0.09564	0.12734	<.001
BMI	0.01132	0.00080	0.00975	0.01290	<.001
Age	0.00779	0.00816	-0.00820	0.02378	.339
Loading score	0.00007	0.00002	0.00003	0.00012	**.002**
Vitamin D	0.00045	0.00015	0.00016	0.00074	.002
LMC by sex	-0.03558	0.01602	-0.06697	-0.00418	**.026**

	β	S.E.	95% Confidence interval Lower	Upper	p
Nonpreferred arm BMD (Ln)					
Intercept	-0.83789	0.18402	-1.19856	-0.47723	<.001
LMC	-0.02178	0.01471	-0.05060	0.00705	.139
Sex	0.08062	0.00879	0.05340	0.09785	<.001
BMI	0.01189	0.00097	0.00998	0.01380	<.001
Age	0.01110	0.00912	-0.00676	0.02897	.223
Loading score	0.00005	0.00003	-0.00001	0.00011	.091
Vitamin D	0.00047	0.00016	0.00016	0.00079	.003
LMC by sex	-0.01578	0.01814	-0.05133	-0.01976	.384
Preferred arm BMD (Ln)					
Intercept	-0.81803	0.18665	-1.18385	-0.45220	<.001
LMC	-0.03841	0.01353	-0.06492	-0.01190	**.005**
Sex	0.08734	0.00894	0.06981	0.10486	<.001
BMI	0.01305	0.00101	0.01106	0.01503	<.001
Age	0.00909	0.00923	-0.00900	0.02718	.325
Loading score	0.00011	0.00003	0.00006	0.00016	**<.001**
Vitamin D	0.00048	0.00017	0.00016	0.00081	.003
LMC by sex	0.00333	0.01806	-0.03207	0.03872	.854

Note. β beta coefficient; S.E. standard error; p p-value; LMC Low motor competence

Table B6

General Linear Model Accounting for LMC Status and Sedentary Behaviour

	β	S.E.	95% Confidence interval Lower	Upper	p
Total BMD (Ln)					
Intercept	-0.47243	0.15382	-0.77392	-0.17095	.002
LMC	-0.02044	0.00748	-0.03510	-0.00578	**.006**
Sex	0.09474	0.00637	0.08226	0.10722	<.001
BMI	0.01166	0.00090	0.00990	0.01342	<.001
Age	0.00904	0.00757	-0.00580	0.02389	.232
Sedentary behaviour	-0.00000	0.00001	-0.00002	0.00001	.787
Vitamin D	0.00057	0.00013	0.00031	0.00082	<.001

	β	S.E.	95% Confidence interval Lower	Upper	p
Head BMD (Ln)					
Intercept	0.07925	0.21085	-0.33400	0.49250	.707
LMC	0.00712	0.01020	-0.01288	0.02712	.485
Sex	0.01331	0.00881	-0.00396	0.03057	.131
BMI	0.00568	0.00101	0.00369	0.00767	<.001
Age	0.01574	0.01043	-0.00471	0.03619	.131
Sedentary behaviour	0.00001	0.00001	-0.00001	0.00003	.318
Vitamin D	0.00022	0.00019	-0.00014	0.00058	.235
Pelvis BMD (Ln)					
Intercept	-0.41317	0.19433	-0.79406	-0.03229	.033
LMC	-0.02026	0.00917	-0.03823	-0.00228	**.027**
Sex	0.13131	0.00792	0.11578	0.14684	<.001
BMI	0.01545	0.00094	0.01361	0.01729	<.001
Age	0.00204	0.00957	-0.01670	0.02079	.831
Sedentary behaviour	0.00005	0.00001	-0.00002	0.00003	.641
Vitamin D	0.00094	0.00017	0.00062	0.00127	<.001
Non-preferred leg BMD (Ln)					
Intercept	-0.43563	0.16991	-0.76864	-0.10262	.010
LMC	-0.02805	0.00824	-0.04420	-0.01191	**.001**
Sex	0.10932	0.00712	0.09537	0.12326	<.001
BMI	0.01214	0.00083	0.01051	0.01377	<.001
Age	0.01012	0.00837	-0.00628	0.02653	.227
Sedentary behaviour	-0.00000	0.00001	-0.00002	0.00002	.931
Vitamin D	0.00063	0.00015	0.00034	0.00092	<.001
Preferred leg BMD (Ln)					
Intercept	-0.39149	0.16775	-0.72028	-0.06270	.020
LMC	-0.02531	0.00814	-0.04126	-0.00937	**.002**
Sex	0.10841	0.00703	0.09464	0.12218	<.001
BMI	0.01172	0.00082	0.01011	0.01333	<.001
Age	0.00844	0.00827	-0.00776	0.02465	.307
Sedentary behaviour	0.00000	0.00001	-0.00002	0.00002	.860
Vitamin D	0.00056	0.00015	0.00027	0.00085	<.001

			95% Confidence interval		
	β	**S.E.**	**Lower**	**Upper**	**p**
Non-preferred arm BMD (Ln)					
Intercept	-0.84502	0.18642	-1.21040	-0.47963	<.001
LMC	-0.02322	0.00890	-0.04065	-0.05778	**<.001**
Sex	0.08103	0.00763	0.06607	0.09598	<.001
BMI	0.01205	0.00098	0.01012	0.01397	<.001
Age	0.01130	0.00920	-0.00673	0.02933	.219
Sedentary behaviour	-0.00000	0.00001	-0.00002	0.00002	.989
Vitamin D	0.00057	0.00016	0.00026	0.00088	<.001
Preferred arm BMD (Ln)					
Intercept	-0.84288	0.19075	-1.21675	-0.46901	<.001
LMC	-0.03759	0.00915	-0.05552	-0.01966	**<.001**
Sex	0.09512	0.00786	0.07972	0.11052	<.001
BMI	0.01334	0.00105	0.01129	0.01538	<.001
Age	0.01166	0.00939	-0.00674	0.03006	.214
Sedentary behaviour	-0.00002	0.00001	-0.00004	0.00000	.123
Vitamin D	0.00061	0.00016	0.00028	0.00093	<.001

Note. β beta coefficient; S.E. standard error; p p-value; LMC low motor competence

Table B7

General Linear Model Accounting for LMC Status, Sedentary Behaviour, and Lean Mass

			95% Confidence interval		
	Beta	S.E.	Lower	Upper	p
Total BMD (Ln)					
Intercept	-0.48643	0.13182	-0.74481	-0.22806	<.001
LMC	-0.00295	0.00652	-0.01573	0.00983	.651
Sex	-0.04712	0.01113	-0.06894	-0.02530	<.001
BMI	0.00578	0.00087	0.00407	0.00748	<.001
Age	0.00446	0.00650	-0.00828	0.01719	.493
Sedentary behaviour	-0.00000	0.00001	-0.00001	0.00002	.840
Vitamin D	0.00007	0.00012	-0.00016	0.00031	.528
Lean mass	0.00001	0.00001	0.00001	0.00001	<.001

			95% Confidence interval		
	Beta	S.E.	Lower	Upper	p
Head BMD (Ln)					
Intercept	0.11782	0.20567	-0.28528	0.52093	.567
LMC	0.01532	0.01007	-0.00443	0.03506	.128
Sex	-0.05049	0.01348	-0.07692	-0.02406	<.001
BMI	0.00733	0.00102	0.00532	0.00934	<.001
Age	0.00489	0.01032	-0.01532	0.02511	.635
Sedentary behaviour	0.00001	0.00001	-0.00001	0.00004	.208
Vitamin D	0.00006	0.00018	-0.00030	0.00042	.748
Lean mass	0.00006	0.00001	0.00004	0.00007	<.001
Pelvis BMD (Ln)					
Intercept	-0.45641	0.18146	-0.81206	-0.10077	.012
LMC	-0.00836	0.00864	-0.02530	0.00857	.333
Sex	0.03541	0.01204	0.01181	0.05902	.003
BMI	0.00982	0.00104	0.00778	0.01185	<.001
Age	-0.00063	0.00893	-0.01814	0.01688	.933
Sedentary behaviour	0.00001	0.00001	-0.00001	0.00003	.358
Vitamin D	0.00060	0.00016	0.00029	0.00091	<.001
Lean mass	0.00004	0.00000	0.00003	0.00005	<.001
Non-preferred leg BMD (Ln)					
Intercept	-0.47839	0.15175	-0.77583	-0.18096	.002
LMC	-0.01375	0.00744	-0.02834	0.00083	.065
Sex	0.00234	0.01045	-0.01815	0.02282	.823
BMI	0.00549	0.00090	0.00371	0.00726	<.001
Age	0.00826	0.00748	-0.00640	0.02291	.270
Sedentary behaviour	-0.00000	0.00001	-0.00002	0.00002	.994
Vitamin D	0.00022	0.00014	-0.00005	0.00049	.107
Lean mass	0.00004	0.00000	0.00003	0.00004	<.001

			95% Confidence interval		
	Beta	S.E.	Lower	Upper	p
Preferred leg BMD (Ln)					
Intercept	-0.36104	0.14953	-0.65412	-0.06796	.016
LMC	-0.01381	0.00730	-0.02813	0.00051	.059
Sex	0.00193	0.01030	-0.01827	0.02213	.851
BMI	0.00468	0.00091	0.00290	0.00646	<.001
Age	0.00347	0.00738	-0.01098	0.01793	.638
Sedentary behaviour	0.00000	0.00001	-0.00001	0.00002	.705
Vitamin D	0.00015	0.00013	-0.00012	0.00041	.268
Lean mass	0.00004	0.00000	0.00003	0.00004	<.001
Non-preferred arm BMD (Ln)					
Intercept	-0.72688	0.17320	-1.06633	-0.38742	<.001
LMC	-0.00700	0.00839	-0.02345	0.00944	.404
Sex	-0.04461	0.01392	-0.07189	-0.01733	.001
BMI	0.00821	0.00098	0.00628	0.01013	<.001
Age	0.00382	0.00856	-0.01295	0.02060	.655
Sedentary behaviour	-0.00000	0.00001	-0.00001	0.00002	.604
Vitamin D	0.00016	0.00015	-0.00014	0.00046	.299
Lean mass	0.00007	0.00001	0.00006	0.00009	<.001
Preferred arm BMD (Ln)					
Intercept	-0.76322	0.17343	-1.10314	-0.42331	<.001
LMC	-0.02021	0.00845	-0.03677	-0.00366	**.017**
Sex	-0.04967	0.01438	-0.07786	-0.02148	.001
BMI	0.00886	0.00102	0.00686	0.01087	<.001
Age	0.00599	0.00854	-0.01076	0.02273	.483
Sedentary behaviour	-0.00001	0.00001	-0.00003	0.00001	.248
Vitamin D	0.00018	0.00015	-0.00012	0.00048	.235
Lean mass	0.00009	0.00007	0.00007	0.00010	<.001

Note. β beta coefficient; S.E. standard error; p p-value; LMC low motor competence

Table B8

General Linear Model Accounting for LMC Status, Sedentary Behaviour and Puberty Category

			95% Confidence interval		
	β	**S.E.**	**Lower**	**Upper**	**p**
Total BMD (Ln)					
Intercept	-0.42499	0.15660	-0.73193	-0.11806	.007
LMC	-0.01911	0.00761	-0.03403	-0.00420	**.012**
Sex	0.09422	0.00697	0.08056	0.10788	<.001
BMI	0.01150	0.00092	0.00971	0.01330	<.001
Age	0.00698	0.00772	-0.00815	0.02210	.366
Sedentary behaviour	-0.00001	0.00001	-0.00002	0.00002	.919
Vitamin D	0.00053	0.00013	0.00027	0.00079	<.001
Puberty category 3	-0.05415	0.02133	-0.09596	-0.01234	.011
Puberty category 4	-0.00272	0.00778	-0.01797	0.01253	.727
Head BMD (Ln)					
Intercept	0.11059	0.21631	-0.31337	0.53456	.609
LMC	0.00501	0.01053	-0.01563	0.02565	.634
Sex	0.00878	0.00984	-0.01050	0.02806	.372
BMI	0.00547	0.00104	0.00343	0.00752	<.001
Age	0.01497	0.01072	-0.00605	0.03598	.163
Sedentary behaviour	-0.00001	0.00001	-0.00001	0.00004	.323
Vitamin D	0.00017	0.00019	-0.00020	0.00054	.365
Puberty category 3	-0.06015	0.03104	-0.12099	0.00069	.053
Puberty category 4	-0.01869	0.01102	-0.04029	0.00292	.090
Pelvis BMD (Ln)					
Intercept	-0.29112	0.19796	-0.67912	0.09687	.141
LMC	-0.01982	0.00939	-0.03822	-0.00143	**.035**
Sex	0.13288	0.00877	0.11558	0.14995	<.001
BMI	0.01507	0.00096	0.01319	0.01696	<.001
Age	-0.00324	0.00975	-0.02235	0.01586	.739
Sedentary behaviour	0.00002	0.00001	-0.00002	0.00002	.892
Vitamin D	0.00092	0.00017	0.00059	0.00125	<.001
Puberty category 3	-0.06357	0.02761	-0.11768	-0.00945	.021
Puberty category 4	0.00319	0.00987	-0.01615	0.02253	.747

			95% Confidence interval		
	β	**S.E.**	**Lower**	**Upper**	**p**
Nonpreferred leg BMD (Ln)					
Intercept	-0.39429	0.17372	-0.73477	-0.05381	.023
LMC	-0.02547	0.00847	-0.04207	-0.00887	**.003**
Sex	0.11116	0.00790	0.09568	0.12665	<.001
BMI	0.01186	0.00085	0.01019	0.01353	<.001
Age	0.00825	0.00856	-0.00853	0.02504	.335
Sedentary behaviour	0.00001	0.00001	-0.00002	0.00002	.884
Vitamin D	0.00060	0.00015	0.00030	0.00090	<.001
Puberty category 3	-0.06830	0.02432	-0.11598	-0.02063	.005
Puberty category 4	0.00134	0.00877	-0.01585	0.01853	.879
Preferred leg BMD (Ln)					
Intercept	-0.32668	0.17177	-0.66334	0.00998	.057
LMC	-0.02328	0.00837	-0.03970	-0.00687	**.005**
Sex	0.11070	0.00781	0.09539	0.12601	<.001
BMI	0.01138	0.00084	0.00973	0.01303	<.001
Age	0.00514	0.00847	-0.01146	0.02174	.544
Sedentary behaviour	0.00001	0.00001	-0.00001	0.00003	.516
Vitamin D	0.00054	0.00015	0.00025	0.00083	<.001
Puberty category 3	-0.06517	0.02405	-0.11231	-0.01803	.007
Puberty category 4	0.00229	0.00867	-0.01471	0.01929	.792
Non-preferred arm BMD (Ln)					
Intercept	-0.77998	0.19208	-1.15644	-0.40352	<.001
LMC	-0.02259	0.00916	-0.04055	-0.00464	**.014**
Sex	0.08371	0.00848	0.06708	0.10034	<.001
BMI	0.01173	0.00101	0.00975	0.01371	<.001
Age	0.00846	0.00948	-0.01012	0.02704	.372
Sedentary behaviour	0.00001	0.00001	-0.00002	0.00002	.947
Vitamin D	0.00054	0.00016	0.00022	0.00085	.001
Puberty category 3	-0.06596	0.02652	-0.11793	-0.01399	.013
Puberty category 4	0.00663	0.00955	-0.01210	0.02535	.488

			95% Confidence interval		
	β	S.E.	Lower	Upper	p
Preferred arm BMD (Ln)					
Intercept	-0.82930	0.19720	-1.12158	-0.44280	<.001
LMC	-0.03756	0.00946	-0.05611	-0.01901	**<.001**
Sex	0.09617	0.00880	0.07892	0.11342	<.001
BMI	0.01305	0.00108	0.01093	0.01518	<.001
Age	0.01154	0.00971	-0.00749	0.03058	.235
Sedentary behaviour	0.00002	0.00001	-0.00004	0.00001	.126
Vitamin D	0.00058	0.00017	0.00025	0.00090	.001
Puberty category 3	-0.03801	0.02771	-0.09232	0.01630	.170
Puberty category 4	0.00447	0.00988	-0.01489	0.02383	.651

Note. β beta coefficient; S.E. standard error; p p-value; LMC low motor competence

Table B9

General Linear Model Including LMC Status, Loading Score, and LMC by Loading Interaction Effect

			95% Confidence interval		
	β	S.E.	Lower	Upper	p
Total BMD (Ln)					
Intercept	-0.46688	0.15089	-0.76262	-0.17114	.002
LMC	-0.02011	0.00996	-0.03964	-0.00058	**.044**
Sex	0.08971	0.00647	0.07703	0.10239	<.001
BMI	0.01150	0.00089	0.00976	0.01324	<.001
Age	0.00872	0.00747	-0.00592	0.02336	.243
Loading score	0.00007	0.00002	0.00002	0.00012	**.004**
Vitamin D	0.00046	0.00013	0.00020	0.00072	.001
LMC by loading	0.00000	0.00004	-0.00009	0.00008	.962
Head BMD (Ln)					
Intercept	0.08431	0.20849	-0.32432	0.49294	.686
LMC	0.00249	0.01354	-0.02405	0.02902	.854
Sex	0.01512	0.00896	-0.00244	0.03268	.092
BMI	0.00576	0.00100	0.00380	0.00772	<.001
Age	0.01670	0.01035	-0.00360	0.03699	.107
Loading score	-0.00003	0.00003	-0.00010	0.00003	.310
Vitamin D	0.00022	0.00019	-0.00015	0.00058	.252
LMC by loading	0.00002	0.00006	-0.00010	0.00013	.772

			95% Confidence interval		
	β	**S.E.**	**Lower**	**Upper**	**p**
Pelvis BMD (Ln)					
Intercept	-0.39167	0.19050	-0.76504	0.01830	.040
LMC	-0.01345	0.01208	-0.03712	0.01022	.266
Sex	0.12380	0.00799	0.10814	0.13946	<.001
BMI	0.01525	0.00092	0.01345	0.01704	<.001
Age	0.00161	0.00941	-0.01684	0.02006	.864
Loading score	0.00011	0.00003	0.00005	0.00017	**<.001**
Vitamin D	0.00077	0.00017	0.00044	0.00110	<.001
LMC by loading	-0.00005	0.00005	-0.00015	0.00005	.347
Non-preferred leg BMD (Ln)					
Intercept	-0.41716	0.16691	-0.74430	-0.09003	.012
LMC	-0.02197	0.01089	-0.04331	-0.00062	**.044**
Sex	0.10404	0.00722	0.08988	0.11820	<.001
BMI	0.01197	0.00081	0.01037	0.01356	<.001
Age	0.00919	0.00827	-0.00702	0.02540	.267
Loading score	0.00009	0.00003	0.00003	0.00014	**.002**
Vitamin D	0.00052	0.00015	0.00022	0.00081	.001
LMC by loading	-0.00004	0.00005	-0.00013	0.00005	.403
Preferred leg BMD (Ln)					
Intercept	-0.36949	0.16509	-0.69306	-0.04592	.025
LMC	-0.01856	0.01077	-0.03967	0.00256	.085
Sex	0.10286	0.00715	0.08886	0.11687	<.001
BMI	0.01140	0.00081	0.00982	0.01298	<.001
Age	0.00772	0.00818	-0.00831	0.02376	.345
Loading score	0.00008	0.00003	0.00003	0.00014	**.002**
Vitamin D	0.00046	0.00015	0.00017	0.00075	.002
LMC by loading	-0.00004	0.00005	-0.00014	0.00005	.355

Supp 6C Young Adult Study: General Linear Models Divided by Sex

Table C1

General Linear Model Accounting for Loading Score, Male Only Model

	β	S.E.	95% Confidence interval Lower	Upper	p
Total BMD (Ln)					
Intercept	-0.61586	0.22161	-1.05021	-0.18151	.005
LMC	-0.03113	0.01035	-0.05142	-0.01084	**.003**
BMI	0.01454	0.00137	0.01186	0.01722	<.001
Age	0.01697	0.01104	-0.00467	0.03861	.124
Loading score	0.00007	0.00003	0.00002	0.00013	**.011**
Vitamin D	0.00053	0.00021	0.00012	0.00094	.012
Head BMD (Ln)					
Intercept	-0.14871	0.29280	-0.72258	0.42518	.612
LMC	0.00777	0.01363	-0.01895	0.03448	.569
BMI	0.00761	0.00156	0.00456	0.01066	<.001
Age	0.02649	0.01460	-0.00213	0.05511	.070
Loading score	-0.00004	0.00004	-0.00011	0.00004	.326
Vitamin D	0.00033	0.00028	-0.00023	0.00088	.248
Pelvis BMD (Ln)					
Intercept	-0.48866	0.27389	-1.02547	-0.04815	.074
LMC	-0.03542	0.01255	-0.06002	-0.01082	**.005**
BMI	0.01808	0.00147	0.01519	0.02097	<.001
Age	0.00937	0.01361	-0.01730	0.03603	.491
Loading score	0.00012	0.00003	0.00005	0.00018	**.001**
Vitamin D	0.00078	0.00026	0.00027	0.00129	.003
Nonpreferred leg BMD (Ln)					
Intercept	-0.53810	0.25026	-1.02860	-0.04759	.032
LMC	-0.05062	0.01165	-0.07347	-0.02778	**<.001**
BMI	0.01684	0.00137	0.01416	0.01952	<.001
Age	0.01577	0.01242	-0.00857	0.04010	.204
Loading score	0.00008	0.00003	0.00002	0.00014	**.012**
Vitamin D	0.00031	0.00024	-0.00017	0.00078	.205

			95% Confidence interval		
	β	**S.E.**	**Lower**	**Upper**	**p**
Preferred leg BMD (Ln)					
Intercept	-0.41304	0.24398	-0.89124	0.06515	.090
LMC	-0.04421	0.01136	-0.06648	-0.02194	**<.001**
BMI	0.01616	0.00133	0.01355	0.01877	<.001
Age	0.01005	0.01210	-0.01368	0.03377	.407
Loading score	0.00008	0.00003	0.00001	0.00014	**.015**
Vitamin D	0.00036	0.00024	-0.00010	0.00083	.123
Nonpreferred arm BMD (Ln)					
Intercept	-0.93745	0.26387	-1.45463	-0.42026	<.001
LMC	-0.02940	0.01209	-0.05311	-0.00570	**.015**
BMI	0.01563	0.00147	0.01275	0.01852	<.001
Age	0.01524	0.01316	-0.01056	0.04104	.247
Loading score	0.00007	0.00003	0.00004	0.00013	**.039**
Vitamin D	0.00055	0.00025	0.00006	0.00103	.028
Preferred arm BMD (Ln)					
Intercept	-0.97034	0.27110	-1.50169	-0.43899	<.001
LMC	-0.03531	0.01247	-0.05975	-0.01086	**.005**
BMI	0.01677	0.01603	0.01363	0.01991	<.001
Age	0.01622	0.01349	-0.01022	0.04266	.229
Loading score	0.00015	0.00003	0.00008	0.00021	**<.001**
Vitamin D	0.00052	0.00025	0.00003	0.00102	.039

Note. β beta coefficient; S.E. standard error; p p-value; LMC low motor competence

Table C2

General Linear Model Accounting for Loading Score, Female Only Model

	β	S.E.	95% Confidence interval Lower	Upper	p
Total BMD (Ln)					
Intercept	-0.19989	0.20037	-0.58150	0.20394	.346
LMC	-0.00574	0.01036	-0.02605	0.01456	.579
BMI	0.00856	0.00114	0.00633	0.01078	<.001
Age	-0.00139	0.00983	-0.02065	0.01788	.888
Loading score	0.00004	0.00003	-0.00002	0.00011	.149
Vitamin D	0.00034	0.00017	0.00002	0.00066	.040
Head BMD (Ln)					
Intercept	0.36634	0.29822	-0.21816	0.95085	.219
LMC	0.00345	0.01516	-0.02627	0.03316	.820
BMI	0.00483	0.00131	0.00176	0.00689	.001
Age	0.00483	0.01469	-0.02396	0.03363	.742
Loading score	-0.00003	0.00005	-0.00012	0.00006	.477
Vitamin D	0.00006	0.00025	-0.00043	0.00056	.804
Pelvis BMD (Ln)					
Intercept	-0.10586	0.26070	-0.61682	0.40509	.685
LMC	-0.00229	0.01279	-0.02736	0.02277	.858
BMI	0.01290	0.00114	0.01067	0.01513	<.001
Age	-0.00934	0.01277	-0.03436	0.01569	.465
Loading score	0.00005	0.00004	-0.00003	0.00012	.206
Vitamin D	0.00067	0.00021	0.00025	0.00109	.002
Nonpreferred leg BMD (Ln)					
Intercept	-0.24502	0.21109	-0.65875	0.16870	.246
LMC	-0.00032	0.01078	-0.02145	0.02080	.976
BMI	0.00863	0.00094	0.00678	0.01048	<.001
Age	0.00430	0.01040	-0.01609	0.02470	.679
Loading score	0.00005	0.00003	-0.00002	0.00011	.151
Vitamin D	0.00057	0.00018	0.00022	0.00092	.002

	β	S.E.	95% Confidence interval Lower	Upper	p
Preferred leg BMD (Ln)					
Intercept	-0.25345	0.21438	-0.67363	0.16674	.237
LMC	-0.00103	0.01095	-0.02249	0.02042	.925
BMI	0.00810	0.00096	0.00622	0.00998	<.001
Age	0.00596	0.01057	-0.01475	0.02667	.573
Loading score	0.00004	0.00003	-0.00002	0.00011	.209
Vitamin D	0.00043	0.00018	0.00007	0.00079	.018
Nonpreferred arm BMD (Ln)					
Intercept	-0.55294	0.25161	-1.04565	-0.05934	.028
LMC	-0.01497	0.01264	-0.03976	0.00981	.236
BMI	0.00829	0.00126	0.00581	0.01076	<.001
Age	0.00165	0.01232	-0.02250	0.02580	.894
Loading score	0.00003	0.00004	-0.00004	0.00011	.383
Vitamin D	0.00032	0.00020	-0.00008	0.00072	.113
Preferred arm BMD (Ln)					
Intercept	-0.51395	0.24928	1.00254	-0.02536	.039
LMC	-0.03719	0.01265	-0.06198	-0.01241	**.003**
BMI	0.00973	0.00126	0.00726	0.01219	<.001
Age	-0.00141	0.01222	-0.02535	0.02254	.908
Loading score	0.00002	0.00004	-0.00005	0.00010	.539
Vitamin D	0.00039	0.00021	-0.00023	0.00079	.065

Note. β beta coefficient; S.E. standard error; p p-value; LMC low motor competence

Table C3

General Linear Model Accounting for Loading Score and Puberty, Male Only Model

			95% Confidence interval		
	β	**S.E.**	**Lower**	**Upper**	**p**
Total BMD (Ln)					
Intercept	-0.05032	0.22137	-0.93710	-0.06936	.023
LMC	-0.02866	0.01051	-0.04925	-0.00807	**.006**
BMI	0.01472	0.00139	0.01198	0.01745	<.001
Age	0.01126	0.01103	-0.01035	0.03288	.307
Loading score	0.00007	0.00003	0.00002	0.00013	**.012**
Vitamin D	0.00048	0.00021	0.00008	0.00089	.020
Puberty category 3	-0.06079	0.03161	-0.12274	0.00117	.054
Puberty category 4	0.02022	0.01433	-0.00787	0.04831	.158
Head BMD (Ln)					
Intercept	0.00320	0.30228	-0.58926	0.59566	.992
LMC	0.00828	0.01427	-0.01968	0.03625	.562
BMI	0.00717	0.00163	0.00397	0.01037	<.001
Age	0.01968	0.01509	-0.00990	0.04926	.192
Loading score	-0.00004	0.00004	-0.00012	0.00003	.276
Vitamin D	0.00031	0.00029	-0.00026	0.00088	.280
Puberty category 3	-0.11575	0.04408	-0.20214	-0.02935	.009
Puberty category 4	0.00818	0.02002	-0.03107	0.04742	.683
Pelvis BMD (Ln)					
Intercept	-0.33920	0.27457	-0.87736	0.19895	.217
LMC	-0.03321	0.01277	-0.05824	-0.00819	**.009**
BMI	0.01847	0.00151	0.01550	0.02143	<.001
Age	0.00154	0.01364	-0.02520	0.02828	.910
Loading score	0.00012	0.00003	0.00005	0.00019	**<.001**
Vitamin D	0.00072	0.00026	0.00021	0.00123	.006
Puberty category 3	-0.05982	0.03939	-0.13702	0.01739	.129
Puberty category 4	0.03135	0.01814	-0.00420	0.06691	.084

			95% Confidence interval		
	β	**S.E.**	**Lower**	**Upper**	**p**
Nonpreferred leg BMD (Ln)					
Intercept	-0.44692	0.25190	-0.94062	0.04679	.076
LMC	-0.04709	0.01188	-0.07038	-0.02380	**<.001**
BMI	0.01692	0.00139	0.01419	0.01964	<.001
Age	0.01122	0.01248	-0.01324	0.03569	.369
Loading score	0.00008	0.00003	0.00002	0.00014	**.014**
Vitamin D	0.00026	0.00024	-0.00022	0.00073	.289
Puberty category 3	-0.07479	0.03526	-0.14389	-0.00569	.034
Puberty category 4	0.02760	0.01669	-0.00512	0.06032	.098
Preferred leg BMD (Ln)					
Intercept	-0.30060	0.24604	-0.78283	0.18164	.222
LMC	-0.04147	0.01161	-0.06422	-0.01872	**<.001**
BMI	0.01622	0.00136	0.01356	0.01889	<.001
Age	0.00439	0.01219	-0.01951	0.02829	.719
Loading score	0.00008	0.00003	0.00001	0.00014	**.018**
Vitamin D	0.00033	0.00024	-0.00014	0.00079	.169
Puberty category 3	-0.06446	0.03444	-0.13196	0.00304	.061
Puberty category 4	0.03222	0.01631	0.00026	0.06418	.048
Nonpreferred arm BMD (Ln)					
Intercept	-0.83395	0.27106	-1.36523	-0.30268	.002
LMC	-0.02775	0.01258	-0.05240	-0.00309	**.027**
BMI	0.01508	0.00153	0.01208	0.01807	<.001
Age	0.01080	0.01351	-0.01569	0.03729	.424
Loading score	0.00006	0.00003	-0.00008	0.00013	.085
Vitamin D	0.00056	0.00025	0.00006	0.00106	.027
Puberty category 3	-0.07674	0.03847	-0.15213	-0.00135	.046
Puberty category 4	0.00426	0.01773	-0.03048	0.03900	.810
Preferred arm BMD (Ln)					
Intercept	-0.94034	0.27918	-1.48752	-0.39316	.001
LMC	-0.03475	0.01305	-0.06032	-0.00919	**.008**
BMI	0.01657	0.00168	0.01328	0.01985	<.001
Age	0.01501	0.01389	-0.01222	0.04223	.280
Loading score	0.00014	0.00003	0.00007	0.00021	**<.001**
Vitamin D	0.00052	0.00026	0.00000	0.00103	.048
Puberty category 3	-0.04494	0.04145	-0.12618	0.03630	.278
Puberty category 4	0.01022	0.01824	-0.02554	0.04597	.576

Note. β beta coefficient; S.E. standard error; p p-value; LMC low motor competence

Table C4

General Linear Model Accounting for Loading Score and Puberty, Female Only Model

	β	S.E.	95% Confidence interval Lower	Upper	p
Total BMD (Ln)					
Intercept	-0.22242	0.02089	-0.63183	0.18699	.287
LMC	-0.00737	0.01067	-0.02829	0.01355	.490
BMI	0.00855	0.00117	0.00627	0.01084	<.001
Age	0.00046	0.01027	-0.01967	0.02059	.964
Loading score	0.00005	0.00003	-0.00001	0.00012	.118
Vitamin D	0.00035	0.00017	0.00002	0.00068	.038
Puberty category 3	-0.03515	0.02750	-0.08905	0.01875	.201
Puberty category 4	-0.00734	0.00882	-0.02463	0.00995	.405
Head BMD (Ln)					
Intercept	0.25194	0.30185	-0.33968	0.84356	.404
LMC	-0.00600	0.01536	-0.03610	0.02411	.696
BMI	0.00431	0.00131	0.00174	0.00687	.001
Age	0.01134	0.01491	-0.01788	0.04056	.447
Loading score	-0.00003	0.00005	-0.00012	0.00006	.564
Vitamin D	0.00005	0.00025	-0.00045	0.00055	.845
Puberty category 3	-0.00031	0.04292	-0.08443	0.08381	.994
Puberty category 4	-0.02843	0.01299	-0.05389	-0.00296	.029
Pelvis BMD (Ln)					
Intercept	-0.04841	0.26977	-0.57714	0.48033	.858
LMC	-0.00704	0.01324	-0.03300	0.01892	.595
BMI	0.01250	0.00116	0.01022	0.01478	<.001
Age	-0.01182	0.01324	-0.03777	0.01413	.372
Loading score	0.00006	0.00004	-0.00002	0.00014	.138
Vitamin D	0.00072	0.00022	0.00030	0.00115	.001
Puberty category 3	-0.04770	0.03687	-0.11996	0.02457	.196
Puberty category 4	-0.00414	0.01121	-0.02610	0.01783	.712

			95% Confidence interval		
	β	S.E.	Lower	Upper	p
Nonpreferred leg BMD (Ln)					
Intercept	-0.27783	0.21988	-0.70878	0.15313	.206
LMC	-0.00115	0.01122	-0.02313	0.02084	.918
BMI	0.00843	0.00097	0.00653	0.01034	<.001
Age	0.00614	0.01087	-0.01515	0.02744	.572
Loading score	0.00005	0.00003	-0.00001	0.00012	.117
Vitamin D	0.00059	0.00018	0.00023	0.00095	.001
Puberty category 3	-0.03758	0.03110	-0.09852	0.02337	.227
Puberty category 4	-0.00352	0.00946	-0.02206	0.01503	.710
Preferred leg BMD (Ln)					
Intercept	-0.25149	0.22331	-0.68917	0.18619	.260
LMC	-0.00283	0.01139	-0.02515	0.01950	.804
BMI	0.00783	0.00099	0.00590	0.00976	<.001
Age	0.00618	0.01103	-0.01545	0.02781	.575
Loading score	0.00005	0.00003	-0.00002	0.00011	.181
Vitamin D	0.00046	0.00019	0.00010	0.00083	.013
Puberty category 3	0.04342	0.03158	-0.10531	0.01848	.169
Puberty category 4	-0.00499	0.00961	-0.02383	0.01385	.604
Nonpreferred arm BMD (Ln)					
Intercept	-0.52944	0.26248	-1.04389	-0.01500	.044
LMC	-0.01409	0.01310	-0.03977	0.01158	.282
BMI	0.00838	0.00130	0.00584	0.01093	<.001
Age	0.00019	0.01288	-0.02505	0.02543	.988
Loading score	0.00003	0.00004	-0.00005	0.00011	.457
Vitamin D	0.00031	0.00021	-0.00009	0.00072	.134
Puberty category 3	-0.03908	0.03538	-0.10843	0.03026	.269
Puberty category 4	0.01130	0.01089	-0.01005	0.03265	.300
Preferred arm BMD (Ln)					
Intercept	-0.50851	0.26127	-1.02059	0.00357	.052
LMC	-0.03647	0.01319	-0.06233	-0.01061	**.006**
BMI	0.00971	0.00131	0.00715	0.01227	<.001
Age	-0.00188	0.01283	-0.02703	0.02327	.884
Loading score	0.00002	0.00004	-0.00005	0.00010	.632
Vitamin D	0.00039	0.00022	-0.00003	0.00081	.069
Puberty category 3	-0.01498	0.03523	-0.08403	0.05407	.671
Puberty category 4	0.00883	0.01109	-0.01291	0.03056	.426

Note. β beta coefficient; S.E. standard error; p p-value

Table C5

General Linear Model, Including DCD Status and Lean Mass, Male Only Model

			95% Confidence interval		
	Beta	**S.E.**	**Lower**	**Upper**	**p**
Total BMD (Ln)					
Intercept	-0.66960	0.19064	-1.04344	-0.29576	<.001
LMC	-0.01443	0.00905	-0.03217	0.00331	.111
BMI	0.00637	0.00142	0.00359	0.00915	<.001
Age	0.01189	0.00951	-0.00676	0.03053	.211
Loading score	0.00005	0.00002	0.00000	0.00010	.041
Vitamin D	-0.00004	0.00019	-0.00041	0.00033	.822
Lean mass	0.00001	0.00000	0.00001	0.00001	<.001
Head BMD (Ln)					
Intercept	-0.25681	0.28528	-0.81595	0.30233	.368
LMC	0.01895	0.01345	-0.00741	0.04530	.159
BMI	0.00902	0.00154	0.00601	0.01204	<.001
Age	0.02069	0.01423	-0.00721	0.04859	.146
Loading score	-0.00005	0.00004	-0.00012	0.00002	.148
Vitamin D	0.00012	0.00028	-0.00042	0.00066	.661
Lean mass	0.00006	0.00001	0.00003	0.00008	<.001
Pelvis BMD (Ln)					
Intercept	-0.59400	0.25985	-1.10330	-0.08469	.022
LMC	-0.02370	0.01202	-0.04726	-0.00014	**.049**
BMI	0.01104	0.00177	0.00758	0.01450	<.001
Age	0.00947	0.01288	-0.01579	0.03472	.463
Loading score	0.00009	0.00003	0.00003	0.00016	**.003**
Vitamin D	0.00051	0.00025	0.00002	0.00100	042
Lean mass	0.00003	0.00001	0.00002	0.00004	<.001
Nonpreferred leg BMD (Ln)					
Intercept	-0.58463	0.23055	-1.03650	0.13277	.011
LMC	-0.03606	0.01090	-0.05742	-0.01470	**.001**
BMI	0.00843	0.00166	0.00517	0.01169	<.001
Age	0.01329	0.01144	-0.00913	0.03571	.245
Loading score	0.00007	0.00003	0.00001	0.00012	**.022**
Vitamin D	-0.00005	0.00023	-0.00050	0.00039	.811
Lean mass	0.00003	0.00000	0.00002	0.00004	<.001

			95% Confidence interval		
	Beta	**S.E.**	**Lower**	**Upper**	**p**
Preferred leg BMD (Ln)					
Intercept	-0.36576	0.22141	-0.79971	0.06819	.099
LMC	-0.03283	0.01039	-0.05320	-0.01245	**.002**
BMI	0.00686	0.00163	0.00366	0.01006	<.001
Age	0.00330	0.01101	-0.01828	0.02488	.765
Loading score	0.00006	0.00003	0.00001	0.00012	**.032**
Vitamin D	0.00003	0.00022	-0.00040	0.00046	.887
Lean mass	0.00003	0.00000	0.00003	0.00004	<.001
Nonpreferred arm BMD (Ln)					
Intercept	-0.85267	0.24388	-1.33066	-0.37468	<.001
LMC	-0.00989	0.01144	-0.03230	0.01252	.387
BMI	0.00993	0.00154	0.00691	0.01294	<.001
Age	0.00745	0.01220	-0.01645	0.03135	.541
Loading score	0.00005	0.00003	-0.00001	0.00011	.121
Vitamin D	0.00006	0.00024	-0.00040	0.00053	.784
Lean mass	0.00007	0.00001	0.00005	0.00008	<.001
Preferred arm BMD (Ln)					
Intercept	-0.92924	0.24476	-1.40896	-0.44952	<.001
LMC	-0.01608	0.01147	-0.03856	0.00641	.161
BMI	0.01115	0.00158	0.00805	0.01425	<.001
Age	0.00955	0.01220	-0.01436	0.03347	.434
Loading score	0.00012	0.00003	0.00006	0.00018	**<.001**
Vitamin D	-0.00001	0.00024	-0.00047	0.00046	.978
Lean mass	0.00008	0.00001	0.00006	0.00009	<.001

Note. β beta coefficient; S.E. standard error; p p-value; LMC low motor competence

Table C6

General Linear Model, Including DCD Status and Lean Mass, Female Only Model

			95% Confidence Interval		
	Beta	S.E.	Lower	Upper	P
Total BMD (Ln)					
Intercept	-0.34762	0.17739	-0.69531	0.00006	.050
LMC	0.00714	0.00923	-0.01096	0.02524	.440
BMI	0.00521	0.00107	0.00313	0.00730	<.001
Age	-0.00199	0.00866	-0.01896	0.01499	.818
Loading score	0.00001	0.00003	-0.00005	0.00006	.798
Vitamin D	0.00003	0.00015	0.00026	0.00032	.841
Lean mass	0.00001	0.00000	0.00001	0.00001	<.001
Head BMD (Ln)					
Intercept	0.50361	0.29249	-0.06966	1.07688	.085
LMC	0.00653	0.01490	-0.02267	0.03573	.661
BMI	0.00632	0.00136	0.00367	0.00898	<.001
Age	-0.01198	0.01481	-0.04101	0.01705	.419
Loading score	-0.00005	0.00004	-0.00014	0.00004	.265
Vitamin D	0.00005	0.00025	-0.00054	0.00045	.850
Lean mass	0.00006	0.00001	0.00003	0.00010	<.001
Pelvis BMD (Ln)					
Intercept	-0.18270	0.24391	-0.66075	0.29534	.454
LMC	0.00594	0.01201	-0.01761	0.02948	.621
BMI	0.00863	0.00123	0.00622	0.01105	<.001
Age	-0.01300	0.01195	-0.03641	0.01042	.277
Loading score	0.00002	0.00004	-0.00005	0.00009	.591
Vitamin D	0.00039	0.00020	-0.00001	0.00079	.057
Lean mass	0.00004	0.00001	0.00003	0.00005	<.001
Nonpreferred leg BMD (Ln)					
Intercept	-0.37878	0.18737	-0.74602	-0.01154	.043
LMC	0.00831	0.00958	-0.01048	0.02709	.386
BMI	0.00387	0.00098	0.00196	0.00579	<.001
Age	0.00404	0.00921	-0.01401	0.02209	.661
Loading score	0.00003	0.00003	-0.00003	0.00009	.295
Vitamin D	0.00024	0.00016	-0.00008	0.00055	.145
Lean mass	0.00004	0.00000	0.00003	0.00005	<.001

			95% Confidence Interval		
	Beta	S.E.	Lower	Upper	P
Preferred leg BMD (Ln)					
Intercept	-0.33049	0.19440	0.71151	0.05052	.089
LMC	0.00709	0.00996	-0.01244	0.02661	.477
BMI	0.00320	0.00105	0.00114	0.00525	.002
Age	0.00387	0.00957	-0.01490	0.02263	.686
Loading score	0.00003	0.00003	-0.00003	0.000-9	.392
Vitamin D	0.00009	0.00017	-0.00024	0.00042	.591
Lean mass	0.00004	0.00001	0.00003	0.00005	<.001
Nonpreferred arm BMD (Ln)					
Intercept	-0.60250	0.24142	-1.07568	-0.12932	.013
LMC	-0.00806	0.01219	-0.03197	0.01584	.508
BMI	0.00676	0.00125	0.00432	0.00921	<.001
Age	-0.00085	0.01182	-0.02402	0.02233	.943
Loading score	0.00002	0.00004	-0.00005	0.00009	.658
Vitamin D	0.00008	0.00020	-0.00031	0.00048	.682
Lean mass	0.00008	0.00002	0.000005	0.00011	<.001
Preferred arm BMD (Ln)					
Intercept	-0.64039	0.23474	-1.10048	-0.18030	.006
LMC	-0.02729	0.01197	-0.05074	-0.00383	**.023**
BMI	0.00639	0.00129	0.00386	0.00892	<.001
Age	-0.00020	0.01147	-0.02267	0.002228	.986
Loading score	-0.00001	0.00004	-0.00008	0.00006	.841
Vitamin D	0.00020	0.00020	-0.00019	0.00069	.318
Lean mass	0.00011	0.00002	0.00007	0.00014	<.001

Note. β beta coefficient; S.E. standard error; p p-value; LMC low motor competence

Table C7

General Linear Model Including LMC Status, Loading Score, and LMC by Loading Interaction Effect, Male Only Model

			95% Confidence Interval		
	Beta	S.E.	Lower	Upper	P
Total BMD (Ln)					
Intercept	-0.61193	0.22245	-1.04793	-0.17594	.006
LMC	-0.02899	0.01483	-0.05805	-0.00007	.051
BMI	0.01455	0.00137	0.01187	0.01724	<.001
Age	0.01673	0.01110	-0.00503	0.03949	.132
Loading score	0.00008	0.00003	0.00001	0.00014	**.028**
Vitamin D	0.00053	0.00021	0.00011	0.00094	.012
LMC by loading	-0.00001	0.00006	-0.00012	0.00010	.840
Head BMD (Ln)					
Intercept	0.14463	0.29382	-0.72051	0.43125	.623
LMC	0.01000	0.01921	-0.02764	0.04765	.602
BMI	0.00759	0.00156	0.00454	0.01065	<.001
Age	0.02627	0.01466	-0.00246	0.05500	.073
Loading score	-0.00003	0.00005	-0.00012	0.00005	.495
Vitamin D	0.00032	0.00028	-0.00023	0.00087	.255
LMC by loading	-0.00001	0.00007	-0.00016	0.00013	.869
Pelvis BMD (Ln)					
Intercept	-0.47906	0.27500	-1.01806	0.05993	.082
LMC	-0.03068	0.01771	-0.06540	0.00403	.083
BMI	0.01804	0.00148	0.01514	0.02094	<.001
Age	0.00887	0.01367	-0.01791	0.03566	.516
Loading score	0.00013	0.00004	0.00004	0.00021	**.003**
Vitamin D	0.00077	0.00026	0.00026	0.00128	.003
LMC by loading	-0.00002	0.00007	-0.00016	0.00011	.705
Non-preferred leg BMD (Ln)					
Intercept	-0.53446	0.25125	-1.02689	-0.04202	.033
LMC	-0.04870	0.01660	-0.08124	-0.01616	**.003**
BMI	0.01682	0.00137	0.01414	0.01951	<.001
Age	0.01557	0.01247	-0.00887	0.04002	.212
Loading score	0.00008	0.00004	0.00001	0.00016	**.034**
Vitamin D	0.00030	0.00024	-0.00017	0.00078	.210
LMC by loading	-0.00001	0.00006	-0.00014	0.00011	.871

			95% Confidence Interval		
	Beta	S.E.	Lower	Upper	P
Preferred leg BMD (Ln)					
Intercept	-0.40318	0.24487	-0.88313	0.07676	.100
LMC	-0.03899	0.01618	-0.07071	-0.00728	.016
BMI	0.01612	0.00133	0.01351	0.01874	<.001
Age	0.00953	0.01215	-0.01429	0.03335	.433
Loading score	0.00009	0.00004	0.00001	0.00016	**.026**
Vitamin D	0.00036	0.00024	-0.00011	0.00082	.131
LMC by loading	-0.00003	0.00006	-0.00015	0.00009	.651
Non-preferred arm BMD (Ln)					
Intercept	-0.97836	0.26467	-1.49710	-0.45962	<.001
LMC	-0.04654	0.01698	-0.07981	-0.01326	**.006**
BMI	0.01574	0.00147	0.01286	0.01863	<.001
Age	0.01738	0.01321	-0.00851	0.04328	.188
Loading score	0.00003	0.00004	-0.00005	0.00011	.422
Vitamin D	0.00057	0.00025	0.00009	0.00106	.021
LMC by loading	0.00009	0.00007	-0.00003	0.00022	.152
Preferred arm BMD (Ln)					
Intercept	-0.98268	0.27168	-1.51516	-0.45021	<.001
LMC	-0.04301	0.01759	-0.07748	-0.00854	**.014**
BMI	0.01678	0.00160	0.01364	0.01992	<.001
Age	0.01692	0.01353	-0.00959	0.04344	.211
Loading score	0.00013	0.00004	0.00005	0.00021	**.002**
Vitamin D	0.00054	0.00026	0.00004	0.00104	.035
LMC by loading	0.00004	0.00007	-0.00009	0.00017	.535

Note. β beta coefficient; S.E. standard error; p p-value; LMC low motor competence

Table C8

General Linear Model Including LMC Status, Loading Score, and LMC by Loading Interaction Effect, Female Only Model

			95% Confidence Interval		
	Beta	S.E.	Lower	Upper	P
Total BMD (Ln)					
Intercept	-0.15978	0.20236	-0.55640	-0.23683	.430
LMC	-0.01441	0.01377	-0.04141	0.01259	.296
BMI	0.00858	0.00113	0.00636	0.01080	<.001
Age	-0.00272	0.00991	-0.02215	0.01671	.784
Loading score	0.00003	0.00003	-0.00003	0.00010	.306
Vitamin D	0.00032	0.00017	0.00001	0.00064	.056
LMC by loading	0.00009	0.00009	-0.00009	0.00026	.341
Head BMD (Ln)					
Intercept	0.40299	0.30027	-0.18552	0.99151	.180
LMC	-0.00806	0.01935	-0.04599	0.02987	.677
BMI	0.00437	0.00131	0.00181	0.00694	.001
Age	0.00309	0.01478	-0.02588	0.03207	.834
Loading score	-0.00006	0.00005	-0.00016	0.00005	.280
Vitamin D	0.00006	0.00025	-0.00044	0.00056	.818
LMC by loading	0.00010	0.00011	-0.00011	0.00031	.340
Pelvis BMD (Ln)					
Intercept	-0.12780	0.26326	-0.64379	0.38818	.627
LMC	0.00368	0.01638	-0.02843	0.03578	.822
BMI	0.01288	0.00114	0.01066	0.01511	<.001
Age	-0.00830	0.01289	-0.03356	0.01695	.519
Loading score	0.00006	0.00004	-0.00002	0.00015	.164
Vitamin D	0.00067	0.00021	0.00025	0.00109	.002
LMC by loading	-0.00005	0.00009	-0.00023	0.00012	.560
Non-preferred leg BMD (Ln)					
Intercept	-0.24947	0.21260	-0.66616	0.16721	.241
LMC	0.00116	0.01371	-0.02570	0.02803	.932
BMI	0.00862	0.00095	0.00677	0.01048	<.001
Age	0.00451	0.01047	-0.01601	0.02504	.666
Loading score	0.00005	0.00004	-0.00002	0.00012	.175
Vitamin D	0.00057	0.00018	0.00022	0.00092	.002
LMC by loading	-0.00001	0.00008	-0.00017	0.00014	.861

	Beta	S.E.	95% Confidence Interval Lower	Upper	P
Preferred leg BMD (Ln)					
Intercept	-0.25627	0.21592	-0.67947	0.16694	.235
LMC	-0.00009	0.01392	-0.02738	0.02720	.995
BMI	0.00809	0.00096	0.00621	0.00998	<.001
Age	0.00709	0.01064	-0.01476	0.02794	.567
Loading score	0.00004	0.00004	-0.00003	0.00012	.243
Vitamin D	0.00043	0.00018	0.00008	0.00079	.018
LMC by loading	-0.00009	0.00008	-0.00016	0.00015	.913
Non-preferred arm BMD (Ln)					
Intercept	-0.56467	0.25315	-1.06084	-0.06850	.026
LMC	-0.01055	0.01635	-0.04259	0.02149	.519
BMI	0.00830	0.00126	0.00582	0.01078	<.001
Age	0.00219	0.01238	-0.02208	0.02646	.860
Loading score	0.00004	0.00004	-0.00004	0.00012	.331
Vitamin D	0.00033	0.00020	-0.00007	0.00073	.110
LMC by loading	-0.00004	0.00009	-0.00022	0.00014	.669
Preferred arm BMD (Ln)					
Intercept	-0.54678	0.25368	-1.04397	-0.04958	.031
LMC	-0.02993	0.01651	-0.06229	0.00243	.070
BMI	0.00967	0.00126	0.00720	0.01214	<.001
Age	0.00018	0.01243	-0.02417	0.02454	.988
Loading score	0.00004	0.00004	-0.00005	0.00012	.399
Vitamin D	0.00040	0.00021	-0.00001	0.00081	.057
LMC by loading	-0.00007	0.00010	-0.00026	0.00012	.494

Note. β beta coefficient; S.E. standard error; p p-value; LMC low motor competence

Table C9

General Linear Model Accounting for Sedentary Behaviour, Male Only Model

			95% Confidence interval		
	β	**S.E.**	**Lower**	**Upper**	**p**
Total BMD (Ln)					
Intercept	-0.61185	0.22472	-1.05230	-0.17140	.006
LMC	-0.03160	0.01052	-0.05221	-0.01099	.003
BMI	0.01496	0.00137	0.01227	0.01765	<.001
Age	0.01800	0.01119	-0.00393	0.03994	.108
Sedentary behaviour	-0.00002	0.00001	-0.00004	0.00001	.263
Vitamin D	0.00063	0.00021	0.00023	0.00104	.002
Head BMD (Ln)					
Intercept	-0.14734	0.29399	-0.72355	0.42888	.616
LMC	0.00863	0.01379	-0.01840	0.03567	.531
BMI	0.00766	0.00158	0.00369	0.01075	<.001
Age	0.02485	0.01473	-0.00402	0.05371	.092
Sedentary behaviour	0.00001	0.00002	-0.00002	0.00005	.417
Vitamin D	0.00028	0.00027	-0.00026	0.00082	.310
Pelvis BMD (Ln)					
Intercept	-0.49302	0.27827	-1.03843	-0.05238	.076
LMC	-0.03719	0.01285	-0.06237	-0.01201	**.004**
BMI	0.01821	0.00151	0.01524	0.02118	<.001
Age	0.01217	0.01387	-0.01502	0.03935	.380
Sedentary behaviour	0.00003	0.00002	-0.00006	0.00001	.133
Vitamin D	0.00098	0.00026	0.00047	0.00148	<.001
Nonpreferred leg BMD (Ln)					
Intercept	-0.54414	0.25380	-1.04159	-0.00047	.032
LMC	-0.05119	0.01187	-0.07445	-0.02703	**<.001**
BMI	0.01719	0.00139	0.01446	0.01992	<.001
Age	0.01635	0.01258	-0.00831	0.04100	.194
Sedentary behaviour	-0.00001	0.00002	-0.00004	0.00003	.726
Vitamin D	0.00047	0.00024	0.00000	0.00094	.048

			95% Confidence interval		
	β	**S.E.**	**Lower**	**Upper**	**p**
Preferred leg BMD (Ln)					
Intercept	-0.42673	0.24709	-0.91102	0.05756	.084
LMC	-0.04422	0.01156	-0.06687	0.02154	**<.001**
BMI	0.01662	0.00136	0.01396	0.01928	<.001
Age	0.01006	0.01225	-0.01394	0.03407	.411
Sedentary behaviour	0.00000	0.00002	-0.00003	0.00003	.856
Vitamin D	0.00053	0.00023	0.00008	0.00099	.022
Nonpreferred arm BMD (Ln)					
Intercept	-0.93546	0.26595	-1.45672	-0.41420	<.001
LMC	-0.03064	0.01227	-0.05470	-0.00659	**.013**
BMI	0.01578	0.00149	0.01287	0.01870	<.001
Age	0.01705	0.01330	-0.00902	0.04312	.200
Sedentary behaviour	-0.00002	0.00002	-0.00005	0.00001	.212
Vitamin D	0.00066	0.00024	0.00018	0.00113	.007
Preferred arm BMD (Ln)					
Intercept	-0.96384	0.27550	-1.52635	-0.44641	<.001
LMC	-0.03716	0.01274	-0.06214	-0.01218	**.004**
BMI	0.01706	0.00163	0.01387	0.02025	<.001
Age	0.02225	0.01376	-0.00472	0.04922	.106
Sedentary behaviour	-0.00005	0.00002	-0.00009	0.00002	.001
Vitamin D	0.00071	0.00025	0.00022	0.00121	.005

Note. β beta coefficient; S.E. standard error; p p-value; LMC low motor competence

Table C10

General Linear Model Accounting for Sedentary Behaviour, Female Only Model

			95% Confidence interval		
	β	S.E.	Lower	Upper	p
Total BMD (Ln)					
Intercept	-0.20364	0.20367	-0.60283	0.19555	.317
LMC	-0.00523	0.01031	-0.02544	0.01498	.612
BMI	0.00844	0.00114	0.00621	0.01068	<.001
Age	-0.00112	0.00992	-0.02056	0.01832	.910
Sedentary behaviour	0.00001	0.00001	-0.00001	0.00003	.496
Vitamin D	0.00041	0.00016	0.00001	0.00073	.012
Head BMD (Ln)					
Intercept	0.35119	0.30400	-0.24464	0.94703	.248
LMC	0.00680	0.01522	-0.02302	0.03663	.655
BMI	0.00417	0.00134	0.00154	0.00679	.002
Age	0.00439	0.01486	-0.00247	0.03352	.768
Sedentary behaviour	0.00001	0.00002	-0.00002	0.00004	.461
Vitamin D	0.00010	0.00025	-0.00039	0.00060	.680
Pelvis BMD (Ln)					
Intercept	-0.15776	0.26336	-0.697394	-0.35842	.549
LMC	-0.00151	0.01272	-0.02643	-0.02342	.906
BMI	0.01276	0.00115	0.01051	0.01502	<.001
Age	-0.00927	0.01281	-0.03437	0.01583	.469
Sedentary behaviour	0.00003	0.00001	0.00000	0.00005	**.027**
Vitamin D	0.00078	0.00021	0.00036	0.00119	<.001
Nonpreferred leg BMD (Ln)					
Intercept	-0.27210	0.21433	-0.69218	0.14797	.208
LMC	-0.00041	0.01076	-0.02151	0.02069	.970
BMI	0.00852	0.00096	0.00664	0.01041	<.001
Age	0.00530	0.01048	-0.01525	0.02585	.613
Sedentary behaviour	0.00001	0.00001	-0.00001	0.00003	.534
Vitamin D	0.00061	0.00018	0.00026	0.00096	.001

	β	S.E.	95% Confidence interval Lower	Upper	p
Preferred leg BMD (Ln)					
Intercept	-0.27955	0.21764	-0.70612	0.14701	.199
LMC	-0.00135	0.01093	-0.02278	0.02007	.901
BMI	0.00821	0.00098	0.00630	0.01013	<.001
Age	0.00673	0.01064	-0.01413	0.02760	.527
Sedentary behaviour	0.00001	0.00001	-0.00002	0.00003	.597
Vitamin D	0.00047	0.00018	0.00011	0.00082	.010
Nonpreferred arm BMD (Ln)					
Intercept	-0.59736	0.25353	-1.09427	-0.10046	.018
LMC	-0.01437	0.01254	-0.03895	-0.01020	.252
BMI	0.00828	0.00126	0.00581	0.01075	<.001
Age	0.00240	0.01234	-0.02179	0.02659	.846
Sedentary behaviour	0.00002	0.00001	-0.00001	0.00004	.183
Vitamin D	0.00038	0.00020	-0.00002	0.00078	.060
Preferred arm BMD (Ln)					
Intercept	-0.56158	0.25380	-1.05902	-0.06414	.027
LMC	-0.03851	0.01263	-0.06328	-0.01375	**.002**
BMI	0.00992	0.00130	0.00738	0.01246	<.001
Age	-0.00009	0.01232	-0.02423	0.02406	.994
Sedentary behaviour	0.00001	0.00001	-0.00001	0.00003	.404
Vitamin D	0.00040	0.00021	-0.00000	0.00081	.052

Note. β beta coefficient; S.E. standard error; p p-value; LMC low motor competence

Table C11

General Linear Model Accounting for Sedentary Behaviour and Puberty Status, Male Only Model

			95% Confidence interval		
	β	**S.E.**	**Lower**	**Upper**	**p**
Total BMD (Ln)					
Intercept	-0.51435	0.22456	-0.95449	-0.07421	.022
LMC	-0.02918	0.01068	-0.05011	-0.00825	**.006**
BMI	0.01501	0.00141	0.01225	0.01777	<.001
Age	0.01282	0.01118	-0.00909	0.03473	.251
Sedentary behaviour	-0.00001	0.00001	-0.00004	0.00002	.409
Vitamin D	0.00059	0.00021	0.00018	0.00099	.004
Puberty category 3	-0.06269	0.03208	-0.12557	0.00019	.051
Puberty category 4	0.01740	0.01451	-0.01103	0.04584	.230
Head BMD (Ln)					
Intercept	0.00635	0.30308	-0.58768	0.60038	.983
LMC	0.01008	0.01443	-0.01821	0.03837	.485
BMI	0.00732	0.00165	0.00408	0.01056	<.001
Age	0.01696	0.01519	-0.01280	0.04673	.264
Sedentary behaviour	0.00002	0.00002	-0.00001	0.00006	.215
Vitamin D	0.00027	0.00028	-0.00028	0.00083	.332
Puberty category 3	-0.11764	0.04425	-0.20437	-0.03092	.008
Puberty category 4	0.00920	0.02005	-0.03010	0.04851	.646
Pelvis BMD (Ln)					
Intercept	-0.36353	0.27951	-0.91136	0.18431	.193
LMC	-0.03490	0.01311	-0.06059	-0.00922	**.008**
BMI	0.01856	0.00155	0.01551	0.02160	<.001
Age	0.00499	0.01392	-0.02230	0.03228	.720
Sedentary behaviour	-0.00002	0.00002	-0.00006	0.00001	.218
Vitamin D	0.00092	0.00026	0.00042	0.00143	<.001
Puberty category 3	-0.06472	0.04013	-0.14338	0.01394	.107
Puberty category 4	0.02817	0.01845	-0.00799	0.06433	.127

			95% Confidence interval		
	β	S.E.	Lower	Upper	p
Nonpreferred leg BMD (Ln)					
Intercept	-0.47079	0.25533	-0.97123	0.02966	.065
LMC	-0.04747	0.01211	-0.07119	-0.02374	**<.001**
BMI	0.01720	0.00143	0.01441	0.01999	<.001
Age	0.01233	0.01264	-0.01244	0.03710	.329
Sedentary behaviour	0.00000	0.00002	-0.00003	0.00003	.974
Vitamin D	0.00042	0.00024	-0.00005	0.00089	.080
Puberty category 3	-0.08095	0.03570	-0.15091	-0.01099	.023
Puberty category 4	0.02492	0.01687	-0.00814	0.05798	.140
Preferred leg BMD (Ln)					
Intercept	-0.32967	0.24892	-0.81754	0.15820	.185
LMC	-0.04137	0.01180	-0.06450	-0.01824	**<.001**
BMI	0.01659	0.00139	0.01387	0.01932	<.001
Age	0.00495	0.01232	-0.01919	0.02910	.688
Sedentary behaviour	0.00001	0.00002	-0.00002	0.00004	.667
Vitamin D	0.00049	0.00023	0.00003	0.00095	.036
Puberty category 3	-0.07175	0.03480	-0.13995	-0.00355	.039
Puberty category 4	0.02981	0.01644	-0.00242	0.06204	.070
Nonpreferred arm BMD (Ln)					
Intercept	-0.84065	0.27277	-1.37527	-0.30603	.002
LMC	-0.02907	0.01275	-0.05407	-0.00407	**.023**
BMI	0.01051	0.00154	0.01209	0.01814	<.001
Age	0.01297	0.01363	-0.01374	0.03968	.341
Sedentary behaviour	-0.00002	0.00002	-0.00005	0.00001	.270
Vitamin D	0.00065	0.00025	0.00016	0.00114	.009
Puberty category 3	-0.07705	0.03873	-0.15295	-0.00114	.047
Puberty category 4	0.00291	0.01781	-0.03200	0.03782	.870
Preferred arm BMD (Ln)					
Intercept	-0.97592	0.28276	-1.53012	-0.42172	.001
LMC	-0.03711	0.01329	-0.06316	-0.01106	**.005**
BMI	0.01658	0.00170	0.01325	0.01992	<.001
Age	0.02229	0.01412	-0.00538	0.04995	.114
Sedentary behaviour	-0.00005	0.00002	-0.00009	0.00002	**.002**
Vitamin D	0.00069	0.00026	0.00018	0.00119	.008
Puberty category 3	-0.04247	0.04209	-0.12497	0.04002	.313
Puberty category 4	0.00528	0.01848	-0.03093	0.04150	.775

Note. β beta coefficient; S.E. standard error; p p-value; LMC low motor competence

Table C12

General Linear Model Accounting for Sedentary Behaviour and Puberty Category, Female Only Model

			95% Confidence interval		
	β	S.E.	Lower	Upper	p
Total BMD (Ln)					
Intercept	-0.23486	0.21249	-0.65133	0.18160	.269
LMC	-0.00694	0.01062	-0.02776	0.01388	.514
BMI	0.00842	0.00117	0.00613	0.01071	<.001
Age	0.00014	0.01035	-0.02013	0.02042	.989
Sedentary behaviour	0.00001	0.00001	-0.00001	0.00004	.345
Vitamin D	0.00042	0.00017	0.00009	0.00075	**.012**
Puberty category 3	-0.03287	0.02769	-0.08715	0.02140	.235
Puberty category 4	-0.00567	0.00891	-0.02314	0.01180	.524
Head BMD (Ln)					
Intercept	0.23909	0.30833	-0.36523	0.84342	.438
LMC	-0.00257	0.01544	-0.03282	0.02769	.868
BMI	0.00415	0.00134	0.00153	0.00678	.002
Age	0.01115	0.01508	-0.01841	0.04071	.460
Sedentary behaviour	0.00001	0.00002	-0.00003	0.00004	.682
Vitamin D	0.00009	0.00025	-0.00040	0.00059	.713
Puberty category 3	-0.00124	0.04334	-0.08618	0.08371	.977
Puberty category 4	-0.02948	0.01319	-0.05534	-0.00363	.025
Pelvis BMD (Ln)					
Intercept	-0.07996	0.27396	-0.61691	0.45700	.770
LMC	-0.00600	0.01323	-0.03192	0.01992	.650
BMI	0.01233	0.00119	0.01001	0.01466	<.001
Age	-0.01278	0.01332	-0.03888	0.01332	.337
Sedentary behaviour	0.00003	0.00002	-0.00000	0.00006	.071
Vitamin D	0.00081	0.00022	0.00039	0.00123	<.001
Puberty category 3	-0.04237	0.03696	-0.11482	0.03008	.252
Puberty category 4	-0.00022	0.01129	-0.02234	0.02191	.985

			95% Confidence interval		
	β	S.E.	Lower	Upper	p
Nonpreferred leg BMD (Ln)					
Intercept	-0.30109	0.22352	-0.73918	0.13700	.178
LMC	-0.00104	0.01122	-0.02302	0.02094	.926
BMI	0.00832	0.00099	0.00638	0.01027	<.001
Age	0.00645	0.01094	-0.01499	0.02788	.555
Sedentary behaviour	0.00001	0.00001	-0.00001	0.00004	.376
Vitamin D	0.00063	0.00018	0.00027	0.00099	.001
Puberty category 3	-0.03484	0.03125	-0.09609	0.02642	.265
Puberty category 4	-0.00063	0.00955	-0.01936	0.01809	.947
Preferred leg BMD (Ln)					
Intercept	-0.28671	0.22673	-0.73110	0.15767	.206
LMC	-0.00286	0.01138	-0.02516	0.01943	.801
BMI	0.00795	0.00100	0.00598	0.00992	<.001
Age	0.00647	0.01109	-0.01528	0.02821	.560
Sedentary behaviour	0.00002	0.00001	-0.00001	0.00004	.259
Vitamin D	0.00049	0.00019	0.00013	0.00086	.008
Puberty category 3	-0.04005	0.03170	-0.10219	0.02208	.206
Puberty category 4	-0.00228	0.00969	-0.02128	0.01671	.814
Nonpreferred arm BMD (Ln)					
Intercept	-0.58643	0.26425	-1.10434	-0.06851	.026
LMC	-0.01298	0.01298	-0.03842	0.01246	.317
BMI	0.00840	0.00129	0.00586	0.01093	<.001
Age	0.00075	0.01285	-0.02444	0.02594	.953
Sedentary behaviour	0.00002	0.00002	-0.00001	0.00005	.122
Vitamin D	0.00036	0.00021	-0.00005	0.00076	.084
Puberty category 3	-0.03518	0.03533	-0.10442	0.03406	.319
Puberty category 4	0.01428	0.01091	-0.00710	0.03566	.190
Preferred arm BMD (Ln)					
Intercept	-0.57604	0.26639	-1.09815	-0.05394	.031
LMC	-0.03726	0.01316	-0.06306	-0.01146	**.005**
BMI	0.00993	0.00134	0.00729	0.01256	<.001
Age	-0.00064	0.01292	-0.02596	0.02468	.960
Sedentary behaviour	0.00002	0.00002	-0.00001	0.00005	.186
Vitamin D	0.00040	0.00021	-0.00002	0.00081	.060
Puberty category 3	-0.01074	0.03532	-0.07996	0.05849	.761
Puberty category 4	0.01161	0.01118	-0.01031	0.03352	.299

Note. β beta coefficient; S.E. standard error; p p-value; LMC low motor competence

Table C13

General Linear Model Accounting for Sedentary Behaviour and Lean Mass, Male Only Model

			95% Confidence interval		
	Beta	**S.E.**	**Lower**	**Upper**	**p**
Total BMD (Ln)					
Intercept	-0.66681	0.19286	-1.04482	-0.28880	.001
LMC	-0.01455	0.00917	-0.03252	0.00342	.113
BMI	0.00653	0.00143	0.00373	0.00933	<.001
Age	0.01271	0.00961	-0.00613	0.03155	.186
Sedentary behaviour	-0.00001	0.00001	-0.00004	0.00001	.285
Vitamin D	0.00001	0.00019	-0.00035	0.00038	.929
Lean mass	0.00001	0.00000	0.00001	0.00001	<.001
Head BMD (Ln)					
Intercept	-0.24874	0.28680	-0.81085	0.31337	.386
LMC	0.01931	0.01362	-0.00737	0.04600	.156
BMI	0.00896	0.00156	0.00590	0.01202	<.001
Age	0.01914	0.01438	-0.00905	0.04732	.183
Sedentary behaviour	0.00001	0.00002	-0.00002	0.00005	.414
Vitamin D	0.00005	0.00027	-0.00049	0.00058	.861
Lean mass	0.00005	0.00001	0.00003	0.00008	<.001
Pelvis BMD (Ln)					
Intercept	-0.60351	0.26331	-1.11958	-0.08743	.022
LMC	-0.02461	0.01228	-0.04868	-0.00055	**.045**
BMI	0.01090	0.00180	0.00737	0.01443	<.001
Age	0.01190	0.01310	-0.01377	0.03758	.363
Sedentary behaviour	-0.00002	0.00002	-0.00005	0.00001	.186
Vitamin D	0.00065	0.00025	0.00017	0.00114	.008
Lean mass	0.00003	0.00001	0.00002	0.00004	<.001
Nonpreferred leg BMD (Ln)					
Intercept	-0.59213	0.23369	-1.05015	-0.13411	.011
LMC	-0.03624	0.01109	-0.05798	-0.01449	**.001**
BMI	0.00861	0.00170	0.00529	0.01193	<.001
Age	0.01398	0.01158	-0.00872	0.03668	.228
Sedentary behaviour	-0.00001	0.00001	-0.00004	0.00002	.674
Vitamin D	0.00008	0.00022	-0.00036	0.00052	.731
Lean mass	0.00003	0.00000	0.00002	0.00004	<.001

			95% Confidence interval		
	Beta	**S.E.**	**Lower**	**Upper**	**p**
Preferred leg BMD (Ln)					
Intercept	-0.37665	0.22414	-0.81596	0.06265	.093
LMC	-0.03272	0.01057	-0.05343	-0.01201	**.002**
BMI	0.00714	0.00166	0.00388	0.01040	<.001
Age	0.00339	0.01113	-0.01843	0.02521	.760
Sedentary behaviour	0.00000	0.00001	-0.00003	0.00003	.940
Vitamin D	0.00016	0.00021	-0.00026	0.00058	.457
Lean mass	0.00003	0.00000	0.00003	0.00004	<.001
Nonpreferred arm BMD (Ln)					
Intercept	-0.85464	0.24546	-1.33574	-0.37354	<.001
LMC	-0.01021	0.01160	-0.03295	0.01254	.379
BMI	0.01001	0.00155	0.00697	0.01305	<.001
Age	0.00855	0.01231	-0.01558	0.03269	.487
Sedentary behaviour	-0.00001	0.00002	-0.00004	0.00002	.432
Vitamin D	0.00014	0.00023	-0.00032	0.00060	.545
Lean mass	0.00007	0.00001	0.00005	0.00008	<.001
Preferred arm BMD (Ln)					
Intercept	-0.94233	0.24789	-1.42818	-0.45647	<.001
LMC	-0.01700	0.01169	-0.03991	0.00590	.146
BMI	0.01124	0.00160	0.00810	0.01438	<.001
Age	0.01428	0.01241	-0.01004	0.03860	.250
Sedentary behaviour	-0.00004	0.00002	-0.00007	-0.00001	.005
Vitamin D	0.00013	0.00024	-0.00034	0.00059	.590
Lean mass	0.00008	0.00001	0.00006	0.00009	<.001

Note. β beta coefficient; S.E. standard error; p p-value; LMC low motor competence

Table C14

General Linear Model Accounting for Sedentary Behaviour, Female Only Model

			95% Confidence interval		
	Beta	**S.E.**	**Lower**	**Upper**	**p**
Total BMD (Ln)					
Intercept	-0.39596	0.17987	-0.71851	-0.01342	.042
LMC	0.00934	0.00920	-0.00869	0.02737	.310
BMI	0.00511	0.00106	0.00302	0.00720	<.001
Age	-0.00202	0.00872	-0.01911	0.01506	.816
Sedentary behaviour	0.00001	0.00001	-0.00001	0.00003	.277
Vitamin D	0.00008	0.00015	-0.00021	0.00037	.588
Lean mass	0.00001	0.00000	0.00001	0.00001	<.001
Head BMD (Ln)					
Intercept	0.46681	0.29802	-0.11730	1.05092	.117
LMC	0.01073	0.01498	-0.01863	0.04008	.474
BMI	0.00625	0.00139	0.00352	0.00899	<.001
Age	-0.01190	0.01498	-0.04127	0.01746	.427
Sedentary behaviour	0.00002	0.00001	-0.00001	0.00004	.285
Vitamin D	0.00000	0.00025	-0.00050	0.00049	.986
Lean mass	0.00006	0.00001	0.00003	0.00009	<.001
Pelvis BMD (Ln)					
Intercept	-0.24776	0.24555	-0.72903	0.23351	.313
LMC	0.00827	0.01192	-0.01510	0.03163	.488
BMI	0.00861	0.00122	0.00621	0.01101	<.001
Age	-0.01280	0.01193	-0.03619	0.01060	.284
Sedentary behaviour	0.00003	0.00001	0.00000	0.00005	**.018**
Vitamin D	0.00047	0.00020	0.00008	0.00087	.019
Lean mass	0.00004	0.00001	0.00003	0.00006	<.001
Nonpreferred leg BMD (Ln)					
Intercept	-0.39947	0.19055	-0.77295	-0.02600	.036
LMC	0.00955	0.00960	-0.00927	0.02838	.320
BMI	0.00387	0.00099	0.00194	0.00581	<.001
Age	0.00481	0.00930	-0.01341	0.02303	.605
Sedentary behaviour	0.00000	0.00001	-0.00001	0.00002	.651
Vitamin D	0.00028	0.00016	-0.00003	0.00060	.080
Lean mass	0.00004	0.00000	0.00003	0.00005	<.001

Supp 6D Young Adult Study: Bone Health Differences Based on LMC Status for the Whole Group

Table D1

Bone Health Differences Based on DCD Status for The Entire Group

	LMC (n=272) M (SD) [Md] {IQR}	**Non-LMC (n=771) M (SD) [Md] {IQR}**	**U**	**P**
Bone mineral density (g/cm^2)				
Total body	1.056 (0.106) [1.051] {0.991 to 1.140}	1.068 (0.107) [1.058] {0.991 to 1.140}	-1.474	.140
Head	1.792 (0.222) [1.784] {1.628 to 1.928}	1.790 (0.210) [1.772] {1.641 to 1.920}	-0.168	.867
Pelvis	1.151 (0.160) [1.136] {1.041 to 1.245}	1.158 (0.160) [1.143] {1.045 to 1.262}	-0.589	.556
Preferred leg	1.155 (0.141) [1.138] {1.059 to 1.254}	1.167 (0.134) [1.154] {1.073 to 1.258}	-1.359	.174
Non-preferred leg	1.161 (0.136) [1.140] {1.060 to 1.260}	1.168 (0.137) [1.150] {1.070 to 1.260}	-0.773	.439
Preferred arm	0.779 (0.104) [0.769] {0.710 to 0.853}	0.796 (0.095) [0.786] {0.733 to 0.850}	-2.235	.025
Non-preferred arm	0.772 (0.096) [0.770] {0.700 to 0.840}	0.781 (0.090) [0.770] {0.720 to 0.850}	-1.719	.086