# Longitudinal fibular deficiency: Lower limb function and quality of life of children and young people

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Thesis presented for the degree of

Master of Research

Submitted 7 October, 2016

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# Preface

This thesis is made up of for four chapters. **Chapter 1** is a synthesised literature review, providing in-depth background about longitudinal fibular deficiency, its functional classification, management and outcomes. **Chapter 2** investigates the functional consequences of longitudinal fibular deficiency using the International Classification of Function, Disability and Health (ICF) framework. **Chapter 3** is a cross-sectional study using patient-reported outcomes to compare lower limb function and quality of life in children and young people with longitudinal fibular deficiency to a large sample of unaffected peers. This chapter is presented in the exact format of the manuscript which has been submitted to the American Journal of Physical Medicine & Rehabilitation. **Chapter 4** systematically explores the findings of the thesis in greater detail, considers the implications for clinical practice and research, and discusses the limitations of the thesis as well as key recommendations. The references for chapters 1, 2, and 4 are presented together after Chapter 4, while the references for Chapter 3 are presented at the end of the submitted manuscript.

# Thesis Aims

To improve the understanding of longitudinal fibular deficiency within the context of the ICF-CY, the aim of this thesis is to build upon the current understanding of the condition in children and young people, specifically in terms of lower limb function and quality of life. By considering the impact of the condition in terms activity limitations and participation restrictions, a more holistic perspective of affected children and young people can be formed.

To achieve this, the objectives of this thesis are to:

- Critically appraise the available literature on lower limb function and quality of life in longitudinal fibular deficiency, encompassing all aspects of the ICF-CY (Chapter 1-2).
- Compare lower limb function and quality of life of children and young people with longitudinal fibular deficiency to unaffected peers using a cross-sectional study and patient-reported outcomes (Chapter 3).
- Evaluate and explore the findings pertaining to lower limb function and quality of life in children and young people with longitudinal fibular deficiency, and discuss implications for clinical practice and future research, limitations, and key recommendations (Chapter 4).

# Abstract

This thesis builds upon the small evidence-base for longitudinal fibular deficiency in children and young people, specifically in terms of lower limb function and quality of life.

To date, research on individuals with longitudinal fibular deficiency has focused on impairments of body functions and structures with minimal investigation of activity limitations and participation restrictions. Studies suggest that affected adults have similar quality of life to published normative values, but little is known about quality of life and lower limb function of children and young people with this condition.

Therefore, a cross-sectional study was undertaken exploring these outcomes in 17 affected children compared to 213 unaffected peers. Children and young people reported, on average, significantly reduced lower limb function and quality of life compared to unaffected peers. Knee function in younger children was significantly reduced, however, in young adults it was closer to normal. Ankle function was reduced in children and young people when compared to unaffected peers.

Early and individualised clinical assessment of these outcomes appears to be warranted. Further research assessing the effectiveness of treatment interventions, longitudinal studies assessing individual changes over time, and qualitative investigations of a child's function and quality of life are recommended.

# Candidate's Statement

I, Joshua Pate, certify that the work in this thesis entitled "Longitudinal fibular deficiency: Lower limb function and quality of life of children and young people" has not previously been submitted for a degree nor has it been submitted as part of requirements for a degree to any other university or institution other than Macquarie University.

I also certify that the thesis is an original piece of research and it has been written by me. Any help and assistance that I have received in my research work and the preparation of the thesis itself have been appropriately acknowledged.

In addition, I certify that all information sources and literature used are indicated in the thesis. The research presented in this thesis was approved by Sydney Children's Hospital Network (LNR/15/SCHN/327) and by Macquarie University Ethics Review Committee (reference number: 5201500761) on 10 September 2015.

Joshua Pate

Signed: _____

Date: 7 October 2016

# Supervisor's Statement

As the supervisors of Joshua Pate's Master of Research work, we certify that we consider his thesis "Longitudinal fibular deficiency: Lower limb function and quality of life of children and young people" to be suitable for examination.

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# Acknowledgments

I am very thankful for my supervisors, Verity Pacey and Mark Hancock, whose expertise, understanding, guidance and support made it possible for me to complete this thesis. I have enjoyed embarking on the adventure of being a researcher and it is largely due to them. It has been a pleasure working in the team at Macquarie University and I look forward to continuing to work with them in the immediate future.

I would like to thank Louise Tofts for being a great source of advice from a clinical perspective during my candidature. Thank you to Jennifer Baldwin, Marnie McKay, and Joshua Burns, for your helpful input in terms of the 1000 Norms Project for the study. Thanks to all of the clinicians at The Children's Hospital at Westmead and Sydney Children's Hospital for helping along the way.

To my wife Anna, I am incredibly thankful for your support and encouragement.

This project has been a fantastic journey and I hope that it is the first of many more to come!

# List of Abbreviations

| | |
|---|---|
| CAIT | Cumberland Ankle Instability Tool |
| CAIT-Youth | Cumberland Ankle Instability Tool – Youth version |
| CI | Confidence Interval |
| ICF-CY | International Classification of Functioning, Children and Youth version |
| IQR | Inter-Quartile Range |
| ISO | International Standards Organisation |
| ISPO | International Society for Prosthetics and Orthotics |
| KOOS | Knee injury and Osteoarthritis Outcome Score |
| KOOS-Child | Knee injury and Osteoarthritis Outcome Score – Child version |
| QLQ | Quality of Life Questionnaire |
| SD | Standard Deviation |
| SF-36 | Short-Form 36 |

# Chapter One:
# Introduction to longitudinal fibular deficiency

## 1.1. Longitudinal fibular deficiency

Longitudinal fibular deficiency, also known as fibular hemimelia, is most commonly defined as the congenital absence or hypoplasia of the fibula.[1] It is not an isolated anomaly but rather a spectrum of dysplasia of the lower limb.[2] Longitudinal fibular deficiency was first described by Gollier in 1698 as fibular hemimelia.[1] The original term "hemimelia" comes from the Greek "melos" (limb) and "hemi" (half) so the condition was defined by Gollier as the "absence of a large part of the fibula".[3] Other names for the condition have since been developed in attempts to make the definition more specific, such as postaxial hypoplasia of the lower extremity.[4] Despite this, the most common terms used in current literature and practice are longitudinal fibular deficiency and fibular hemimelia.

Longitudinal fibular deficiency is often associated with an equinovalgus[2,5-12] or equinovarus[6-9] foot, in addition to lateral ray deficiencies, anteromedial bowing of the tibia, femoral shortening, genu valgum, tarsal coalition, hypoplastic patella and cruciate ligament deficiency.[7,12] Affected individuals may present with one or more of these anomalies, unilaterally or bilaterally, with varying severity (Figure 1.1). As the fibula normally contributes to the lateral part of the ankle joint, its absence in conjunction with absent or lax ligaments in the ankle and knee, particularly the anterior cruciate ligament, can significantly affect joint stability and may affect lower limb function.[13] Upper limb anomalies have also been reported ranging from syndactyly (webbing of digits) to extensive deficiencies,[6,7,9] but these are not the focus of this thesis. Other non-musculoskeletal anomalies, such as cardiac and renal impairments, have been recently reported on in a review,[6] however, the reports of this refer back to a single case study.[7] Therefore, at present it is unclear if these non-musculoskeletal anomalies form part of the condition or if they are an unassociated co-morbidity in only one research participant.

## 1.2. Aetiology

The aetiology of longitudinal fibular deficiency is unclear.[6] Structural deformities may be due to disruptions during the critical period of embryonic limb development between the fourth and eighth weeks of gestation.[14] Possible disruptions have been theorised and one review suggests vascular dysgenesis, viral infections, trauma and environmental influences may contribute.[6] The condition does

not appear to recur in families which suggests a non-genetic origin; however, this does not entirely exclude a genetic or multifactorial cause in some cases.[6]

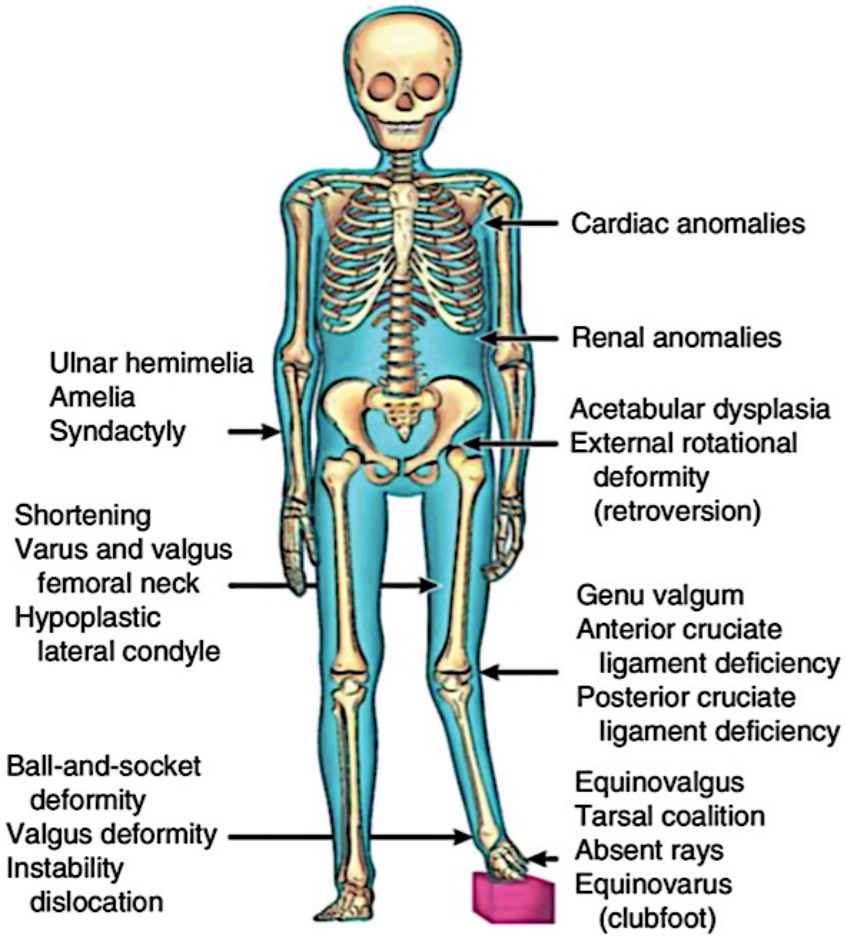


**Figure 1.1. Skeletal diagram of a 13-year-old child demonstrating the associated anomalies of longitudinal fibular deficiency[7]. Figure used with permission. This includes cardiac and renal anomalies which are only reported in one participant in one study.[8]**

## 1.3. Diagnosis

Longitudinal fibular deficiency is usually identified in utero by ultrasound during the second trimester ultrasound examination.[14] A fibrous band is noted instead of the fibula. Diagnosis is typically confirmed after birth by plain radiography in addition to clinical findings.[5] Long bone deficiencies may be a presenting feature in other syndromes or chromosome anomalies.[15] Therefore, differential diagnoses include amniotic band syndrome and thalidomide embryopathy, as well as several skeletal dysplasias and dysostoses (delayed ossification) with an asymmetrical involvement of the lower limbs such as femoral-facial syndrome.[15]

## 1.4. Incidence

The incidence of the condition is poorly understood and minimally studied. Many papers[6,10,12,17-20] quote an estimated incidence of 7.35 to 20 cases per million live births,[21,22] making longitudinal fibular deficiency the most common long-bone deficiency.[23] However, the validity of this reported incidence is uncertain. The earliest literature reports incidence of "absence of the foot" (Table 1.1), but these numbers could not be used to estimate longitudinal fibular deficiency as this phrase may also refer to other conditions such as amniotic band syndrome. As the terminology of diagnoses and presenting features within the literature became more specific, the incidence values became more valid. However, further studies are needed to qualify these estimates used in the consecutive case series listed in Table 1.1, which are based on radiographic evaluation. The extent of associated anatomical involvement, such as ligaments, is not clear at birth.[19] No incidence values have been recorded for particular classifications of the condition, for example, "partial" and "total" deficiencies.[24] It is unclear if one side of the body is affected more commonly or if the condition is more common in males or females.

**TABLE 1.1. Chronology of incidence values referenced in the literature.**

| Author | Years | Location | Participant Age | Description of condition recorded | Incidence reported | Estimated incidence per million |
|---|---|---|---|---|---|---|
| McIntosh et al. (1954)[25] | 1946-1953 | USA | 0-1 | "absence of foot" | 1/5530 | 180.8 |
| Rogala et al. (1974)[22] | 1964-1968 | United Kingdom | 4-9 | "fibula absence" | 0/52029 | <20 |
| Froster & Baird (1993)[21] | 1952-1984 | Canada | 0-7 | "fibula deficiency" | 9/1213913 | 7.35 |

## 1.5. Classification

The first classification system for longitudinal fibular deficiency was developed in 1952, and since then four other systems have been developed (Table 1.2). Historically, classification has been based on length and presence of the fibula, but recently more complex classification systems have been created in an attempt to account for other anatomical variations of the condition. The heterogeneity of longitudinal fibular deficiency and the lack of a widely agreed upon system have complicated the classification process. Clinically, the International Standards Organisation/International Society for Prosthetics & Orthotics (ISO/ISPO) classification of congenital limb deficiencies is utilised, which

**TABLE 1.2. Longitudinal fibular deficiency classification systems.**

| Author | Sample Size (n) | Years Data Collected | Anatomical Variant | Type | Original Description of Characteristic | Suggested Treatment |
|---|---|---|---|---|---|---|
| Coventry & Johnson (1952)[23] | 29 | 1913-1947 | Fibula | I | Hypoplastic fibula | Limb preservation |
| | | | | II | Rudimentary or absent fibula | Foot ablation |
| | | | | III | Bilateral fibular deficiency or the presence of "associated anomalies" | Probable limb preservation as no appreciable limb-length inequality was anticipated |
| Achterman & Kalamchi (1979)[7] | 81 | 1940-1977 | Fibula | IA | Hypoplasia of the fibula in the proximal area, ankle mortise intact | Conservative or epiphysiodesis of unaffected limb |
| | | | | IB | Hypoplasia of the fibula with dysplastic or absent ankle mortise | Prostheses, leg lengthening or amputation |
| | | | | II | Complete absence of the fibula | Prostheses, leg lengthening or amputation |
| Paley (19995)[16] | 0 | N/A | Ankle joint | 1 | Stable normal ankle | Lengthening of tibia and fibula |
| | | | | 2 | Dynamic valgus ankle | + ankle realignment + lengthening of calf muscles |
| | | | | 3a | procurvatum and valgus ankle joint | Types 3 & 4 involve specific osteotomies, leg lengthening and external fixation |
| | | | | 3b | subtalar coalition | |
| | | | | 3c | combination of 3a and 3b | |
| | | | | 3d | malorientation of the subtalar joint | |
| | | | | 4 | Fixed equino-varus ankle (clubfoot type) | |
| Stanitski & Stanitski[#] (2003)[1] | 32 | 1995-2003 | Fibula | I | Nearly normal fibula | Not stated |
| | | | | II | Small or miniature fibula, regardless of its position in the limb | Not stated |
| | | | | III | Complete absence of the fibula | Not stated |
| | | | Tibiotalar joint and distal tibial epiphyseal morphology | H | Horizontal | Not stated |
| | | | | V | Valgus (triangular distal tibial epiphysis) | Not stated |
| | | | | S | Spherical (ball-and-socket) | Not stated |
| | | | Tarsal coalition | c | If present | Not stated |
| | | | Foot rays (medial to lateral) | 1–5 | Number of rays | If 1-2 rays, then Syme's amputation. If 3-5 rays, individualised treatment. |
| Birch et al.* (2011)[9] | 104 | 1971-2005 | Fibula (with 4-5 foot rays) | 1A | <6% inequality | No treatment or orthosis or epiphysiodesis |
| | | | | 1B | 6% to 10% inequality | Epiphysiodesis ± lengthening |
| | | | | 1C | 11% to 30% inequality | 1 or 2 lengthenings ± epiphysiodesis or extension orthosis |
| | | | | 1D | >30% inequality | >2 lengthenings or amputation or extension orthosis |
| | | | Fibula (with 1-3 foot rays) | 2A | Functional upper extremity | Early amputation |
| | | | | 2B | Non-functional upper extremity | Consider salvage |

describes the condition as partial or total.[24] Table 1.2 outlines the different classifications systems created to account for the variable presentation of individuals with longitudinal fibular deficiency.

All five studies presented in Table 1.2 are case series from the USA using radiographic assessments of fibular deficiency of participants of any age. However, the systems vary greatly; some studies include joints,[1,7,16] some focus on anatomical aspects other than the fibula,[1,16,23] some suggest treatments,[7,9,23] and some include other anomalies such as upper limb involvement.[9,23] As diagnosis usually occurs in the newborn, classification may be delayed at this time due to some characteristics not yet being clear. For example, the need to assess radiological joint morphology may delay classification under the Stanitski & Stanitski system.[1] The Paley classification system developed in 1995 is widely recognised by paediatric orthopaedic surgeons and used in clinical practice.[16] Nevertheless, this surgically focused system is not relevant for children who do not have an intact ankle, so it is only potentially beneficial for a proportion of the population. As no clinically useful classification system is available for all of the population at present,[15] clinical experts published a catalogue of better defined skeletal disorders.[26] However, this does not include partial or total longitudinal fibular deficiency as described by the ISO/ISPO classification of congenital limb deficiency.[24] No cohort from the past decade has been considered when developing a classification system so knowledge about the condition changing over time is lacking. No cohorts from ethnicities outside the USA have been considered at the times of system development. Due to a lack of consensus and clinical applicability, recent studies[17] have used the older Achterman and Kalamchi (1979)[7] system despite the development of the newer classification systems.

# Chapter Two:
# Functional consequences of longitudinal fibular deficiency

## 2.1. Conceptualising longitudinal fibular deficiency within the International Classification of Functioning, Disability and Health (ICF)

The functional consequences of the anatomical variations associated with longitudinal fibular deficiency have not been well described in the literature. Longitudinal fibular deficiency can be associated with functional deficits related to foot and ankle deformities, lower limb joint stiffness and loss of muscle strength.[27] A vast spectrum of possible consequences exist that may affect a child's ability to perform an activity or participate in society. To date, no framework or model has been used to conceptualise the condition holistically and incorporate these possible consequences.

## 2.2. The International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY) model

The ICF model was developed by the World Health Organisation as the international standard to describe and measure health and health-related states. The Children & Youth version of this model, referred to as the ICF-CY,[28] was developed specifically for use with children and young people. It acknowledges the inherent differences in disability, health conditions and the environment that are due to rapid phases of development during the paediatric years.

Within the model, the following terms are defined: body functions are the physiological and psychological functions of bodily systems; body structures are anatomical parts of the body such as organs and limbs; an activity is the execution of a task or action by an individual; and participation is involvement in a life situation.[28] Building on these definitions in the context of a health condition, an impairment is defined as a physiological, psychological or physical problem with significant deviation from normal or a loss in body function or structure; activity limitations are difficulties in executing activities; and participation restrictions are problems experienced in involvement in life situations.[28] In addition, the ICF-CY framework includes two contextual factors that influence function and disability. Personal factors are internal influences, and environmental factors are external influences. The dynamic interaction between each of these ICF-CY components is presented in Figure 2.1.

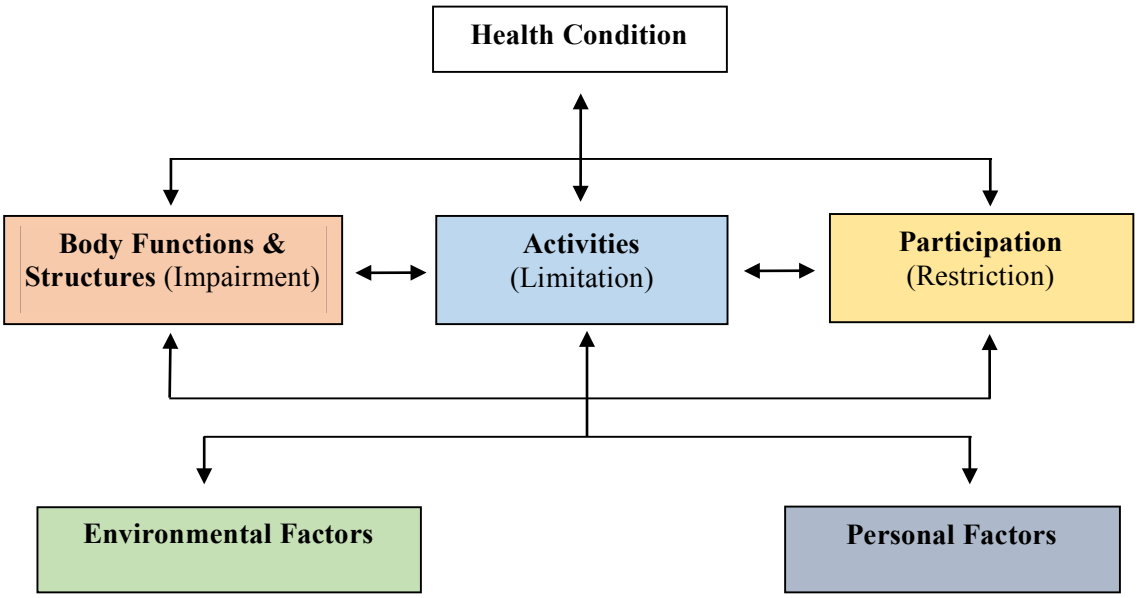


**Figure 2.1. Interactions between the components of the ICF-CY model.**[28]

## 2.3. ICF-CY interactions within an individual

Commonly considered impairments for longitudinal fibular deficiency are readily understandable using the ICF-CY model. For example, a leg length discrepancy due to fibular deficiency (impairment of body structure) may lead to a child having difficulty running (activity limitation) which then impedes on their ability to play football with their peers at school (participation restriction). The child's motivation (personal factor), in addition to the uneven grass on the field and access to appropriate footwear (environmental factors), will also interact with these elements of the model.

However, longitudinal fibular deficiency also impacts on other aspects of health which increase the complexity of the interactions between ICF-CY components. For example, decreased confidence may complicate a particular child's motivation to run and play sport with peers. Therefore, a broader and more complex understanding of the individualised nature of the condition, including personal and environmental influences, will enable clinicians to optimise patient management and allow researchers to appropriately conceptualise the condition in the paediatric population.

The focus of the ICF-CY is the impact on the functioning of the individual. When this framework is applied to children and young people with longitudinal fibular deficiency and the current evidence base is considered (Table 2.1), it is apparent that impairments have historically been investigated more

frequently than activity limitations and participation restrictions. For example, all studies in Table 2.1 reported on body structures using radiographic findings, whereas, very few studies have considered activity limitations and participation restrictions. This demonstrates a clear focus on the anatomy of the condition. However, it is important to note that all published studies to date are retrospective case series (Level IV) and hence are considered a low level of evidence (Appendix 5).[29]

The demographics of participants in the studies listed in Table 2.1 vary significantly. Five studies in Table 2.1 focused only on children, one on young adults, eight on both children and adults, and one on an unknown age range. The percentage of female participants ranged from 25.0 to 65.5% and was reported in only 13 of the 15 studies listed. The percentage of participants who were bilaterally affected ranged from 0 to 29.0%, and it was also reported in only 13 of the 15 studies listed. Because of the variability in these studies, as well as the quality of the evidence and the small sample sizes, it is unclear if specific impairments differ in these demographic characteristics of the condition.

Many of the studies analysed in Table 2.1 cover adulthood and childhood ages, but none report if there is any change in impairments, activity limitations or participation restrictions depending on the age of the individual. Furthermore, as all the currently published studies are retrospective case series, no study to date has provided comparisons with unaffected peers. Therefore, it is unclear if children or adults with longitudinal fibular deficiency have any critical time periods where their function is more or less limited compared to their age expected norms.

The literature on affected children and young people to date has focused primarily on impairments. However, standardised outcome measures have rarely been used, likely due to the retrospective nature of the studies. For example, when considering an altered gait pattern (impairment) or difficulties with walking (activity limitation), two papers[5,11] reported on a binary "Yes/No" outcome of limping based on observation only. Standardised objective measures, such as gait analysis have not been used, and the functional consequences of altered gait on an individual's ability to participate in self-care activities or play sport, have not been well described. Similarly, when considering the most commonly affected joints, the knee and ankle, within this population, standardised reproducible measures such as physical

**TABLE 2.1. References to components of ICF-CY for children and young people with longitudinal fibular deficiency in the literature.**

| | Participants | | | | Lower limb impairments | | | | | | | | | Activity Limitations | | | | Participation Restrictions | | | Environmental Factors | | Personal Factors |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Body Structures | | Body Functions | | | | | | | | | | | | | | | | |
| Author | Sample Size (n) | Age range (years) | % females | % bilateral | Bones of lower leg - fibular deficiency (s75010) | Ankle joint and joints of foot and toes (s75021) | Knee joint (s75011) | Stability of joint functions - knee (b715) | Stability of joint functions - ankle (b715) | Mobility of joint functions – knee/ankle (b710) | Muscle power functions (b730) | Gait pattern functions (b770) | Pain in lower limb (b28015) | Walking (d450) | Running (d4552) | Completing the daily routine (d2302) | Changing basic body position (d410) eg. Sitting to standing | School education (d820) | Doing housework (d640) | Sports (d9201) | Assistive products and technology for personal use in daily living (e1151) | Immediate family (e310) | Confidence (b1266) |
| Coventry & Johnson, 1952[24] | 29 | 0-52 | 65.5 | 20.7 | ✓ | | | | | | | | | | | | | | | | ✓ | | |
| Achterman & Kalamchi, 1979[2] | 81 | * | 43.2 | 19.8 | ✓ | ✓ | | | | | | | | | | | | | | | | | |
| Naudie et al., 1997[12] | 22 | 0-16 | 45.5 | 4.5 | ✓ | | | | | | | ✓ | | | | | | | | | ✓ | ✓ | |
| Birch et al., 1999[28] | 10 | 18-26 | 30.0 | 10.0 | ✓ | | | | | | ✓ | | | | | | | ✓ | | | ✓ | | |
| Stevens & Arms, 2000[6] | 20 | 0-21 | 55.0 | * | ✓ | | | ✓ | | | | | | | | | | | | | | | |
| McCarthy et al., 2000[30] | 25 | 2-33 | 44.0 | 20.0 | ✓ | | | | | | | | ✓ | | | | | | | ✓ | | | |
| Tomas-Gil et al., 2002[7] | 4 | 0-27 | 25.0 | 0 | ✓ | | | | | | | ✓ | ✓ | | | | | | | | | | |
| Stanitski & Stanitski, 2003[3] | 32 | 6-16 | 37.5 | 3.1 | ✓ | ✓ | | | | | | | | | | | | | | | | | |
| Catagni et al., 2010[4] | 32 | 10-32 | 37.5 | 0 | ✓ | | | ✓ | ✓ | ✓ | | | ✓ | | | | | | | | | | |
| El-Sayed et al., 2010[13] | 157 | 1-36 | 61.1 | 14.6 | ✓ | ✓ | | ✓ | ✓ | | | | ✓ | ✓ | | | | | | | | | |
| Birch et al., 2011[10] | 104 | 2-15 | 33.7 | 21.2 | ✓ | ✓ | ✓ | | | | | | | | | | | | | | | | |
| Oberc & Sulko, 2013[9] | 31 | 2-17 | * | 29.0 | ✓ | ✓ | | | | | | | | | | | | | | | | | |
| Shabtai et al., 2014[11] | 18 | 9-49 | 55.6 | 16.7 | ✓ | | | ✓ | | ✓ | | | | | | | | | | | | | |
| Yoong & Mansour, 2014[19] | 5 | 14-31 | 40.0 | 20.0 | ✓ | | ✓ | | | | | | | | | | | | | | | | |
| Popkov et al., 2015[17] | 52 | 4-7 | * | * | ✓ | ✓ | | | | | | | | | | | | | | | | | |

* Not reported

assessment of range of motion[2,10] and radiographic findings,[12] have been used. However, the effect of these impairments on an individual's function, incorporating the use of validated patient-reported outcomes measures, has not been assessed.

Overall, validated patient-reported outcomes have been used minimally in research regarding children and young adults with longitudinal fibular deficiency. For example, one study reported broadly that participants were observed being able to "walk independently".[12] However, no studies to date report on patient-reported walking ability. Patient-reported outcomes have not been used to identify the perceived impact of impairments, such as an altered gait pattern, on an individual's participation in daily activities. Similarly, lower limb joint instability has been reported on physical assessment[4,12] and patient reports of subluxation,[2,10] but this has not been done using a standardised patient-reported outcome measure.

Another example of an impairment in longitudinal fibular deficiency that has not been thoroughly reported on in the literature is pain. Two studies[2,30] reported on pain using non-standardised 5-point pain assessment scales, whereas two other studies[5,12] had a binary "Yes/No" report on the presence of any pain. Given El-Sayed et al. (2010) report the presence or absence of pain in infants through to young adults,[12] the manner in which this data was obtained, and who reported it, is essential to provide a clear understanding of their findings. This is significant because parents and children can perceive pain differently.[31] In each of these studies, it appears that pain was patient-reported, but it was not specified if the parents or children in these studies reported these symptoms. The potential impact of pain on activity limitations and participation restrictions is likely to be significant,[32] but this has been largely ignored in research studies to date. The location of pain, as well as the duration, intensity and type of pain, has not been described well in the current literature.

Activity limitations and participation restrictions are poorly understood for affected children and young adults. No studies to date have reported on the ICF-CY activity limitations (Table 3) such as running, performing daily routines or changing basic body position from sitting to standing. Naudie et al. (1997) reported on the frequency of school participation, but no study has reported on the ability to participate or quality of participation at school. Likewise, Birch et al. (1999) reported on school attendance but not

on a young person's perception of their ability to participate in daily activities at school. In terms of sports participation, only one study (McCarthy et al., 2000) reported on it as a binary "Yes/No" outcome but did not use a standardised outcome measure nor compare to unaffected peers to determine the difference, and hence effect size, of decreased sporting participation.

From an ICF-CY perspective, it is evident that environmental factors and personal factors are also poorly considered in the literature at present. Naudie et al. (1997)[11] commented on the involvement of families in treatment decisions but did not use child or parent/carer reported outcome measures. Some studies commented on the use of prostheses[11,23,27] but this was not in the context of their influence on activities and participation. Additionally, no studies to date have reported on personal factors such as confidence or personal and family difficulties and challenges as a result of longitudinal fibular deficiency.

## 2.4. Lower Limb Function

"Functioning" is a term described by the ICF-CY as encompassing all body functions, activities and participation.[28] When considering the function of the lower limbs, two affected joints in longitudinal fibular deficiency are the knee and ankle.[17] In unaffected populations, the knee provides the ability to flex and extend the lower leg, providing controlled movements during the stance and swing phases of gait. The ankle joint similarly provides movements of the foot. Coordinated movements of these joints are critical for a normal gait pattern. However, it is suspected that various impairments in longitudinal fibular deficiency, such as a leg length discrepancy or absent anterior cruciate ligament (which has been reported in 95% of cases in a retrospective case series of 66 children[33]), may impact on knee and ankle joint function.[13] It is evident from Table 2.1 that impairments to the knee and ankle joints have been emphasised in the literature to date, with little consideration for the functional consequences of these impairments and how they may impact on activities, participation and quality of life.

## 2.5. Quality of Life

Quality of life is defined as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns.[34] It broadly refers to a person's physical, psychological, social wellbeing, as well as aspects

of the environment and a person's standard of living.[35] Evidence suggests that children with congenital physical disabilities have psychosocial adjustment problems,[36,37] and may report reduced quality of life.[38-40] In longitudinal fibular deficiency, quality of life has only been reported in three studies; all of which target the adult population. Firstly, a small case series of young adults who had had a Syme amputation (n=10) by Birch et al. (1999)[27] used the Quality of Life Questionnaire (QLQ)[41] and found participants had no statistically significant difference in their quality of life in comparison to previously published normative adult samples. The findings of this study should be considered cautiously because of the small sample size of only amputees, so there is limited applicability to the broader population of individuals with longitudinal fibular deficiency. Secondly, a cross-sectional study (n=62) by Walker et al. (2009) used the Short-Form 36 (SF-36)[42] and QLQ[41] and in comparison to previously published normative data, reported no statistically significant differences in adults with longitudinal fibular deficiency. Finally, a small adult case control study (n=11) by Crawford et al. (2012)[19] used the SF-36[42] and also found affected adults had very similar scores compared to normative data from the manual published in 1993,[43] with no statistically significant differences. The small sample size and low return rate of only 11/66 participants completing the questionnaire were significant limitations of this study. No study has investigated this outcome in children to date. While it appears at present, overall, affected adults have similar quality of life to their peers, good quality evidence is lacking and research is needed on how affected children and young people perceive their quality of life.[44]

## 2.6. Current clinical management considering the ICF-CY model

A major focus of treatment for longitudinal fibular deficiency is the surgical management of impairments of body structures as defined by the ICF-CY.[11,17] Surgical management varies depending on the condition of the foot, the presence of associated anomalies, bilaterality, family desires and cultural differences.[30] For milder classifications of longitudinal fibular deficiency, a conservative approach is often employed because of the risks involved with invasive surgical interventions and the effectiveness of prostheses in these patients.[6] The two main invasive management options for longitudinal fibular deficiency are amputation and limb lengthening. However, no high quality randomised-controlled trials have been performed to inform this important management decision. Division exists amongst leading clinicians as to whether invasive techniques such as amputation should be considered the last line of

treatment, or an early management option.[2,20,30,45] These management decisions relating to which surgical approach, if any, have to be made in a growing child, but minimal paediatric research on functional outcomes is currently available.[44] Some retrospective research has been conducted on long-term adult outcomes,[19,20,27] but investigating adult outcomes will not sufficiently provide information about participation at school and in sports. In addition, recent advances in surgical techniques and devices have led to a shift to less invasive surgical techniques. For example, the recent development of internal lengthening devices has attempted to reduce the complication rates associated with the previously used Ilizarov external fixators.[10] Therefore, to guide these critical decisions, a need exists for up-to-date high quality prospective research focusing on children and young people.

Management that focuses on improving function requires a multidisciplinary approach involving genetic counsellors, perinatologists, prosthetists, paediatric orthopaedic surgeons, physiotherapists and social workers to provide holistic care not solely focused on impairments.[46] Current amputee guidelines suggest that if a limb deficiency is detected during pregnancy, the parents should be referred antenatally to the appropriate limb clinic,[47] but minimal literature is available to support management guidelines. The surgical and prosthetic management of longitudinal fibular deficiency is often focused on anatomical changes, for example, algorithms based on leg length discrepancies,[8] and not on the activity limitations and participation restrictions resulting from the condition, such as difficulties climbing stairs and playing sports. Although the anatomical changes potentially impact function, this focus restricts treatment planning and goal setting because it assumes that particular anatomical changes always lead to specific functional changes. Families of children with a physical disability are interested in functional outcomes,[48] such as participation in activities of daily living with a prosthetic leg,[44] rather than how anatomically correct a particular limb or joint is. Holistic management that considers all aspects of the ICF-CY could be better informed if evidence was available regarding functional outcomes and quality of life in children and young people, but this evidence is currently lacking.

## 2.7. Outcome measures in the context of the ICF-CY model

Parents of children and young people with any physical disability are vitally concerned about their future performance of activities of daily living and active participation in society.[48] Therefore, high quality

prognostic information would have great value in providing this information. Understanding how longitudinal fibular deficiency affects children and young people is significant because paediatric years are critical years of functional development, for example, learning to participate in sports. As the current data for functional outcomes is limited and only available in adults, it has limited generalisability to the paediatric population.

Currently, the available literature relating to longitudinal fibular deficiency has a strong focus on impairments in terms of the ICF-CY (Table 2.1).[28] Outcome measures used in research for the condition are often focused on surgical outcomes such as healing index, limb length and joint range of motion.[2,8,10] To ensure activity limitations and participation restrictions are considered in addition to impairments, a need exists to use outcome measures assessing lower limb function and quality of life.

*2.7.1. Patient-reported outcome measures*

In order to assess lower limb function and quality of life, patient-reported outcomes are required. Historically, these have not been used often in the clinical paediatric setting, but in recent years, paediatric versions of patient-reported outcomes have been developed and validated. Prime examples of these outcomes are those for the Knee injury and Osteoarthritis Outcome Score (KOOS)[49] and the Cumberland Ankle Instability Tool (CAIT)[50]; namely the KOOS-Child[51] and CAIT-Youth[52] (Appendices 1-4). This has created an opportunity for research focusing on children's activity and participation outcomes. Table 2.2 summarises available outcome measures that are valid and reliable measures of lower limb function or quality of life in children and young people. Measures that have not been validated for children and young people are excluded from the table.

**TABLE 2.2. Valid and reliable patient-reported outcome measures that could be used in longitudinal fibular deficiency research in children and young people to assess lower limb function and quality of life.**

| Outcome Measure | Validated Age Ranges (years) | Purpose | Lower Limb Function | Quality of Life | ICF Components Addressed: Body Functions / Structures | Activity Limitations | Participation Restrictions | Environmental Factors | Personal Factors |
|---|---|---|---|---|---|---|---|---|---|
| Knee injury and Osteoarthritis Outcome Score (KOOS-Child[51] & KOOS[49]) | 7-16 & 17-79 | Assess knee pain, symptoms, activities of daily living, sport and recreation and quality of life. | ✓ | ✓ | ✓ | ✓ | ✓ | | ✓ |
| Cumberland Ankle Instability Tool (CAIT-Youth[52] & CAIT[50]) | 8-16 & >16 | Assess ankle pain and instability. | ✓ | | ✓ | ✓ | ✓ | ✓ | |
| International Knee Documentation Committee (IKDC) Subjective Knee Form[53] | >12 | Measure symptoms, function and sports activity. | ✓ | | ✓ | ✓ | ✓ | | |
| Cincinnati Knee Rating System[54] | 13-65 | Assess overall knee function with respect to work limitations. | ✓ | | ✓ | ✓ | ✓ | | |
| Short-Form Health Survey (SF-36)[42] | 15-52 | Evaluate general health with mental and physical component scores. | | ✓ | ✓ | ✓ | ✓ | | ✓ |
| Paediatric Quality of Life Inventory (PedsQL)[55] | 2-18 | Assess quality of life and ambulatory status. | | ✓ | | ✓ | ✓ | | ✓ |
| Child Health Questionnaire (CHQ)[56] | 5-13 | Measure physical and psychosocial well-being of children | | ✓ | | ✓ | | ✓ | ✓ |

To encompass the assessment of both lower limb function and quality of life, incorporating all aspects of the ICF-CY, the focus of this thesis is on the KOOS/KOOS-Child and CAIT/CAIT-Youth.

*2.7.2. Knee injury and Osteoarthritis Outcome Score (KOOS & KOOS-Child)*

The Knee injury and Osteoarthritis Outcome Score (KOOS) is a patient-reported outcome measure used to assess a patient's opinion about their knee function. It contains 42 questions in five subscales; Pain, other Symptoms, Function in daily living (ADL), Function in sport and recreation (Sport/Rec) and knee-related Quality of life (QOL). The KOOS is a valid and reliable outcome measure[57] that has a comprehensive focus on the activity limitation & participation restrictions components of the ICF-CY (Figure 2.1). A score from 0 (worst) to 100 (best) is given for each of the subscales. The KOOS-Child has been used in children with patellofemoral pain syndrome,[58] demonstrating significantly worse scores compared to pain-free adolescents. In a population-based cohort, Paradowski et al. (2006)[59] found pain, physical function and knee-related quality of life vary with age and gender. This article recommended the use of age and gender matched reference values when evaluating outcomes using the KOOS.

*2.7.3. Cumberland Ankle Instability Tool (CAIT & CAIT-Youth)*

The CAIT is a patient-reported outcome measure used to assess a patient's opinion about their ankle pain and instability. It contains nine questions with a total score out of 30, with a higher score indicating better stability. The CAIT is a valid and reliable outcome measure[50] incorporating some questions that go beyond impairments to also provide insight into the perception of stability associated with activity limitations and participation restrictions. The CAIT-Youth has been used in children with Charcot-Marie-Tooth disease,[52] demonstrating significantly worse scores compared to unaffected children. In 2014, the cut-off score for functional ankle instability using the CAIT in adults was independently recalibrated from ≤27 out of 30[50] to ≤25 out of 30.[60] However, no cut off has been proven valid and reliable in children and young people.

*2.7.4. Summary of outcome measures*

Patient-reported outcomes have not yet been utilised in children and young people with longitudinal fibular deficiency in the literature. It is, therefore, evident that paediatric studies using patient-reported

outcomes, particularly ones related to lower limb function and quality of life, are warranted. Both the KOOS-Child and CAIT-Youth are appropriate outcome measures to use in this population.

# Chapter Three:
# Longitudinal fibular deficiency: A cross-sectional study comparing lower limb function and quality of life of children and young people with unaffected peers

**This chapter is presented in the exact format of the manuscript which has been submitted to the American Journal of Physical Medicine & Rehabilitation.**

# Statement from co-authors confirming authorship contribution of the Master of Research candidate

As co-authors of the paper "Longitudinal fibular deficiency: A cross-sectional study comparing lower limb function and quality of life of children and young people to unaffected peers", we confirm that Joshua Pate has made the following contributions:

- conception and design of the research
- collection and extraction of data
- analysis and interpretation of the findings
- writing of the manuscript and critical appraisal of the content

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| A/Prof Mark Hancock | M. Hancock | Date: 15 September 2016 |
| Dr Louise Tofts | | Date: 16 September 2016 |
| Dr Adrienne Epps | | Date: 15 September 2016 |
| Jennifer Baldwin | Jennifer Baldwin Digitally signed by Jennifer Baldwin DN: cn=Jennifer Baldwin, o=The University of Sydney, ou=Clinical and Rehabilitation Sciences, email=jennifer.baldwin@sydney.edu.au, c=AU Date: 2016.09.15 13:19:11 +10'00' | Date: 15 September 2016 |
| Marnee McKay | | Date: 16 September 2016 |
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**Title:**

Longitudinal fibular deficiency: A cross-sectional study comparing lower limb function and quality of life of children and young people with unaffected peers

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**Author Disclosures:**

*Competing Interests*: None declared.

*Funding*: JP is a Research Assistant employed by Limb Clinic, Kids Rehab at The Children's Hospital at Westmead from funds donated by the Limbless Soldiers Association. The 1000 Norms Project was supported by the National Health and Medical Research Council of Australia (NHMRC, #1031893), and Australian Podiatry Education & Research Fund, Australasian Podiatry Council.

*Financial benefits to the authors*: Nil.

*Details of any previous presentation of the research, manuscript, or abstract in any form* – Abstract accepted to Rehabilitation Medicine Society of Australia and New Zealand Conference (October 16-19, 2016) for poster presentation on 30 May, 2016.

# Abstract

**Objective**

To compare the lower limb function and quality of life of children and young people with longitudinal fibular deficiency to that of unaffected peers.

**Design**

Seventeen (10 males) of an eligible 25 (68%) children and young people with longitudinal fibular deficiency aged 7 - 21 years living in New South Wales, Australia completed the 'Knee injury and Osteoarthritis Outcome Score' (KOOS/KOOS-Child) and the 'Cumberland Ankle Instability Tool' (CAIT/CAIT-Youth) validated questionnaires, and were compared to data from 213 unaffected peers. Linear regression models compared affected children and young people to unaffected peers.

**Results**

Affected participants on average reported lower knee and ankle function and quality of life than unaffected peers (all $P \leq 0.001$). Age significantly affected the difference in all five KOOS domain scores with younger children with longitudinal fibular deficiency having a greater difference to their unaffected peers (all $P \leq 0.02$). Differences in ankle function (CAIT scores) were not affected by age ($P=0.26$).

**Conclusion**

Children and young people with longitudinal fibular deficiency reported reduced lower limb function and quality of life than unaffected peers. Knee function was worse in younger affected children and closer to normal in young adults.

**Key Words:**

Longitudinal fibular deficiency, fibular hemimelia, lower limb function, quality of life.

# Introduction

Longitudinal fibular deficiency, also known as fibular hemimelia, is the congenital partial or complete failure of formation of the fibula.[1] It is not an isolated anomaly but a spectrum of dysplasia of the lower limb.[2] Longitudinal fibular deficiency is the most common long-bone deficiency,[3] with an estimated incidence of 7.4 to 20 cases per million live births.[4,5]

Longitudinal fibular deficiency may present unilaterally or bilaterally, with varying severity and involvement of associated anatomical changes.[6] The integrity and function of both the knee and ankle joint may be affected, as well as the length of the long bones and therefore the leg. As the fibula normally contributes to the structure and stability of the lateral part of the ankle joint, its absence in conjunction with absent or insufficient ligaments in the ankle and knee, particularly the anterior cruciate ligament, can significantly affect joint stability and therefore may affect lower limb function and participation in daily activities.[7] Diagnosis usually occurs on mid to late gestation fetal ultrasound scan or soon after birth.[6] It is commonly associated with an equinovalgus[2,3,7-13] or equinovarus[3,7,9,10] foot, in addition to lateral ray deficiencies, anteromedial bowing of the tibia, femoral shortening, genu valgum, tarsal coalition, hypoplastic patella and cruciate ligament deficiency.[9,13]

Parents of young people with any congenital structural anomaly are concerned about their child's ability to perform activities of daily living and fully participate in society, throughout their life.[14] To date, studies on longitudinal fibular deficiency have focused on impairments rather than the domains of activity limitations and participation restrictions, as described by the International Classification of Functioning Children & Youth Version (ICF-CY).[15] Commonly used outcome measures in the literature, such as healing index, limb length and joint range of motion,[2,3,11] focus on impairments but do not include the impact these impairments have on a young person's function and quality of life. Patient-reported outcomes are likely to better capture the impact longitudinal fibular deficiency has on function and quality of life.

Quality of life of adults with LFD has been reported to be similar to that of their unaffected peers in three studies.[16-18] No published information is available for lower limb function and quality of life in

children and young adults with longitudinal fibular deficiency; life stages where functional skills and social relationships primarily develop. Therefore, the aim of this cross-sectional study was to investigate patient-reported lower limb function on the affected limb, and quality of life, in children and young people with longitudinal fibular deficiency in comparison to unaffected peers.

# Methods

*Study design*

This was a cross-sectional study involving children and young people with longitudinal fibular deficiency who lived in the state of New South Wales, Australia from October 2015 to April 2016. Measures of lower limb function and quality of life were collected and compared to a data subset from the 1000 Norms Project, a cross-sectional study that collected patient-reported outcomes and physical performance measures in 1000 healthy individuals aged 3-101 years (January 2014 – September 2015), also living in New South Wales, Australia at a similar time.[19] Ethics approval was gained for the study from Sydney Children's Hospitals Network (LNR/15/SCHN/327) and Macquarie University (Ref: 5201500761). The 1000 Norms Project had ethical approval from the institutional ethics committee at the University of Sydney (HREC 2013/640).

*Participants*

An attempt was made to identify the complete population of individuals aged 7-21 years of age, with a diagnosis of longitudinal fibular deficiency, who were living in New South Wales during the study period. Exclusion criteria included any individuals with unassociated comorbidities likely to significantly affect lower limb function and quality of life, such as intellectual disability and neurological conditions, those who had undergone previous lower limb joint surgery not related to their condition, and those less than 6 months since most their recent surgical procedure relating to longitudinal fibular deficiency. Based on an estimated incidence of between 7.4 and 20 cases per million live births,[4,5] and the 2014 New South Wales Census population data,[20] the number of possible participants with longitudinal fibular deficiency in the study's age range was estimated to be between 10 and 28. Each participant's condition was classified using the Achterman & Kalamchi (1979) system in which hypoplasia of the fibula is Type Ia, partial absence is Type Ib, and complete absence is Type II.[9]

The control group comprised of a sample of individuals living in New South Wales, Australia who were representative of the healthy 'normal' population across this age range.[19] Participants in this study were healthy by self-report and able to participate in age-appropriate daily activities. Potential participants in the 1000 Norms Project were excluded based on inability to follow instructions, insufficient English language, and any condition affecting neurological function and mobility.[19]

*Identification and recruitment of participants with longitudinal fibular deficiency and of unaffected peers*

Participants with longitudinal fibular deficiency were identified via two sources: (1) through diagnostic codes in the rehabilitation and orthopaedic databases at the Sydney Children's Hospitals Network which provides the only paediatric management clinics for children and young people with longitudinal fibular deficiency in New South Wales; and (2) through a patient support organisation called "Limbs4Life". Potential participants and their parent/carer were sent a letter of invitation, participant information sheet, three questionnaires and a stamped self-addressed envelope. Potential participants who did not respond within two weeks received a follow-up telephone call, email or text message. Three attempts were made to contact potential participants who did not reply to the first letter of invitation. All participants in the 1000 Norms Project that were aged 7-21 years were included as the control group of unaffected peers.

*Data collected*

After obtaining informed consent from participants, questionnaire and demographic data were collected by mail or email depending on participant preference. Demographic data was collected from the participant (ages 17-21 years) or parent/carer (ages 7-16 years), using a standard questionnaire. Data collected included age, gender, affected leg(s), height, weight, prosthetic use, pain, and surgical history. Treating health professionals confirmed reported surgical procedures and dates these occurred.

Control data for unaffected peers was available at an individual participant level for children and young people aged 7-21 years of age who participated in the 1000 Norms Project.[19]

*Outcomes*

Patient-reported knee function and quality of life were assessed through completion of the 'Knee injury and Osteoarthritis Outcome Score' (KOOS/KOOS-Child). The KOOS was used for participants aged 17-21 years, and the paediatric version of the KOOS, the KOOS-Child, was used for participants aged 7-16 years. The KOOS and KOOS-Child are patient-reported outcome measures used to assess an individual's knee function. The KOOS-Child mirrors the KOOS, and both questionnaires have five domains; pain, other symptoms, function in daily living, function in sport and recreation, and quality of life. The KOOS/KOOS-Child are valid and reliable outcome measures[21,22] with a focus on the activity limitation and participation restriction components of the ICF-CY[15]. A score from 0 to 100 is given for each of the domains; a higher score indicating better function.

To investigate functional ankle instability, the 'Cumberland Ankle Instability Tool' (CAIT/CAIT-Youth) was used; the CAIT for participants aged 17-21 years and CAIT-Youth for participants aged 7-16 years. It contains nine questions with a total score out of 30; a higher score indicating better function. The CAIT/CAIT-Youth are valid and reliable patient-reported outcome measures[23,24] and questions relate to ankle pain and functional instability in a variety of environmental contexts including sports participation.

If participants did not complete all questions in the KOOS or CAIT, each domain with missing data was scored following the standard instructions provided in each questionnaire. Individuals without an intact ankle or knee joint were not requested to complete the associated outcomes. The most affected limb was used in all analyses for participants who had bilateral limb involvement. The control participants from the 1000 Norms Project completed the same outcomes as the participants with longitudinal fibular deficiency.

An open-ended question was asked to identify the challenges of growing up with longitudinal fibular deficiency from the perspective of the patients and/or their parents/carers. All affected participants were asked, "Have you [or has your child] faced challenges growing up where you could have been assisted to prepare and deal with these challenges? If 'Yes', please list the top 3 (in priority order)". Common

themes raised in these responses were identified and the frequency of responses relating to identified themes was recorded.

*Data Analysis*

A descriptive analysis of the demographics of the individuals with longitudinal fibular deficiency and control participants was performed. The paediatric versions of the KOOS and CAIT, the KOOS-Child and CAIT-Youth respectively, are similar measures to the adult versions but with simplified language to make it appropriate for children. Therefore, a combined analysis was performed for the two versions of each outcome. As individual participant data was available for both children and young people with longitudinal fibular deficiency and the unaffected peers, the data was combined in a single data set. Comparison of KOOS and CAIT scores for children and young people with longitudinal fibular deficiency and unaffected peers was performed using linear regression models. Separate models were built for each outcome including the five KOOS domains and a total CAIT score. For each outcome a simple model was built where longitudinal fibular deficiency status ("yes" or "no") was the only variable entered. Next a model was built adjusting for age, gender, and Body Mass Index-For-Age Percentile.[25] Finally, a model was built adjusting for the same variables but it also included the interaction between age and longitudinal fibular deficiency. The interaction term was included to assess if differences in outcomes between individuals with longitudinal fibular deficiency and unaffected peers were systematically related to age. The data was assessed for normality by visual inspection, and as all outcomes were normally distributed, means (SD) were used. All analyses were conducted using Statistical Package for the Social Sciences Version 22.0.[26]

# Results

A total of 25 potential participants were initially identified through the clinic database and an attempt to contact them was made. Two potential participants contacted the researchers through Limbs4Life, but both were too young to participate in the study. Two potential participants declined to participate and 6 did not respond to contact attempts. Therefore, 17 children and young people (68%) agreed to participate in the study and all completed the questionnaires. One was initially excluded due to recent surgery, but then re-entered the study 6 months post-surgery (still within study recruitment period). Normative data

was obtained from 213 unaffected peers who were in the appropriate age range from the 1000 Norms study.[19]

Details of included participants are provided in Table 1 and a comparison with unaffected peers is provided in Table 2. Within the group of individuals with longitudinal fibular deficiency, there were 13 unilateral cases with the right side affected in 5 participants and the left in 8. Four participants had bilateral involvement. Total fibula absence was identified in 2 participants, and Syme's amputations had been performed on 7 participants. Five children with longitudinal fibular deficiency, all under the age of 15 years, reported 1-3 falls in the past week.

The KOOS/KOOS-Child questionnaire was fully completed by 16 of 17 participants, and partially completed by one participant who completed 2 of the KOOS domains and had missing data for the other 3 domains and did not respond to requests to complete these questions. The CAIT/CAIT-Youth was completed by 13 of 17 participants, as there were 4 participants who did not have intact affected ankles due to Syme's amputations. One participant had both intact ankles affected but scored the same on both sides, so this was the score used in the analyses.

The outcome scores for individuals with longitudinal fibular deficiency and unaffected peers are presented in Table 3 along with unadjusted and adjusted differences. There was a statistically significant difference between participants with longitudinal fibular deficiency and unaffected peers for all KOOS domains and the CAIT score. The between-group differences from the unadjusted model were similar to the between-group differences from the adjusted model. Adjusted between-group differences ranged from 11.0 points for KOOS Pain domain through to 25.3 points for KOOS quality of life domain. Unaffected peers scored higher in all outcomes.

For all KOOS domains, age significantly affected the difference in scores between participants with longitudinal fibular deficiency and unaffected peers (Figure 2, all $P \leq 0.02$ for age interaction). The differences between participants with longitudinal fibular deficiency and unaffected peers was greatest for the younger children and reduced over time as demonstrated by the interaction term in the model.

For each year older that participants were, the difference between KOOS scores for participants with longitudinal fibular deficiency and unaffected peers reduced by 2.2 (95% CI: 0.5-3.9) points for pain, 2.2 (95% CI: 0.8-3.6) points for symptoms, 2.1 (95% CI: 1.3-3.0) points for activities of daily living, 3.5 (95% CI: 1.9-5.1) points for sports and recreation and 2.3 (95% CI: 0.6-4.1) points for quality of life. The differences in CAIT scores between participants with longitudinal fibular deficiency and unaffected peers was not influenced by age (P=0.256 for age interaction). Figures 1 and 2 present the outcomes for the CAIT/CAIT-Youth and each domain of the KOOS/KOOS-Child for both participants with longitudinal fibular deficiency and unaffected peers for the range of included ages.

12 out of 17 participants with longitudinal fibular deficiency reported challenges in the open-ended question. The most frequent responses related to anxiety (5 mentions), social acceptance (4 mentions), and sports participation (4 mentions).

# Discussion

This study found that children and young people with longitudinal fibular deficiency on average report reduced lower limb function and quality of life when compared to unaffected peers. A novel finding from this study was that knee function for people with longitudinal fibular deficiency is significantly worse than unaffected peers in younger children, but is similar to unaffected peers in young adults. In contrast, ankle function is reduced in both children and young adults with longitudinal fibular deficiency when compared to unaffected peers.

The findings of this study that knee function and quality of life approximates that of unaffected peers in the older participants is supported by previous literature for adults[17,18] which found that adults with longitudinal fibular deficiency had active lives similar to age-matched controls and high levels of general function using the Short Form 36 (SF-36). Likewise, Birch et al. (1999)[16] investigated quality of life in young adults and adults with longitudinal fibular deficiency and found it similar to that of the unaffected adult population. For the younger participants in our study, and for ankle function specifically, there is no previous literature to use for comparison. The novel findings in this younger age group warrant further investigation.

A strength of this study was the large unaffected peers control group who were similar in terms of the baseline characteristics collected, geographical area and time period when data was collected. By having the same patient level data for both cases and controls, adjusted between-group differences were able to be calculated using modelling which included covariates. This study was also able to introduce interactions between age and longitudinal fibular deficiency status into the models. Although this study only had 17 participants with longitudinal fibular deficiency, this represents a large proportion of the whole population (68%) in the state of NSW. It is possible that some youth with longitudinal fibular deficiency living in NSW were not identified; however, the approach used was very thorough. Estimates of the longitudinal fibular deficiency population from the census data and incidence rates suggest most if not all potential participants are likely to have been identified.

While this study did adjust for some variables, other factors such as severity of disease were not adjusted for which could have impacted the findings. To compare between the different severity classifications of longitudinal fibular deficiency, large multi-center trials would need to be undertaken to achieve a sufficient sample size. In addition, no condition-specific quality of life measure currently exists. Although the KOOS and CAIT have been widely used in a variety of different patient populations, these measures have not been specifically validated in assessing individuals with longitudinal fibular deficiency. To inform the development of such a measure, the main challenges presented by the participants of this study could be used as the basis of more qualitative work.

The finding that younger children with longitudinal fibular deficiency are substantially behind unaffected peers with regards to knee function suggests that early intervention targeting this outcome may be important. Guidelines state that comprehensive multidisciplinary services incorporating both physical and psychological management are likely to improve the outcomes for children with longitudinal fibular deficiency.[27] While current practice in Australia appears to broadly adhere to these guidelines, the majority of affected children do not receive interventions specifically aiming to improve knee function as it has not been routinely assessed in the clinical setting. This is potentially because it was not previously known that knee function was substantially reduced in comparison to their unaffected

peers. While providing intervention targeting knee function seems appropriate based on our findings, especially in younger children, there is a need for randomised controlled trials to provide rigorous evidence that the interventions are actually effective and help younger patients improve knee function. Additionally, longitudinal studies following individual children over time are needed to further investigate this study's finding that knee function of affected children gradually improves to become closer to unaffected peers as they grow older. Interventions focused on improving knee function in younger children with longitudinal fibular deficiency, such as physiotherapy and prosthetic prescription, may be important in meeting their functional potential and 'catching-up' with their unaffected peers sooner.

Ankle function scores were lower for children and young people with longitudinal fibular deficiency regardless of age, and currently no studies exist providing evidence on strategies to improve this. Currently no literature on the role of physiotherapy exists for ankle instability in people with this condition, and due to the nature of the anatomical consequences, further research is needed. The benefits of physiotherapy have been well established in unaffected young adults with chronic functional ankle instability.[28] Physiotherapy aimed at improving functional ankle stability in people with longitudinal fibular deficiency may be important at any age and this should be investigated.

Important areas for future research include investigations to better understand the factors contributing to the range of functional levels in children and young people with longitudinal fibular deficiency. While we found on average function was below that of unaffected peers, some individuals scored at or above average levels of unaffected peers. Future studies could look at trying to delineate why some children and young people have reduced function and other do not. For example, comparing outcomes for children affected unilaterally or bilaterally. A Dutch study found that children with bilateral limb deficiencies appeared to be functioning less adequately than the other amputee children,[29] but this information is not specific to longitudinal fibular deficiency so further research into this would be important. Also, investigating the impact of the severity of the condition could lead to better function and quality of life outcomes in children and young people with longitudinal fibular deficiency. The responses to the open-ended question highlight the difficulties with anxiety and social acceptance for

families of children and young people with longitudinal fibular deficiency; a broader area where further research is required.[30]

The results of this study provide helpful and relevant clinical information to families and health professionals regarding the functional outcomes of children and young people with longitudinal fibular deficiency and how this is different for different ages. Detailed information about the longitudinal fibular deficiency population from a more holistic perspective in terms of the ICF-CY is provided that could enable improved education. Provision of this information may reduce anxiety for families, particularly in the early stages of the child's life regarding the likely functional impact of the condition, and it could also assist families to make better long-term management decisions.

# Conclusion

Children and young people with longitudinal fibular deficiency on average report reduced lower limb function and quality of life compared to unaffected peers. A novel finding of this study is that knee function is worse in younger affected children and closer to normal in young adults. This study provides information which is important to patients and families and also opportunities for improving clinical care and directing future research.

**Acknowledgements:**

Kate Knox (Physiotherapist, The Children's Hospital Westmead) and Margaret Patterson (Physiotherapist, Rehab2Kids, Sydney Children's Hospital) for providing additional clinical advice. Limbs4Life http://www.limbs4life.org.au/ for enabling additional potential recruitment of participants.

*Control group information:*

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# Figure Legends

Figure 1. Scores of children and young people with longitudinal fibular deficiency for intact ankles on the affected limb and trendline, and unaffected peers trendline for the CAIT/CAIT-Y against age (years).

Figure 2. Scores of children and young people with longitudinal fibular deficiency for intact knees on the affected limb and trendline, and unaffected peers trendline for each KOOS/KOOS-Child domain against age (years).

**Table 1. Demographics of the participants with longitudinal fibular deficiency**

| Characteristic | Longitudinal fibular deficiency (n=17) |
|---|---|
| Bilateral (%) | 4/17 (23.5%) |
| Unilateral side affected (right, %) | 5/13 (38.5%) |
| Classification of every affected limb* (IA, IB, II) | 16, 3, 2 |
| Number of foot rays (Median, IQR) | 4 (3.75-4.25) |
| Number of orthopaedic procedures (median, IQR) | 1 (1-2) |
| Amputation (%) | 8** (47.1%) |
| Leg lengthening (%) | 3 (17.6%) |
| Epiphysiodesis (%) | 6 (35.3%) |
| Median number of falls in past week (IQR) | 0 (0-1) |

** Participants affected limbs were classified using the Achterman and Kalamchi (1979) system as Type IA, IB or II[9]. The values are given here are the number of participants. Type IA - Fibula hypoplastic but whole; Type IB - Part of fibula absent; Type II - True agenesis of the fibula.*

*** 7 participants had a Syme's amputation, 1 participant had toes amputated.*

**Table 2. Comparison between the 2 populations.**

| Characteristic | Longitudinal fibular deficiency (n=17) | Unaffected peers (n=213) |
|---|---|---|
| **Age in years [mean (SD), range]** | 14.4 (3.7), 8-20 | 13.7 (3.8) 8-20 |
| **Gender [Number of Females/Total (percentage)]** | 7/17 (41.2%) | 110/213 (51.6%) |
| **Body Mass Index For Age Percentile [mean (SD), range]** | 54.2% (28.5), 5.9-97.7 | 59.8% (27.0), 2.3-98.8 |

**Table 3. KOOS and CAIT outcomes for the 2 groups.**

| | *Outcome* | Longitudinal fibular deficiency group | Unaffected peers group | Unadjusted difference between groups (95%CI) | P value | Adjusted*** difference between groups (95%CI) | P value (adjusted difference) |
|---|---|---|---|---|---|---|---|
| ***Knee function**** | ***Pain (/100)*** | n=16**** | n=211 | | | | |
| | *Mean score (SD)* | 83.7 (17.9) | 94.9 (11.4) | -11.2 (-17.3 to -5.1) | <0.001 | -11.0 (-17.2 to -4.9) | <0.001 |
| | ***Symptoms (/100)*** | n=16**** | n=211 | | | | |
| | *Mean score (SD)* | 81.9 (19.2) | 94.4 (9.2) | -12.5 (-17.7 to -7.3) | <0.001 | -11.3 (-16.5 to -6.1) | <0.001 |
| | ***Activities of Daily Living (/100)*** | n=17 | n=211 | | | | |
| | *Mean score (SD)* | 90.4 (15.2) | 98.2 (5.4) | -7.8 (-11.1 to -4.5) | <0.001 | -8.4 (-11.7 to -5.1) | <0.001 |
| | ***Sports/Recreation (/100)*** | n=17 | n=211 | | | | |
| | *Mean score (SD)* | 76.8 (23.2) | 95.6 (10.3) | -18.8 (-24.6 to -13.0) | <0.001 | -18.8 (-24.6 to -13.0) | <0.001 |
| | ***Quality of life (/100)*** | n=16**** | n=211 | | | | |
| | *Mean score (SD)* | 71.6 (24.2) | 95.6 (10.7) | -24.0 (-30.2 to -17.8) | <0.001 | -25.3 (-31.6 to -19.0) | <0.001 |
| ***Ankle function**** | ***Total (/30)*** | n=13 | n=208 | | | | |
| | *Mean score (SD)* | 19.7 (8.3) | 25.6 (4.8) | -5.9 (-8.7 to -3.1) | <0.001 | -7.0 (-9.7 to -4.2) | <0.001 |

** Knee function measured with Knee Osteoarthritis Outcome Score (KOOS/KOOS-Child) – higher scores indicate better function.*
*** Ankle function measured with Cumberland Ankle Instability Tool (CAIT/CAIT-Youth) - higher scores indicate better function.*
**** Adjusted for age, gender, and Body-Mass-Index-For-Age Percentile*
***** Missing data and participant did not respond to follow-up*

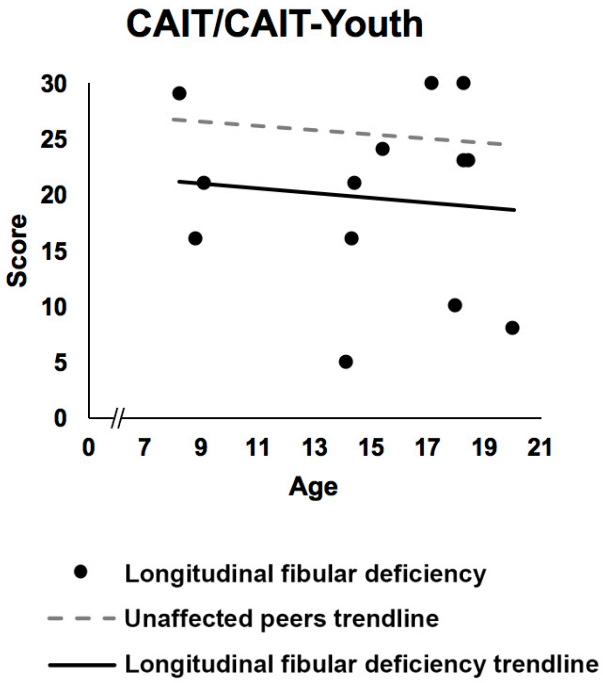


**Figure 1. Scores of children and young people with longitudinal fibular deficiency for intact ankles on the affected limb and trendline, and unaffected peers trendline for the CAIT/CAIT-Y against age (years).**

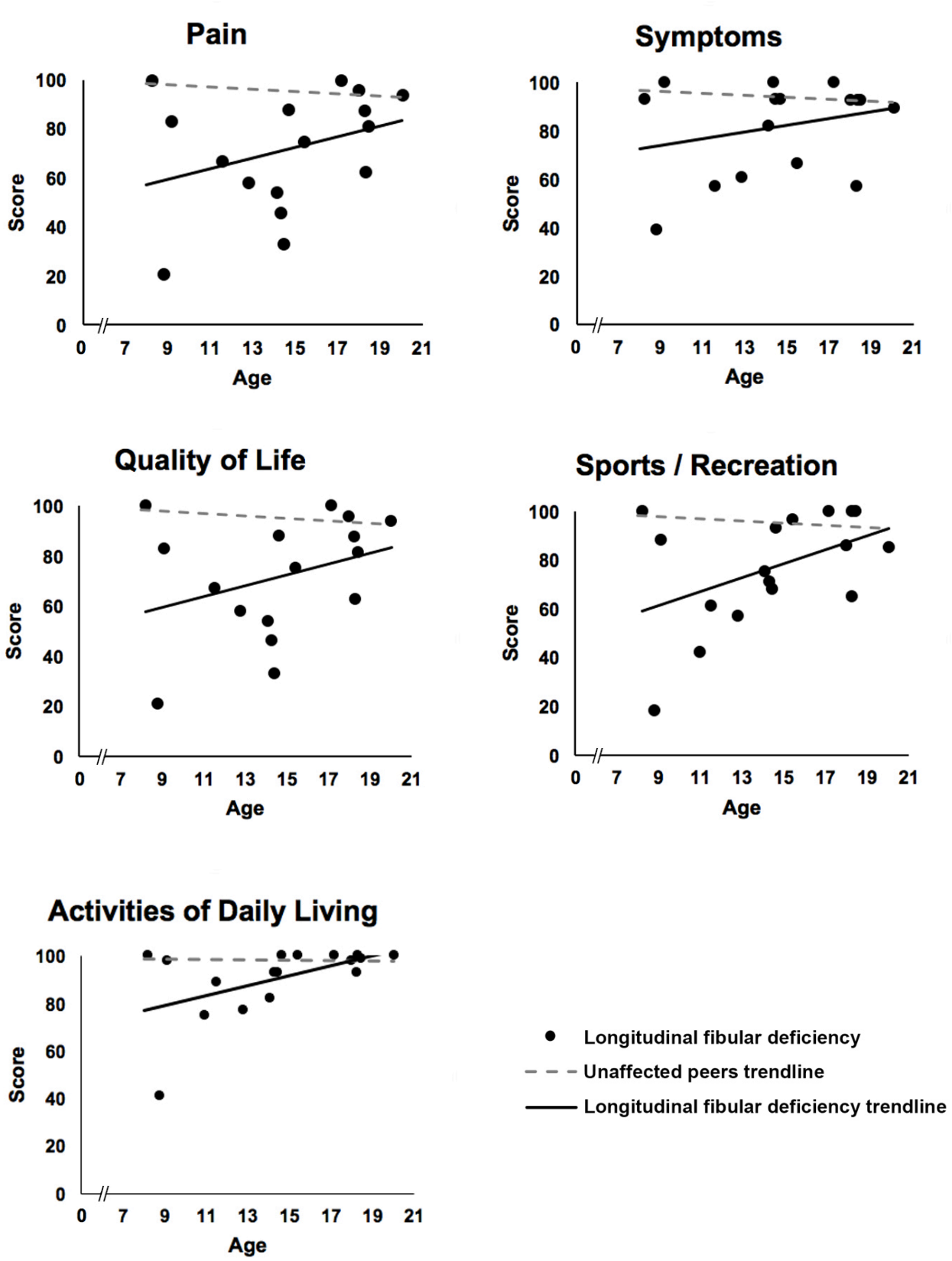


**Figure 2. Scores of children and young people with longitudinal fibular deficiency for intact knees on the affected limb and trendline, and unaffected peers trendline for each KOOS/KOOS-Child domain against age (years).**

# Chapter Four:
# Discussion

## 4.1. Overview

This chapter explores the findings of this thesis in greater depth than covered in the manuscript submitted to the American Journal of Physical Medicine & Rehabilitation, presented in Chapter 3. Each key finding is systematically discussed in terms of the implications for both clinical practice and research.

The key findings are:

1. Knee function in children with longitudinal fibular deficiency is significantly worse than unaffected peers in younger children, but is similar to unaffected peers in young adults.
2. Ankle function is worse in both children and young adults with longitudinal fibular deficiency when compared to typically developing unaffected peers.
3. Wide variability exists in the lower limb function and quality of life of children and young people with longitudinal fibular deficiency.
4. The most commonly reported challenges growing up with longitudinal fibular deficiency are anxiety, social acceptance and difficulties with sports participation.
5. All of the components of the ICF-CY framework are impacted in children and young people with longitudinal fibular deficiency.

## 4.2. Thesis findings and implications for clinical practice and research

### *4.2.1. Finding 1: Knee function in children with longitudinal fibular deficiency is significantly worse than unaffected peers in younger children, but is similar to unaffected peers in young adults.*

Children with longitudinal fibular deficiency report worse knee function on average than unaffected peers. However, this difference is significantly smaller when comparing affected young adults to unaffected peers (Figure 2 and Table 3 of the study). This finding is consistent across all domains of knee function assessed using the KOOS/KOOS-Child, including pain, symptoms, activities of daily living, sports and recreation, and quality of life. The difference in function between children and young adults with longitudinal fibular deficiency, in comparison with their unaffected peers, has not previously been reported.

*4.2.1.1. Clinical implications*

This finding suggests clinicians should assess knee function early in childhood to identify the presence of impairments, activity limitations and participation restrictions. Early assessment of knee function is not current recommended practice within the congenital amputee guidelines. These guidelines state that parents should have access to specialised physiotherapy,[47] however they do not recommend specific screening or assessment of knee function, nor the timing of assessment. Utilising patient-reported outcomes, such as the KOOS/KOOS-Child, could be a helpful adjunct to physical assessments in the clinical setting to ensure that assessment covers all components of the ICF-CY.

The early assessment of knee function may identify children with longitudinal fibular deficiency performing poorly in comparison to their unaffected peers, who may benefit most from intervention. At present, there are no randomised controlled studies assessing the effectiveness of interventions aiming to improve knee function in these children. Two examples of potentially beneficial interventions are physiotherapy and prostheses. In terms of physiotherapy, one specific impairment to address may be knee instability. This is identified in the literature as a common impairment of adults with longitudinal fibular deficiency.[19,20,27] Knee instability could be attributed to anterior cruciate ligament deficiency; an associated finding that has been reported in 95% of affected children in a retrospective case series (n=66).[33] A previous study reported that knee instability was a particular concern in individuals with longitudinal fibular deficiency undergoing limb lengthening procedures, possible due to altered joint and muscle function during the limb lengthening procedures.[10] Reduced stability in a child's knee joint may decrease their ability to do daily activities and participate in sports. This may be a contributing factor to our study finding that 5 of the 17 participants with longitudinal fibular deficiency reported 1-3 falls in the past week. Physiotherapy has been shown in multiple studies to improve functional stability regardless of ligamentous integrity in individuals with anterior cruciate ligament deficiency.[61,62] In addition, a clinical trial of 26 participants with ruptures of the anterior cruciate ligament highlighted that sports participation can significantly improve with physiotherapy input using perturbation training techniques.[63] Therefore, when a clear deficit has been identified, clinicians should consider a trial of physiotherapy aiming to improve knee function. However, given the lack of evidence specific to the condition, careful monitoring of outcomes will be essential to assess the value of the intervention for

individual patients. It is also important to note that such measures would provide short term benefit as this study showed that knee function in young adults with fibula hemimelia is not significantly different to unaffected peers.

The finding of reduced knee function also suggests the need for careful assessment at each time point that a young person with longitudinal deficiency who has undergone an amputation has a new type of prosthesis prescribed by their healthcare team. Specific prosthetic devices have demonstrated the ability to improve mobility and functionality of lower limb amputees, such as those that can store and return energy during gait.[64,65] Clinical experience suggests that adapting prosthetic trim lines to provide mechanical stability to the knee may be of benefit, but no research to test this has been conducted. Theoretically, higher trim lines, where the firm fibreglass of the socket covers the femoral condyles, provides more mediolateral and anteroposterior stability, however, the stiff and tight socket limits knee flexion range of motion. Therefore, a clinical assessment of knee function prior to, and following, each prosthetic prescription will enable appropriate support to be provided via the design of the prosthesis depending on patient goals. Due to the lack of evidence to support prosthetic designs for individuals with longitudinal fibular deficiency, monitoring outcomes on an individualised basis is vital to support clinical decision-making.

*4.2.1.2. Research implications*

Future research may help to better understand the factors contributing to knee function of children and young people with longitudinal fibular deficiency. It is important to understand which factors most strongly contribute to reduced knee function to guide assessment and provide a theoretical basis for appropriate treatment interventions. Multiple congenital structural changes in longitudinal fibular deficiency may contribute to reduced knee function, to differing degrees. An obvious potential contributor is the almost universal anterior cruciate ligament deficiency, as mentioned above. However, other impairments may also be important contributors to reduced knee function. For example, weakness in quadriceps or gluteal muscles could be present in children with longitudinal fibular deficiency, but neither the presence of this impairment or its potential relationship with knee function has been investigated. The role of personal and environmental influences on knee function should also be

assessed. Studies investigating contributing factors should, therefore, investigate a wide range of potential contributing factors to identify patient characteristics which are potentially amenable to change with interventions.

The effectiveness of any prescribed interventions targeting improvements in knee function, such as physiotherapy, prosthetic rehabilitation, or surgery, are yet to be rigorously tested. Randomised controlled trials have not yet been conducted to assess the effectiveness of any intervention in individuals with longitudinal fibular deficiency. For example, no surgically-focused studies performed to date have involved randomisation.[8,10,11,17,20,30] The lack of randomised controlled trials in this population is likely due to the many challenges associated with conducting these studies in this patient population. As the condition is uncommon, obtaining an adequate sample size would require a coordinated approach across multiple centres which is time-consuming, expensive and may be difficult to coordinate due to inherent differences in clinical practice between centres. Ethical challenges relating to family-centred care, equipoise and sham surgery also limit the feasibility of this study design because of the invasive nature of surgical interventions.[66]

Our study used different children and young people of various ages to draw the conclusion that knee function is worse in younger children than in young adults, compared to unaffected peers. However, a longitudinal study design would provide more robust evidence to confirm these findings as it would allow individual children to be followed over time and assess if their function approaches that of similar aged unaffected peers as they get older. This design would have better control for individual differences that may have impacted on our findings, such as the severity of the condition, especially given the small sample size of affected children and young people (n=17).

In our study, we assumed that the adult and child versions of the knee function outcome measure, the KOOS and KOOS-Child, were comparable. The KOOS-Child was specifically designed to be comparable to the adult version to enable a smooth transition between the versions in long term follow-ups.[51] We made this assumption so that the knee function of every participant across the ages of 7-21 could be compared to the unaffected population in a combined analysis adjusting for the effect of age,

which has not previously been considered in the literature. This is common practice in a paediatric setting, for example, the PedsQL has multiple versions for different age ranges and combined analyses are performed.[55] However, future research could investigate the similarities between the KOOS and KOOS-Child to confirm they are comparable.

### *4.2.2. Finding 2: Ankle function is reduced in both younger and older children with longitudinal fibular deficiency when compared to typically developing unaffected peers.*

Children and young people with longitudinal fibular deficiency had reduced perceived ankle function compared to unaffected peers. The mean adjusted difference between groups for the CAIT/CAIT-Youth questionnaire was -7.0 (95% CI: -9.7 to -4.2). This finding of significantly reduced perceived ankle function has implications for both clinical practice and future research.

#### *4.2.2.1. Clinical implications*

The finding of reduced perceived ankle function has several similar assessment and treatment implications to those related to the finding of reduced knee function. However, as reduced perceived ankle function was not found to be age-dependant, regular assessment of ankle function may guide the need for specific individualised treatment throughout childhood and in young people, not just the focus on younger years. Physical interventions such as physiotherapy may also be important in improving ankle function when deficits are identified. A recent systematic review assessing the efficacy of physiotherapy for individuals with chronic ankle instability suggested that balance and strengthening exercises may be advantageous in reducing 'giving way' episodes and improving function.[68] However, the heterogeneity of the various rehabilitation programs included in this review made it difficult to pinpoint the potentially effective components of the programs. Therefore, when instability has been observed in children with longitudinal fibular deficiency, clinical management should include physiotherapy input with a goal of improving ankle function. However, the absence of direct evidence in children and young people with longitudinal fibular deficiency suggests close monitoring of outcomes will be essential in assessing the value of the intervention for individuals.

*4.2.2.2. Research implications*

A need exists to explore the finding that children and young people have decreased perceived ankle function when compared to unaffected peers. Studies focused on long-term adult outcomes suggest that knee and hip function is similar to unaffected adults,[19,20,27] but perceptions of ankle function have not been previously assessed. For each year older that participants were in our study, the difference between perceived ankle function (CAIT) scores for children and young people with longitudinal fibular deficiency and unaffected peers did not reduce (P=0.256 for age interaction) as they did for knee function (KOOS) scores. Future research could investigate why perceived ankle function does not appear to get closer to normal in young adults, despite this occurring for perceived knee function. Given that perceptions of ankle function in children and young people remains reduced in comparison to unaffected peers, it is important to investigate whether this deficit continues throughout adulthood or improves at a later stage of life.

As previously discussed, the CAIT/CAIT-Y measures the perception of ankle stability and function as reported by the child. To obtain a broader perspective on self-reported ankle function, other measures may be useful to assess in both the research and clinical setting. However, at present, there are no other self-report measures of ankle function which have been validated in children. For example, while the Foot and Ankle Ability Measure (FAAM) has been used in musculoskeletal physiotherapy patients aged 8-83 years, [67] it was originally validated using the SF-36[43] which is not valid in children. Further studies on the FAAM and other potential measures of ankle function would be required before utilising other questionnaires as a measure of function in young people with longitudinal fibular deficiency.

Future research could investigate the development of a CAIT/CAIT-Youth cut-off score for functional ankle instability in children and young people. To date, no score has been validated in children. Despite this, one study in 2013 used the adult cut-off score of ≤27 out of 30[50] in children and found that 36% of children with no history of ankle sprains scored below the cut-off score.[52] This adult cut-off score was independently recalibrated in 2014 to ≤25 out of 30 in a study investigating individuals with chronic ankle instability.[60] In our study, 73 unaffected peers (35.1%) scored below this new adult cut-off, and 3 children and young people with longitudinal fibular deficiency (23.1%) scored above this cut-off score

(Figure 1, Chapter 3). It is worth noting that the unaffected peers group were not asked about ankle sprains history and so it is possible that this figure may include healthy children who have a history of ankle sprains which would lower CAIT/CAIT-Youth scores. These findings suggest that the cut-off for use in children may be different and needs to be validated.

As per the KOOS and KOOS-Child for knee function, a combined analysis was also performed for the CAIT and CAIT-Youth measuring ankle function. Although the CAIT and CAIT-Youth are very similar, and both have been shown to be are valid and reliable, more research is required to ensure these measures are comparable and can be combined.

### *4.2.3. Finding 3: Wide variability exists in the lower limb function and quality of life of children and young people with longitudinal fibular deficiency.*

While group averages showed reduced lower limb function and quality of life compared to unaffected peers, children and young people with longitudinal fibular deficiency had quite variable outcomes (Figure 1, Chapter 3), with some individual participants functioning at normal levels and some functioning well below normal. As an example of the variability of individual responses, Figure 1 in the manuscript shows KOOS/KOOS-Child Domain scores ranged from 18-100/100 and CAIT/CAIT-Youth scores ranged from 5-30/30.

#### *4.2.3.1. Clinical implications*

The finding of wide variations in the responses to the patient-reported outcomes used in the study suggests that careful individual assessment is required as opposed to presuming functional levels based on group averages. As ranges and individual function scores are not given in the current available literature for adults with longitudinal fibular deficiency,[19,20,27] it is unclear if there continues to be the same amount of heterogeneity in the adult population as there is in children and young people. Targeting treatment to the specific needs of individual children and young people with longitudinal fibular deficiency can only be done if the appropriate assessment is performed. Equally, in children without clear difficulties with lower limb function, it is unlikely that treatment will be warranted or produce important benefits.

*4.2.3.2. Research implications*

The finding of wide variability in the outcomes measured in the study suggests that a need exists to understand the factors contributing to this variability. Longitudinal cohort studies could investigate a range of prognostic factors from different domains, such as structural and socioeconomic factors. High quality prognostic information would enable parents to be given more accurate and individualised predictions of their child's likely outcomes as they get older. If prognostic factors are modifiable then they would also become potential targets for interventions.

The identification of prognostic factors could be critical in further developing a classification system for longitudinal fibular deficiency that can provide both prognostic information and guidance in management. While the Paley system is currently used in clinical practice by orthopaedic surgeons,[16] research literature is yet to confirm a system for all of this heterogeneous population.[15] Currently in a clinical setting, classification is broadly described as "partial" or "total" longitudinal fibular deficiency as per the ISO/ISPO Classification of congenital limb deficiency.[24] This simplified classification does not provide enough information for clinicians to inform all treatment decisions. If a particular individual could be appropriately classified from a functional perspective, patient education regarding future function would significantly improve and individuals could be considered more holistically. This is particularly important because families of children with a physical disability are interested in functional outcomes,[48] such as participation in activities of daily living with a prosthetic leg,[44] rather than how anatomically correct a particular limb or joint is. Researching a detailed system that can predict function and guide treatment in young children and infants would, therefore, be very beneficial in this population.

### *4.2.4. Finding 4: The most commonly reported challenges growing up with longitudinal fibular deficiency are anxiety, social acceptance and difficulties with sports participation.*

Prior to the study, no findings pertaining to psychosocial challenges for children and young people with longitudinal fibular deficiency were available, which may be attributed to the historical focus on impairments rather than function. Although only one open-ended question was asked in our study, it did

provide some insight into difficulties experienced by children growing up with longitudinal fibular deficiency.

#### *4.2.4.1. Clinical implications*

Clinical assessment should include assessment of psychosocial factors such as anxiety and feelings of social acceptance, which were reported as common concerns. Currently, psychological input is limited in the multidisciplinary teams in the limb clinics in Australia. The Amputee Care Standards state that experienced clinical counselling and psychological support is to be made available for all children and their families,[69] but our findings suggest that this resource is likely not being accessed sufficiently, and a greater emphasis on the availability of psychological support may be required.[47]

Sports participation was also identified as a challenge for children and young people growing up with longitudinal fibular deficiency. The importance of this issue has been highlighted in the literature.[70] Research suggests that parents of children with a physical disability are concerned with their child's social participation in activities such as sport, but note that this is rarely recognised as a goal in therapy.[48] Assessing and acknowledging the value that some children and young people and their families place on sports participation may be of importance from a multidisciplinary perspective. Management teams could work with families to ensure that this challenge is considered throughout childhood.

#### *4.2.4.2. Research implications*

A more in-depth understanding of the challenges children and young people reported in this study could be explored through qualitative research. This research approach has the benefit of participants being encouraged to expand on their responses, which can unveil new topic areas not initially considered. For example, if it was found that a particular source of anxiety was common, then intervention studies specifically providing support around this source of concern may be considered.[71] Studies exploring the reasons behind children and parents' specific psychosocial challenges would inform both clinicians and researchers when developing educational and treatment programmes. Furthermore, assessment of relevant psychosocial influences, such as anxiety, may also be beneficial to incorporate in future research designs when assessing changes in function and quality of life of children over time.

### *4.2.5. Finding 5: All of the components of the ICF-CY framework are impacted in children and young people with longitudinal fibular deficiency.*

From an ICF-CY perspective, the results of the study highlight the impact of longitudinal fibular deficiency on activity limitations and participation restrictions, in addition to body functions and structures. This contrasts with previous research which focuses more on impairments to body functions and structures, as explored in Chapter 2. In this chapter, the ICF-CY was outlined and many significant knowledge gaps were identified. The study then added significantly to the evidence base. The specific contributions of the study are highlighted in Figure 4.1.

#### *4.2.5.1. Clinical implications*

The finding that all components of the ICF-CY are affected in a young person with longitudinal fibular deficiency suggests that a holistic consideration of an affected patient in a clinical setting is vital. This would enable a shift away from only focusing on impairments to body functions and structures, and allow for an additional focus on activity performance and participation in school and sport. If our study was added to Table 2.1, it becomes apparent that it fills several gaps in the literature in terms of all of the components of the ICF-CY. Specifically, the study considers activity limitations, participation restrictions, personal factors, environmental factors, the effect of age, as well as the benefits of patient-reported outcomes and standardised measures to enhance the overall picture of longitudinal fibular deficiency within the framework of the ICF-CY. By considering more than anatomical impairments when devising management plans, children and young people with longitudinal fibular deficiency will be cared for holistically.

Relevant patient-reported outcomes could be utilised clinically in an attempt to identify any components of the ICF-CY that may be missed in current practice. They are an adjunct to good clinical questioning to provide objective data, by assessing treatment effects or informing clinicians of changes over time. The choice of these outcomes depends on the individual's presentation. Importantly, the use of patient-

reported outcomes may identify other ICF-CY components, such as activity limitations and participation restrictions, not commonly identified or objectively assessed in a clinical setting.

It is common practice in Australian limb clinics to provide multidisciplinary care as per therapeutic guidelines,[15,48] but it is not common to provide specific lower limb physiotherapy interventions. This is because physiotherapy-amenable activity limitations and participation restrictions have not previously been highlighted as a problem. For example, running is one of the activity limitations listed in Figure 4.1 where physiotherapy may be able to contribute to improved function, then improving sports

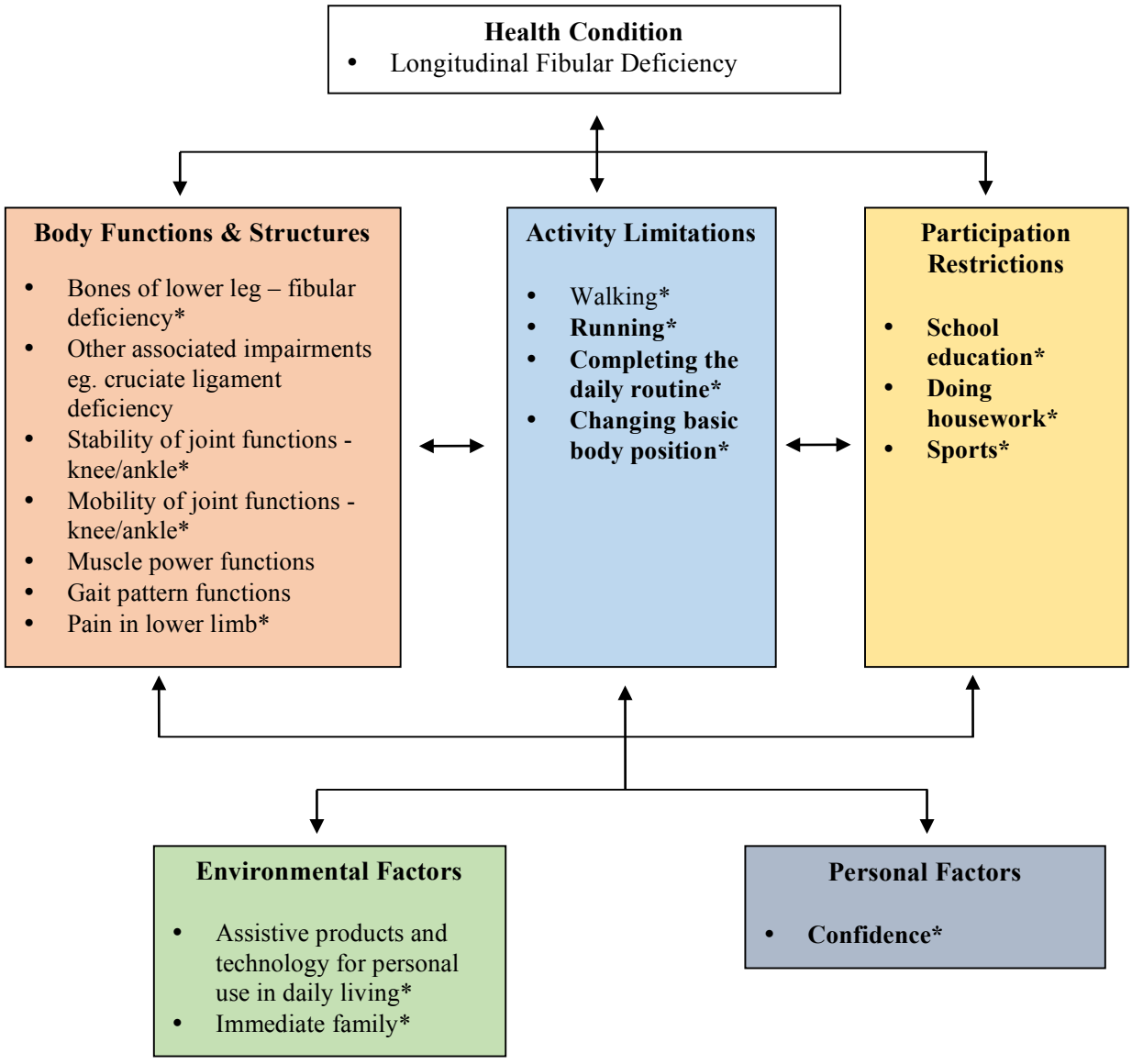


***Figure 4.1. Additions to the current evidence base using the ICF-CY model for a child with longitudinal fibular deficiency. Aspects covered in our study have an asterisk (*), and new findings resulting from our study are in bold.***

participation and confidence. A multidisciplinary team approach to addressing each component of the ICF-CY will allow for holistic care and targeted interventions.

*4.2.5.2. Research implications*

A thorough examination of each relevant ICF-CY component is warranted so that impairments are not the sole focus of future research. By using patient-reported outcomes focused on function, our study was able to identify limitations to daily activities and restrictions in participating in sport and school. In light of this, a combination of patient-reported outcomes and objective measures in future research, monitored throughout the paediatric years due to potential changes with age, would provide insight into patients from a holistic perspective. Until the recent validation of the KOOS-Child [51] and CAIT-Youth,[52] validated and reliable patient-reported outcomes of paediatric knee and ankle function encompassing all aspects of the ICF-CY were not obtainable. These knee and ankle patient-reported outcomes are highly appropriate measures to achieve the aim of assessing activity limitations and participation restrictions in addition to impairments.

Pain is an impairment that has not been thoroughly reported on in the literature in this population. Our study showed the adjusted between-group difference for the KOOS Pain domain was 11.0 points (95% CI: -17.2 to -4.9), with unaffected peers scoring higher. Future studies should measure the location of pain, as well as the duration, intensity and type of pain, as opposed to the current literature reports which have used non-standardised 5-point pain assessment scales[2,30] and a binary "Yes/No" report on the presence of any pain.[5,12] Pain has a large potential impact on activity limitations and participation restrictions,[32] but this has yet to be focused on in studies to date.

Investigations into a condition-specific outcome measure encompassing all components of the ICF-CY would be beneficial as it would enable future research to have increased specificity to the population. Alternatively, in addition to the KOOS/KOOS-Child and CAIT/CAIT-Youth, an overall quality of life questionnaire such as the PedsQL[55] could have been administered to address quality of life in more depth. The PedsQL has been validated in children of all ages[55] and would have been appropriate given the study aims have a particular focus on quality of life as an outcome. To reduce the burden on

participants a further self-report measure was not used within the current study. This study did not use a condition-specific outcome measure as no such measure currently exists. However, by incorporating measures that are commonly used and appropriate across multiple populations, the external validity of the findings of future studies can be improved. Hence, comparisons could then be made between longitudinal fibular deficiency and other physical disability and amputee populations. Use of these measures in our study allowed the comparison of affected children and young people with their unaffected peers.

## 4.3. Conclusion

This thesis built upon the limited evidence-base for longitudinal fibular deficiency in children and young people, specifically in terms of lower limb function and quality of life. It was found that they, on average, report reduced lower limb function and quality of life compared to unaffected peers. Knee function is worse in younger affected children and closer to normal in young adults.

Key recommendations for clinical practice include considering early and regular assessment of knee and ankle function, and providing targeted treatment where indicated. In addition, the use of patient-reported outcomes, such as the KOOS/KOOS-Child and CAIT/CAIT-Youth, enable the assessment of activity limitations and participation restrictions as well as impairments. A multidisciplinary approach considering all aspects of the ICF-CY is recommended for patients with longitudinal fibular deficiency to address the functional consequences of the condition.

Key recommendations for research include investigating the benefits of early intervention on knee function, and exploring the possible causes regarding reduced knee and ankle function and the correlation between these and quality of life. Future research should continue to look at activity limitations and participation restrictions, in addition to impairments of body functions and structures, including patient-reported outcomes.

The findings from this thesis provide information which is valuable to patients and families and also identifies opportunities for improving clinical care and directing future research.

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# Appendices

## Appendix 1: Knee injury and Osteoarthritis Outcome Score (KOOS)

Reprinted with permission from Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynnon BD. Knee Injury and Osteoarthritis Outcome Score (KOOS)—development of a self-administered outcome measure. Journal of Orthopaedic & Sports Physical Therapy. 1998;28(2):88-96.

# KOOS KNEE SURVEY

Today's date:_____/_____/_____ Date of birth:_____/_____/_____

Name: _____

**INSTRUCTIONS:** This survey asks for your view about your knee. This information will help us keep track of how you feel about your knee and how well you are able to perform your usual activities.
Answer every question by ticking the appropriate box, only one box for each question. If you are unsure about how to answer a question, please give the best answer you can.

### Symptoms

These questions should be answered thinking of your knee symptoms during the **last week**.

S1. Do you have swelling in your knee?

| Never | Rarely | Sometimes | Often | Always |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

S2. Do you feel grinding, hear clicking or any other type of noise when your knee moves?

| Never | Rarely | Sometimes | Often | Always |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

S3. Does your knee catch or hang up when moving?

| Never | Rarely | Sometimes | Often | Always |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

S4. Can you straighten your knee fully?

| Always | Often | Sometimes | Rarely | Never |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

S5. Can you bend your knee fully?

| Always | Often | Sometimes | Rarely | Never |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

### Stiffness

The following questions concern the amount of joint stiffness you have experienced during the **last week** in your knee. Stiffness is a sensation of restriction or slowness in the ease with which you move your knee joint.

S6. How severe is your knee joint stiffness after first wakening in the morning?

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

S7. How severe is your knee stiffness after sitting, lying or resting **later in the day**?

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

### Pain

P1. How often do you experience knee pain?

| Never | Monthly | Weekly | Daily | Always |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

What amount of knee pain have you experienced the **last week** during the following activities?

P2. Twisting/pivoting on your knee

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

P3. Straightening knee fully

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

P4. Bending knee fully

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

P5. Walking on flat surface

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

P6. Going up or down stairs

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

P7. At night while in bed

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

P8. Sitting or lying

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

P9. Standing upright

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

**Function, daily living**

The following questions concern your physical function. By this we mean your ability to move around and to look after yourself. For each of the following activities please indicate the degree of difficulty you have experienced in the **last week** due to your knee.

A1. Descending stairs

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

A2. Ascending stairs

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

For each of the following activities please indicate the degree of difficulty you have experienced in the **last week** due to your knee.

A3. Rising from sitting

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

A4. Standing

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

A5. Bending to floor/pick up an object

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

A6. Walking on flat surface

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

A7. Getting in/out of car

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

A8. Going shopping

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

A9. Putting on socks/stockings

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

A10. Rising from bed

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

A11. Taking off socks/stockings

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

A12. Lying in bed (turning over, maintaining knee position)

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

A13. Getting in/out of bath

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

A14. Sitting

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

A15. Getting on/off toilet

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

For each of the following activities please indicate the degree of difficulty you have experienced in the **last week** due to your knee.

A16. Heavy domestic duties (moving heavy boxes, scrubbing floors, etc)

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

A17. Light domestic duties (cooking, dusting, etc)

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

**Function, sports and recreational activities**

The following questions concern your physical function when being active on a higher level. The questions should be answered thinking of what degree of difficulty you have experienced during the **last week** due to your knee.

SP1. Squatting

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

SP2. Running

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

SP3. Jumping

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

SP4. Twisting/pivoting on your injured knee

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

SP5. Kneeling

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

**Quality of Life**

Q1. How often are you aware of your knee problem?

| Never | Monthly | Weekly | Daily | Constantly |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

Q2. Have you modified your life style to avoid potentially damaging activities to your knee?

| Not at all | Mildly | Moderately | Severely | Totally |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

Q3. How much are you troubled with lack of confidence in your knee?

| Not at all | Mildly | Moderately | Severely | Extremely |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

Q4. In general, how much difficulty do you have with your knee?

| None | Mild | Moderate | Severe | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

***Thank you very much for completing all the questions in this questionnaire.***

## Appendix 2: Knee injury and Osteoarthritis Outcome Score - Child (KOOS-Child)



# KOOS-Child KNEE SURVEY

Today's date:_____ Date of birth: _____

Name: _____

## INSTRUCTIONS

These questions collect information about how your injured knee affects you. Answer every question by ticking the appropriate box, only one box for each question. If you are unsure about how to answer a question, please select the best answer you can.

### KNEE PROBLEMS

S1. During the past 7 days, how often has your knee been swollen?

| Never | Rarely | Sometimes | Often | Always |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

S2. During the past 7 days, how often has your knee made any noise/sounds?

| Never | Rarely | Sometimes | Often | Always |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

S3. During the past 7 days, how often did your knee get stuck?

| Never | Rarely | Sometimes | Often | Always |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

S4. During the past 7 days, how often have you been able to fully straighten your knee on your own?

| Always | Often | Sometimes | Rarely | Never |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

S5. During the past 7, days how often have you been able to fully bend your knee on your own?

| Always | Often | Sometimes | Rarely | Never |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

S6. During the past 7 days, how much difficulty have you had moving your knee just after waking up in the morning?

| No difficulty | A little | Some | A lot | Extreme difficulty |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

S7. During the past 7 days, how much difficulty have you had later in the day moving your knee after being sedentary for a while?

| None | A little | Some | A lot | Extreme |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

P1. During the past month, how often have you experienced knee pain?

| Never | Rarely | Sometimes | Often | All the time |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

**HOW PAINFUL**

**How much knee pain** have you experienced **in the past 7 days** during the following activities? Check the best answer for each item

| | No pain | A little pain | Some pain | A lot of pain | Extreme pain |
|---|---|---|---|---|---|
| P2. Twisting/pivoting on your injured knee when walking/standing/running | | | | | |
| P3. Fully straightening your injured knee | | | | | |
| P4. Fully bending your injured knee | | | | | |
| P6a. Walking up stairs | | | | | |
| P6b. Walking down stairs | | | | | |
| P8a. Sitting with your injured knee bent | | | | | |
| P9. Standing upright on both legs for any amount of time | | | | | |

**DIFFICULTY DURING DAILY ACTIVITIES**

A1. During the past 7 days, how much difficulty have you had walking down stairs?

No difficulty ☐ | A little ☐ | Some ☐ | A lot ☐ | Extreme difficulty ☐

A2. During the past 7 days, how much difficulty have you had walking up stairs?

No difficulty ☐ | A little ☐ | Some ☐ | A lot ☐ | Extreme difficulty ☐

A3. During the past 7 days, how much difficulty have you had standing up from a chair?

No difficulty ☐ | A little ☐ | Some ☐ | A lot ☐ | Extreme difficulty ☐

A5. During the past 7 days, how much difficulty have you had to bend down and pick up an object from the floor?

No difficulty ☐ | A little ☐ | Some ☐ | A lot ☐ | Extreme difficulty ☐

A7. During the past 7 days, how much difficulty have you had getting in to/out of a car?

No difficulty ☐ | A little ☐ | Some ☐ | A lot ☐ | Extreme difficulty ☐

A10. During the past 7 days, how much difficulty have you had to get out of bed?

No difficulty ☐ | A little ☐ | Some ☐ | A lot ☐ | Extreme difficulty ☐

A12. During the past 7 days, how much difficulty have you had to change knee position when lying in bed?

No difficulty ☐ | A little ☐ | Some ☐ | A lot ☐ | Extreme difficulty ☐

A13. During the past 7 days, how much difficulty have you had getting in to/out of the bathtub/shower?

No difficulty | A little | Some | A lot | Extreme difficulty

| | | | | |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

A14. During the past 7 days, how much difficulty have you had to sit in a chair with your injured knee bent?

| No difficulty | A little | Some | A lot | Extreme difficulty |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

A16. During the past 7 days, how much difficulty have you had to carry heavy bags /backpacks etc?

| No difficulty | A little | Some | A lot | Extreme difficulty |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

A17. During the past 7 days, how much difficulty have you had to do light chores such as cleaning your room, filling/emptying the dishwasher, making your bed, etc?

| No difficulty | A little | Some | A lot | Extreme difficulty |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

**DIFFICULTY DURING SPORTS AND PLAYING**

| | |
|---|---|
| SP1. During the past 7 days, how much difficulty have you had to squat down during play or sports activities?<br><br>No difficulty ☐ A little ☐ Some ☐ A lot ☐ Extreme difficulty ☐ |  |
| SP2. During the past 7 days, how much difficulty have you had to run during play or sports activities?<br><br>No difficulty ☐ A little ☐ Some ☐ A lot ☐ Extreme difficulty ☐ |  |
| SP3. During the past 7 days, how much difficulty have you had to jump during play or sports activities?<br><br>No difficulty ☐ A little ☐ Some ☐ A lot ☐ Extreme difficulty ☐ |  |
| SP4. During the past 7 days, how much difficulty have you had to twist/pivot because of your injured knee during play or sports activities?<br><br>No difficulty ☐ A little ☐ Some ☐ A lot ☐ Extreme difficulty ☐ |  |
| SP5. During the past 7 days, how much difficulty have you had to kneel because of your injured knee?<br><br>No difficulty ☐ A little ☐ Some ☐ A lot ☐ Extreme difficulty ☐ |  |
| SPN6. During the past 7 days, how much difficulty have you had to keep your balance when walking /running on uneven ground?<br><br>No difficulty ☐ A little ☐ Some ☐ A lot ☐ Extreme difficulty ☐ |  |

SPN7. During the past 7 days, how much difficulty have you had playing sports because of your injured knee?

| No difficulty | A little | Some | A lot | Extreme difficulty |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

**HOW HAS YOUR INJURY AFFECTED YOUR LIFE?**

Q1. How often do you think about your knee problem?

| Never | Rarely | Sometimes | Often | All the time |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

Q2. How much have you changed your lifestyle because of your injured knee?

| Not at all | A little | Some | A lot | Very much |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

Q3. How much do you trust your injured knee?

| Not at all | A little | Some | A lot | Completely |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

Q4. Overall, how much difficulty do you have with your injured knee?

| No difficulty | A little | Some | A lot | Extreme difficulty |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

QN5. How much difficulty have you had getting to school or walking around in school (climbing stairs, opening doors, carrying books, participating during recess) because of your injured knee?

| No difficulty | A little | Some | A lot | Extreme difficulty |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

QN6**.** How much difficulty have you had to do things with friends because of your injured knee?

| No difficulty | A little | Some | A lot | Extreme difficulty |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

**Thank you very much for completing all the questions in this questionnaire!**

## Appendix 3: Cumberland Ankle Instability Tool (CAIT)

Reprinted with permission from Hiller CE, Refshauge KM, Bundy AC, Herbert RD, Kilbreath SL. The Cumberland Ankle Instability Tool: A Report of Validity and Reliability Testing. *Archives of Physical Medicine and Rehabilitation.* 2006;87(9):1235-1241.

Please tick the ONE statement in EACH question that BEST describes your ankles.

| | LEFT | RIGHT | Score |
|---|---|---|---|
| 1. I have pain in my ankle | | | |
| Never | □ | □ | 5 |
| During sport | □ | □ | 4 |
| Running on uneven surfaces | □ | □ | 3 |
| Running on level surfaces | □ | □ | 2 |
| Walking on uneven surfaces | □ | □ | 1 |
| Walking on level surfaces | □ | □ | 0 |
| 2. My ankle feels UNSTABLE | | | |
| Never | □ | □ | 4 |
| Sometimes during sport (not every time) | □ | □ | 3 |
| Frequently during sport (every time) | □ | □ | 2 |
| Sometimes during daily activity | □ | □ | 1 |
| Frequently during daily activity | □ | □ | 0 |
| 3. When I make SHARP turns, my ankle feels UNSTABLE | | | |
| **Never** | □ | □ | 3 |
| Sometimes when running | □ | □ | 2 |
| Often when running | □ | □ | 1 |
| When walking | □ | □ | 0 |
| 4. When going down the stairs, my ankle feels UNSTABLE | | | |
| **Never** | □ | □ | 3 |
| If I go fast | □ | □ | 2 |
| Occasionally | □ | □ | 1 |
| Always | □ | □ | 0 |
| 5. My ankle feels UNSTABLE when standing on ONE leg | | | |
| Never | □ | □ | 2 |
| On the ball of my foot | □ | □ | 1 |
| With my foot flat | □ | □ | 0 |
| 6. My ankle feels UNSTABLE when | | | |
| Never | □ | □ | 3 |
| I hop from side to side | □ | □ | 2 |
| I hop on the spot | □ | □ | 1 |
| When I jump | □ | □ | 0 |
| 7. My ankle feels UNSTABLE when | | | |
| Never | □ | □ | 4 |
| I run on uneven surfaces | □ | □ | 3 |
| I jog on uneven surfaces | □ | □ | 2 |
| I walk on uneven surfaces | □ | □ | 1 |
| I walk on a flat surface | □ | □ | 0 |
| 8. TYPICALLY, when I start to roll over (or "twist") on my ankle, I can stop it | | | |
| Immediately | □ | □ | 3 |
| Often | □ | □ | 2 |
| Sometimes | □ | □ | 1 |
| Never | □ | □ | 0 |
| I have never rolled over on my ankle | □ | □ | 3 |
| 9. After a TYPICAL incident of my ankle rolling over, my ankle returns to "normal" | | | |
| Almost immediately | □ | □ | 3 |
| Less than one day | □ | □ | 2 |
| 1–2 days | □ | □ | 1 |
| More than 2 days | □ | □ | 0 |
| I have never rolled over on my ankle | □ | □ | 3 |

NOTE: The scoring scale is on the right. The scoring system is not visible on the subject's version.

## Appendix 4: Cumberland Ankle Instability Tool - Youth (CAIT-Youth)

Reprinted with permission from Mandarakas M, Hiller CE, Rose KJ, Burns J. Measuring Ankle Instability in Pediatric Charcot-Marie-Tooth Disease. *Journal of Child Neurology.* 2013;28(11):1456-1462.

This survey is all about your ankles. We want to know if your ankles are steady or unsteady. If your ankle is unsteady, it can sometimes feel wobbly or unstable.
**Tick the box that best describes your ankles. Only tick one box for each question.**

| | LEFT  |  RIGHT | Score |
|---|---|---|---|
| 1. My ankle HURTS | | | |
| **Never** | □ | □ | 5 |
| **When I play sport** | □ | □ | 4 |
| **When I run on uneven ground** | □ | □ | 3 |
| **When I run on flat ground** | □ | □ | 2 |
| **When I walk on uneven ground** | □ | □ | 1 |
| **When I walk on flat ground** | □ | □ | 0 |
| 2. My ankle feels UNSTEADY | | | |
| **Never** | □ | □ | 4 |
| **Some of the time when I play sport** | □ | □ | 3 |
| **Every time I play sport** | □ | □ | 2 |
| **Some of the time during the day** | □ | □ | 1 |
| **Most of the day** | □ | □ | 0 |
| 3. When I make a quick turn, my ankle feels UNSTEADY | | | |
| **Never** | □ | □ | 3 |
| **Some of the time when I run** | □ | □ | 2 |
| **Most of the time when I run** | □ | □ | 1 |
| **When I walk** | □ | □ | 0 |
| 4. When I go down stairs my ankle feels UNSTEADY | | | |
| **Never** | □ | □ | 3 |
| **If I go fast** | □ | □ | 2 |
| **Some of the time** | □ | □ | 1 |
| **All of the time** | □ | □ | 0 |
| 5. When I stand on ONE leg, my ankle feels UNSTEADY | | | |
| **Never** | □ | □ | 2 |
| **On my toes** | □ | □ | 1 |
| **With my foot flat on the ground** | □ | □ | 0 |
| ***I can't stand on one leg*** | □ | □ | 0 |
| 6. My ankle feels UNSTEADY | | | |
| **Never** | □ | □ | 3 |
| **When I hop from side to side on the** | □ | □ | 2 |
| **When I hop on the spot** | □ | □ | 1 |
| **When I jump** | □ | □ | 0 |
| ***I can't hop or jump*** | □ | □ | 0 |
| 7. My ankle feels UNSTEADY | | | |
| **Never** | □ | □ | 4 |
| **When I run fast on uneven ground** | □ | □ | 3 |
| **When I run slowly on uneven ground** | □ | □ | 2 |
| **When I walk on uneven ground** | □ | □ | 1 |
| **When I walk on flat ground** | □ | □ | 0 |
| 8. If I start to roll or twist my ankle, I CAN STOP | | | |
| **Most of the time** | □ | □ | 2 |
| **Some of the time** | □ | □ | 1 |
| **Never** | □ | □ | 0 |
| **Straight away** | □ | □ | 3 |
| ***I have never rolled my ankle*** | □ | □ | 3 |
| 9. If I do roll my ankle it FEELS FINE | | | |
| **Almost straight away** | □ | □ | 3 |
| **In less than a day** | □ | □ | 2 |
| **In 1 or 2 days** | □ | □ | 1 |
| **In more than 2 days** | □ | □ | 0 |
| ***I have never rolled my ankle*** | □ | □ | 3 |

NOTE: The scoring scale is on the right. The scoring system is not visible on the subject's version.

## Appendix 5: National Health and Medical Research Council Levels of Evidence

Reprinted with permission from Coleman K, Norris S, Weston A, et al. NHMRC additional levels of evidence and grades for recommendations for developers of guidelines STAGE 2 CONSULTATION Early 2008-end June 2009, viewed 26 March 2011. *Canberra, Australia.* 2009.

**NHMRC Evidence Hierarchy: designations of 'levels of evidence' according to type of research question** (including explanatory notes)

| Level | Intervention [1] | Diagnostic accuracy [2] | Prognosis | Aetiology [3] | Screening Intervention |
|---|---|---|---|---|---|
| I [4] | A systematic review of level II studies | A systematic review of level II studies | A systematic review of level II studies | A systematic review of level II studies | A systematic review of level II studies |
| II | A randomised controlled trial | A study of test accuracy with: an independent, blinded comparison with a valid reference standard,[5] among consecutive persons with a defined clinical presentation[6] | A prospective cohort study[7] | A prospective cohort study | A randomised controlled trial |
| III-1 | A pseudorandomised controlled trial (i.e. alternate allocation or some other method) | A study of test accuracy with: an independent, blinded comparison with a valid reference standard,[5] among non-consecutive persons with a defined clinical presentation[6] | All or none[8] | All or none[8] | A pseudorandomised controlled trial (i.e. alternate allocation or some other method) |
| III-2 | A comparative study with concurrent controls:<br>▪ Non-randomised, experimental trial[9]<br>▪ Cohort study<br>▪ Case-control study<br>▪ Interrupted time series with a control group | A comparison with reference standard that does not meet the criteria required for Level II and III-1 evidence | Analysis of prognostic factors amongst persons in a single arm of a randomised controlled trial | A retrospective cohort study | A comparative study with concurrent controls:<br>▪ Non-randomised, experimental trial<br>▪ Cohort study<br>▪ Case-control study |
| III-3 | A comparative study without concurrent controls:<br>▪ Historical control study<br>▪ Two or more single arm study[10]<br>▪ Interrupted time series without a parallel control group | Diagnostic case-control study[6] | A retrospective cohort study | A case-control study | A comparative study without concurrent controls:<br>▪ Historical control study<br>▪ Two or more single arm study |
| IV | Case series with either post-test or pre-test/post-test outcomes | Study of diagnostic yield (no reference standard)[11] | Case series, or cohort study of persons at different stages of disease | A cross-sectional study or case series | Case series |

*Source: National Health and Medical Research Council*

## NHMRC Evidence Hierarchy Explanatory notes

1 Definitions of these study designs are provided on pages 7-8 *How to use the evidence: assessment and application of scientific evidence* (NHMRC 2000b*)*.

2 The dimensions of evidence apply only to studies of diagnostic accuracy. To assess the effectiveness of a diagnostic test there also needs to be a consideration of the impact of the test on patient management and health outcomes (Medical Services Advisory Committee 2005, Sackett and Haynes 2002).

3 If it is possible and/or ethical to determine a causal relationship using experimental evidence, then the 'Intervention' hierarchy of evidence should be utilised. If it is only possible and/or ethical to determine a causal relationship using observational evidence (ie. cannot allocate groups to a potential harmful exposure, such as nuclear radiation), then the 'Aetiology' hierarchy of evidence should be utilised.

4 A systematic review will only be assigned a level of evidence as high as the studies it contains, excepting where those studies are of level II evidence. Systematic reviews of level II evidence provide more data than the individual studies and any meta-analyses will increase the precision of the overall results, reducing the likelihood that the results are affected by chance. Systematic reviews of lower level evidence present results of likely poor internal validity and thus are rated on the likelihood that the results have been affected by bias, rather than whether the systematic review itself is of good quality. Systematic review *quality* should be assessed separately. A systematic review should consist of at least two studies. In systematic reviews that include different study designs, the overall level of evidence should relate to each individual outcome/result, as different studies (and study designs) might contribute to each different outcome.

5 The validity of the reference standard should be determined in the context of the disease under review. Criteria for determining the validity of the reference standard should be pre-specified. This can include the choice of the reference standard(s) and its timing in relation to the index test. The validity of the reference standard can be determined through quality appraisal of the study (Whiting et al 2003).

6 Well-designed population based case-control studies (eg. population based screening studies where test accuracy is assessed on all cases, with a random sample of controls) do capture a population with a representative spectrum of disease and thus fulfil the requirements for a valid assembly of patients. However, in some cases the population assembled is not representative of the use of the test in practice. In diagnostic case-control studies a selected sample of patients already known to have the disease are compared with a separate group of normal/healthy people known to be free of the disease. In this situation patients with borderline or mild expressions of the disease, and conditions mimicking the disease are excluded, which can lead to exaggeration of both sensitivity and specificity. This is called spectrum bias or spectrum effect because the spectrum of study participants will not be representative of patients seen in practice (Mulherin and Miller 2002).

7 At study inception the cohort is either non-diseased or all at the same stage of the disease. A randomised controlled trial with persons either non-diseased or at the same stage of the disease in *both* arms of the trial would also meet the criterion for this level of evidence.

8 All or none of the people with the risk factor(s) experience the outcome; and the data arises from an unselected or representative case series which provides an unbiased representation of the prognostic effect. For example, no smallpox develops in the absence of the specific virus; and clear proof of the causal link has come from the disappearance of small pox after large-scale vaccination.

9 This also includes controlled before-and-after (pre-test/post-test) studies, as well as adjusted indirect comparisons (ie. utilise A vs B and B vs C, to determine A vs C with statistical adjustment for B).

10 Comparing single arm studies ie. case series from two studies. This would also include unadjusted indirect comparisons (ie. utilise A vs B and B vs C, to determine A vs C but where there is no statistical adjustment for B).

11 Studies of diagnostic yield provide the yield of diagnosed patients, as determined by an index test, without confirmation of the accuracy of this diagnosis by a reference standard. These may be the only alternative when there is no reliable reference standard.

**Note A:** Assessment of comparative harms/safety should occur according to the hierarchy presented for each of the research questions, with the proviso that this assessment occurs within the context of the topic being assessed. Some harms are rare and cannot feasibly be captured within randomised controlled trials; physical harms and psychological harms may need to be addressed by different study designs; harms from diagnostic testing include the likelihood of false positive and false negative results; harms from screening include the likelihood of false alarm and false reassurance results.

**Note B:** When a level of evidence is attributed in the text of a document, it should also be framed according to its corresponding research question eg. level II intervention evidence; level IV diagnostic evidence; level III-2 prognostic evidence.

**Source:** Hierarchies adapted and modified from: NHMRC 1999; Bandolier 1999; Lijmer et al. 1999; Phillips et al. 2001.

# Appendix 6: American Journal of Physical Medicine & Rehabilitation Author Guidelines

American Journal of Physical Medicine & Rehabilitation. Instructions for Authors. http://edmgr.ovid.com/ajpmr/accounts/ifauth.htm. Accessed 20 September, 2016.

## INSTRUCTIONS FOR AUTHORS

### Mission Statement

The mission of the *American Journal of Physical Medicine & Rehabilitation* is to publish articles about all aspects of PM&R and to promote excellence in education, scientific research, clinical practice, health policy, and administration.
The *American Journal of Physical Medicine & Rehabilitation* is the official scholarly journal of the Association of Academic Physiatrists (AAP).
The scope of the *Journal* emphasizes all aspects of the specialty of physiatry, including pediatric, adult, and geriatric physical medicine, rehabilitation, and electrodiagnostic medicine. The practice focus is on the clinical and administrative aspects of physical medicine, rehabilitation, and electrodiagnostic medicine. The research focus emphasizes clinical inquiry and also explores basic science. The educational focus is on the application of modern teaching techniques/technology to graduate, undergraduate, and postgraduate physiatric instructional programs.
The overall goal of the *Journal* is to enhance the interrelationship of practice, research, and education to advance the field of physiatric medicine for the ultimate benefit of the patient.

### Conditions for Submission

The author:

1. Assures that the manuscript is an original work that has not been previously published
2. Assures that the manuscript has not been previously submitted to any other publication
3. Accepts full responsibility for the accuracy of all content, including findings, citations, quotations, and references contained within the manuscript
4. Releases and assigns all rights for the publication of the manuscript to Lippincott Williams & Wilkins
5. Discloses on the title page any conflicts of interest related to the research or the manuscript
6. Discloses on the title page any previous presentation of the research, manuscript, or abstract;
7. Assures that authorship has been granted only to those individuals who have contributed substantially to the research or manuscript
8. Discloses in the methods section of the manuscript that any investigation involving human subjects or the use of patient data for research purposes was approved by the committee on research ethics at the institution in which the research was conducted in accordance with the Declaration of the World Medical Association (www.wma.net) and that any informed consent from human subjects was obtained as required
9. Attaches documents showing all relevant permissions to publish quotations, text, tables, or illustrations from copyrighted sources
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### Categories of Manuscripts

1. *Research Article:* Original scientific investigations that advance the field of physiatric medicine. These papers include: (1) randomized controlled trials, (2) cohort studies; (3) case-control studies; (4) cross-sectional studies; and (5) Meta-analyses.

- **LIMITS:** 6,000 words; 4 Tables; 4 Figures, **Maximum 30 References. Please note that if you are unable to adhere to our reference list limit, your article may be published online-only**

2. *Education & Administration Article:* Short papers or surveys addressing issues concerning education, student training, and administration in the field of physical medicine & rehabilitation.

- **LIMITS:** 4,000 words; 3 Tables; 3 Figures

3. *Brief Report:* Short papers reporting on research techniques, statistical techniques, and clinical aspects of physical medicine & rehabilitation.

**LIMITS:** 3,000 words; 2 Tables; 2 Figures

4. ***Case Report:* Short reports explaining the diagnosis, treatment, and outcomes of individual cases of specific conditions to clarify and improve patient care. Cases must be unique to the published medical literature. Any treatment recommendations should reflect current medical practice and cite references from previously published research.

**LIMITS:** 2,000 words; 1 Table; 1 Figure

5. *Clinical Note:* Brief comment on patient diagnosis or treatment resulting from personal clinical experience.

**LIMITS:** 1,000 words; 1 Table; 1 Figure

6. *Commentary:* Short editorial-like paper promoting a particular viewpoint on matters relating to the clinical, scientific, and educational aspects of physical medicine & rehabilitation. Papers that follow the format for a commentary do not have abstracts. Include four key words.

**LIMITS:** 2,000 words; 1 Table; 1 Figure

7. *Analysis:* In-depth systematic examination of complex issues of significant interest to readers and authored by a recognized expert in the field of physical medicine & rehabilitation.

**LIMITS:** 5,000 words; 4 Tables; 4 Figures

8. *Perspective:* In-depth elaboration of viewpoints and personal experiences of interest to readers and authored by a recognized expert in the field of physical medicine & rehabilitation.

**LIMITS:** 5,000 words; 4 Tables; 4 Figures

9. *Literature Review:* In-depth critical summaries and assessments of previously published information on topics related to the field of physical medicine & rehabilitation and authored by a recognized expert. The Journal primarily publishes systematic reviews. Please note that all meta-analyses should be considered Research Articles rather than Literature Reviews

- **LIMITS:** 5,000 words; 4 Tables; 4 Figures, **Maximum 30 References. Please note that if you are unable to adhere to our reference list limit, your article may be published online-only**

10. ***Letters to the Editor:* Intellectual and scholarly letters of comment about articles published in the *Journal* or other matters of general interest. References may be included to support opinions. The Editor reserves the right to determine which letters shall be published and to shorten letters as necessary.

a. **NOTE:** If a Letter to the Editor is written about an article previously published in AJPMR, the corresponding author of the original article will be contacted with a blinded copy of the submitted Letter to the Editor and given a chance to respond. If a response is received and accepted, the two Letters to the Editor will be published together

11. ** *Visual Vignettes:* A rapid, interesting, and enjoyable mechanism by which to further educate and stimulate the readers of the *Journal* using both visual aids and written information. The visual aids that authors submit may include any of the following:

- X-rays
- CT scans
- MRI scans
- Graphs or diagrams
- Photos of electron microscope findings
- EKG printouts
- Electrodiagnostic printouts (NCS or needle exam)
- Photo of a patient or medical device
- Other similar images

All images must be high resolution and may be submitted in either black & white or color. Please follow the Figure Guidelines when submitting images. Accompanying text should include a brief and concise clinical review of the specific patient or clinical issue. This should be followed by a description of the visual aid and an explanation of how such aid may have influenced/affected the management of the patient (diagnosis, treatment, medical and/or PM&R management issues). As appropriate, a summary of the particular pathology or disease process may be included. Finally, any clinical or academic "pearls" to be learned from the visual aid should be included.

**LIMITS:** 200-400 words; **Maximum of 4 References**; Must fit on one page of the published Journal

12. ***Video Galleries:* Combines text with video in the presentation and discussion of a topic of interest in physical medicine and rehabilitation. The Journal encourages submission of high quality digital video to explain medical techniques or procedures of interest to the readership. Educational or instructional videos should accompany a written report to explain the technique or procedure. Visit www.AJPMR.com for current examples. Please follow the Video Guidelines when submitting. Both the manuscript and video will be reviewed for quality of content. Authors may be asked to revise the text and/or video if accepted for publication. **A video checklist is required for Video Gallery submissions and can be found here:** http://edmgr.ovid.com/ajpmr/accounts/Standalone_Video_Checklist.doc

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