The Identification of Gait Asymmetry in Children with Juvenile Idiopathic Arthritis

By

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DECLARATION

I, **Miss Lindiwe Mpaka**, declare that the content of this unique mini dissertation submission is my own unaided work, except for the information acquired from literature sources and my prescribed supervisors. All formal sources of information from literature have been adequately acknowledged and referenced in honor of the efforts of all the authors and their work. I havenot received assistance from any other source in completing this work. This dissertation has also not been, is not being and is not to be submitted for another degree at the University of Cape Town or any other university. I consent to the University of Cape Town to reproduce either the whole or any part of the contents of this work in any manner whatsoever for the purpose of research.

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LIST OF ABBREVIATIONS

APDM	Active Postural dynamic Model
BMI	Body Mass Index
ERA	Enthesitis-Related arthritis
ILAR	International League of Association for Rheumatology
JIA	Juvenile idiopathic Arthritis
M	Meters
m/s	Meters per second
MonoJIA	Monoarticular Juvenile idiopathic Arthritis
MS	Multiple Sclerosis
MRI	Magnetic Resonance Imaging
WS	Wearable sensors
NWS	Non-wearable sensors
OJIA	Oligoarticular Juvenile idiopathic Arthritis
PA	Physical activity
PolyJIA	Polyarticular Juvenile idiopathic Arthritis
RA	Rheumatoid Arthritis
ROM	Range of motion
S	Seconds
SeroJIA	Seronegative Juvenile Idiopathic Arthritis
QoL	Quality of life
SJIA	Systemic Juvenile idiopathic arthritis
SD	Standard deviation
VAS	Visual Analogue Scale
6MWT	Six Minute Walk Test
%GCT	Gait Cycle Time

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ABSTRACT

Background: Gait abnormalities are common in children with Juvenile idiopathic arthritis (JIA), and early detection is crucial to reduce walking disability, which is a significant aspect of daily life. Analyzing gait in this population provides vital information about joint issues and walking patterns, guiding treatment goals. Addressing gait asymmetry can enhance a child's functional abilities, participation in activities, and overall quality of life (QoL).

Purpose: To determine the incidence of gait asymmetry in children with JIA and to further determine the association between gait asymmetry and disease severity and functional capacity

Study design: Cross-sectional Observational study.

Methods: A total number of 14 children between 6-16 years of age (accompanied by their parents) that are diagnosed with JIA, were recruited. They were recruited between April and October 2023 at Tygerberg Hospital, Bellville, Cape Town during routine medical check-ups. The six minute walk test (6MWT) was used to assess gait-related variables using the Active Postural Dynamic Model (APDM) wearable Technologies® incorporated within the Mobility Lab software package. We focused on the examination of five gait parameters related to the lower limbs: 1) Gait cycle duration, 2) gait speed, 3) time in stance phase, 4) stride length, and 5) time in swing phase. The test was administered in a 25 meters walkway, which was measured using a tape measurer, two cones were placed on each end, one at the beginning and one cone at the end of the distance.

Results: We found a statistically significant difference in gait speed and stride length ($p=0.031$ and $p=0.046$, respectively) for the total group, considering left and right leg. Gait asymmetry was found in 8 of 14 participants when the effect size was calculated. No significant differences were found when comparing four of the gait variables between the asymmetry and no asymmetry groups. However, a statistically significant difference was observed in stride

length ($p = 0.04$ left and $p = 0.03$ right) in the asymmetry and no asymmetry group. There was no statistical significance between the disease activity and the asymmetry group ($p = 0.627$). No statistically significant difference was observed in the total distance achieved in both the asymmetry and no asymmetry group on the 6MWT.

Conclusion: Our study underscores the significant impact of gait speed and stride length on gait asymmetry in children with JIA. These gait parameters exhibited the greatest discrepancies among participants, with stride length closely associated with gait asymmetry and gait speed significantly correlated with the total distance achieved during the 6MWT. These findings suggest that both stride length and gait speed are critical factors in understanding gait asymmetry and the functional limitations experienced by children with JIA.

Key words: Juvenile idiopathic arthritis, gait analysis, gait asymmetry, disease activity, functional capacity

CHAPTER I: INTRODUCTION AND SCOPE OF THE DISSERTATION

The background of this thesis is introduced in the first chapter. Then, the problem area is discussed next to provide a deeper understanding of the effect of Juvenile Idiopathic Arthritis in children. The research questions and the research aims/ objectives are stated. At the end of the chapter the outline of this research is presented.

1.1 Background

There is limited research on the prevalence of gait asymmetry in children with Juvenile Idiopathic Arthritis (JIA) in South Africa. However, existing studies have highlighted the effects of JIA on gait, including a crouch-like gait with hyperflexion in the hip and knee joints, less plantar flexion in the ankle, slower gait velocity, shortened step length, decreased Range of Motion (ROM) at the hip, knee, and ankle, and decreased joint power (Vincent et al., 2022; Woolnough et al., 2021). These gait deviations can lead to reduced physical capacity and functional limitations, making it crucial to understand the impact of JIA on gait patterns in children (Kuntze et al., 2020). Therefore, gait analysis serves as a valuable tool in identifying gait abnormalities, informing treatment and rehabilitation strategies. Further research is needed to determine the prevalence of gait asymmetry in children with JIA in South Africa and to explore if disease activity is associated with gait asymmetry.

There is an increase in research on gait abnormalities in children with JIA as noted by (Kuntze et al., 2020). Therefore, it is important to detect gait complications early in children with JIA to provide the necessary treatment to reduce walking disability – the most common component of activities of daily living (Vincent et al., 2022). It is imperative that gait is sufficiently analyzed in children with this condition, as it provides important information about joint alterations and gait patterns that will determine the treatment goals (Montefiori et al., 2019).

Gait abnormalities in patients with JIA are typically addressed initially through use of medical drugs, such as disease-modifying agents to try and decrease symptoms and possible disability in children with JIA (Bazarnik-Mucha et al., 2022; Morita et al., 2018). While early medical intervention is generally recommended for JIA patients, a significant number of them still havea progressive functional deficit as well as subsequent limitations such as active joint contractions, decline in muscle strength, and a reduction in physical activity (PA). As a result of these changes, their quality of life (QoL) is negatively affected (Bazarnik-Mucha et al., 2022; Morita et al., 2018; Weiss et al., 2008).

While there is a growing body of literature on gait analysis and juvenile idiopathic arthritis, there is a noticeable gap in research specific to gait asymmetry in children with JIA in the South African context. This dissertation aims to fill this gap by investigating the identification of gait asymmetry and its implications on the lives of children with JIA in Western Cape, South Africa. The rationale behind this research is rooted in the need for tailored interventions that consider the unique socio-cultural and healthcare landscape of South Africa to address the specific challenges faced by these children.

1.2 Purpose of the study

This study was conducted as a sub study within a larger project led by Stellenbosch University. The primary study, titled "Assessing the validity and reliability of a physical performance test battery for children with JIA," aimed to evaluate various physical performance tests including the six-minute test (6MWT) to ensure they are accurate and reliable for use in children with JIA. Within the scope of this broader research, our study chose to focus specifically on the 6MWT as a tool to evaluate gait asymmetry in children with JI This research topic was chosen as there is a significant lack of evidence on gait asymmetry in children with JIA, therefore, we aimed to contribute to the understanding of this important aspect of physical function in this population.

The purpose of this study is to identify gait asymmetry in children with JIA in Western Cape, South Africa, and explore its impact on their functional performance and PA. It is important that gait is evaluated as the disease impacts their physical performance, which further has animpact on their cardiorespiratory fitness, muscle strength, bone density, ROM, functional ability, and QoL (Klepper et al., 2019). By identifying and understanding these gait abnormalities, healthcare professionals can better assess the severity of the condition, track disease progression, and develop targeted interventions to improve the QoL and functional ability of children with JIA. Furthermore, this research aims to contribute to the literature and inform future research, policy development, and interventions to improve the QoL and overall mobility in children with JIA.

This study is significant because it will contribute to the existing body of knowledge on gait asymmetry in children with JIA, particularly in the South African context. By identifying gait asymmetry and its impact on functional performance and PA, we can inform interventions and policies aimed at improving the QoL for children with JIA in SouthAfrica and beyond. Finally, by addressing gait asymmetry early in the lives of these children, the study seeks to enhance their overall QoL and future outcomes.

This thesis will employ a kinematic approach to analyze the gait patterns in children withJIA. The Active Postural Dynamic Model (APDM) wearable Technologies from Mobility Lab software package was used to analyze gait patterns through the 6MWT in order to quantify any abnormalities and identify key features of gait in children with JIA, such as gait speed, stride length, gait cycle, time in swing phase and time in stance phase.

1.3 Research questions

According to the literature reviewed the following questions arise: 1. Are there gait asymmetries in children diagnosed with JIA that are between the age of six and sixteen years? 2. Is there a relationship between gait asymmetry, disease activity and functional capacity in children

diagnosed with JIA?

1.4 Research aims and objectives

Therefore, the primary aim of this present study is to investigate the presence of gait asymmetries in children diagnosed with JIA between the age six and sixteen years old. The secondary aim is to investigate if there is a relationship between gait asymmetry, functional capacity and disease activity in children diagnosed with JIA.

1.5 Objectives

Based on the research questions, this study seeks to identify gait spatiotemporal parameters affecting gait asymmetry and determine how this knowledge can be applied in clinical settings for a more specialized treatment goals in children with JIA. Therefore, the specific objectives are as follows; To assess gait asymmetry and how they will perform in the 6MWT protocol, analyze the data to determine the presence and the extent of gait asymmetries in the study population, and observe if there is any correlation between gait asymmetry and functional capacity with the levels of disease activity in children with JIA.

1.6 Hypothesis

We hypothesize that children with JIA will exhibit significant spatiotemporal gait asymmetries. Furthermore, we expect that there is a positive relationship between the degree of spatiotemporal gait asymmetry and the level of disease activity in this population.

1.7 Outline of the dissertation

This thesis is divided into six (6) chapters. In the first chapter the background of this thesis is presented followed by the rationale and problem statement, this chapter also includes research

aim, objectives, and conceptual model. In chapter two, we reviewed the existing literature on children with JIA, highlighting the gaps and limitations of previous research and the need for the present study. Methodology is fully presented in chapter three which describes the research methods used to collect and analyze data, ensuring the validity and reliability of the findings. Chapter four presented the findings of the study, including any trends, patterns, or relationships identified in the data. Lastly, chapter five will delve deeper into the discussion of the main findings of the study and compared them to previous researchers, as well as the limitations and future recommendation and ended with the conclusion.

CHAPTER II: LITERATURE REVIEW

The following chapter provides a narrative literature review summarizing the most recent and relevant studies that are related to our research questions presented in the previous chapter. This chapter delves deeper into the disease, its effects on gait and previous research conducted on the topic.

2.1 Introduction

Juvenile idiopathic arthritis (JIA) is an autoimmune condition resulting in heterogenic inflammatory joint disease and is considered the most prevalent chronic rheumatologic disease in children (Kuntze et al., 2020) . It encompasses a diverse group of arthritic conditions with an unknown etiology, typically starting before the age of 16 (Bazarnik-Mucha et al., 2022; Kuntze et al., 2020). The exact cause of the disease remains poorly understood, but it appears to be influenced by both genetic and environmental factors, leading to the wide range of signs and symptoms observed (Barut et al., 2017). Furthermore, prolonged periods of active arthritis can hinder muscle development, resulting in overall growth delay, uneven limb lengths, joint erosion, and reduced quality of life (QoL) (Barut et al., 2017; Klepper et al., 2019). While there are no curative drugs available, considerable progress has been made in managing the disease, resulting in improved prognosis (Al-Mayouf et al., 2021; Weiss et al., 2008) for this widespread chronic disease, however, additional research into the disease and aspects affecting their QoL, such as gait asymmetry, could aid in creating more specific treatment modalities.

The prevalence of JIA varies across different regions across the world. However, due to the lack of standardized classification methods and the diverse frequency of the disease in various regions, the exact prevalence and incidence of JIA remains inconclusive (Thatayatikom & De Leucio, 2020). Numerous studies on JIA have yielded inconsistent results. Globally, the prevalence of this disease is estimated at 3.8 per 100 000 with an incident rate of 1.6-23 per 100

000 children (Al-Mayouf et al., 2021). In contrast, Khodra et al. (2020) has reported an incidence of the disease ranging from 1-23 cases per 100 000 children with a prevalence of 3.8 to 400 cases per 100 000 children in Alaska. Furthermore, a study conducted in Africa and Middle East reported a prevalence of 3.8 to 400 cases per 100 000 children with JIA (Al-Mayouf et al., 2021). Notably, a study conducted in Australia revealed a remarkably high prevalence of 400 cases per 100 000 children (Adrovic et al., 2021). Understanding the epidemiological characteristics of the disease is crucial for assessing the impact of genetic and environmental factors on its prognosis. Thus, providing valuable insights into appropriate treatment approaches and improving preventive healthcare methods.

Thus far there is still no exact consensus regarding the precise prevalence of this condition in developing countries, this may be attributed by the lack of trained pediatric rheumatologists in African countries (Weakley et al., 2012) . For instance, according to statistics from South Africa there are only nine trained pediatric rheumatologists in the country and training each specialist costs around one million. Moreover, in South Africa, the prevalence of JIA has been poorly documented (Weakley et al., 2012) . As a result of delayed specialist referrals, children commonly face a delay in receiving an early diagnosis, typically occurring around the age of eight years. Presently, the median age at which children are diagnosed with JIA is 13 years (Weakley et al., 2012). A delay in diagnosis can have a huge detrimental effect on the development of children and their QoL and can result in short- or long-term disability (Klepper et al., 2019). Therefore, it is important that diagnosis is made on time, as this condition can result in disability and in severe cases mortality.

2.2 Diagnosis and treatment of Juvenile Idiopathic Arthritis (JIA)

According to the International League of Associations for Rheumatology (ILAR) diagnosis is made after all other forms of inflammation that affect joints (synovitis/ bursitis) have been excluded (Ringold et al., 2019). The main criteria for diagnosing the disease include the onset

of symptoms before the age of 16 and inflammation in at least one joint persisting for more than six weeks while excluding other potential causes of joint inflammation (Weiss et al., 2008). Complications of the disease can range from growth retardation and osteoporosis resulting from both treatment and disease activity to a severe condition which further results in complications with diagnosis (Barut et al., 2017). Furthermore, the disease subtype is determined at the onset and may be reassessed during the follow-up. Initial classification is based on the clinical features observed within the first six months of the disease (Barut et al., 2017). The emergence of new clinical features during the disease course determines the final subtype.

The impact of JIA Is further observed by the significant decrease in the QoL in affected children, extending beyond the physical symptoms associated with the disease (Vincent et al., 2022). Consequently, the chronic pain, joint stiffness, and limitations in mobility can restrict a child's ability to engage in age-appropriate activities, participate in sports, and socialize with peers as previously reported in literature (Gueddari et al., 2014). Furthermore, the unpredictable nature of JIA flares and the need for frequent medical appointments and treatments can disrupt school attendance and academic performance, leading to feelings of frustration and isolation (Lelieveld et al., 2005). In addition, the emotional toll of living with a chronic condition can result in anxiety, depression, and reduced self-esteem in children withJIA (Moorthy et al., 2010). The overall QoL is profoundly affected by the interplay of physical, social, and psychological factors.

There are six subtype groups in which JIA is divided into, with the primary purpose of enhancing communication among physicians worldwide regarding epidemiology, therapeutic strategies, and patient outcomes (Weiss et al., 2008). The most prevalent subtype of the disease is Oligoarticular JIA which affects about 50%-60% of the population (Weiss et al., 2008). In

addition, it is mostly prevalent in young females and typically affects up to four or more joints after the first six months (Saurenmann et al., 2007). Followed by Systemic JIA (sJIA), which affects 10-20% of the population and is characterized by recurrent fever and rash episodes (Barut et al., 2017). Seropositive polyarticular JIA, shares similarities with adult rheumatoid arthritis (RA), and is observed in fewer than 10% of pediatric patients and is mostly prevalent within the South African population (Barut et al., 2017; Weakley et al., 2012). On the other hand, seronegative polyarticular JIA involves widespread inflammation affecting both large and small joints throughout the body (Zaripova et al., 2021). The enthesitis-related arthritis (ERA) is a distinct subtype of the disease, characterized by inflammation at the sites where tendons and ligaments attach to the bone, and non-symmetrical JIA primarily affects the lower extremities (Barut et al., 2017). Subtype classification enables a method to standardize the diverse groups, establish appropriate treatment options, devise follow-up strategies, and predict disease prognosis (Weiss et al., 2008).

The treatment for JIA has evolved over the last two decades. A body of literature has reported that nearly all children with JIA experience persistent or recurring pain and almost 60%-70% of them have limitations in participating in physical activities (Vincent et al., 2022). However, the introduction of new therapies in the past two decades has led to a significant advancement in the treatment of JIA, resulting in improved long-term outcomes. For instance, a study published by Murray et al. (2021) mentioned that treatments such as methotrexate and, less often, sulfasalazine and leflunomide have long been used for polyarticular JIA with success for most patients. In addition, a review by Beukelman (2014) mentioned that recent developments in the treatment of systemic JIA demonstrate beneficial features, including marked clinical benefit and confirmation of the pathogenic role of molecular targets.

Managing JIA requires a collaborative approach involving a skilled team of healthcare professionals, including a pediatric rheumatologist, ophthalmologist, orthopedist, pediatric psychiatrist, and physical therapist Stinson et al. (2012). The main treatment goals are to eliminate active disease, restore normal joint function, support healthy growth, and prevent long term joint damage (Backström et al., 2019; Barut et al., 2017). Often PA and movement therapies can induce beneficial results towards children with JIA achieving functional and independent lifestyles. Understanding gait and gait patterns form a large component of functional movement and potential effective interventions, and thus exploring JIA-specific gait patterns is of great value. For this study's purpose, it is important to first understand gait biomechanics and then explore JIA specific gait deviations.

2.3 Gait

Walking is a complex physical process that is predominantly regulated by both the neural and musculoskeletal systems (Fang et al., 2018). Normal gait is a series of smooth and well-structured rhymical movements, that is characterized by symmetrical loading patterns (the left and right limbs behave similarly), long stride length, increased cadence, and normal gait speed (Fang et al., 2018; Vazquez-Galliano et al., 2014; Woolnough et al., 2021). Walking speed, cadence (number of steps per minute), and stride length (linear distance travelled by one gait cycle) have been widely studied in literature as they are crucial in walking (Carroll et al., 2015; Weiss et al., 2008) . The ability to walk is a crucial component of everyday life activities that is however often impaired in children with JIA (Morita et al., 2018). Therefore, it is crucial that these gait complications observed in children with JIA are detected early in order to provide necessary therapy.

2.4 Gait Cycle

The gait cycle is a fundamental concept in the study of human locomotion, extensively

investigated in research related to biomechanics and rehabilitation. It encompasses a complete sequence of events that occur during walking, from one heel strike of a foot to the subsequent heel strike of the same foot (Kharb et al., 2011). It is conventionally divided into two main phases: the stance phase and the swing phase. During the stance phase (which accounts for 60% of the gait cycle),the foot is in contact with the ground, providing stability and propulsion (Kharb et al., 2011). It is further divided into sub-phases, including initial contact, loading response, mid-stance, terminal stance, and pre-swing. The swing phase, on the other hand (40% of the gait cycle), involves the leg being lifted and propelled forward, preparing for the next stance phase (Kharb et al., 2011). It is divided into three sub-phases: initial swing, mid-swing, and terminal swing.Throughout the gait cycle, various joints, muscles, and body segments work synergistically to generate efficient and coordinated movement (Kharb et al., 2011). Understanding the complexes of the gait cycle is crucial for assessing normal and pathological walking patterns, evaluating interventions, and developing effective rehabilitation strategies for individuals with gait impairments like JIA.

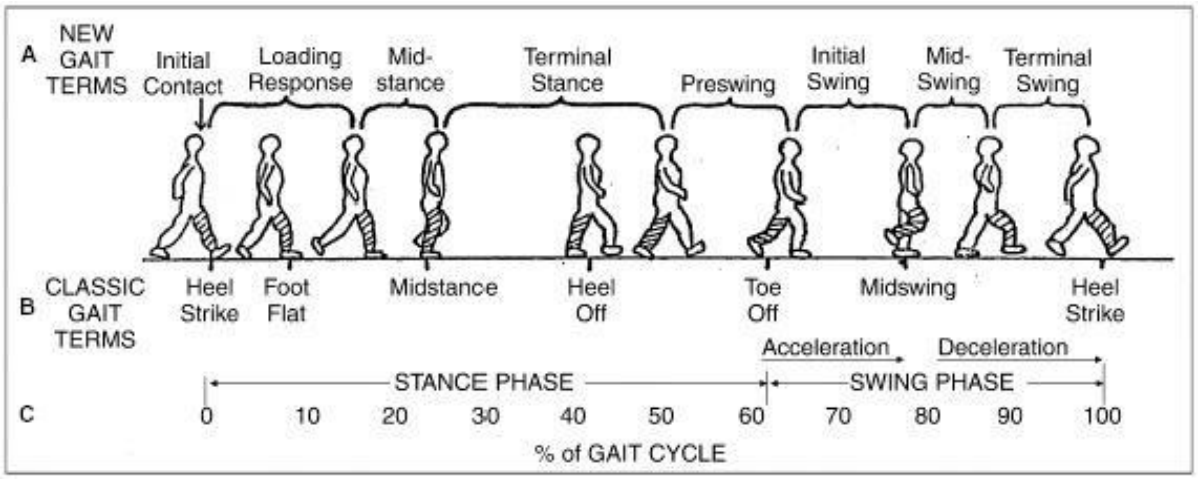


Figure 2.1: A figure presenting the phases of gait cycle (extracted with permission from a study by Castermans and colleagues, *Brain Sciences*, 2014, 4, p. 4 (Castermans et al. 2014; doi:10.3390/brainsci4010001).

The phases of the gait cycle most affected were believed to be initial and final contact. A study conducted by Hartmann et al. (2010), has found some gait deviations during the stance phase in the lower extremities in children with JIA. Moreover, the impact is observed through a decrease in muscular strength/atrophy, bone density, Range of Motion (ROM), and aerobic capacity, and thus affecting their QoL (Hartmann et al., 2010; Kuntze et al., 2020). Furthermore, JIA canlead to joint deformities which can lead to long-term health problems, including fatigue duringPA, contractures, or subluxations, which further affect joint alignment and mechanics during walking (Woolnough et al., 2021). For instance, knee joint involvement may result in flexed or extended knees, further distorting the gait pattern as previously observed (Hartmann et al., 2010). Therefore, these distinct gait differences require targeted treatment options to improve function such as focusing on knee strengthening and gait retraining to enhance mobility. These gait alterations in children with JIA highlight the significant impact of the disease on their mobility and emphasize the need for comprehensive assessment and targeted interventions to improve their gait function and overall QoL.

2.5 Juvenile Idiopathic Arthritis (JIA) and Gait Characteristics

Gait characteristics in children with JIA have been a focal point in understanding the impact of the disease on walking and overall QoL. Children with JIA exhibit distinct characteristics in their walking patterns which are often different from their healthy counterparts (Hartmann et al., 2010) (Broström et al., 2002). Previous research has been done on this population and it has been established that their gait often displays to be characterized by a trend towards flexion at the hip, knee and ankle joints, leading to a crouch-like gait (Hartmann et al., 2010; Merker et al., 2018). Additionally, abnormal joint kinematics such as decreased dorsiflexion and plantarflexion at the ankle and altered knee flexion-extension cycles have been associated with uneven and asymmetric gait patterns (Merker et al., 2018).

The compensatory mechanisms, such as increased pelvic tilt and reduced gait speed are common in this population as they attempt to minimize pain and discomfort during walking (Hartmann et al., 2010; Kuntze et al., 2020).The slowed walking speed is often accompanied by shortened step length, which can be attributed to the reduced ROM in the affected joints (Hartmann et al., 2010; Vincent et al., 2022). This characteristic was associated with pain and inflammation, which results in compensation mechanisms to avoid inflamed and painful joints.

Furthermore, previous studies have suggested that gait abnormalities reflect the overall functional ability of children with chronic arthritis (Kuntze et al., 2020; Woolnough et al., 2021). Evaluating gait may be at the least a tool to assess their functional ability in tracking disease progression.

2.6 Gait spatiotemporal parameters

In recent years, research has evolved and investigating the spatiotemporal gait parameters has increased in children with JIA. Studies have consistently reported a decrease in gait speed, cadence, step length and stride length in this population. According to Merker et al. (2018), children with JIA showed a notable decrease in walking speed associated with an anterior tilt of the pelvis and a restricted extension of the lower limb joints. In addition, Broström et al. (2002) examined the gait in children with JIA with reference to gait velocity, ground reaction force and temporal parameters and found that the mean walking velocity for children with JIA was significantly less than for the healthy controls. Furthermore, Shaw et al. (2006) revealed that children with JIA exhibited decreased walking speed, shorter stride length, increased stance time, and altered joint motion as compared to their healthy counterparts. These studies, among others, contribute to our understanding of gait parameter abnormalities and their impact on functional mobility in children with JIA. However, it is worth noting that some of these studies did not consider the potential influencing factors, such as the current state of disease activity (active or inactive), when assessing gait parameters.

2.7 Gait Analysis in Juvenile Idiopathic Arthritis (JIA)

Objectively analyzing the gait of children without specialized methods such as three-dimensional motion sensors which are considered gold standard (Muro-de-la-Herran et al., 2014), in a clinical setting poses challenges due to the complex and rapid nature of their movements, and the often expensive and cumbersome equipment it requires. Traditional methods such as observation, video analysis on a walkway or treadmill, and gait scales and questionnaires are subjective and often lack the ability to provide quantitative, objective measures of gait parameters (Muro-de-la-Herran et al., 2014). Furthermore, these methods cannot assess factors such as kinetics and muscle activity involved in gait, with their accuracy dependent on the clinician's experience (Kyriazis, 2001).

Therefore, in recent years they have started using motion sensors for gait analysis as opposed to observational gait analysis (like observational gait scale and Edinburgh visual gait score), video analysis or gait scales and questionnaires which were subjective and lacked the ability to provide quantitative, objective measurements of gait parameters (Hulleck et al., 2022; Muro-de-la-Herran et al., 2014). Furthermore, these traditional methods could not assess factors such as kinetics and muscle activity involved in gait, and the accuracy was dependent on the clinician's experience (Kyriazis, 2001). The emergence of instrumented gait analysis using motion sensors allowed for a more comprehensive, qualitative evaluation and evaluation in gait analysis (Muro-de-la-Herran et al., 2014). In this study, we utilized the use of APDM sensor to analyze gait in a 25-meter walkway to capture the children's natural walking patterns in a clinical setting.

Gait analysis can be used as a method to measure the progress of the disease as it provides valuable insights into the biomechanical characteristics, walking patterns, and functional limitations associated with JIA (Broström et al., 2002). Assessing gait during the early stages of

the disease may be useful in identifying both the progression of the disease and the effectiveness of the treatment interventions (Fairburn et al., 2002). Gait analysis in children can be evaluated using various methods, categorized into non-wearable sensors (NWS) and wearable sensors (WS), where NWS systems rely on specialized research facilities and controlled by walkways to gather data, while WS systems allow for a collection of gait information during a person's normal daily routines, outside of a laboratory setting (Muro-de-la-Herran et al., 2014).

These different methods have been previously used by different researchers. For example, Fairburn et al. (2002) used an in-house visual vector system and the novel PEDAR in-shoe plantar pressure measurement system, which incorporates both non-wearable (NWS) and wearable sensors (WS) for gait analysis. The combination of NWS and WS allows for a more comprehensive assessment of gait by capturing external visual data (NWS) and internal foot pressure distribution (WS), providing a detailed understanding of the biomechanical gait abnormalities in children with JIA. They have found four different gait patterns in this population for example a near normal gait (pattern I), gait affected by lower limb pain (pattern II), gait affected by lower limb deformity (pattern III), and a combination of pain and deformity affecting gait (pattern IV) were identified (Fairburn et al., 2002).

More research has been conducted on NWS. For example, Montefiori et al. (2019) proposed a Magnetic Resonance Imaging based methodology to analyze the link between joint impairment and joint loading when they were walking. A notable finding from the study was the correlation between impairment in one limb and increased load on the opposite limb, suggesting compensatory mechanisms that might put the contralateral limb at risk, particularly at the knee joint level. Furthermore, a study conducted by Merker et al. (2018) using three-dimensional (Vicon) motion analysis system to assess functional deficits in children with JIA, has found that children with JIA showed slower gait as compared to their healthy counterparts.

Moreover, some studies have utilized the use of WS in this population to assess gait while walking. For example, Kuntze et al. (2020) assessed for gait adaptations in this population using reflective spherical markers attached to the skin (WS) gait kinematics betweenJIA and typically developing youth and observed deviations in joint angles, suggesting that even with low disease activity, youth with JIA adapt their gait to avoid joint inflammation andpain. It is important to note that these systems as much as they provide valuable data, they are considered expensive, time consuming and more suitable for laboratory assessments than in clinical settings.

With evolving technology, inertial sensors are increasingly being used in research and clinical settings. In addition to WS, there has been an increase in the use of inertial sensors for gait analysis in clinical settings. The use of the different gait analysis methods helps provide valuable information to address specific gait deviations, prevent further restrictions, and improve overall mobility their QoL. Moreover, using inertial sensors for spatiotemporal gait analysis may be acceptable as it shows good validity compared to video or camera-based motion capture analysis systems (Kluge et al., 2017).

In this thesis we focused on assessing gait using the APDM sensor during the 6MWT. The APDM sensor is part of the Inertial measurement unit. This system provides a valuable tool for clinicians and researchers to evaluate and interpret gait impairments, aiding in the development of rehabilitation plans and training interventions.

2.8 Six-Minute Walk Test as a measure of gait assessment

The six-minute walk test (6MWT) is a self-paced walking test that is commonly used to objectively analyze gait in various chronic populations such as neurological disorders, multiple sclerosis (MS) as well as cerebral palsy (CP) (Graser et al., 2016; Shema-Shiratzky et al., 2019; Thompson et al.,

2008). It is easy to administer, safe, inexpensive, and feasible to use in clinical settings. The 6MWT provides an assessment of dynamic changes while the individual is walking which may provide valuable clinical information such as the quality of gait, asymmetries between the legs and gait speed(Shema-Shiratzky et al., 2019). Additionally, the test measures exercise tolerance necessary for activities of daily living (ADL) such as walking to school, making it a well-tolerated and informative tool for clinicians (Thompson et al., 2008).

Research on the use of the 6MWT and gait analysis on the pediatric population is still lacking, especially JIA population. However, extensive research has been conducted on the adult population (Bartels et al., 2013; Hadouiri et al., 2021; Shema-Shiratzky et al., 2019). A study conducted by Mian et al. (2022) is the first study that established the 6MWT distance references values in the JIA population of the same group (6 to 16 years old). The study found that children with JIA had achieved a lower mean 6MWT distances compared to those without JIA. Moreover, on average, the distance achieved were 84% and 78% of the predicted values for children without JIA. The reference values established in this study, along with the predictive model developed, can be utilized to assess the exercise capacity of children with JIA(Mian et al., 2022). Another study by Kasović et al. (2021) conducted on the 6MWT in healthy children between the age of 11 to 14 years old, has provided standardized references for clinicians and researchers evaluating exercise capacity in children with chronic diseases, enhancing the interpretation of the 6MWT results in clinical settings.

Studies comparing shorter tests (two-minute walk test) to 6MWT have shown that longer tests, such as the 6MWT better correlate with real-life mobility metrics like walking speed, daily walking and total distance (Shema-Shiratzky et al., 2019). For instance, Sandroff et al. (2015) found that the 6MWT distance was associated with walking performance rather than aerobic and muscular

fitness. In addition, they found that measures of walking performance, such as the timed 25-foot walk speed and gait velocity, contributed more to the six-minute walk distance, whereas physical fitness measures made a minimal contribution in people with MS (Sandroff et al., 2015). Similarly, Pilutti et al. (2013) identified cadence and stride length as key gait variables explaining differences in six-minute walk performance between people with MS and healthy controls (HC). Moreover, this suggests that longer walking may have greater ecological validity and may be a more effective measure of gait discrepancies as well as the level of fatigue during sustained walking. (Shema-Shiratzky et al., 2019). The assessment of gait using the 6MWT has been shown to be valid and reliable in both adults and the pediatric populations (Hadouiri et al., 2021).

In the context of JIA, factors like pain and fatigue can significantly affect spatiotemporal gait parameters over longer distances which can be analyzed and used to enhance treatment, unlike shorter distances like the ten-meter walk test. Moreover, studies have shown that the 6MWT can reveal variations in gait parameters that may not be evident in shorter tests, such as fatigue-related changes or adaptations that occur with prolonged walking (Geiger et al., 2007; Pires et al., 2022). In addition, a more natural walking pattern is likely to be observed during the 6MWT as children do not feel they are being observed for a brief, intense period therefore, this longer duration allows them to walk more naturally and comfortably (Jeon et al., 2023).

2.9 Juvenile Idiopathic Arthritis (JIA) and Disease Activity

Disease activity refers to the level of inflammation and symptoms experienced by an individual with JIA. In particular, gait asymmetry can be influenced by the severity of joint inflammation, pain, and limitations caused by the disease (Backström et al., 2019). During periods of active disease flare-ups, when inflammation and symptoms are heightened, gait asymmetry may be

more pronounced. The increased joint pain, swelling, and stiffness can lead to altered movement patterns and compensatory mechanisms, resulting in noticeable gait abnormalities (Weiss et al., 2008). Furthermore, the degree of gait asymmetry may correlate with the level of joint inflammation and tenderness (Turner et al., 2008). Assessing disease activity is an essential part of the clinical evaluation of children with JIA since ongoing active disease significantly contributes to joint damage and physical functional limitations (Consolaro et al., 2009).

Studies have found that the level of disease activity can significantly affect gait. This impact may manifest as a reduction in gait speed, a decrease in stride length, and an increase in the duration of double support while walking (Hartmann et al., 2010; Vincent et al., 2022). Therefore, suggesting that as disease activity increases, gait function may be negatively affected. However, it is important to note that individual variations exist, and the specific impact of disease activity on gait may depend on factors such as the subtype and severity of JIA, as well as the joints involved.

There is a high prevalence of gait abnormalities in children suffering from JIA (Kuntze et al., 2020; Woolnough et al., 2021). It is important to detect gait complications early in children with JIA to provide the necessary treatment to reduce walking disability, the most common component of activities of daily living (Vincent et al., 2022). It is important that gait is sufficiently analyzed in children with this condition, as it provides essential information about joint alterations and gait patterns that will determine the treatment goals (Montefiori et al., 2019). By addressing gait asymmetry, healthcare professionals can help improve a child's functional abilities, promote participation in activities, and enhance their overall QoL. Therefore, the purpose of this study is to determine the incidence of gait asymmetry in children with JIA and to further determine the association between gait asymmetry and disease severity.

CHAPTER III: METHODOLOGY

This chapter will present a detailed idea about how the research was conducted. This includes the study design, participants recruited, inclusion and exclusion criteria, how descriptive information was collected, administration of the Juvenile Arthritis Disease Activity Score (JADAs 10) and the 6 Minute Walk Test (6MWT).

3.1 Introduction

The current study is part of a larger study paired with Stellenbosch University conducted by Su-Ane Zwiegelaar, (*title: Assessing the validity and reliability of a physical performance test battery for children with JIA*). Ethical approval was submitted and accepted from Stellenbosch University (ethics number: S22/03/051). Please see Appendix 3 for a memorandum of understanding (MoU) between authors from the University of Cape Town and Stellenbosch University respectively, stating the differences in the research aims of the project between the two students. This sub-study assisted in data collection in exchange for access and exclusive usage of certain variables to address the research question. Our study was approved by the Health Sciences Human Research Ethics Committee of the University of Cape Town (HREC 492/2023) and adhered to the principles of the Declaration of Helsinki (Association, 2013) (Appendix 4).

3.2 Study design

We conducted a literature search on gait analysis in children with Juvenile Idiopathic Arthritis (JIA) from January 2023 to October 2023. The search included databases such as PubMed, Scopus, Google Scholar, Web of Science, and the University of Cape Town's library. Keywords and synonyms related to various aspects of gait analysis and children with JIA were used. The specific queries used in the title and/or abstract were: ("JIA" OR "juvenile idiopathic arthritis"), ("gait analysis" OR "gait assessment"), ("6MWT" OR "six-minute walk test" OR "six-minute walking test" OR "6MWD" OR "6-min walk test" OR "six-minute walk test"), AND ("IMU" OR "inertial measurement unit" OR "MIMU" OR "magneto inertial measurement unit" OR

“inertial sensor” OR “accelerometer” OR “wearable sensor” OR “activity tracker” OR "APDM sensor" OR “Ambulatory Parkinson's Disease Monitoring”). Initially, the search was limited to studies from the last ten years (2013 to 2023), but due to the limited research on this topic, we extended the search to include the last 20 years (2003 to present). The inclusion criteria for the studies were: 1) JIA defined by the ILAR criteria, 2) age between 6 to 16 years, 3) studies focused on gait analysis in children with JIA, and 4) the use of the 6MWT in children. Additionally, gait analysis was based on spatiotemporal gait parameters.

This was a cross-sectional observational study. A total number of 14 children between 6-16 years of age (accompanied by their parents) that are diagnosed with Juvenile Idiopathic Arthritis (JIA), were recruited. They were recruited between April and November 2023 at Tygerberg Hospital, Bellville, Cape Town during routine medical check-ups. All ethical considerations were considered and comprehensively shared with the participants on the consent forms (Appendix 5 and 6).

3.3 Inclusion and exclusion criteria

The following inclusion and exclusion criteria were formulated from studies previously conducted within the JIA population (Bourdier et al., 2021; Calık et al., 2020; Connelly et al., 2019) . Furthermore, most of the criteria have been established to ensure participant safety and minimize the risk of harm or injury.

3.3.1 Inclusion criteria:

Participants included in the study were between the ages of 6-16 years, and JIA diagnosed by a pediatric rheumatologist as per International League of Associations for Rheumatology (ILAR). Participants were included if their parents signed the consent/assent forms, they did not have any contraindications to physical activity (PA), and they had pain in more than one

joint over six months. Lastly, they were included if they were receiving medication for synthetic or disease modifying anti-rheumatic drugs.

3.3.2 Exclusion criteria:

Participants who were younger than six years and over the age of 16 years were excluded, based on the definition of JIA, which is used to distinguish JIA from other forms of arthritis that may occur in older adults (Calık et al., 2020; Klepper et al., 2019). They were excluded if they had an active acute infection, which may result in decreased performance. Those using corticosteroids either orally or injection for the past three months, had a fever two weeks prior to testing or had any surgical operations within the last six months were excluded. Lastly, those who had a severe cognitive impairment which may alter their ability to understand instructions were excluded.

3.4 Experimental procedures

The study procedure followed the following sequence. Descriptive data was collected which included the consent forms and assent forms (Appendix 5 and 6) Then followed by the assessment process; the JADAS10 (prioritizing non-fatiguing tests). Subsequently, the 6MWT was administered by a qualified Biokineticist who was trained in the testing procedures.

The child was required to wear appropriate clothing, including athletic wear such as shorts and a t-shirt with a vest/or sports bra for females, as well as correct footwear, specifically closed shoes (trainers/tekkies). For those who use assistive devices they were asked to bring it along to the appointment. However, the study had no participants who used assistive devices. Finally, medication was advised to be taken as required for the child before testing on the day of the visit.

Instructions on how to conduct the assessments were provided by the Biokineticist and they

made sure that the participant understood the instructions before the assessment started. If the participant did not clearly understand the instructions, the Biokineticist provided demonstrations. Furthermore, participants were informed that if they want to stop the assessment, they can do so without any consequences. For their safety, participants were notified about the availability of the first aid kit, and automated electronic defibrillator and the Biokineticist is a certified first aider in case of an emergency.

3.4.1 Descriptive data

During their visit participants were asked to sign an informed consent form and descriptive data was collected. Descriptive data included basic anthropometric measures (age, height, sex, weight), disease/condition and medical history questionnaire (subtype, time since diagnosis, pain level and location, medication and dosages, recent operations), and the physical readiness questionnaire (Appendix 7).

3.4.2 Juvenile Arthritis Disease Activity Score

The Juvenile Arthritis Disease Activity Score (JADAS) is a comprehensive tool for assessing disease severity, inactive disease, and clinical remission which includes these four components: joint assessment (ROM, pain/tenderness, swelling), physician global assessment, patient global assessment, and ESR measurement, all normalized to a visual analog scale (VAS) of zero to ten (Backström et al., 2019; Consolaro et al., 2016). It is considered a reliable and widely accepted tool for assessing disease activity in pediatric rheumatology (Backström et al., 2023). It is commonly used by pediatric rheumatologists to guide treatment decisions and achieve targeted therapeutic goals. Importantly, the cJADAS does not necessitate the measurement of an acute phase reactant, which enhances its practicality and accessibility in resource-limited settings where cost-effective testing is crucial.

The JADAS10 was used to observe and record joints disease activity score specific to JIA. The

investigator palpated all joints, beginning with the fingers and progressing to the shoulder, spine, hips, knees, ankles, and toes. The joints were evaluated specifically for swelling, tenderness, and subjective ROM, which was scored on a scale of one to ten, with each tender, swollen, or reduced ROM joint increasing the scale score (active joint count).

Once the number of joints affected were identified and subsequently evaluated using a geometry (digital device from Easy Angle® by Meloq Devices), which is a method used by the Biokineticist to assess the overall activity of the disease. In particular, the joints mentioned in the JADAS10 that exhibit limited ROM were measured. Each joint was measured based on the location of the joint axis, the reference line, the measurement line, and the plane in which the movement happens. After measuring the joint's resting position, the participant was requested to do the specific joint movement, and the digital goniometer was moved along with the joint to the maximum point, where the final ROM was recorded. ROM was recorded once according to the following order of position, sitting, supine, side-lying (right), prone, side- lying (left), and standing.

Finally, joints that were scored on the JADAS10 were evaluated and scored on a scale of one to ten based on the percentage of full ROM achieved within a joint. Thus, for 100% of the optimum ROM achieved, a score of one was given, 99-90% was given a score of two, 89-80% was given a score of three, 79-70% was awarded a score of four, 69-60% was given ascore of five, and so on until a ten was awarded if only 19% or less of the optimum ROM was achieved. The scores of one to ten for each joint assessed was then averaged to provide the overall ROM domain score of one to ten for the ROM domain (see Appendix 8)

3.4.3 Instrumented Six-Minute Walk Test (6MWT)

The 6MWT is a widely accepted and validated functional exercise capacity test for children and adolescents with juvenile idiopathic arthritis (JIA). It measures the distance a person can walk in

six minutes, following a standardized protocol set by the American Thoracic Society (ATS) (Mian et al., 2022). The test is conducted on a 30-meter surface, with verbal encouragement provided every minute, and measurements of blood pressure, heart rate, oxygen saturation, and perceived exertion taken before and after the test.

Although the 6MWT shows moderate correlations with VO2peak but it is also reflective of joint status (Pritchard et al., 2022). The test has demonstrated good to excellent reliability (ICC = 0.86) for children aged 7 to 17 years (Pritchard et al., 2022). In addition to the 6MWT being used in various chronic populations such as neurological disorders, multiple sclerosis (MS) as well as cerebral palsy (CP) (Graser et al., 2016; Shema-Shiratzky et al., 2019; Thompson et al., 2008), it has also been used to test functional capacity in JIA population (Lelieveld et al., 2005). It is easy to administer, safe, inexpensive, and feasible to use in clinical settings. The 6MWT provides an assessment of dynamic changes while the individual is walking which may provide valuable clinical information such as the quality of gait, asymmetries between the legs and gait speed(Shema-Shiratzky et al., 2019).

Therefore, using a longer test like the 6MWT for gait analysis is advantageous over shorter tests due to its comprehensive evaluation of gait and mobility. While traditionally used to measure functional capacity, the 6MWT is also highly relevant for gait analysis. Clinically, the test has been shown to have a strong ecological validity, meaning that the test closely resembles real-world situations where children engage in prolonged walking activities. Moreover, this extended duration allows for the observation of fatigue effects and compensatory strategies that might not be evident in shorter duration tests, thus offering a holistic view of children's gait and overall mobility.

The 6MWT was used to measure gait variables using the Active postural Dynamic Model (APDM) wearable Technologies® from Mobility Lab software package. The APDM sensor has been

previously used to measure gait analysis using the 6MWT in various adult populations and in children (Howell et al., 2018; Muthukrishnan et al., 2020; Shema-Shiratzky et al., 2019). The APDM system consists of wearable sensors that can be attached to various parts of the body, such as the wrists, ankles, and torso (Yang & Li, 2012). These sensors collect detailed data on movement patterns, providing clinicians with valuable insights into a child's motor development and potential abnormalities (Bisi et al., 2018). Furthermore, this system provides a valuable tool for clinicians and researchers to evaluate and interpret gait impairments, aiding in the development of rehabilitation plans and training interventions (Muro-de-la-Herran et al., 2014).

Studies have shown the validity and reliability of the APDM sensor that has been used in children with different chronic conditions for gait analysis (Lanovaz et al., 2017; Shieh et al., 2022; Sivarajah et al., 2018; Voss et al., 2020). One of the significant advantages of using APDM sensors in children is their non-invasive nature. Traditional methods of assessing motor skills often involve clinical observations and subjective assessments, which can be inconsistent and imprecise. In contrast, APDM sensors offer objective, quantitative data that can be recorded over extended periods, even during a child's daily activities (Howell et al., 2018).

This continuous monitoring capability allows for a more comprehensive understanding of a child's motor functions and the identification of subtle issues that might not be evident in a clinical setting (Prosser et al., 2018). By providing precise and reliable data on movement patterns, APDM sensors can help identify these conditions at an early stage, allowing for timely intervention that can significantly improve outcomes.

The APDM sensor offers portability, ease of use and the ability to provide objective gait information making it a valuable tool for continuous monitoring in various settings, including clinics, laboratories and even community environments. Despite its compact size and lightweight

nature, this system offersgreat sensitivity and proves to be an affordable and convenient option for clinical testing as compared to the other motion sensors like the 3-dimensional sensors or the Vicon system, which are considered the "gold standard" measures but are expensive and not clinically and practically suitable for practitioners. For this reason, we decided to utilize the APDM sensor to objectively measure and analyze spatiotemporal parameters of gait and the results were automatically recorded in the computer to be analyzed.

For the purpose of this project, five gait parameters of the lower limb were used for our analysis: 1) gait peed [m/s], 2) gait cycle duration [s], 3) time in stance phase [%GCT], 4) time in swing phase [%GCT], 5) stride length [m]. Before the APDM sensor was placed it was calibrated. Once calibrated, the APDM Wearable Technologies® from Mobility Lab was attached to the participants, six sensors- 2 on the feet, two on the wrist, one on lower back and one on the sternum. During the 6MWT the signals were sampled and recorded automatically on to the investigators' laptop and calculated via the corresponding Mobility Lab software (see Appendix 7).

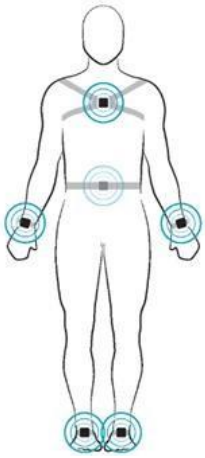


Figure 3.1: *APDM sensor placement on the sternum, one on each wrist, one on each foot, and one on the lower back.*

The test was administered in a 25 meters walkway, which was measured using a tape measurer, two cones were placed on each end, one at the beginning and one cone at the end of the distance (Mian et al., 2021). Once the setup of the test was completed. Participants were encouraged to cover the largest distance they can in the six minutes period at their preferred walking pace without running, as done by Lelieveld and colleagues (2005).

During the test, participants were expected to walk through the 25-meter walkway, once they reach the end they had to return to the starting cone, which was recorded as one lap. Time was measured and recorded using a stopwatch. For every minute participants wereinformed about their progress. Throughout the test, participants were encouraged, "keep going" "you are doing well" as done by Lilieveld et al., (2005). During the test participants were asked about their Rate Perceived Exertion (RPE) using the Borg scale from one to ten (1 = no exertion and 10 = maximal exertion), to measure their overall fatigue.

When the time was at six minutes, participants were asked to stop and stand still where they are, and the distance covered was measured using a measuring tape and recorded. Distance covered

was calculated by multiplying the number of laps by 25 and adding the additional meters in the final partial lap. Distance was rounded to the nearest meter.

Additionally, a termination criterion was implemented such as participant can decide to stop if they did not want to participate anymore, if there was an equipment failure, if there were any signs of poor blood circulation, pain, and extreme fatigue.

3.5 Data analysis

The statistical tests used for data analysis were selected with the assistance of Laerd Statistics (Laerd Statistics, 2013). Data analyses were conducted using IBM SPSS statistics version 28 software and with GraphPad Prism 10.0.0 (for Windows, GraphPad Software, Boston, Massachusetts USA). Descriptive statistics were analyzed, mean and standard deviation (SD) was used for continuous variable and frequencies and percentages for categorical variables as they were calculated on baseline demographics. All continuous data analyses were performed using non-parametric tests due to the small sample sizes of the total group (n=14) and no asymmetry and asymmetry groups (n=6 and n=8) (Pett, 2015).

A Wilcoxon signed-ranked test was conducted between left and right spatiotemporal gait parameters within the total group (n=14) to determine if any discrepancies between left and right parameters were observed. The outcome variables: gait speed, gait cycle duration, time in stance phase, time in swing phase and stride length, 6MWT outcomes and physical measurements were analyzed for possible differences between the Asymmetry (n=8) and no asymmetry group (n=6). For all latter statistics, the Mann-Whitney u test was performed. The Mann-Whitney U test was also used to assess whether there were differences between the spatiotemporal variables on the left and right side.

The chi square test of two proportions was conducted between the nominal/ factorial data to

determine if the distribution of individuals/factors in one group are significantly different compared to the distribution in the other group (asymmetry versus no asymmetry) (Statistics, 2013). During Chi-square analyses, the Fisher Exact Statistic were used when the expected count for any of the proportions were < 5. The outcome variable for each gait parameter during the 6MWT resulted in a mean and SD result over the 6 minutes of walking. Statistical significance was set at $P < 0.05$.

To determine the effect size in the absence of a reference group or non-diseased control group, we quantified the magnitude of the differences between left and right spatiotemporal outcome variables to determine if they were clinically meaningful. We determined the effect size of the differences between the average and SD of the left and the right side for each outcome variable. We selected the smallest clinically meaningful effect size of 0.20 or higher as indicative of a real difference between left and right side. The use of 0.2 threshold was based on the minimal clinically importance difference (MCID). The literature suggests that a small effect size of 0.2 is commonly used to define MCID, which is a patient-centered measure that expresses both the extent of the improvement and the value that patients place on it (Franceschini et al., 2022). Therefore, we used the threshold of 0.2 to ensure that our results are based on a widely accepted and established standard in the clinical field, ensuring that the MCID is meaningful and relevant to the patients and clinicians involved.

This small or greater effect size was selected as the cut-off for a clinical significance between left and right, based on the type of variables that were analyzed. If three of the five spatiotemporal parameters resulted in an effect size greater than 0.2 the participant was categorized as having "gait asymmetry." If not, they were classified as having "no asymmetry." The effect size formula used was:

$$d = \frac{M1 - M2}{SD}$$

where M1 is the mean of the left leg and M2 is the mean of the right leg, divided by the SD (Becker, 2000). This formula enabled us to qualify the magnitude of the difference between the left and right legs, thereby establishing the true clinically meaningful difference between asymmetry and no asymmetry groups spatiotemporal patterns.

3.5.1 Six-Minute Walk Test: Total Distance Achieved

The final score was expressed as the distance covered in meters during the six-minute period. After allocating participants into asymmetry and no asymmetry groups, we used the prediction equation provided by Mian et al. (2022) to determine the expected distance JIA children should cover. We calculated the difference between Mian et al. (2022) predicted distance and our measured 6MWT distance using the following formula:

$$Difference\ (\%) = \frac{Predicted\ value - measured\ values}{Predicted\ value}\ X100$$

If the difference was more than 10% of Mian's predicted value, it indicated that the participant's distance covered was significantly less than expected.

Additionally, we used the paper by Kasović et al. (2021) to compare and group the distances according to percentiles. We established that participants who achieved the 50th percentile or higher were considered to have acceptable performance. Participants were informed that they were being observed for the distance walked rather than walking patterns to avoid compensation.

A Spearman Rank-order correlation was conducted to determine any possible associations between spatiotemporal gait parameters and the total distance achieved during the 6MWT.

CHAPTER IV: RESULTS

This chapter will present data that has been collected and analyzed through statistics using the SPSS software. First, we provide descriptive information for the whole group as well as the subgroups identified as showing asymmetry or not, followed by the gait variables of the left and right leg for the group of a whole. Next the effect sizes of participants are shown per gait variable, which showcases the methods we used to differentiate between participants who showed asymmetry and those without asymmetry, and thereafter the results of difference between these two subgroups are shown. Lastly any correlation with disease severity and asymmetry are presented.

4.1. Demographic characteristics

Fourteen participants volunteered to participate in the study. The demographic data were not normally distributed (due to the small sample size), and the participants' characteristics are summarized in **Table 4.1**. However, demographic characteristics are presented as mean ± SD. A chi square test was conducted between the demographic variables between the asymmetry, and no asymmetry groups. three out of four expected cell frequencies were less than five, therefore, a Fisher's exact test was conducted.

We found no statistical differences in all the demographics data between the asymmetry (n = 8) and no asymmetry (n = 6) $p > 0.05$. Furthermore, 8 (57.1%) of the participants had active disease, as assessed by the Juvenile Arthritis disease Activity Score (JADAS10) based on a score from1-10 which measures the percentage of full range of motion (ROM) achieved within a joint. The total JADAS scores ranged from 0-7.7, with a Visual Analogue Scale (VAS) score ranging from zero to seven. Nine participants had active joints (inflammation and/or pain that resulting in limping), with the knee joint being the most affected. Additionally, 43% of the participants had more than one joint affected. All participants were onmedication, with the number of medications ranging from one to seven.

Table 4.1: Demographic characteristics of children with JIA

Characteristics	Total (n=14)	Asymmetry (n=8)	No asymmetry(n=6)	P value
Age (yrs.)	10.71±2.81	10.00 ± 2.83	11.67 ± 2.73	0.35
Gender (Girls, %)	9 (64%)	5 (56%)	4 (44%)	
Height (cm)	143.1±11.51	139.45 ± 12.13	147.98 ± 9.39	0.23
Weight (kg)	39.93±15.38	34.54 ± 14.38	47.12 ± 14.73	0.59
BMI (kg/m^2)	18.93±4.73	17.31 ± 4.70	21.10 ± 4.17	0.12
Disease Duration (mnth)	45±36.35	39.36 ± 35.68	54.33 ± 38.71	0.35
6MWT: Total distance (m)	461.01±90.61	456.96±105.88	482.55±82.69	0.76

Note: yrs.: years %: percentage, cm: centimeterKg: kilograms BMI: Body mass Index, Kg/m^2: kilograms per meter squared.Mnth: months, 6MWT: six-minute walk test, m: meters

4.2 Distribution of JIA Subtypes

Distribution of JIA subtypes are summarized in **Figure 4.1**. Oligoarticular and enthesitis-related arthritis (ERA) as the top two subtypes of JIA accounting for 63% of all the cases of JIA in the group.

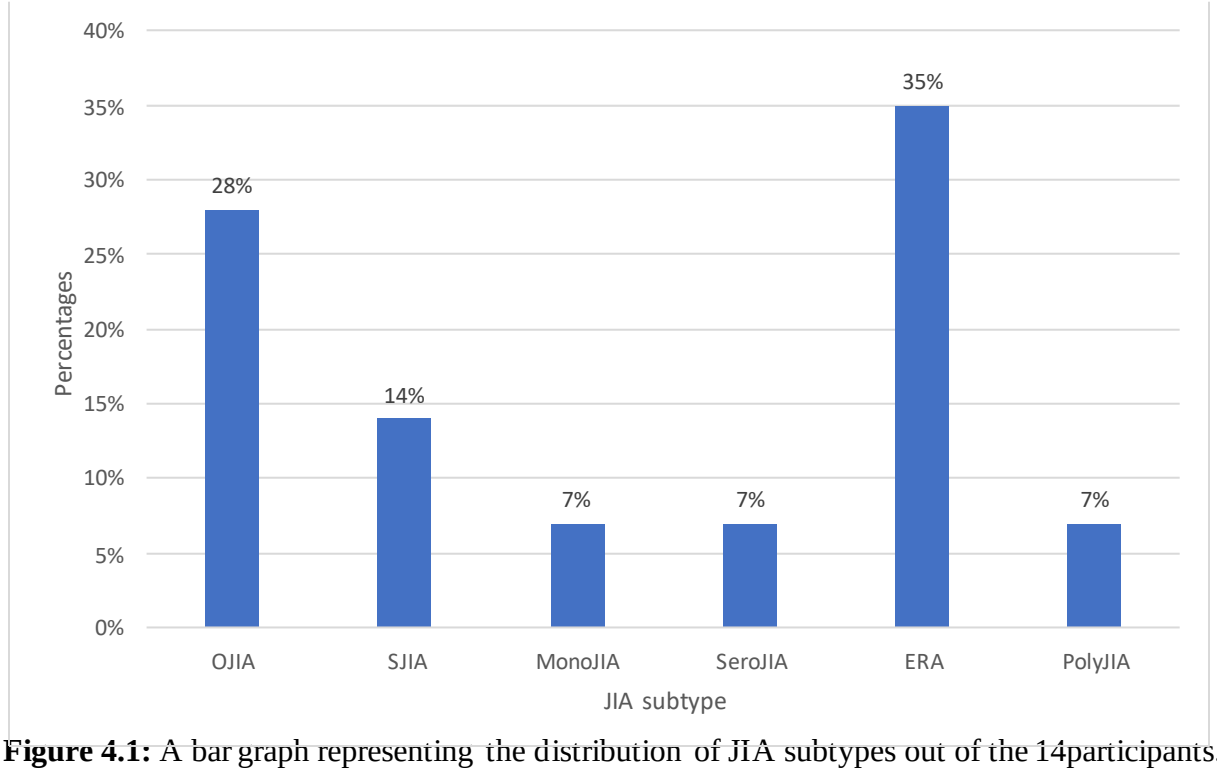


Figure 4.1: A bar graph representing the distribution of JIA subtypes out of the 14participants.

Note JIA: Juvenile idiopathic arthritis,OJIA: oligoarticular, SJIA: systemic, MonoJIA: Monoarticular SeroJIA: Seronegative Polyarticular, ERA: enthesitis-related arthritis, polyJIA: polyarticular

4.3 Gait Parameters

Spatiotemporal parameters are depicted in **Table 4.2**. A Mann Whitney U test was conducted to determine if there were any differences between the gait variables of the left and right side. The results indicate that there was a statistically significant difference in gait speed ($p=0.031$) and stride length ($p=0.046$). However, no significant differences were found in gait cycle, time in stance phase and time in swing phase between the left and right leg $p>0.05$.

Table 4.2 The spatiotemporal parameters for gait asymmetry between the left and right lower limbs were measured on the 14 participants. Values are presented as means ± SD.

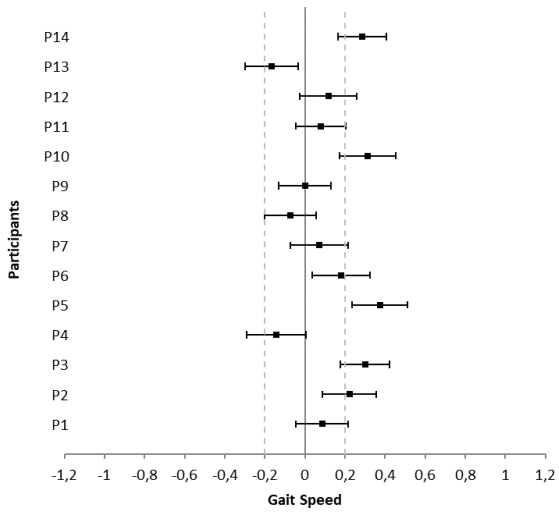
Variable	Left	Right	Standard test statistic	P value
Gait speed (m/s)	1.355 ± 0.233	1.342 ± 0.230	-2.160	**0.031**
Gait cycle duration (s)	0.844 ± 0.105	0.844 ± 0.107	0.577	0.564
Stance phase (%GCT)	56.534 ± 2.368	56.672 ± 1.907	1.036	0.300
Swing phase (%GCT)	43.466 ± 2.368	43.328 ± 1.908	-1.036	0.300
Stride length (m)	1.124 ± 0.109	1.114 ± 0.109	-1.997	**0.046**

Note: m/s: meters per second, s: seconds, %GCT: gait cycle time, m: meters

4.4 Effect size to determine gait asymmetry

The results of the effect sizes are presented in **Figure 4.2**. Effect size was calculated to establish gait asymmetry. A threshold of 0.2 was established, where an effect size of greater than 0.2 indicated a true difference (asymmetry), while an effect size of less than 0.2 indicated no difference (no asymmetry) between left and right limb. If a participant showed an effect size higher than 0.2 for three or more variables, they were included in the asymmetry group. Eight out of the fourteen participants had gait asymmetry (effect size >0.2).

A **B**


P14
P13
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P7
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P4
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Participants
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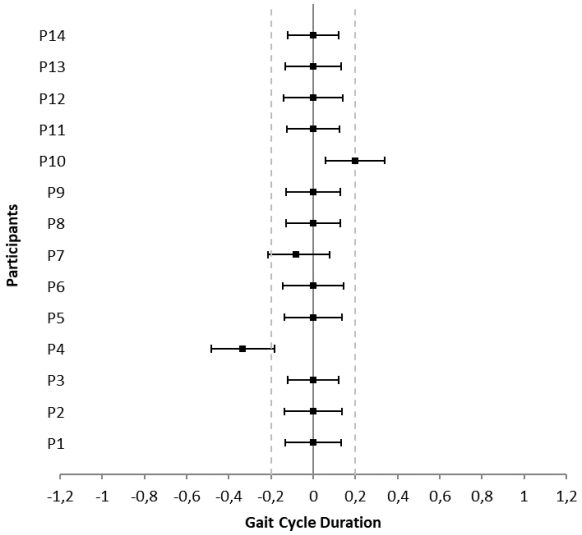
Gait Speed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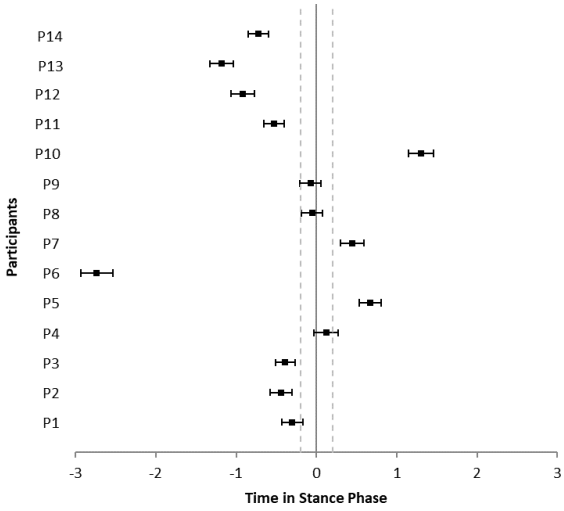
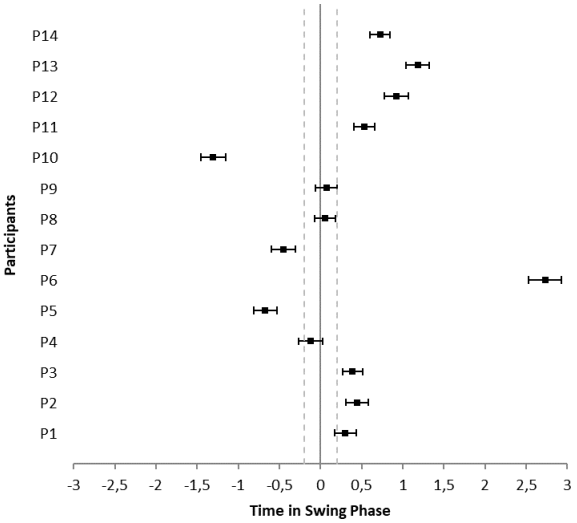
Participants
-1,2 -1 -0,8 -0,6 -0,4 -0,2 0 0,2 0,4 0,6 0,8 1 1,2
Gait Cycle Duration

C


P14
P13
P12
P11
P10
P9
P8
P7
P6
P5
P4
P3
P2
P1
Participants
-3 -2 -1 0 1 2 3
Time in Stance Phase

D


P14
P13
P12
P11
P10
P9
P8
P7
P6
P5
P4
P3
P2
P1
Participants
-3 -2,5 -2 -1,5 -1 -0,5 0 0,5 1 1,5 2 2,5 3
Time in Swing Phase

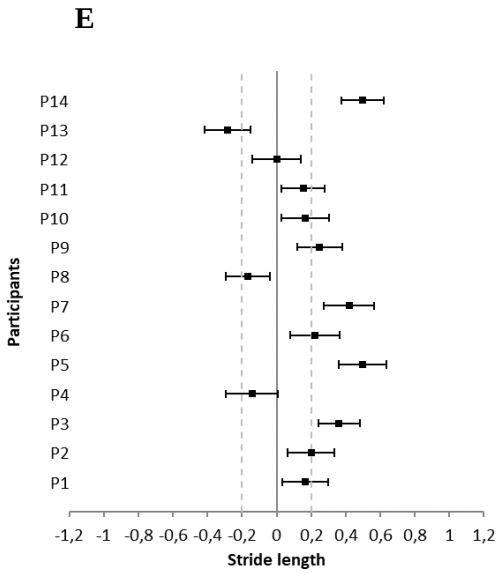
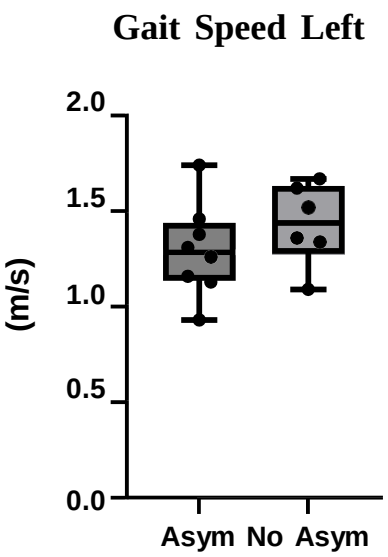


Figure 4.2: Forest plots representing an effect size difference between the left and right limb of all the participants from A-E.

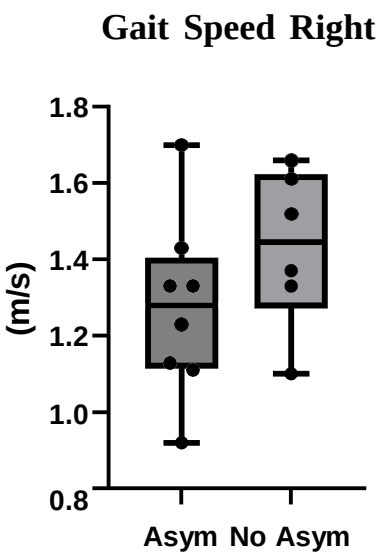
4.5 Asymmetry versus No asymmetry

The gait variables of the participants with asymmetry (n = 8) were compared to the participants with no asymmetry (n = 6) for the left and the right side, and the results are presented in **Figure 4.3**. A Mann-Whitney U test was run to determine if there were differences in left and right gait parameters between the asymmetry and no asymmetry groups. There was no statistical significance difference in the observed variables between the asymmetry and no asymmetry groups for the left and the right legs ($p > 0.05$), except for stride length (left, $p = 0.04$; right, $p = 0.03$).

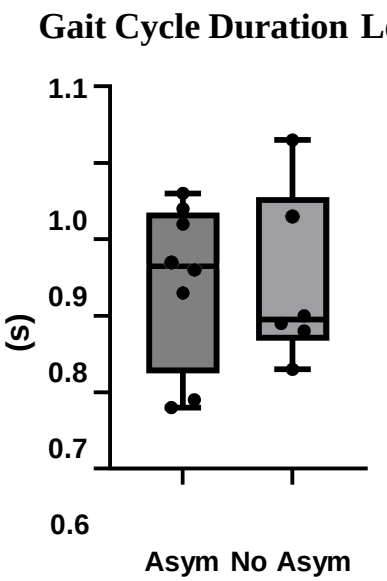
A


Gait Speed Left
2.0
1.5
1.0
0.5
0.0
(m/s)
Asym
No Asym

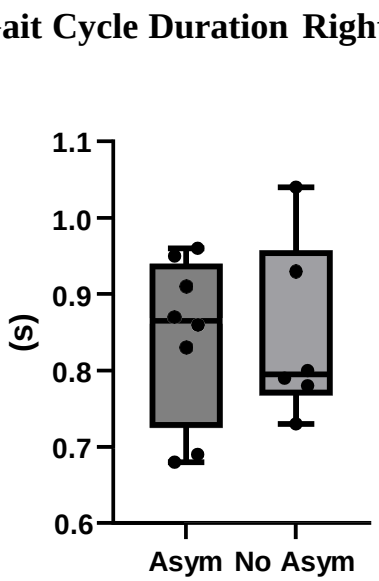
B


Gait Speed Right
1.8
1.6
1.4
1.2
1.0
0.8
(m/s)
Asym
No Asym

C

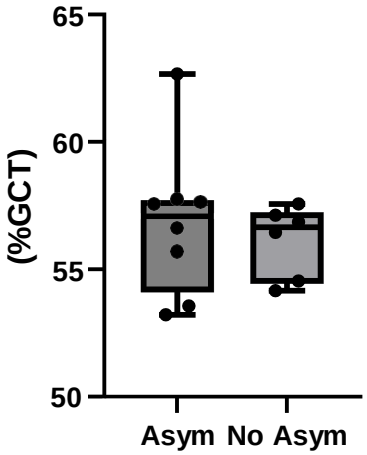

Gait Cycle Duration Left
1.1
1.0
0.9
0.8
0.7
0.6
(s)
Asym
No Asym

D


Gait Cycle Duration Right
1.1
1.0
0.9
0.8
0.7
0.6
(s)
Asym
No Asym

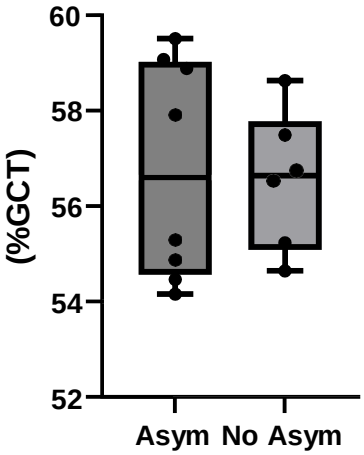
E

Time in stance phase Left



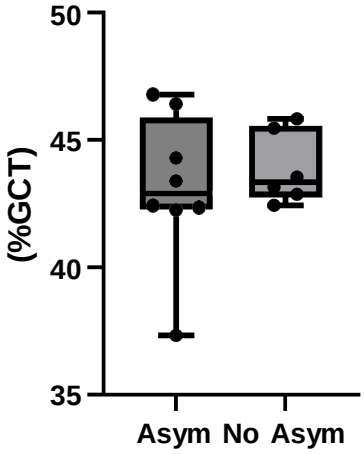
F

Time in stance phase Right



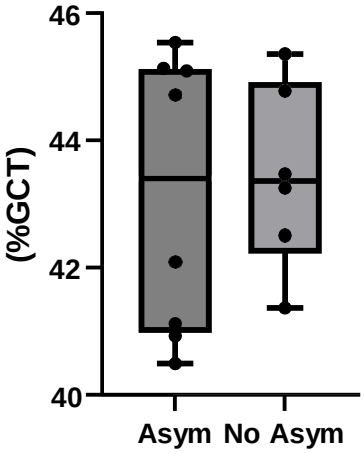
G

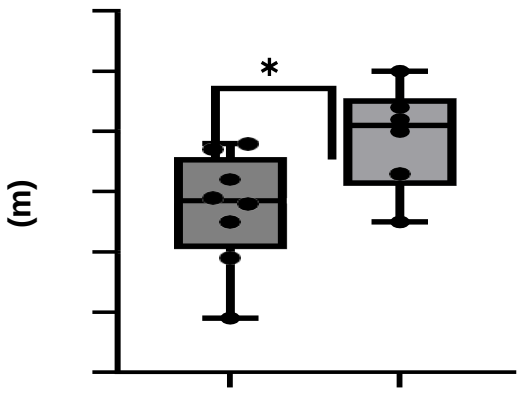
Time in Swing Phase Left



H

Time in Swing Phase Right





Stride length Left

1.4
1.3
1.2
1.1
1.0
0.9

0.8

Asym No Asym

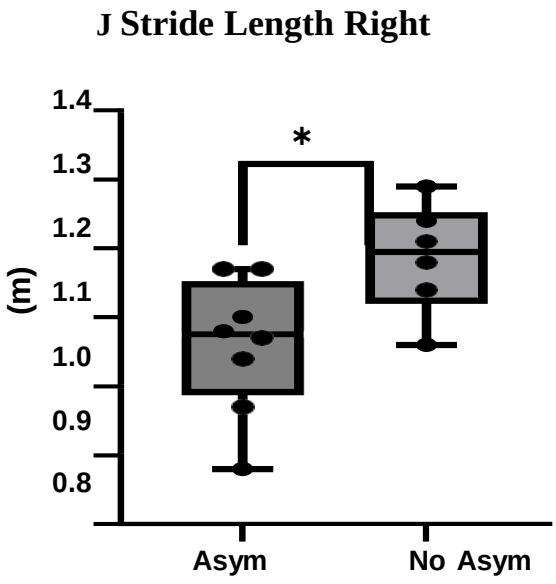


Figure 4.5: Dot over Box & Whisker plots illustrating individual data points, median, interquartile range, minimum and maximum values between the asymmetry (n = 8) vs no asymmetry groups (n = 6) for the five gait parameters A to J. representing all the variables from **A-J** comparing participants with gait asymmetry (n = 8) and no gait asymmetry (n = 6),on the left and right-side **A, C, E, and I are the left legs and B, D, F and J are the right leg*** Represents the p value ($p < 0.05$).

4.6 Comparison of disease activity, pain, medication and total distance of the asymmetry and no asymmetry group

A chi square test was conducted between the disease activity, pain, individuals who took more than four or more medication and the total distance achieved during the 6MWT between the asymmetry and no asymmetry groups. Three out of four expected cell frequencies were less than five, therefore, a Fisher's exact test was conducted. Inboth groups asymmetry and no asymmetry four participants had an active disease. 50% of theparticipants in the asymmetry group were taking more than four medications. We found no statistically significant differences for the 6MWT total distance achieved, $p>0.05$.

Table 4.3: A comparison of the disease activity, pain, number of medications, acceptable percent of predicted range and below 50th percentile range between the asymmetry and no asymmetry group.

Characteristics	Asymmetry (n=8)	No asymmetry. (n=6)	Fischer Exact's P value
Disease Activity	4 (50%)	4 (66.6%)	0.627
Pain	2 (25%)	4 (66.6%)	0.277
4 or More Meds	4 (50%)	2 (33.3%)	0.627
6MWT: % predicted distance	4(50%)	3(50%)	0.704
Below 50th percentile	5(62.5%)	4(66.7%)	0.657

Note: meds: number of medications taken, 6MWT % predicted total distance: the number of participants achieved the predicted distance from Mian et al., (2022), Below 50th percentile: grouping according to the percentiles by Kasovic et al., (2021)

4.7 Spearman correlation between all gait variables and total distance achieved

A correlation between the gait parameters and the total distance achieved in the 6MWT was conducted. There was a strong negative correlation (r= -0.705, p=0.005) between the difference in gait speed and the total distance covered in the 6MWT. However, we found no correlation between gait cycle, time in stance and swing phase and stride length p>0.05.

Table 4.4: Correlation between differences in gait parameters of all the 14 participants and the total distance achieved in the six-minute walk test.

Differences (Delta, Δ) between L &R Gait parameters	Total Distance (m) 6MWT	
	Spearman r	p-value
Δ Gait Speed (m/s)	-0.705	**0.005**
Δ Gait cycle (%GCT)	-0.458	0.099
Δ Stance phase (%GCT)	-0.077	0.794
Δ Swing phase (%GCT)	0.218	0.445
Δ Stride length (m)	-0.345	0.227

Note: m/s: meters per second, s: seconds, %GCT: gait cycle time, m: meters

CHAPTER V: DISCUSSION AND CONCLUSION

This research provided insights into the differences in gait asymmetry in children with Juvenile Idiopathic Arthritis (JIA). In this chapter, we discussed the findings of this research process including the limitations and future recommendations. The chapter ended with a summary of the findings ofthe research.

5.1 Main findings

The main aim of this study was to determine if children with JIA experience gait asymmetry. We hypothesized that the majority of gait parameters in the total group of participants will show significant differences between left and right gait parameters, but only found significant differences in gait speed and stride length between the left and right legs. No normative values for gait assessment in children with JIA using the APDM device have been established yet. Based on this shortcoming we investigated an alternative way to determine indices of gait asymmetry in the 14 participants. We calculated the effect size between the left and right leg parameters for each participant indicative of a clinical meaningful difference between left and right and identified the participant as having asymmetry if they showed a clinical meaningful difference (Effect size >= 0.2) in three or more of the five spatiotemporal parameters. Using these indices, we found that eight participants (57%) showed gait asymmetry and six with no gait asymmetry.

These results do not fully support our hypothesis, as gait asymmetry was not observed in all the spatiotemporal gait parameters as expected. These findings may suggest that gait asymmetry in children with JIA may be more specific to certain parameters, such as gait speed, and stride length, than generalized asymmetry across all spatiotemporal gait parameters. To our knowledge, this is the first study to examine gait asymmetry (specifically between the left and right legs) during a 6MWT in children diagnosed with JIA using the APDM sensor monitor.

Therefore, these results should be interpreted with caution due to the differences in the methods utilized in gait analysis of children with JIA.

The examination of demographic and clinical variables differences between the total, asymmetry, and no asymmetry groups, including age, gender, weight, height, BMI, and disease activity, aimed to identify potential factors influencing the observed gait asymmetry. The absence of significant differences in any of the outcomes: age, weight, and gender, suggests that these demographic and clinical characteristics may not be decisive factors in the manifestation of gait asymmetry in this specific cohort. For instance, Vincent et al., (2022) found comparable results, as there was no significant difference between age, gender, and weight in children with JIA. This underscores the need for a more delicate exploration of factors contributing to gait asymmetry in JIA, potentially involving joint-specific considerations and detailed kinematic assessments.

We found a statistically significant difference when comparing the gait speed of all participants' left and right legs. This significant difference indicates that there was a notable asymmetry in gait speed between the left and right legs in this population. These findings may be possibly attributed to joint damage (inflammation and pain) in the affected leg, resulting in muscle imbalances and newly adopted gait patterns (Hartmann et al., 2010; Kuntze et al., 2020). When we compared the asymmetry and no asymmetry groups, we found that there was no significant difference between the two groups. These findings suggest that although there was a significant difference in gait speed between the left and right legs when considering all participants together, this asymmetry did not translate into a significant difference when the groups are divided into asymmetry and no asymmetry groups. We therefore suggest that our method of gait asymmetry determination may not be sensitive enough to statistically identify where the differences exist, and that an equal distribution of left and right differences in gait speed occurs in researcher-defined asymmetry vs no asymmetry. It also raises the need for further investigation into this method of determining gait asymmetry.

Previous studies have reported on the consistent decrease in gait speed in children with JIA (Hartmann et al., 2010; Vincent et al., 2022). However, due to the difference in the methods utilized, such as the difference in the equipment used to assess gait and different aims, we could not establish a consensus of whether gait speed was different to them. Furthermore, we found that there are no reference values for gait analysis on investigating individual legs in children with JIA. In addition to this, a study conducted by Hartmann et al. (2010) looking at children with JIA (n = 35, aged 13.2± 4.2 years), has shown that individuals with JIA preferred a slower gait speed with an average of 1.06 ± 0.17m/s when they were compared to their healthy counterparts (n =16, age 17.9 ±6.5 years) (1.32 ± 0.08 m/s). However, our study found contrasting results as our participants have shown an increase in their preferred gait speed (average of 1.36 ± 0.12m/s on the left and 1.34 ± 0.12m/s on the right) as compared to the previous study. However, it should be noted that these results may be influenced by variations in the methods used to measure gait speed (even though they were instructed to walk at self-selected pace in both studies), thus, limiting the direct comparisons with the study by Hartmann and colleagues. The current study evaluated gait in a 25 meter (m) long walkway using the APDM sensor, while the study conducted by Hartmann and colleagues was conducted in a 9m and 3m long laboratory that was equipped with 3D-motion systems.

Walking speed is known to vary with age as well as other factors such as height and leg length (Broström et al., 2002). Therefore, it is imperative to acknowledge the growth disturbances such as height when comparing this population. These divergent results underline the variability in gait characteristics within the JIA population and highlight the necessity of considering diverse factors, such as disease activity, age, weight, height, and individual variability. While previous researchers have examined various gait variables, such gait speed and step length and kinetic variables, there is lack of evidence regarding the impact of gait cycle as an independent variable in children with JIA.

In terms of stride length, it was interesting to find a statistically significant difference when we

investigated the differences in left vs right legs in all 14 participants; and differences when the participants were grouped into asymmetry and no asymmetry groups. These findings indicate that, when we compared the asymmetry group to the no asymmetry group, we have found that the stride length of the asymmetry group was shorter than those of the no asymmetry group in both left and right legs. This study is in contrast with a study conducted by Vincent et al. (2022) as they found no significant differences in inactive and active JIA participants with Healthy controls. It should be noted that these results may have been due to the differences in the testing methods in terms of the device used to measure gait and the walking tests utilized in these studies.

There is limited evidence that supports the impact of stride length in the gait of this population. One study conducted by Vincent et al. (2022) found no significant difference in stride length of children with JIA and the control group. The discrepancy in these findings, particularly the statistically significant difference in stride length between the asymmetry and no asymmetry groups, warrants further investigation. Alterations in stride length may have functional implications for individuals with JIA, and understanding the underlying mechanisms and clinical relevance of this finding could provide valuable insights for the management of gait-related issues in this population.

The limited evidence in this variable limit our ability to find possible factors that may have led to this finding. However, plantarflexion, knee and hip extension restriction may be attributed for the shorter stride length as these are all the elements you need when doing toe-off, pushing off your back foot to take a step forward. Thus, if an individual does not havethis triple extension during gait, it may result in shorter steps (Broström et al., 2002). Therefore, further research is needed to better understand the impact of stride length on the gait of children with JIA. These unexpected outcomes also highlight a need for additional studies on the factors influencing stride length in children with gait asymmetry such as fatigue and standardized testsin children with JIA.

5.2 Secondary Findings

The secondary aim of this study was to determine if gait asymmetry was influenced by disease activity. We hypothesised that higher disease activity, characterized by inflammation and joint dysfunction in children with JIA, could potentially disrupt normal gait patterns, leading to greater asymmetry (Vincent et al., 2022). However, contrary to our hypothesis, the results did not show a significant correlation between the two variables. This may suggest that factors other than disease activity might play a more prominent role in influencing gait asymmetry in children with JIA. Further research is needed to explore these factors, as well as to determine whether other measures of disease severity or functional impairment might have a stronger association with gait abnormalities.

Previous research has reported low physical activity levels in children with JIA due to the effect of active disease (Gueddari et al., 2014). A study conducted by Vincent et al. (2022) compared gait of active and inactive disease in children with JIA and found no interlimb asymmetries inthese groups. Similarly, our study found no association between gait asymmetry and the level of disease activity. While disease activity may not be the sole determinant of gait asymmetry, other factors may contribute to the observed gait variations in this population. Possible contributors may include joint damage, pain, and compensatory mechanisms employed by children with JIA to navigate their physical challenges. Understanding these delicate factors becomes crucial for tailoring interventions that address the specific needs of children with JIAand gait asymmetry.

The absence of significant differences between left and right limbs in gait variables for the nine participants with active joint involvement suggests a relatively symmetric gait pattern in this subgroup. It is important to note that this is the first study looking at gait asymmetry between the left and right legs. Therefore, this warrants more research to investigate discrepancies between the left and the right leg focusing on the gait parameters. These discrepancies may

stem from the diversity of JIA, emphasizing the importance of subgroup analyses in future investigations. Additionally, gait analysis is a complex process that involves the evaluation of multiple parameters, and the interpretation of results can be influenced by several factors. Further research is needed to better understand the relationship between gait parameters and JIA, and to develop targeted interventions to address gait abnormalities in this population.

An advantage of this study is that we looked at both gait asymmetry and disease activity. Therefore, we further investigated whether gait asymmetry affects functional capacity during the six-minute walk test (6MWT) in this population. Functional capacity in children with JIA has been extensively studied by previous researchers (Ozdemir et al., 2024; Paap et al., 2005; Pritchard et al., 2022). However, the aim of this current study was to examine if gait asymmetry affected functional capacity during the 6MWT. Normative values to measure gait asymmetry using the 6MWT are still rare; therefore, we decided to use the normative values by Mian et al. (2022) to establish a difference in our population.

Our results indicate that 50% of the participants in both the asymmetry and no asymmetry group achieved the predicted distance, while the other 50% did not achieve the predicted distance, with no difference between the two groups. These results may suggest that asymmetry did not have a notable impact on the physical performance of individuals as measured by the 6MWT. The comparable performance between the two groups may indicate that other factors, such as overall fitness level, motivation, or specific health conditions, might play a more critical role in determining 6MWT outcomes than asymmetry.

We further investigated the 6MWT using the normative values by Kasović et al. (2021) where they grouped the participants into percentiles (below the 50th percentile means did not perform well). We found that 62.5% of the participants in the asymmetry group were below the 50th percentile. Similarly, 66.7% of the participants in the no asymmetry group were below the 50th percentile. This further supports the notion that asymmetry did not significantly hinder physical

performance in this context. Previous research has indicated that physical function is often impaired in children with JIA (Mian et al., 2022; Ozdemir et al., 2024). Currently, there are no studies that investigate gait asymmetry and its influence on 6MWT. One study conducted by Ozdemir et al. (2024) has found that children with JIA showed decreased levels of functional exercise capacity when compared with healthy, however, the method used to measure gait asymmetry was different to the current study.

Finally, we conducted a correlation to determine the association between the spatiotemporal parameters and the 6MWT. Our results indicate that the association difference in gait speed correlated with their aerobic capacity. To our knowledge, no similar studies could be found to compare this finding to previous researchers. In addition, these results aid the finding of another study by Ozdemir et al. (2024), who found that gait speed in JIA participants were lower compared to healthy controls and result in a lower 6MWT distance achieved. However, it must be noted that the studies methods to measure gait asymmetry were different. Lastly, the JIA participants in the study by Ozdemir and colleagues showed signs of fatigue, pain and muscle weakness which may have contributed to the impaired performance in this population.

5.3 Limitations and future recommendations

It is important to acknowledge the limitations of the study. Firstly, the study's sample size was relatively small, consisting of only 14 participants (because patients with JIA fulfilling the criteria were rare). This limited sample size may have affected the generalizability of our findings to a broader population of children with JIA. In addition, all the participants were tested at a specific hospital in the Western Cape, and even though the hospital serves quite a large diverse community, it is not possible to generalize the results to other individuals with JIA in the western cape or south Africa, especially due to the small sample size.

Future studies with larger sample sizes, normative data, and inclusion of control groups are essential to strengthen the validity and generalizability of findings in this research domain.

Secondly, we did not attribute for the dominant limb, only the limb that was affected was randomly selected for statistical analysis concerning disease activity. Therefore, we cannot comment on possible differences between legs and functional deficits could be underestimated. Furthermore, to better understand the disease impact on these outcomes as pain flares over time, it would be clinically informative tocollect pain measures in parallel with our study.

Thirdly, the lack of a control group further restricts our ability to make direct comparisons and draw conclusive insights into the extent of gait asymmetry in children with JIA as previously done by other researchers. Furthermore, the absence of a control group for comparison necessitated the use of effect size to identify gait asymmetry, which may have introduced potential confounders and limited the ability to draw direct comparisons with a control group. Finally, there was a lack of established normative values for gait parameters in children, as well as normative values allowed for differences between the left and right gait parameters in healthy individuals, that will be able to set off and classify if there is asymmetry or no asymmetry, which could have affected the interpretation of the results and the ability to compare them with existing data.

The study being among the first to use the APDM sensor in children with JIA meant that the technology was still relatively novel to this population, and its limitations and potential sources of error may not have been fully understood or addressed. These factors collectively underscore the need for caution in interpreting the results and highlight the potential for advancements in the use of the APDM sensor for gait analysis in similar studies. Furthermore, due to the study being the first to assess gait asymmetry in children with JIA, it was difficult to compare results of our findings with other studies due to the different devices used to measure gait and the length of the walking test. However, despite these limitations, the use of the APDM sensor provided valuable insights into gait assessment in children with JIA and may pave the way for future

studies using this technology. Future research in this area should aim to conduct larger studies with more diverse populations to further explore the relationship between gait asymmetry and disease activity in children with JIA.

The lack of greater distribution of disease activity in the asymmetry group compared to no asymmetry group underscores the multifactorial nature of motor dysfunction in JIA. Future studies should delve deeper into these contributing factors, exploring their individual and collective impact on gait patterns. Additionally, longitudinal studies may provide insights into the dynamic nature of gait asymmetry over the course of the disease, offering a more comprehensive understanding of its evolution.

5.4 Conclusion

In conclusion, our study highlights that the clinical determination of gait asymmetry in children with JIA may assist in the clinician in understanding where gait imperfections may occur during ambulation in children with JIA. This subsequently can aid treatment to correct the imperfections and limitations experiences by children with JIA. It is important to note that these gait parameters – gait speed and stride length - showed the greatest discrepancies among participants with JIA. Stride length was shorter in participants experiencing gait asymmetry, strengthening the finding that stride length may is an aspect of gait that requires rehabilitation focus.

The lack of showing more differences in terms of gait and other anthropometric and functional variables between participants with asymmetry vs no asymmetry, poses the question to whether the method of determination of asymmetry can be used as a valid method. It requires further investigation. Furthermore, gait speed influenced asymmetry between the left and right legs and was significantly correlated with the total distance achieved during the 6MWT. These findings may suggest that both stride length and gait speed are critical factors in understanding

functional limitations experienced by children with JIA. These findings emphasize the complexity of gait analysis in children with JIA and the necessity of tailored interventions to address their specific gait needs.

Based on these findings, it is important for future research on children with JIA to focus on these key gait parameters - gait speed and stride length. Understanding how these factors affect functionality and mobility in this population can provide valuable insights to guide rehabilitation and treatment approaches. For future research, it is essential to focus on these gait parameters to determine their specific effects on functionality and to develop targeted interventions that can improve gait symmetry and overall physical performance in this population. By addressing these key aspects, we can enhance the quality of life and mobility of children living with JIA.

REFERENCES

Adrovic, A., Yildiz, M., Köker, O., Şahin, S., Barut, K., & Kasapçopur, Ö. (2021). Biologics in juvenile idiopathic arthritis-main advantages and major challenges: A narrative review. *Arch Rheumatol*, *36*(1), 146-157. https://doi.org/10.46497/ArchRheumatol.2021.7953

Al-Mayouf, S. M., Al Mutairi, M., Bouayed, K., Habjoka, S., Hadef, D., Lotfy, H. M., Scott, C., Sharif, E. M., & Tahoun, N. (2021). Epidemiology and demographics of juvenile idiopathic arthritis in Africa and Middle East. *Pediatr Rheumatol Online J*, *19*(1), 166. https://doi.org/10.1186/s12969-021-00650-x

Association, W. M. (2013). World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *Jama*, *310*(20), 2191-2194.

Backström, M., Salo, H., Kärki, J., Aalto, K., Rebane, K., Levälampi, T., Grönlund, M. M., Kröger, L., Pohjankoski, H., Hietanen, M., Korkatti, K., Kuusalo, L., Rantalaiho, V., Huhtakangas, J., Relas, H., Pääkkö, T., Löyttyniemi, E., Sokka-Isler, T., & Vähäsalo, P. (2023). The feasibility of existing JADAS10 cut-off values in clinical practice: a study of data from The Finnish Rheumatology Quality Register. *Pediatr Rheumatol Online J*, *21*(1), 35. https://doi.org/10.1186/s12969-023-00814-x

Backström, M., Tynjälä, P., Aalto, K., Grönlund, M. M., Ylijoki, H., Putto-Laurila, A., Kärki, J., Keskitalo, P., Sard, S., Pohjankoski, H., Hietanen, M., Witter, S., Lehto, H., Löyttyniemi, E., & Vähäsalo, P. (2019). Validating 10-joint juvenile arthritis disease activity score cut-offs for disease activity levels in non-systemic juvenile idiopathic arthritis. *RMD Open*, *5*(1), e000888. https://doi.org/10.1136/rmdopen-2018-000888

Bartels, B., de Groot, J. F., & Terwee, C. B. (2013). The six-minute walk test in chronic pediatric conditions: a systematic review of measurement properties. *Phys Ther*, *93*(4), 529-541. https://doi.org/10.2522/ptj.20120210

Barut, K., Adrovic, A., Şahin, S., & Kasapçopur, Ö. (2017). Juvenile Idiopathic Arthritis. *Balkan Med J*, *34*(2), 90-101. https://doi.org/10.4274/balkanmedj.2017.0111

Bazarnik-Mucha, K., Guzik, A., Szczepanik, M., Snela, S., & Drużbicki, M. (2022). Validity of the Gait Deviation Index in children and adolescents with juvenile idiopathic arthritis. *Acta Bioeng Biomech*, *24*(2), 75-82.

Becker, L. A. (2000). Effect size (ES).

Beukelman, T. (2014). Treatment advances in systemic juvenile idiopathic arthritis. *F1000Prime Rep*, *6*, 21. https://doi.org/10.12703/p6-21

Bisi, M. C., Tamburini, P., Panebianco, G. P., & Stagni, R. (2018). Nonlinear Analysis of Human Movement Dynamics Offers New Insights in the Development of Motor Control During

Childhood. *J Biomech Eng*, *140*(11). https://doi.org/10.1115/1.4040939
Bourdier, P., Birat, A., Rochette, E., Doré, É., Courteix, D., Dutheil, F., Pereira, B., Ratel, S., Merlin, E., & Duché, P. (2021). Muscle function and architecture in children with juvenile idiopathic arthritis. *Acta Paediatr*, *110*(1), 280-287. https://doi.org/10.1111/apa.15335
Broström, E., Haglund-Åkerlind, Y., Hagelberg, S., & Cresswell, A. (2002). Gait in children with juvenile chronic arthritis. *Scandinavian journal of rheumatology*, *31*(6), 317-323.
Calık, B. B., Kabul, E. G., Korkmaz, C., Tekin, Z. E., Yener, G. O., & Yuksel, S. (2020). The efficacy of clinical Pilates exercises in children and adolescents with juvenile idiopathic arthritis: A pilot study. *Revista Colombiana de Reumatología (English Edition)*, *27*(4), 269-277.
Carroll, M., Parmar, P., Dalbeth, N., Boocock, M., & Rome, K. (2015). Gait characteristics associated with the foot and ankle in inflammatory arthritis: a systematic review and meta-analysis. *BMC Musculoskelet Disord*, *16*, 134. https://doi.org/10.1186/s12891-015-0596-0
Castermans, T., Duvinage, M., Cheron, G., & Dutoit, T. (2013). Towards effective non-invasive brain-computer interfaces dedicated to gait rehabilitation systems. *Brain sciences*, *4*(1), 1-48. https://doi:10.3390/brainsci4010001
Connelly, M., Schanberg, L. E., Ardoin, S., Blakley, M., Carrasco, R., Chira, P., Hayward, K., Ibarra, M., Kimura, Y., Kingsbury, D. J., Klein-Gitelman, M. S., Lawson, E., & Stinson, J. (2019). Multisite Randomized Clinical Trial Evaluating an Online Self-Management Program for Adolescents With Juvenile Idiopathic Arthritis. *J Pediatr Psychol*, *44*(3), 363-374. https://doi.org/10.1093/jpepsy/jsy066
Consolaro, A., Giancane, G., Schiappapietra, B., Davì, S., Calandra, S., Lanni, S., & Ravelli, A. (2016). Clinical outcome measures in juvenile idiopathic arthritis. *Pediatr Rheumatol Online J*, *14*(1), 23. https://doi.org/10.1186/s12969-016-0085-5
Consolaro, A., Ruperto, N., Bazso, A., Pistorio, A., Magni-Manzoni, S., Filocamo, G., Malattia, C., Viola, S., Martini, A., & Ravelli, A. (2009). Development and validation of a composite disease activity score for juvenile idiopathic arthritis. *Arthritis Rheum*, *61*(5), 658-666. https://doi.org/10.1002/art.24516
Fairburn, P. S., Panagamuwa, B., Falkonakis, A., Osborne, S., Palmer, R., Johnson, B., & Southwood, T. R. (2002). The use of multidisciplinary assessment and scientific measurement in advanced juvenile idiopathic arthritis can categorise gait deviations to guide treatment. *Arch Dis Child*, *87*(2), 160-165. https://doi.org/10.1136/adc.87.2.160
Fang, X., Liu, C., & Jiang, Z. (2018). Reference values of gait using APDM movement monitoring inertial sensor system. *R Soc Open Sci*, *5*(1), 170818. https://doi.org/10.1098/rsos.170818
Geiger, R., Strasak, A., Treml, B., Gasser, K., Kleinsasser, A., Fischer, V., Geiger, H., Loeckinger, A., & Stein, J. I. (2007). Six-minute walk test in children and adolescents. *The Journal of pediatrics*, *150*(4), 395-399. e392.
Graser, J. V., Letsch, C., & van Hedel, H. J. A. (2016). Reliability of timed walking tests and temporo-spatial gait parameters in youths with neurological gait disorders. *BMC Neurol*, *16*, 15. https://doi.org/10.1186/s12883-016-0538-y
Gueddari, S., Amine, B., Rostom, S., Badri, D., Mawani, N., Ezzahri, M., Moussa, F., Shyen, S., Abouqal, R., Chkirat, B., & Hajjaj-Hassouni, N. (2014). Physical activity, functional ability, and disease activity in children and adolescents with juvenile idiopathic arthritis. *Clin Rheumatol*, *33*(9), 1289-1294. https://doi.org/10.1007/s10067-014-2576-4
Hadouiri, N., Monnet, E., Gouelle, A., Decavel, P., & Sagawa, Y. (2021). Evaluation of Prolonged Walking in Persons with Multiple Sclerosis: Reliability of the Spatio-Temporal Walking Variables during the 6-Minute Walk Test. *Sensors (Basel)*, *21*(9). https://doi.org/10.3390/s21093075
Hartmann, M., Kreuzpointner, F., Haefner, R., Michels, H., Schwirtz, A., & Haas, J. P. (2010). Effects of juvenile idiopathic arthritis on kinematics and kinetics of the lower extremities call for consequences in physical activities recommendations. *Int J Pediatr*, *2010*. https://doi.org/10.1155/2010/835984

Howell, D. R., Meehan, W. P., 3rd, Barber Foss, K. D., Reches, A., Weiss, M., & Myer, G. D. (2018). Reduced dual-task gait speed is associated with visual Go/No-Go brain network activation in children and adolescents with concussion. *Brain Inj*, *32*(9), 1129-1134. https://doi.org/10.1080/02699052.2018.1482424

Hulleck, A. A., Menoth Mohan, D., Abdallah, N., El Rich, M., & Khalaf, K. (2022). Present and future of gait assessment in clinical practice: Towards the application of novel trends and technologies. *Front Med Technol*, *4*, 901331. https://doi.org/10.3389/fmedt.2022.901331

Jeon, J., Kwon, S. Y., Lee, Y. M., Hong, J., Yu, J., Kim, J., Kim, S. G., & Lee, D. (2023). Influence of the Hawthorne effect on spatiotemporal parameters, kinematics, ground reaction force, and the symmetry of the dominant and nondominant lower limbs during gait. *J Biomech*, *152*, 111555. https://doi.org/10.1016/j.jbiomech.2023.111555

Kasović, M., Štefan, L., & Petrić, V. (2021). Normative data for the 6-min walk test in 11-14 year-olds: a population-based study. *BMC Pulm Med*, *21*(1), 297. https://doi.org/10.1186/s12890-021-01666-5

Kharb, A., Saini, V., Jain, Y., & Dhiman, S. (2011). A review of gait cycle and its parameters. *IJCEM International Journal of Computational Engineering & Management*, *13*(01).

Khodra, B., A, M. S., & Ferucci, E. D. (2020). Prevalence of Juvenile Idiopathic Arthritis in the Alaska Native Population. *Arthritis Care Res (Hoboken)*, *72*(8), 1152-1158. https://doi.org/10.1002/acr.23997

Klepper, S., Mano Khong, T. T., Klotz, R., Gregorek, A. O., Chan, Y. C., & Sawade, S. (2019). Effects of Structured Exercise Training in Children and Adolescents With Juvenile Idiopathic Arthritis. *Pediatr Phys Ther*, *31*(1), 3-21. https://doi.org/10.1097/pep.0000000000000555

Kluge, F., Gaßner, H., Hannink, J., Pasluosta, C., Klucken, J., & Eskofier, B. M. (2017). Towards mobile gait analysis: concurrent validity and test-retest reliability of an inertial measurement system for the assessment of spatio-temporal gait parameters. *Sensors*, *17*(7), 1522.

Kuntze, G., Nesbitt, C., Nettel-Aguirre, A., Esau, S., Scholz, R., Brooks, J., Twilt, M., Toomey, C., Mosher, D., Ronsky, J. L., Benseler, S., & Emery, C. A. (2020). Gait Adaptations in Youth With Juvenile Idiopathic Arthritis. *Arthritis Care Res (Hoboken)*, *72*(7), 917-924. https://doi.org/10.1002/acr.23919

Kyriazis, V. (2001). Gait analysis techniques. *Journal of orthopaedics and traumatology*, *2*, 1-6.

Lanovaz, J. L., Oates, A. R., Treen, T. T., Unger, J., & Musselman, K. E. (2017). Validation of a commercial inertial sensor system for spatiotemporal gait measurements in children. *Gait & posture*, *51*, 14-19.

Lelieveld, O. T., Takken, T., van der Net, J., & van Weert, E. (2005). Validity of the 6-minute walking test in juvenile idiopathic arthritis. *Arthritis Rheum*, *53*(2), 304-307. https://doi.org/10.1002/art.21086

Merker, J., Hartmann, M., Haas, J. P., & Schwirtz, A. (2018). Combined three-dimensional gait and plantar pressure analyses detecting significant functional deficits in children with juvenile idiopathic arthritis. *Gait Posture*, *66*, 247-254. https://doi.org/10.1016/j.gaitpost.2018.08.041

Merker, J., Hartmann, M., Kreuzpointner, F., Schwirtz, A., & Haas, J. P. (2015). Pathophysiology of juvenile idiopathic arthritis induced pes planovalgus in static and walking condition: a functional view using 3D gait analysis. *Pediatr Rheumatol Online J*, *13*, 21. https://doi.org/10.1186/s12969-015-0022-z

Mian, Q., Rumsey, D. G., Verschuren, O., Moez, E. K., Roy, M., Kaup, C., & Pritchard, L. (2022). Reference Values for the Six Minute Walk Test in Children with Juvenile Idiopathic Arthritis. *Phys Occup Ther Pediatr*, *42*(2), 187-197. https://doi.org/10.1080/01942638.2021.1934239

Montefiori, E., Modenese, L., Di Marco, R., Magni-Manzoni, S., Malattia, C., Petrarca, M., Ronchetti, A., de Horatio, L. T., van Dijkhuizen, P., Wang, A., Wesarg, S., Viceconti, M., & Mazzà, C. (2019). Linking Joint Impairment and Gait Biomechanics in Patients with Juvenile Idiopathic Arthritis. *Ann Biomed Eng*, *47*(11), 2155-2167. https://doi.org/10.1007/s10439-019-02287-0

Moorthy, L. N., Peterson, M. G., Hassett, A. L., & Lehman, T. J. (2010). Burden of childhood-onset

arthritis. *Pediatr Rheumatol Online J*, *8*, 20. https://doi.org/10.1186/1546-0096-8-20
Morita, Y., Ito, H., Torii, M., Hanai, A., Furu, M., Hashimoto, M., Tanaka, M., Azukizawa, M., Arai, H., Mimori, T., & Matsuda, S. (2018). Factors affecting walking ability in female patients with rheumatoid arthritis. *PLoS One*, *13*(3), e0195059. https://doi.org/10.1371/journal.pone.0195059
Muro-de-la-Herran, A., Garcia-Zapirain, B., & Mendez-Zorrilla, A. (2014). Gait analysis methods: an overview of wearable and non-wearable systems, highlighting clinical applications. *Sensors (Basel)*, *14*(2), 3362-3394. https://doi.org/10.3390/s140203362
Murray, G. M., Sen, E. S., & Ramanan, A. V. (2021). Advancing the treatment of juvenile idiopathic arthritis. *Lancet Rheumatol*, *3*(4), e294-e305. https://doi.org/10.1016/s2665-9913(20)30426-4
Muthukrishnan, N., Abbas, J. J., & Krishnamurthi, N. (2020). A Wearable Sensor System to Measure Step-Based Gait Parameters for Parkinson's Disease Rehabilitation. *Sensors (Basel)*, *20*(22). https://doi.org/10.3390/s20226417
Ozdemir, B. C., Savci, S., Tanriverdi, A., Ozcan Kahraman, B., Isguder, R., Makay, B., & Unsal, E. (2024). Determinants of physical activity level in children and adolescents with juvenile idiopathic arthritis. *Zeitschrift für Rheumatologie*, *83*(Suppl 1), 71-77.
Paap, E., Net, J. v. d., Helders, P., & Takken, T. (2005). Physiologic response of the six-minute walk test in children with juvenile idiopathic arthritis. *Arthritis Care & Research: Official Journal of the American College of Rheumatology*, *53*(3), 351-356.
Pett, M. A. (2015). *Nonparametric statistics for health care research: Statistics for small samples and unusual distributions*. Sage Publications.
Pilutti, L. A., Dlugonski, D., Sandroff, B. M., Suh, Y., Pula, J. H., Sosnoff, J. J., & Motl, R. W. (2013). Gait and six-minute walk performance in persons with multiple sclerosis. *J Neurol Sci*, *334*(1-2), 72-76. https://doi.org/10.1016/j.jns.2013.07.2511
Pires, I. M., Denysyuk, H. V., Villasana, M. V., Sá, J., Marques, D. L., Morgado, J. F., Albuquerque, C., & Zdravevski, E. (2022). Development Technologies for the Monitoring of Six-Minute Walk Test: A Systematic Review. *Sensors (Basel)*, *22*(2). https://doi.org/10.3390/s22020581
Pritchard, L., Verschuren, O., Roy, M., Kaup, C., & Rumsey, D. G. (2022). Reproducibility of the Six-Minute Walk Test in Children and Youth With Juvenile Idiopathic Arthritis. *Arthritis Care Res (Hoboken)*, *74*(4), 686-690. https://doi.org/10.1002/acr.24492
Prosser, L. A., Pierce, S. R., Dillingham, T. R., Bernbaum, J. C., & Jawad, A. F. (2018). iMOVE: Intensive Mobility training with Variability and Error compared to conventional rehabilitation for young children with cerebral palsy: the protocol for a single blind randomized controlled trial. *BMC Pediatr*, *18*(1), 329. https://doi.org/10.1186/s12887-018-1303-8
Ringold, S., Angeles-Han, S. T., Beukelman, T., Lovell, D., Cuello, C. A., Becker, M. L., Colbert, R. A., Feldman, B. M., Ferguson, P. J., Gewanter, H., Guzman, J., Horonjeff, J., Nigrovic, P. A., Ombrello, M. J., Passo, M. H., Stoll, M. L., Rabinovich, C. E., Schneider, R., Halyabar, O., . . . Reston, J. (2019). 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Treatment of Juvenile Idiopathic Arthritis: Therapeutic Approaches for Non-Systemic Polyarthritis, Sacroiliitis, and Enthesitis. *Arthritis Care Res (Hoboken)*, *71*(6), 717-734. https://doi.org/10.1002/acr.23870
Sandroff, B. M., Pilutti, L. A., & Motl, R. W. (2015). Does the six-minute walk test measure walking performance or physical fitness in persons with multiple sclerosis? *NeuroRehabilitation*, *37*(1), 149-155. https://doi.org/10.3233/nre-151247
Saurenmann, R. K., Rose, J. B., Tyrrell, P., Feldman, B. M., Laxer, R. M., Schneider, R., & Silverman, E. D. (2007). Epidemiology of juvenile idiopathic arthritis in a multiethnic cohort: ethnicity as a risk factor. *Arthritis Rheum*, *56*(6), 1974-1984. https://doi.org/10.1002/art.22709
Shaw, K., Southwood, T., Duffy, C., & McDonagh, J. (2006). Health-related quality of life in adolescents with juvenile idiopathic arthritis. *Arthritis Care & Research: Official Journal of the American College of Rheumatology*, *55*(2), 199-207.
Shema-Shiratzky, S., Gazit, E., Sun, R., Regev, K., Karni, A., Sosnoff, J. J., Herman, T., Mirelman, A., & Hausdorff, J. M. (2019). Deterioration of specific aspects of gait during the

instrumented 6-min walk test among people with multiple sclerosis. *J Neurol*, *266*(12), 3022-3030. https://doi.org/10.1007/s00415-019-09500-z

Shieh, V., Zampieri, C., Sansare, A., Collins, J., Bulea, T. C., & Jain, M. (2022). Validation of Body-Worn Sensors for Gait Analysis During a 2-min Walk Test in Children. *J Meas Phys Behav*, *5*(2), 111-119. https://doi.org/10.1123/jmpb.2021-0035

Sivarajah, L., Kane, K. J., Lanovaz, J., Bisaro, D., Oates, A., Ye, M., & Musselman, K. E. (2018). The feasibility and validity of body-worn sensors to supplement timed walking tests for children with neurological conditions. *Physical & Occupational Therapy in Pediatrics*, *38*(3), 280-290.

Statistics, L. (2013). Chi-Square. *Retrieved November*, *7*, 2014.

Stinson, J. N., Feldman, B. M., Duffy, C. M., Huber, A. M., Tucker, L. B., McGrath, P. J., Tse, S. M., Hetherington, R., Spiegel, L. R., Campillo, S., Benseler, S., Gill, N., White, M. E., Baker, N., & Vijenthira, A. (2012). Jointly managing arthritis: information needs of children with juvenile idiopathic arthritis (JIA) and their parents. *J Child Health Care*, *16*(2), 124-140. https://doi.org/10.1177/1367493511430679

Thatayatikom, A., & De Leucio, A. (2020). Juvenile idiopathic arthritis (JIA). *StatPearls, National Library of Medicine (NLM): Bethesda, MD, USA*.

Thompson, P., Beath, T., Bell, J., Jacobson, G., Phair, T., Salbach, N. M., & Wright, F. V. (2008). Test-retest reliability of the 10-metre fast walk test and 6-minute walk test in ambulatory school-aged children with cerebral palsy. *Dev Med Child Neurol*, *50*(5), 370-376. https://doi.org/10.1111/j.1469-8749.2008.02048.x

Turner, D. E., Helliwell, P. S., Siegel, K. L., & Woodburn, J. (2008). Biomechanics of the foot in rheumatoid arthritis: identifying abnormal function and the factors associated with localised disease 'impact'. *Clin Biomech (Bristol, Avon)*, *23*(1), 93-100. https://doi.org/10.1016/j.clinbiomech.2007.08.009

Vazquez-Galliano, J., Kimawi, I., & Chang, L. (2014). Biomechanics of gait and treatment of abnormal gait patterns. *Physical Medicine and Rehabilitation*.

Vincent, H. K., Sharififar, S., Abdelmalik, B., Lentini, L., Chen, C., & Woolnough, L. U. (2022). Gait parameters, functional performance and physical activity in active and inactive Juvenile Idiopathic Arthritis. *Gait Posture*, *98*, 226-232. https://doi.org/10.1016/j.gaitpost.2022.09.080

Voss, S., Joyce, J., Biskis, A., Parulekar, M., Armijo, N., Zampieri, C., Tracy, R., Palmer, A. S., Fefferman, M., Ouyang, B., Liu, Y., Berry-Kravis, E., & O'Keefe, J. A. (2020). Normative database of spatiotemporal gait parameters using inertial sensors in typically developing children and young adults. *Gait Posture*, *80*, 206-213. https://doi.org/10.1016/j.gaitpost.2020.05.010

Weakley, K., Esser, M., & Scott, C. (2012). Juvenile idiopathic arthritis in two tertiary centres in the Western Cape, South Africa. *Pediatr Rheumatol Online J*, *10*(1), 35. https://doi.org/10.1186/1546-0096-10-35

Weiss, R. J., Wretenberg, P., Stark, A., Palmblad, K., Larsson, P., Gröndal, L., & Broström, E. (2008). Gait pattern in rheumatoid arthritis. *Gait Posture*, *28*(2), 229-234. https://doi.org/10.1016/j.gaitpost.2007.12.001

Woolnough, L., Pomputius, A., & Vincent, H. K. (2021). Juvenile idiopathic arthritis, gait characteristics and relation to function. *Gait Posture*, *85*, 38-54. https://doi.org/10.1016/j.gaitpost.2020.12.010

Yang, S., & Li, Q. (2012). Inertial sensor-based methods in walking speed estimation: a systematic review. *Sensors (Basel)*, *12*(5), 6102-6116. https://doi.org/10.3390/s120506102

Zaripova, L. N., Midgley, A., Christmas, S. E., Beresford, M. W., Baildam, E. M., & Oldershaw, R. A. (2021). Juvenile idiopathic arthritis: from aetiopathogenesis to therapeutic approaches. *Pediatr Rheumatol Online J*, *19*(1), 135. https://doi.org/10.1186/s12969-021-00629-8

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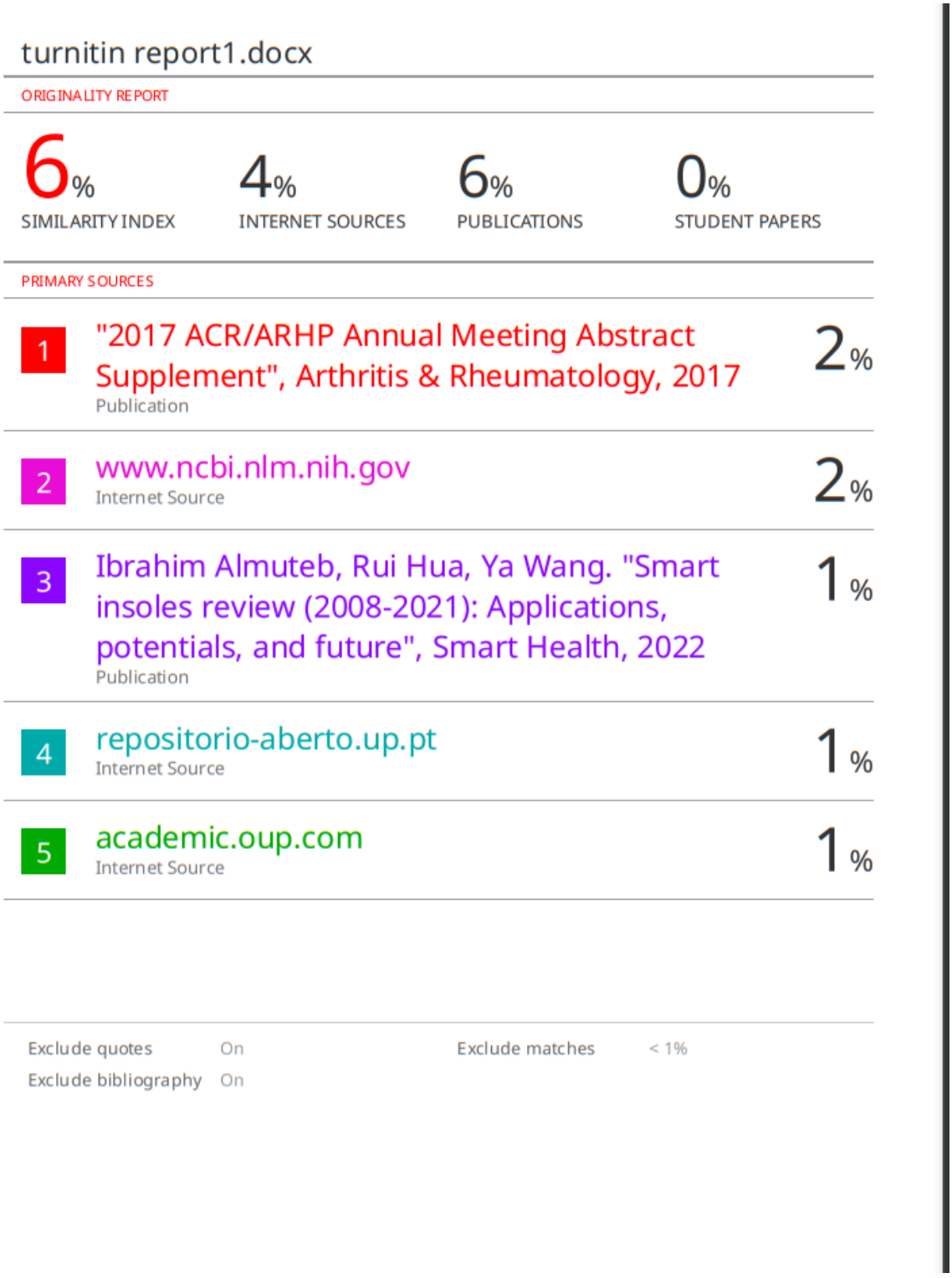

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MEMORANDUM OF UNDERSTANDING

Assessing the Validity and Reliability of a Physical Performance Test Battery for Children with Juvenile Idiopathic Arthritis

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E-Mail Address	ematterbury@gmail.com

Co-Supervisor 1 Information

Name of Co-Supervisor	Jacolene Kroff
Telephone Number	0216505126
Email Address	jacolene.kroff@uct.ac.za

Background

Stellenbosch University HREC Reference Number: S22/03/051

Phase One: Semi-Structured Questionnaire

A semi-structured questionnaire will be posed to children with juvenile idiopathic arthritis (JIA), who are willing to participate in Phase One of the study at the Tygerberg Biokinetics Pediatric Rheumatology (TBPR) Clinic. The questionnaire is meant to derive information from the child's daily life and how their daily living (ADL) activities are impacted by their condition within a home, school, and societal context.

The principal investigator (**Stellenbosch University [SU] postgraduate student**) will have no prior contact with the child participating as a researcher. The sub-investigator (**University of Cape Town [UCT] postgraduate student**) will conduct the questionnaire after the physical examination, with their conversation voice recorded. Hence, the questions have been clearly outlined in the questionnaire that follows at the end of this document, which has been provided to the **UCT postgraduate student**.

Prior to initiating the interview, the **UCT postgraduate student** will first explain to the child and parent/guardian what the study is about by using the assent and consent forms. If the child and parent both agree, the **UCT postgraduate student** will take assent from the child and consent from the parent/guardian. Such a setup reduces bias and undue influence, as the **UCT postgraduate student** has no connection to phase one of the research study. Furthermore, a parent/guardian will be present in the interview, which is the standard operating procedure of the Pediatric Rheumatology and Immunology Clinic at Tygerberg Hospital. Additionally, no social circumstances or sensitive questions will be asked during the recorded interview, as outlined in the questionnaire.

Through Phase One of the study, fifteen participants will be needed using maximum variation sampling based on age. Consequently, three participants will be recruited per age range (6-7, 8-9, 10-11, 12-13, and 14-16). Once a participant has been recruited, the study explained, assent and consent are received and signed, the **UCT postgraduate student** will collect the necessary data listed on the questionnaire document (*Appendix I*) and then read the prompt to the child. Additionally, voice recordings will contain no identifiers, and pseudonyms will be used where needed. After the prompt has been read, the voice recording may start before question one is read. When the voice recording has started, the first question will be read to the child, and time will be given for the child to respond. The **UCT postgraduate student** will determine whether the child hesitates to answer or whether any party has requested to stop the recording. The process will continue until the last answer to the last question has been given. At this point, the voice recording will be stopped.

The **UCT postgraduate student** will share the voice recordings through a OneDrive folder only accessible by the two parties involved, the **UCT postgraduate student** and the **SU postgraduate student**. OneDrive is chosen as the shared platform due to its at-rest and intransit encryption of files, which increases the safety of files as stipulated by Microsoft 365®. After the **SU postgraduate student** completes the download, the file will be deleted from the shared folder. Additionally, the **UCT postgraduate student** agrees that it is their ethical duty to delete the voice recording from their device after it has been uploaded to the shared folder.

Phase Two: Six-Minute Walk Test

A six-minute walk test (6MWT) will be evaluated in children diagnosed with JIA willing to participate in Phase Two of the study at the Department of Exercise, Sport, and Lifestyle Medicine at Stellenbosch University. The 6MWT will be a component of a larger test battery and is meant to assess functional exercise capacity, along with gait variables as measured by the APDM Wearable

Technologies® from Mobility Lab. As part of the larger test battery, disease activity will be recorded using the clinical Juvenile Arthritis Disease Activity Score – 10 (cJADAS10).

Recruitment will occur in the TBPR Clinic, and purposeful sampling will be used based on the study's inclusion and exclusion criteria. Participants will be randomized before data collection through simple randomization to either the first **(SU postgraduate student)** or second assessor for the participant's first visit. The sample size for Phase Two of the study is fourteen participants.

The **SU postgraduate student** and/or second assessor will conduct informed consent and assent upon the participant's first visit. Once informed assent and consent are received, descriptive data will be collected (i.e., age, height, sex, weight, subtype, time since diagnosis, pain level and location, medication and dosages, recent operations or illnesses, and physical activity readiness).

In accordance with the test battery, the cJADAS10 will be conducted first to determine disease activity. The cJADAS10 has three components: 1) an assessment of joint tenderness, swelling, and range of motion (ROM); 2) a clinician global assessment using a visual analog scale (VAS); and 3) patient/parent global assessment using the Wong-Baker FACES scale. These components are combined to provide a cJADAS10 score.

The 6MWT will be conducted last in the test battery. A walkway of twenty-five meters will be measured using the tape measurer, and the center of each cone will be placed at the beginning and end of the distance. Once the setup of the test is completed, as done by Mian and colleagues (2021) who conducted the 6MWT on the JIA population, instructions will be initiated following the "American Thoracic Society Statement: Guidelines for the Six-Minute Walk Test," with modification for the young participants to understand as written in *Appendix II*.

Once all data is collected, participants' agreed-upon de-identified data will be shared by the **SU postgraduate student** with the **UCT postgraduate student.** All de-identified data will be placed into a password-protected Excel spreadsheet and placed in the same OneDrive folder used during Phase One. Once the **UCT postgraduate student** downloads the Excel spreadsheet, it will immediately be deleted from the OneDrive folder, and the folder will be permanently deleted.

Agreement

The bottom of this page is to be initialized by all parties involved to confirm that all the listed expectations are understood and that questions have been asked and clarified where needed.

Stellenbosch University Research Team Expectations:

- The **UCT postgraduate student** agrees to interview during the clinic consultation hours on Tuesday between 8:30 and 12:30, starting on the 28th of March and ending on the 25th of April.
- The **UCT postgraduate student** understands the recruitment strategy and agrees to collect data until the sample size (15) is reached or data is saturated, with the appropriate considerations for the age groups lined out in the *Background – Phase One: Semi-Structured Questionnaire*.
- The **UCT postgraduate student** will follow the interview process directly (i.e., informed assent/consent, descriptive data, voice recording, name usage, stopping of a voice recording) as stipulated in the shared research protocol and within the *Background – Phase One: Semi-Structured Questionnaire* of this MoU.

- The **UCT postgraduate student** agrees to voice record the questions and answers on their device and to upload it to the shared OneDrive folder as the only sharing platform or mechanism.

- The **UCT postgraduate student** agrees to delete the voice recording and all related data from their device immediately after the voice recording has been uploaded to OneDrive.

- The **UCT postgraduate student** understands that the **SU postgraduate student** will download and store the voice recording and immediately delete it from the OneDrive folder.

- The **SU research team** (student, supervisor, and co-supervisors) will be granted authorship (not first authorship or last) of all scientific outputs (i.e., article publications and conference presentations) related to the data used by the **UCT postgraduate student** from any part of the current study.

- The **SU postgraduate student** will be granted authorship (not first authorship) on any scientific outputs (i.e., article publications and conference presentations) related to a topic drawn from the current study by the **UCT postgraduate student**.

University of Cape Town Research Team Expectations:

- The **SU postgraduate student** agrees to conduct data collection ethically and according to the outlined procedure for the cJADAS10 and 6MWT.

- The **SU postgraduate student** will conduct recruitment with the appropriate sampling method to collect data for a sample size of fourteen participants or until data is saturated.

- The **SU postgraduate student** understands and agrees to the research questions:
    - Are there gait asymmetries present in children diagnosed with JIA in South Africa?
    - Is there a relationship between gait asymmetry differences and disease activity in children diagnosed with JIA in South Africa?

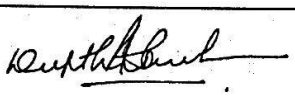
- The **SU postgraduate student** will provide the following de-identified data variables to the **UCT postgraduate student**:
    - Demographic/ descriptive information
        - Age, sex, height, weight, BMI.
        - Subtypes, time since diagnosis, pain level and location, medications and dosages, recent operations or illness, physical activity readiness.
    - Disease activity score as measured by the cJADAS10
    - Gait variables collected using APDM Wearable Technologies® from Mobility Lab during the 6MWT:
        - Time in swing phase.
        - Time in stance phase.
        - Gait speed.

    - Stride length.
    - Stride velocity.

- The **SU postgraduate student** will provide the **UCT postgraduate student** with both assessor one's trials of de-identified data collected for the cJADAS10 and 6MWT regarding the above agreed-upon data variables.
- The **SU postgraduate student** will place all agreed-upon de-identified data into a password-protected Excel spreadsheet and onto the agreed-upon OneDrive folder, to be downloaded by the **UCT postgraduate student.**
- The **SU postgraduate student will** share all agreed-upon de-identified data with the **UCT postgraduate student** no later than June 2023**.**
- The **UCT postgraduate student** will be granted authorship (not first or last authorship) on any scientific outputs (i.e., article publications and conference presentations) related to the semi-structured questionnaire.
- The **UCT research team** will have first, second, and senior authorship on any scientific outputs (i.e., article publications and conference presentations) that relates to the agreed-upon research question(s).

The signatures below serve to confirm that all parties agree to the role and responsibilities as set out in this Memorandum of Understanding:

Signatures of Stellenbosch University Research Team

	SIGNATURE	DATE
STUDENT		14 March 2023
SUPERVISOR		13 March 2023
CO-SUPERVISOR 1		13 March 2023
CO-SUPERVISOR 2		13 March 2023

Signatures of the University of Cape Town Research Team

	SIGNATURE	DATE
STUDENT		11 April 2023
SUPERVISOR		13 March 2023
CO-SUPERVISOR 1		13 March 2023

Appendix 4: Ethics letter approval

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room 45 E-52-E-Floor- Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: hrec-submissions@uct.ac.za
Website: www.health.uct.ac.za/home/human-research-ethics

04 August 2023

HREC REF: 492/2023

A/Prof J Kroff
Division of Physiological Sciences
Human Biology-SSISA
Email: Jacolene.kroff@uct.ac.za
Student: mpklin003@myuct.ac.za

Dear A/Prof Kroff

PROJECT TITLE: THE IDENTIFICATION OF GAIT ASYMMETRY IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS-
(MPHIL CANDIDATE-MS LINDIWE MPAKA)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 August 2024.

Please submit a progress form, using the standardised Annual Report Form (FHS016) if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledge that the student: Ms Lindiwe Mpaka will also be involved in this study.

Please quote HREC REF 492/2023 in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FACULTY OF HEALTH SCIENCES HUMAN RESEARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637. Institutional Review Board (IRB) number: IRB00001938 NHREC-registration number: REC-210208-007
This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Council for Harmonisation of

Appendix 5: Parent consent form

EXT 6
MFULENI, 7100
TelNo:

PARTICIPANT INFORMATION LEAFLET AND CONSENT FORM

TITLE OF RESEARCH PROJECT:	
Assessing the Validity and Reliability of a Physical Performance Test Battery for Children with Juvenile Idiopathic Arthritis	
DETAILS OF PRINCIPAL INVESTIGATOR (PI):	
Title, first name, surname: **Ms. Su-ané Zwiegelaar**	**Ethics reference number:** **S22/03/051**
Full postal address: Sport Science Department, Suidwal Street, Stellenbosch, 7600	**PI Contact number:** 0798923378

We would like to invite your child to take part in a research project. Please take some time to read the information presented here, which will explain the details of this project. Please ask the researcher or doctor any questions about any part of this project that you do not fully understand. It is very important that you are completely satisfied that you clearly understand what this research entails and how your child could be involved. Also, your child's participation is **entirely voluntary,** and you are free to decline to participate. It will not affect you negatively if you say no to participation, as there will be no penalty or loss of benefits or reduction in the level of care to which your child is otherwise entitled. Your child is also free to withdraw from the study at any point, even if you do agree to take part initially.

The Health Research Ethics Committee at Stellenbosch University has approved this study. The study will be conducted according to the ethical guidelines and principles of the international Declaration of Helsinki, the South African Guidelines for Good Clinical Practice (2006), the Medical Research Council (MRC) Ethical Guidelines for Research (2002), and the Department of Health Ethics in Health Research: Principles, Processes, and Studies (2015).

What is this research study all about?

- The study will be conducted at_____
- The total number of participants recruited for the study is 40 across the whole of South Africa.
- The study aims to establish a valid and reliable physical performance test battery for children diagnosed with juvenile idiopathic arthritis (JIA) based on the specific body systems impacted by the condition.
- The following procedures will be followed throughout the research study:
  1. First, informed consent and assent (permission) will be completed; therefore, you and your child need to agree to participate in the study. Only once these two forms are completed will the official procedure of the study start.
  2. At each visit, descriptive data will be collected, which includes your child's age, weight, height, body mass index (BMI), sex, JIA subtype, time since diagnosis, current pain level and location, current medication and dosage, recent operation or sickness, cognitive status, and physical activity readiness.
  3. Next, a series of exercise tests will be done with your child. Your child will be asked to perform different activities throughout the test battery, which involves the researcher

entering your child's personal space. To be more precise, your child will be asked to do the following:

- Stand, sit, or lay down, so the researcher can palpate (touch) and move the body's joints to check for pain, tenderness, swelling, or reduced movement.
- Measure the degrees of movement a joint has.
- Balance will be tested through your child standing heel-to-toe with their hands on their hip bones, on a stable and unstable surface, with their eyes open and closed.
- Joints will be tested for how strong they are through the researcher manually applying resistance to the joint.
- Perform functional activities such as lay-to-stand, stair climbing, hopping, skipping, walking on their heels and toes, and squatting.
- Walking up and down a 15-meter walkway for six minutes, with measurements of heart rate, blood pressure, rate of perceived exertion, and oxygen saturation levels also made.

➢ The above procedures will be conducted on three separate visits. On either the first or second visit, your child will be assessed by a second assessor, Ms. Liesje Myburgh. On the first or second visit conducted by the principal investigator, your child will be asked to do the activities twice.

➢ Duration of visits:

- First and second visit: one visit will be 60-minutes in length and the other visit will be 120 to 140 minutes in duration, depending on whether the first administrator is the principal investigator or the second assessor.
  - Principal investigator's visit will be 120 to 140 minutes in length.
  - Second assessor: 60 minutes in length.
- Third and fourth visit: 60 minutes in duration.
  - If you cannot attend the fourth visit a telephonic call of 15 minutes will be made to provide you with the information on your child's performance.

Why do we invite your child to participate?

➢ Your child is invited to participate in the study as they are diagnosed with juvenile idiopathic arthritis and are between the ages of six and 16 years. Additionally, they fit certain criteria which will be confirmed by your physician; hence you permit the researchers to access past medical records. The specific criteria include:

i. safety to participate in physical activity (PA)
ii. no fever or sickness within the past two weeks before
iii. pain in one or more joints over the past six months
iv. receiving medication
v. no steroid use in the past three months
vi. no severe cognitive impairment that would prevent understanding of instructions and research being conducted
vii. no surgical operations in the past six months

What will your responsibilities be?

➢ As the parent, your responsibility entails ensuring that you bring your child to each appointment and that you are present at all appointments. Additionally, you must ensure that your child is appropriately dressed in exercise shorts above the knee and an exercise vest. There will be three to four different meeting points, lasting a maximum of two hours, in the following time frame:

- First meeting: signing of informed consent/assent, collecting descriptive data, and the initial test battery administration.
- Second meeting: 48 to 96 hours post the first meeting; collecting descriptive data, and the second test battery administration.
- Third meeting: 60 days post the first meeting; collecting descriptive data, and the third test battery administration.
- Fourth meeting: you may choose to attend an informative talk regarding the study results. Suppose you cannot or choose not to attend this meeting, a telephonic conversation will be performed to inform you of your child's performance and the study results.

Will your child benefit from taking part in this research?

- Juvenile idiopathic arthritis can result in short- and long-term disability, which can impact a child's physical health and quality of life (QoL). Exercise has been shown to be a good tool to combat these negative effects, but before exercise can be prescribed, they need to be assessed on how their body moves. Therefore, the personal benefits of participation in the study include understanding how JIA impacts your child's physical performance and physical health status.

Are there any risks involved in your child's participation in this research?

- There are no direct risks of participation for your child. However, during the performance of the activities, there is the risk of injury if activities are performed incorrectly or under poor supervision. Therefore, the researcher will be supervising your child constantly and ensuring their performance of the activities are with the correct technique. The principal researcher is also certified in Basic Life Support.

If you do not agree to take part, what alternatives do you have?

- If you wish to not partake in the study, no disadvantage will come to you or your child. Your child will still be provided with the highest care the researcher, as a Biokineticist, can offer, including consultation, exercise prescription, and follow-up.

Who will have access to your child's medical records?

- Your child's medical records will only be shared with the investigators in the study and with no other parties unless you have given written consent. Additionally, suppose you provide consent to share, then your child's data will be shared anonymously with a code assigned to your child's data. Hence, neither your name nor your child's name will be released at any point in time.

Even though it is unlikely, what will happen if your child gets injured somehow because you took part in this research study?

- The sponsor of a trial must ensure that the participants in health research are covered by comprehensive insurance in the event of physical (bodily) harm or injury, including death. This means that the insurance company will compensate a participant for medical expenses which may have resulted directly from their participation in research without the participant having to prove that the sponsor was at fault.
- Stellenbosch University has insurance to cover participants in all non-industry-sponsored research studies registered with the HREC.
- Please note the following important information:

- By agreeing to participate in this study, you agree that there is a risk that the study procedure(s) may cause harm. If it does, the sponsor will reimburse you for your medical expenses without the participant proving that the sponsor was at fault.
- As the participant's guardian, you may, however, still claim emotional pain and suffering if you so choose. In this event, you will have to prove that the sponsor was negligent and did not take all reasonable and foreseeable steps to prevent the injury or emotional trauma. This will be a separate legal matter.

➢ Stellenbosch University will provide comprehensive no-fault insurance and pay for any medical costs that came about because participants took part in the research (either because the participant used the medicine in this study or took part in another way). Therefore, the participant will not need to prove that the sponsor was at fault.

Will you be paid to take part in this study and are there any costs involved?

➢ You will be compensated to take part in the study and your expenses will be reimbursed for each study visit. In accordance with the Stellenbosch University Health Research Ethics Committee, for a visit of fewer than three hours, R300 reimbursement for travel, inconvenience, and expenses will be given. Additionally, a voucher worth R200 will also be provided for a 30-minute Kinderkinetics session, which will either be in person or online, if there is a Kinderkineticist near you.

Is there anything else that you should know or do?

➢ You should tell your family practitioner or usual doctor that you are taking part in a research study.

➢ You should also tell your medical insurance company that you are participating in a research study.

➢ You can phone Su-ané Zwiegelaar at 0798923378 if you have any further queries or encounter any problems.

➢ You can phone the Health Research Ethics Committee at 021 938 9677/9819 if there still is something that your study doctor has not explained to you, or if you have a complaint.

➢ You will receive a copy of this information and a consent form for you to keep safe.

Declaration by participant

By signing below, I ……..…… agree to take part in a research study entitled Assessing the Validity and Reliability of a Physical Performance Test Battery for Children with Juvenile Idiopathic Arthritis. I declare that:

- I have read this information and consent form, or it was read to me, and it is written in a language in which I am fluent and with which I am comfortable.
- I have had a chance to ask questions and I am satisfied that all my questions have been answered.
- I understand that taking part in this study is **voluntary,** and I have not been pressurised to take part.
- I may choose to leave the study at any time and nothing bad will come of it – I will not be penalised or prejudiced in any way.
- I may be asked to leave the study before it has finished, if the study doctor or researcher feels it is in my best interests, or if I do not follow the study plan that we have agreed on.

Signed at (*place*) ……..…….. on (*date*) ……...…….. 2022….

…… ……

Signature of participant **Signature of witness**

Declaration by investigator

I *(name)* ……..…… declare that:

- I explained the information in this document in a simple and clear manner to ……..
- I encouraged him/her to ask questions and took enough time to answer them.
- I am satisfied that he/she completely understands all aspects of the research, as discussed above.
- I did/did not use an interpreter. (*If an interpreter is used then the interpreter must sign the declaration below.)*

Signed at (*place*) ……..…….. on (*date*) ……...…….. 20….

…… ……

Signature of investigator **Signature of witness**

Permission to have all anonymous data shared with journals:

Please carefully read the statements below (or have them read to you) and think about your choice. No matter what you decide, it will not affect whether you can be in the research study or your routine health care

When this study is finished, we would like to publish the results of the study in journals. Most journals require us to share data anonymously with them before they publish the results. Therefore, we would like to obtain your permission to have your child's anonymous data shared with journals.

Permission for sharing samples and/or information with other investigators:

Please carefully read the statements below (or have them read to you) and think about your choice. No matter what you decide, it will not affect whether you can be in the research study or your routine health care.

In order to do the research, we have discussed, we must collect and store participant information, which will be stored for six years in hard copy form (stored in locked file cabinets) and soft copies (on a password-protected hard drive) and health information from individuals like your child with juvenile idiopathic arthritis. We will do some of the tests right away. Other tests may be done in the future, but only after ethical clearance has been re-applied for. Once we have done the research that we are planning for this research project, we would like to store your child's information. Information will be stored for any reason that the methodology and data are queried or in question and is a standard operating procedure in the Department of Sport Science. To protect your child's privacy, we will replace your child's name with a unique study number. We will only use this code for your child's information. We will do our best to keep the code private. It is however always possible that someone could find out about your child's name, but this is very unlikely to happen. Therefore, we would like to ask for your permission to share your child's information with other investigators.

Tick the option you choose for anonymous data sharing with journals:

I agree to have my anonymous data shared with journals during the publication of the results of this study

☐ Signature_____

OR

I do not agree to have my anonymous data shared with journals during the publication of the results of this study

☐ Signature_____

Tick the option you choose for sharing samples and/or information with other investigators:

I do not want my sample and/or information to be shared with other investigators

☐ Signature_____

OR

My sample and/or information may be shared with other investigators for further analysis and future research in a field related to juvenile idiopathic arthritis.

☐ Signature_____

Appendix 6: Child assent form

STELLENBOSCH UNIVERSITY
FACULTY OF HEALTH SCIENCES

PARTICIPANT INFORMATION LEAFLET AND ASSENT FORM

TITLE OF THE RESEARCH PROJECT: Assessing the Validity and Reliability of a Physical Performance Test Battery for Children with Juvenile Idiopathic Arthritis

RESEARCHERS NAME(S): Su-ané Zwiegelaar, Ms. Liesje Myburgh, Professor Karen Welman, Dr. Dee Abraham, and Dr. Kasha Dickie

ADDRESS: Sport Science Department, Suidwal Street, Stellenbosch, 7600

CONTACT NUMBER: 0798923378

What is RESEARCH?
Research is something we do to find new information about how things (and people) work. For example, we use research studies to help us find out more about disease or illness. Research also helps us find better ways of helping or treating children who may require extra attention to be super healthy.

What is this research project all about?
Children with joint pain and stiffness from juvenile idiopathic arthritis can be helped through exercise. Before you can exercise, an exercise expert (Biokineticist) needs to measure and observe how your body moves. So, this project is about how best to measure and watch how your body moves using different tests.

Why have I been invited to take part in this research project?
You have been invited to be part of this study as you have been diagnosed with juvenile idiopathic arthritis, which means that the exercise tests are designed especially for you. To give you exercises to do we first need to look at how your body moves, which is what this research study will try to do. You are also invited to be part of the study because you are old and young enough to do so.

Who is doing the research?
My name is Su-ané Zwiegelaar, and I will be the main researcher looking and measuring how your body moves. Later in the study, you may also see another researcher, Ms. Liesje Myburgh who may test you during the study.

Assent Form. Faculty of Health Sciences SU. Version 1. June 2009

What will happen to me in this study?

As a participant in the study, you will be asked to do some activities. In order for you to do these activities, you will need to be in exercise shorts and shirt. Here are some activities that will be done or that you will be expected to do:

- Signing this form to ensure you want to participate.
- Measuring your height and weight.
- Seeing if you have any pain around your joints.
- Measuring how far your joints move.
- Balancing on the floor and on a soft pillow.
- Measurement of how strong your joints and muscles are.
- Functional movements such as laying down, standing up, climbing steps, hopping, walking on your heels and toes, skipping, and squatting.
- Walking for six minutes.

These activities will be done at different time points, you will do them once, then again two to four days later, and a third time 60 days later. In one visit you will also be asked to do the activities twice.

Can anything bad happen to me?

We would wish for you to have no pain during the study, but if you currently have sore or stiff joints daily at home, it may cause discomfort and pain. Also, if your joints are sore and stiff, some activities that you do may be filled with discomfort. For example, you may also get very tired with the walking activity, or a joint may get sore. It is okay if you get so tired that you feel you cannot continue. If you also feel like you cannot continue because of pain in a joint, you must say so to the researcher to stop the activity. If you are feeling sick or in more pain than you normally do from juvenile idiopathic arthritis, please tell your parents to tell the researchers.

Can anything good happen to me?

Research has shown that exercise is good for children with juvenile idiopathic arthritis. Children who participate in exercise will move their body's better by being stronger, having better balance, more fitness, and better quality of life. Exercise also reduces the pain, puffiness, and stiffness that may bother your joints. Doing these tests will help get you better and special exercises. Also, there will be a better way to see how you are doing and how exercise helps you.

Will anyone know I am in the study?

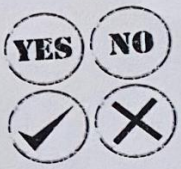
Your participation in the study will be kept secret and will only be shared with the people doing the research. If we share anything about you, it will only be shared by saying we are allowed to. Your real name will not be used but rather a code name. Also, your parent(s)/guardian(s) also need to give us their permission for you to participate, so they will also know that you are in the study. At any time in the study, you can say that you no longer want to be in the study, and nothing bad will happen to you.

Who can I talk to about the study?

The people listed below are individuals you can contact with regard to your participation in the study:

Researcher: Su-ané Zwiegelaar, telephone: 0798923378, email: 20715692@sun.ac.za

What if I do not want to do this?
You are free to choose to not participate in this study, even if your parents have said you can. Suppose you choose to participate and at any time during the study, you feel you no longer want to participate, then you are free to say so without anything bad happening or getting in trouble.



Do you understand this research study, and are you willing to take part in it?

YES ☑ NO ☐

Has the researcher answered all your questions?

YES ☑ NO ☐

Do you understand that you can stop being part of this study at any time?

YES ☑ NO ☐

Zaydah
Signature of Child

17/10/23
Date

Appendix 7: Descriptive Information template

Descriptive information:

DOB: _____ JIA Subtype: _____ Date of Diagnosis: _____

Weight: _____ Height: _____ BMI: _____ Sex: _____

Current Medication Regime: _____

Current Pain and Affected Joints: _____

Recent Operations: _____ Recent Sickness: _____ Physical Activity Readiness: _____

Physical Activity Readiness Questions

	Questions	Yes	No
1	Has your doctor ever said that you have a heart condition or high blood pressure?		
2	Do you feel pain in your chest during your daily activities of living, OR when you do physical activity?		
3	Do you lose balance because of dizziness OR have you lost consciousness in the last 12 months? Please answer NO if your dizziness was associated with over-breathing (including during vigorous exercise).		
4	Have you ever been diagnosed with another chronic medical condition (other than heart disease or high blood pressure)? PLEASE LIST CONDITION(S) HERE:		
5	Are you currently taking prescribed medications for a chronic medical condition? PLEASE LIST CONDITION(S) HERE:		
6	Do you currently have (or have had within the past 12 months) a bone, joint, or soft tissue (muscle, ligament, or tendon) problem that could be made worse by becoming more physically active? Please answer NO if you had a problem in the past, but it does not limit your current ability to be physically active? PLEASE LIST CONDITION(S) HERE:		
7	Has your doctor ever said that you should only do medically supervised physical activity?		

Appendix 8: JADAS10 questionnaire

Impact of Juvenile Idiopathic Arthritis on Activities of Daily Living – A Semi-Structured Questionnaire

Name: _____ Guardian Present: _____
Age: _____ Interviewer: _____
Native Language: _____ Recording Number: _____
Date: _____ Place: _____

Prompt: Please answer the following questions with regards to how you feel physically.

1. What do you enjoy about playing outside and what may be difficult for you when playing outside?

   Hesitancy to answer the question? Yes No

   Request to stop recording before continuing? Yes No

2. How do you take care of yourself and the space you live in at home?

   Hesitancy to answer the question? Yes No

   Request to stop recording before continuing? Yes No

3. Whom do you like going out to the shops with and why?

   Hesitancy to answer the question? Yes No

   Request to stop recording before continuing? Yes No

4. What is your favorite part about going to the shops and what do you not like at all?

   Hesitancy to answer the question? Yes No

   Request to stop recording before continuing? Yes No

5. How would you like to get to school and why?

   Hesitancy to answer the question? Yes No

   Request to stop recording before continuing? Yes No

6. How does your school help you to be able to participate in different activities or class work?

   Hesitancy to answer the question? Yes No

   Request to stop recording before continuing? Yes No

Appendix 9: APDM mobility lab software results

Overview Metric Values

Lower Limb

UNILATERAL	NORMATIVE	2014-05-01 12:16	CHANGE FROM 2014-04-29 10:26
Cadence(steps/min)	83.0 -- 124	106	↓ 6.5%
Gait Cycle Duration(s)	0.972 -- 1.45	1.13	↑ 6.9%
Gait Speed(m/s)	0.850 -- 1.44	1.34	↓ 14.7%
Double Support(%GCT)	16.1 -- 26.8	20.4	↑ 8.9%

Lower Limb

BILATERAL	NORMATIVE	2014-05-01 12:16	CHANGE FROM 2014-04-29 10:26
Foot Clearance(cm)	2.72 -- 3.92	3.90 | 3.57	↑ 2.1% | 14.7% ↑
Lateral Step Variability(cm)	1.94 -- 2.94	3.38 | 3.64	↓ 18.9% | 24.7% ↓
Circumduction(cm)	2.09 -- 6.53	4.17 | 3.37	↓ 23.7% | 16.7% ↓
Foot Strike Angle(°)	17.6 -- 28.7	32.9 | 32.5	↑ 20.8% | 11.8% ↓
Toe Off Angle(°)	28.0 -- 39.5	38.0 | 37.9	↓ 0.1% | 3.5% ↓
Stance(%GCT)	58.1 -- 63.3	60.2 | 60.3	↑ 2.4% | 0.7% ↑
Step Duration(s)	0.486 -- 0.730	0.559 | 0.585	↑ 5.0% | 11.5% ↑
Stride Length(m)	1.20 -- 1.41	1.53 | 1.50	↓ 7.8% | 9.7% ↓
Swing(%GCT)	36.7 -- 41.9	39.8 | 39.7	↓ 3.4% | 1.0% ↓
Toe Out Angle(°)	3.35 -- 17.6	3.18 | 13.0	↓ 87.2% | 51.8% ↑

Upper Limb

BILATERAL	NORMATIVE	2014-05-01 12:16	CHANGE FROM 2014-04-29 10:26
Arm Swing Velocity(°/s)	94.5 -- 303	--	-- | --
Arm Range of Motion(°)	20.2 -- 74.1	--	-- | --

Appendix 10: Synopsis (for ethical considerations)

The Identification of Gait Asymmetry in Children with Juvenile Idiopathic Arthritis.

Principal Investigator (PI) and Co-Investigators

PI	A/Prof Jacolene Kroff	jacolene.kroff@uct.ac.za
Co-investigator	Dr Elizma Atterbury	ematterbury@gmail.com
Co-investigator	Ms Su-ané Swiegelaar	suanezwieg@gmail.com
Student/Co-investigator	Ms Lindiwe Mpaka	MPKLIN003@myuct.ac.za

Background and Purpose of the Study

There is a high prevalence of gait abnormalities in children suffering from Juvenile Idiopathic Arthritis (JIA) (Kuntze et.al, 2019; Woolnough et.al, 2021). It is important to detect gait complications early in children with JIA to provide the necessary treatment to reduce walking disability – the most common component of activities of daily living (Vincent et.al, 2022). It is important that gait is sufficiently analysed in children with this condition, as it provides important information about joint alterations and gait patterns that will determine the treatment goals (Montefori et.al, 2019). The purpose of this study is to determine the incidence of gait asymmetry in children with JIA, as well as the association between gait asymmetry and disease severity.

Gait abnormalities in patients with JIA are typically addressed initially through use of medical drugs, such as disease-modifying agents to try and decrease symptoms and possible disability in children with JIA (Bazarnik-Mucha et.al, 2022; Morita et.al, 2017). While early medical intervention is generally recommended for JIA patients, a significant number of them still have a progressive functional deficit as well as subsequent limitations such as active joint contractions, decline in muscle strength, and a reduction in PA. As a result of these changes, their quality of life (QoL) is negatively affected (Morita et.al, 2018; Mucha et.al, 2022; Weiss et.al, 2007; Weiss et.al, 2007).

Previous research has investigated gait parameters such as cadence, gait speed, step/stride length in relation to disease activity (Carrol.al, 2015; Morita et.al, 2018; Woolnough et.al, 2021, Montefori et.al, 2019), however there was an insufficient report data on the gait parameters and gait asymmetry observed (Vincent et.al, 2022).

It is important that gait is sufficiently analysed, as it provides important information to functionally characterise alterations in the joints, analyse asymmetrical gait patterns, and most importantly to determine and recommend better treatment goals (Thorpe et.al, 2005).

Aims

The primary aim of the study is to examine the occurrence of gait asymmetries (assessed via 6-minute walk test) present in children diagnosed with JIA between the ages of 6 and 16 years.

The secondary aim is to determine the association between gait asymmetry and disease activity in children diagnosed with JIA.

Proposed Outcomes

Methods

The current study is part of a larger study in collaboration with Stellenbosch University conducted by Su-ane Zwiegelaar, (title: Assessing the validity and reliability of a physical performance test battery for children with JIA). Ethical approval has already been submitted and accepted from Stellenbosch University (ethics number: S22/03/051). Clear and distinctively separate research questions are investigated by the Stellenbosch University student and the UCT student, as described in memorandum of understanding attached to the main protocol.

This study will be a cross-sectional observational study. Participants (children diagnosed with JIA between six - 16 years of age, accompanied by their parent) will be recruited during routine medical check-ups at the Tygerberg Biokinetics Paediatric Rheumatology Clinic (TBPR), Tygerberg Hospital, Bellville, Cape Town. After volunteering to participate, both the child and the parent/guardian will be instructed on how to prepare for their visit at the testing venue on a different day. The child is required to wear appropriate clothing, including athletic wear such as shorts and a t-shirt with a vest/or sports bra for females, as well as correct footwear, specifically closed shoes (trainers/tekkies). For those who use assistive devices they should bring it along to the appointment. Finally, medication must be taken as required for the child before testing on the day of the visit.

The following assessments will be completed during the study visit, chronologically in order of appearance:

- Parent/guardian sign an informed consent form and descriptive data will be collected.
- Descriptive data that includes basic anthropometric measures (age, height, sex, weight), disease/condition and medical history questionnaire (subtype, time since diagnosis, pain level and location, medication and dosages, recent operations), and the physical readiness questionnaire.
- The Juvenile Arthritis Disease Activity Score-10 (JADAS10).
- Joint status measurements (digital goniometer) of the affected joints.
- The 6 Minutes' Walk test (6MWT) with automated portable gait sensor (measure parameters of gait).

Additionally, further assessments will include manual muscle testing, functional assessments, heart rate, blood pressure and rate of perceived exertion (modified Borg Scale) measures. The additional tests forms part of the research questions of the broader study and are not described in this protocol. However, the additional tests will

be conducted prior to the 6MWT.

Participants

A total number of fourteen (14) children between the age of 6-16 years old with Juvenile idiopathic arthritis will be recruited from Tygerberg Biokinetics Paediatric Rheumatology Clinic (TBPR). After participants have volunteered to take part in the study following the recruitment process, the participants will be invited to attend a testing session where data collection will take place.

Inclusion and exclusion criteria

Inclusion criteria

- Between the age of 6-16 years
- JIA diagnosed by a paediatric rheumatologist as per International League of Associations for Rheumatology (ILAR)
- Able to understand and provide informed consent
- No contraindications to physical activity
- Pain in more than one joint over six months.
- Receiving medication such as synthetic or disease modifying anti-rheumatic drugs.

Exclusion criteria

- >16 years
- Active acute infection which may result in decreased performance.
- Corticosteroid use either orally or injection for the past three months.
- Fever two weeks prior to testing
- Any surgical operations within the last six months
- Severe cognitive impairments which may alter their ability to understand instructions.

Risks to Participants

Instructions on how to conduct the assessments will be provided by the investigator and the investigator will make sure the participant understands the instructions before the assessment starts. If the participant does not clearly understand the instructions, the investigator will have to provide demonstrations. Furthermore, participants will be informed that if they want to stop the assessment they can do so without any consequences. For their safety, participants will be notified that there is a first aid kit, automated electronic defibrillator and the investigator is a certified first aider in case of an emergency. During all the tests, each participant will receive standardized encouragement. All assessments during this study visit will be administered at Stellenbosch University, specifically in the Faculty of Medicine and Health Sciences. Participants may experience some or

any of the following discomforts during assessments:

Anthropometry:

- Participants will be asked to be dressed in minimal clothing for the weight measurement.
- All measures of anthropometry will be done by a qualified scientists and will attempt to put the participant at ease as much as possible.

Medical history questionnaire:

- Some questions during the medical history questionnaire may cause participants to experience shyness and emotional discomfort to declare disabilities, limitations, and medical conditions.
- Participants will be put to ease by the administrator by explaining beforehand that they do not have to answer any question if they feel that the question can cause negative feelings.

Six-minute walk test (6MWT):

- Participants will be asked to wear appropriate shoes and floors will be checked for environmental hazards to minimise the risk of tripping or falling. Despite best efforts, there is always some risk of losing balance, falling, or becoming physically fatigued. Therefore, the investigator will provide full attention to the participants throughout the tests, observe for proper form, pain, and provide additional instruction. Before the test starts, the assessor will provide thorough instruction to the participant. Most importantly the participants will be asked if they have any symptoms such as, pain, feeling dizzy, any heart palpitations and or fever.
- Some participants may experience maximal effort for a prolonged period of time; therefore, a polar heart rate monitor will be attached to the participants chest to accurately measure heart rate throughout the walk test.
- Participants who walk using a walking aid may be at greater risk for falling. The participant will be advised to perform the 6MWT with their walking aid. The assessor will provide full attention throughout the test and can also walk behind the participant as an additional safety measure.

JADAS and Joint Status assessments:

- Participants might feel uncomfortable asjoint range of motion is measured. However, assessment will be performed by a qualified healthcare professional in a private room.
- Participant may experience physical exertion during these assessments for it requires the participant to change their body positions into several anatomical planes (supine, prone, left side, right side, sitting and standing).

Lastly, all COVID-19 protocols will be observed.

Precaution will be taken during participant visits to uphold their safety, which will include the following:

- All equipment and surfaces will be sanitized and sterilized before each individual use.

- Where possible, a 2-meter social distancing will be maintained throughout the visit between the researchers and parents/guardians, with the researcher only invading the participant space when required to perform part of the test battery.

If a participant, parent/guardian, or investigator tests positive for COVID-19, assessments will be rescheduled after an eight-to-10-day isolation period (as per the Director General Health RSA, 23.12.2021 updates); hence the test battery will need to be conducted from the initial time point of administration

Benefits to the Participant

As participants and parents will be offering their time and energy to be part of the study, their transportation will be covered by Stellenbosch University. Furthermore, on the day of the tests, refreshments will be provided to the participants at the site. At the end of the study a report on the participant's results will be provided to them, along with an individually prescribed exercise program, and a voucher to schedule a Pro Bono session with a Kinderkineticist nearest to them or an online session with the Stellenbosch Kinderkinetics Center. Furthermore, participants will benefit by adding to the knowledge pool which could then lead to better assessment and treatment by clinicians. The study will provide more insight into objective gait assessment tools for clinicians, which will assist them in providing better and more accurate assessment, and consequently more suitable and efficient exercise programmes. Furthermore, this will help the clinicians to get greater insight into the condition and participants will be able to get more personalized attention from the healthcare practitioner.

Ethical Considerations

Participants will only be included in the study after they provide written and verbal consent. The consent form and researcher will clearly explain to the participants the aims and methods of the study, if there are any possible conflicts, institutional affiliations of the researcher and if there any potential risks or discomforts of the study. The results will be aggregated and anonymised to maintain participants' confidentiality.

Participants will be asked to complete the consent form prior to their participation. Once the form is completed and consent has been provided, a hard copy and an excel spreadsheet will be opened where all their information will be stored. For confidentiality and safety, the hard copy file will be locked in a cabinet in an office at the Department of Sport Science at Stellenbosch University and the soft copy will be protected with a password for each file. Both the hard and soft copy will be protected, and access is only given to the MSc student, sub investigator, supervisor, including co supervisors and the investigator conducting the interrater reliability tests. All original paperwork, including the signed consent form, assent form, inclusion and exclusion criteria, descriptive data, and the tests conducted (cJADAS10, Joint Status and 6MWT), gathered during the session are all included in the safely preserved hard copy file. Only the MSc student, supervisor, co-supervisors, and sub-

investigator conducting the tests will have access to each participant's hard copy and electronic file, which will only be kept for up to six years.

The results will not be shared, however if the participant provides written and verbal consent for the data to be shared, that will be taken into consideration. The informed consent form provides information in which the participants' parents/guardians can indicate to which parties their results may be shared with. In addition, all results (individual and averages) will be anonymous during the publication process, thesis, and possible conferences, with no personal or medical details shared.

The study will follow the Health Sciences Human Research Ethics Committee of the University of Cape Town & Stellenbosch University as well as the principles of the Declaration of Helsinki (General Assembly of the World Medical Association. 2014). Some of the principles include autonomy, confidentiality, right to withdraw without prejudice, protection of participant health and following local regulatory norms. This study will be performed in accordance with the principles of the International Conference on Harmonization and the European Good Clinical Practice (GCP) guidelines, the South African GCP guidelines, and the laws of South Africa. The study will be covered by the liability insurance policy of Stellenbosch University.