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University  
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Health Care

**STUDY OF THE PREVALENCE OF  
MUSCULOSKELETAL  
ABNORMALITIES, PARTICULARLY  
ARTHRITIS,  
IN CHILDREN WITH DOWN'S  
SYNDROME IN THE GLASGOW  
POPULATION**

**MAUREEN ANN TODD**

**THESIS SUBMITTED TO UNIVERSITY  
OF GLASGOW FOR THE DEGREE OF  
MASTER OF SCIENCE BY RESEARCH**

**MATRICULATION NUMBER 1010891**



*Frontispiece: Picture of young girl with Down's syndrome taken by John Langdon Down in the 1800s showing marked arthritic changes in her hands (picture quality poor as old photo)  
([www.intellectualdisability.info](http://www.intellectualdisability.info))*

## ABSTRACT

Down's syndrome (DS) is associated with multiple musculoskeletal (MSK) features, including hypermobility and inflammatory arthritis. MSK disorders are not included in the screening programme for these children and correct diagnosis of MSK problems can be missed or delayed.

This study aimed to identify and examine the population of children with DS resident in Greater Glasgow to determine the frequency of musculoskeletal disorders and the levels of associated physical disability, particularly hypermobility, podiatric disorders, arthritis and obesity levels.

Between Jan 2011-2012 147 children with DS, aged between two and sixteen years and resident in Greater Glasgow and Clyde Health Board by postcode were identified from the Glasgow Thyroid and community paediatricians' register. They were invited to a single study visit encompassing musculoskeletal and podiatric examinations, anthropometric measurements and completion of study questionnaires. Focus groups were carried out to establish knowledge of MSK disorders in professionals likely to encounter this population.

Seventy three children participated in the study. A high level of hypermobility was identified, characterized by predominance in the weight bearing joints of the lower limbs, especially hips (77%), ankles (56%) and feet (59%). Standard measures of hypermobility failed to identify the extent and severity of hypermobility in these children, identifying only 15% of children as having hypermobility syndrome. No new cases of arthritis were identified in the study cohort. Families reported a lack of expression of pain. Ten percent of the cohort were obese, compared to 20% in the UK cohort from which DS growth charts are derived. Focus groups identified concerns from professionals about knowledge and skills in identifying musculoskeletal problems in these children, and challenges in ascribing an appropriate diagnosis.

This study identified barriers to care for a range of MSK pathologies in DS which targeted education and disease specific structuring of services could address. Rheumatologists found that expectations for MSK functioning in this population were low. Education focusing on the recognition and accurate assessment of altered or deteriorating MSK function is required. Severe and extensive hypermobility combined with altered expression of pain were found in this population, adding diagnostic challenges. Current MSK examination tools for hypermobility and hypotonia did not perform well in this population. Current health screening structures, the education and expectations of those providing health screening were identified as further barriers to MSK diagnosis. Facilitating early and accurate MSK diagnosis through the development of MSK examination tools, targeted education and structuring services for this population are important for the MSK and broader health of these children.



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Finally, a huge thank you to all the wonderful children with Down's syndrome and their parents who participated in the study.

## **AUTHOR'S DECLARATION**

I declare that, except where explicit reference is made to the contribution of others, that this dissertation is the result of my own work and has not been submitted for any other degree at the University of Glasgow or any other institution.

Signed \_\_\_\_\_

Printed Name Maureen Todd

## **LIST OF ABBREVIATIONS**

AAI	Atlanto-axial instability
AAOD	Atlanto-odontoid distance
AHP	Allied Health Professional
BIA	Bioelectrical Impedence Analysis
BJHS	Benign Joint Hypermobility Syndrome
BMI	Body Mass Index
C1	Cervical vertebrae 1
C2	Cervical vertebrae 2
CHAQ	Childhood Health Assessment Questionnaire
CHQ	Child Health Questionnaire
CMAS	Childhood Myositis Assessment Scale
DMARDS	Disease Modifying Antirheumatic Drugs
DS	Downs syndrome
FO	Foot Orthoses
GALS	Gait Arms Legs Spine
GP	General Practitioner
HLA B27	Human Leucocyte Antigen B27
ILAR	International League of Associations for Rheumatology
JAFAR	Juvenile Arthritis Function Assessment Report
JH	Joint Hypermobility
JHS	Joint Hypermobility Syndrome
JIA	Juvenile Idiopathic Arthritis
JRA	Juvenile Rheumatoid Arthritis
LD	Learning Disability
MCP	Metacarpophalangeal joints
MSK	Musculoskeletal
MTP	Metatarsophalangeal joints
PAOD	Posterior Atlanto-odontoid distance
pGALS	Paediatric Gait Arm Legs Spine
PIP	Proximal interphalangeal joints

pREMS	Paediatric Regional Examination of the Musculoskeletal System
PsA	Psoriatic Arthritis
PsJIA	Psoriatic Juvenile Idiopathic Arthritis
REMS	Regional Examination of the Musculoskeletal System
RHSC	Royal Hospital for Sick Children
ROM	Range of Movement
ST	Sub-talar joint
TN	Talonavicular joint
VAS	Visual Analogue Scale

# **CHAPTER 1**

## **INTRODUCTION**

Children with Down's Syndrome (DS) are well described as having a wide range of musculoskeletal (MSK) problems ranging from atlanto-axial subluxation to inflammatory arthritis. This study aimed to determine the prevalence and characteristics of MSK problems in a population of children with DS resident in Greater Glasgow.

### *Research Objective*

To determine the frequency of musculoskeletal disorders in children with Down's syndrome and the levels of associated physical disability.

### *Secondary research objectives*

1. To determine the proportion of children with Down's syndrome who are hypermobile and the associated levels of impairment and disability.
2. To determine the proportion of significant foot abnormalities and associated levels of disability.
3. To determine the proportion with arthritis and the associated levels of disability
4. To determine the proportion who are significantly overweight contributing to their musculoskeletal disability.
5. To determine barriers to prompt diagnosis and treatment.
6. To carry out focus groups to determine current level of knowledge of and concerns regarding MSK disorders in this population

Literature has described children with Down's syndrome as having with a chronic inflammatory arthritis that is similar to juvenile idiopathic arthritis (JIA) and suggested this may be more prevalent in children with Down's syndrome than the prevalence of JIA in the general population (Yancey et al (1984), Olson et al (1990), Padmakumar et al (2002), Juj et al (2009)). Within the rheumatology department at RHSC, Glasgow, a pilot study assessing the numbers of children who attended with Down's arthritis, compared to the number of children attending with JIA, suggested that inflammatory arthritis was more common in the Down's population. The children with Down's syndrome who attended our service also displayed evidence of prolonged, undiagnosed and severe

disease. This was despite multiple documented consultations with different health professionals who documented the features, but who failed to diagnose inflammatory arthritis (Cruickshanks et al, 2008).

This study aimed to screen children (before their 16<sup>th</sup> birthday) with Down's syndrome who were resident in Glasgow during the study period for a wide range of MSK problems. A single study visit involved a full examination of the musculoskeletal system, documenting any signs and symptoms of musculoskeletal disorders such as atlantoaxial instability, hypermobility, hip instability and patellofemoral instability, inflammatory arthritis, a detailed foot exam and gait assessment, anthropomorphic characteristics, a parent interview and questionnaires.

It is known from literature that these children are more prone to hypotonia, hypermobility and common podiatric disorders and from the above examinations we aimed to determine the level and prevalence of musculoskeletal disability caused by these problems and assess for possible arthritis. Height and weight were recorded to assess obesity levels within the study population and questionnaires used to ascertain any parental concerns.

It also aimed to identify any training needs for health professionals within the community setting to improve the early diagnosis of MSK problems. The RHSC pilot study (Cruickshanks et al, 2008) raised concerns over delay to diagnosis as the children with DS were presenting with severe disease. It was decided to carry out focus groups with a group of community paediatricians to determine level of knowledge of MSK disorders in this population and with paediatric rheumatology specialists to determine concerns regarding referral and diagnosis. Discussion with the community paediatricians included current practice within the annual health review these children receive, and whether they included a musculoskeletal examination. Discussion with the paediatric rheumatology specialists included experience of DS children presenting with arthritis and response to treatment to assess delay to diagnosis and prognosis at presentation. We intend to develop an educational package to raise awareness of MSK problems in this population for the healthcare professionals who see these children regularly and to allow them to feel confident examining for musculoskeletal disorders, and highlight the MSK features of DS to the children's parents to facilitate early presentation.

I have worked in various settings during my nursing career but started working in research three years ago within the rheumatology team at the Royal Hospital for Sick Children (RHSC), Glasgow and have very much enjoyed evolving my role as a nurse in this new direction. I have found it very rewarding working with children and their families on studies and learning the processes involved in a number of research projects. In particular I have found the children with Down's syndrome a delight to work with.

This thesis commences with a literature review followed by a chapter on methodology. The fourth chapter is about the themes obtained from focus groups discussions. Chapters five, six, seven cover results in hypermobility, musculoskeletal and podiatry and Chapter eight concludes with my discussion chapter.



## **CHAPTER 2**

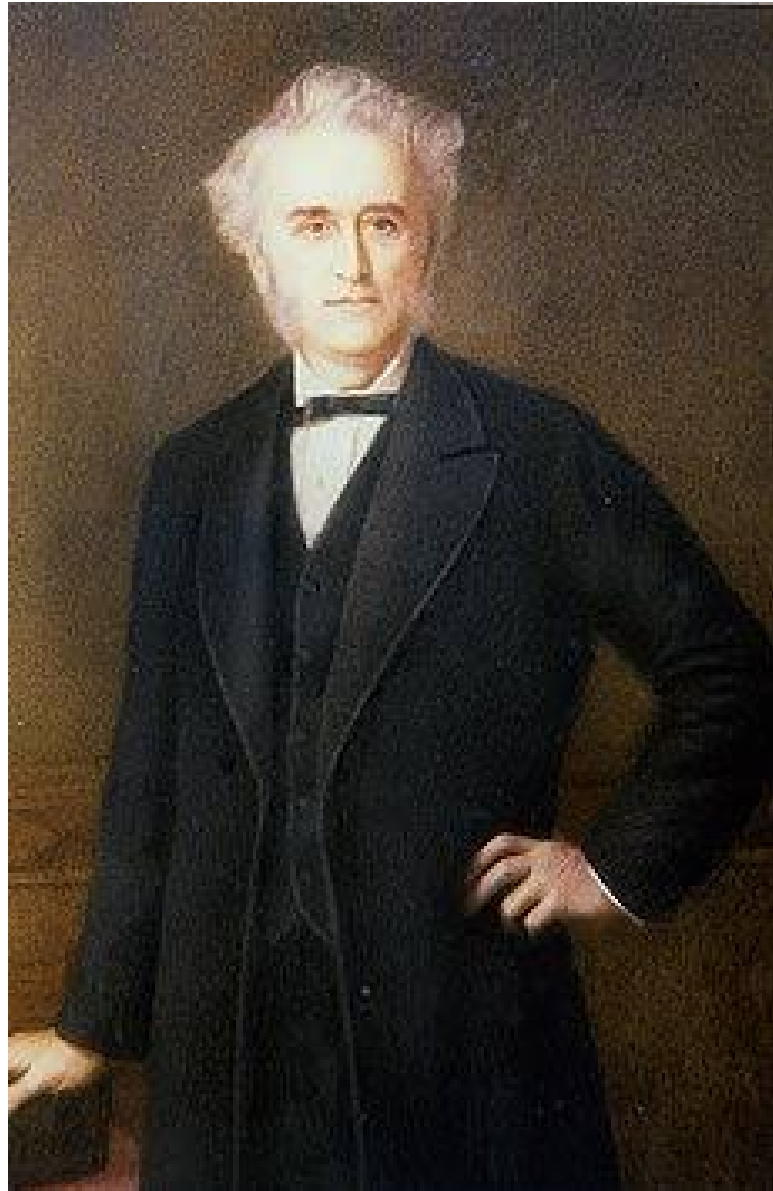
### **LITERATURE REVIEW**

#### *2.1 Literature search strategy*

A literature search was carried out using PubMed UK, Glasgow University Library (Cinahl, Medline and Biomedical Reference Collection), Greater Glasgow & Clyde Health Board Knowledge network, Wiley Online Library and Google Scholar. The phrases 'arthritis in Down\* syndrome', 'arthritis', 'Down\* syndrome', 'children with Down\* syndrome', 'Down\* syndrome and general practice', 'joints', 'psoriatic arthritis', 'psoriatic arthritis in children', 'arthropathy', 'inflammatory arthropathies', 'podiatric', 'podiatry', 'leg length discrepancy in children', 'metatarsal formula', 'pain and Down\* syndrome', 'general care in Down\* syndrome', 'head circumference and Down\* syndrome', 'communication in Down\* syndrome', 'Special Olympics', 'Special Olympics exclusion', 'Down\* syndrome athletes', 'musculoskeletal', 'musculoskeletal exam', 'CHAQ', 'pGALS', 'hypermobility', 'medical ethics', 'principles of medical ethics' and 'unethical research' were entered into the databases. No specific year restrictions were added to the search as quite a number of the relevant articles date back over 30 years but, mainly, literature from 2000 and 2011 was used for current relevance. Only English articles were included in the search. Numerous results were returned for each phrase of which many were not relevant. Papers were generally eliminated based on the title but a small number were eliminated due to abstract if the title appeared relevant. A large number of relevant results were returned, particularly on atlanto-axial instability, and other musculoskeletal disorders. A number of the articles found were reviews of the literature of their particular subject. The Google search engine was also used to search for 'John Langdon Down', the man who originally described Down's syndrome, which provided various versions of his life story and a link to his original paper classifying Down's syndrome.

## 2.2 Historical Perspective

### Classification of Down's syndrome and John Langdon Down



Picture 2.1 - John Langdon Down ([www.langdondowncentre.org.uk](http://www.langdondowncentre.org.uk))

Down's syndrome (DS) was originally described by John Langdon Down (Picture 2.1) in his 1866 paper 'Observations on an Ethnic Classification of Idiots'. His observation was that some patients had features that could be likened to different ethnicities such as Ethiopian and Malayan. In particular he was intrigued by a large group of patients who displayed the same physical features. Down likened these features to the people of Mongolia. He described the similarity in their facial features in depth and remarked that this was so marked that these children could be siblings. He noted that these were features present in more than 10% of his cases and it is always a congenital condition. He concentrated his time measuring head circumferences, studying photographs and examining the brains of these children post mortem.

Following publication of his paper these patients were then described as Mongols or Mongolian Idiots until the 1960s. They were then reclassified as Down's syndrome. The Editor of the Lancet opted for the description Down's syndrome after a group of 20 leading geneticists wrote suggesting differing options. The World Health Organisation confirmed this change in 1965. (Ward, 2002). This decision was taken after a request from the People's Republic of Mongolia. However, despite this reclassification, the term mongol was still used into the 1980s. (Kinnell, 1984)

In 1866 mentally ill patients were termed as idiots, imbeciles and lunatics and placed in institutions. Although Down's paper would be considered inappropriate in current times, it was written at a time when these terms were used widely and John Langdon Down was not describing his patients in a derogatory fashion. His description of racial similarity was a recognition of consistently found clinical features which has led to an understanding of distinct clinical syndromes and the discovery of the genetic process involved. This has provided further understanding of the mechanisms of DS and contributes to understanding of congenital disorders generally.

Down became concerned that all people with any sign of mental illness or disability were branded as idiots with no distinction between levels of learning disability. He discovered that people with DS improved better than he would have expected with direct involvement and teaching. He preferred the term 'feeble minded' rather than idiots and, after being Medical Superintendent of Earlswood Asylum for Idiots for 10 years, he opened up his own home, Normansfield, as a residential training and care centre for the learning disabled ([www.langdondowncentre.org.uk](http://www.langdondowncentre.org.uk)).

Normansfield started as a family home with 20 patients but over 23 years, was expanded and grew to a home housing 150 patients. The patients were encouraged to learn, play and interact. The home incorporated a theatre (Picture 2.2) where they had Sunday services and put on shows and concerts. It appears that John Langdon Down was a very liberal, open minded person at a time when opinions were considerably narrower than today. He was also known for supporting the suffragette movement. Normansfield remained as a home for people with learning disabilities and run by the

Langdon Down family for 100 years (the advert in Picture 2.3 shows his sons as the medical superintendents). It is now occupied by the Down's Syndrome Association and the theatre is used for professional productions. By a strange twist of fate, one of John Langdon Down's grandchildren was born with DS (after his death) and lived at Normansfield until he died aged 65.



Picture 2.2 Normansfield Theatre ([www.langdowndowncentre.co.uk](http://www.langdowndowncentre.co.uk))

ADVERTISEMENTS. 813

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*Medical Superintendents:*

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PERCIVAL L. LANGDON-DOWN, M.A., M.B., B.C.

---

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Picture 2.3 Advert for Normansfield

### 2.3 Down's syndrome

Following John Langdon Down's description, many different studies examined the epidemiology of DS. One of the earliest conclusions to an increased risk of a pregnancy with DS was that increased maternal age was a factor (Penrose, 1933; Howells, 1989; Bosch, 2003; Roizen and Patterson, 2003; Bittles and Glasson, 2004; Kava et al, 2004; Sherman et al, 2007; Weijerman et al, 2010). Penrose (1933) examined maternal and paternal age in relation to DS births and discovered that increased maternal age was much more significant than increased paternal age.

In 1959 the presence of an extra chromosome 21 was discovered in DS due to the introduction of karyotyping (Roizen and Patterson, 2003; Sherman et al, 2007) and has subsequently also become known as trisomy 21.

Prenatal testing for DS was introduced in the 1970s (Roizen, 2001) and was originally an invasive amniocentesis in the second trimester but has progressed to a less invasive combined test of nuchal transparency screening using ultrasound and a blood test for beta-human chorionic gonadotrophin and pregnancy-associated plasma protein-A (Nice Guidelines CG62, 2008). Introduction of screening has appeared to affect the number of children born with DS as it has allowed women to have the choice to terminate or continue with the pregnancy. However not all countries have widespread access to screening. Kava et al (2004) comment that screening is only offered to women over 35 or those with a previous DS pregnancy in India. It is noticeable that the abortion law in Eire means the incidence of DS is 10 fold higher than in Glasgow despite a similar sized population. (O Killeen and C Foley personal communication)

DS is now considered to be one of the most common chromosomal abnormalities (Howells, 1989; Sherman et al, 2007; Weijerman and de Winter, 2010). Prevalence reports of DS have changed over the years with Howells (1984) breaking the reporting down into maternal age difference of 1 in 2500 for mothers under 30, 1 in 1200 for mothers between 29 & 34, 1 in 200 for mothers aged between 35 and 39 and 1 in 35 for mothers aged between 39 & 47. More recent studies in the United States suggest approximately 1 in 700 births are children with DS (Kava et al, 2004; Sherman et al, 2010; Prows et al, 2013). Weijerman and de Winter (2010) commented on a world wide prevalence of 10 per 10,000 live births but also discussed differences in prevalence around the world. One of the reasons for this may be due to attitude and laws surrounding termination of pregnancy. Countries where abortion is illegal such as Ireland and United Arab Emirates have higher prevalence rates and some countries such as France show lower prevalence rates.

### 2.3.1 Signs and symptoms

The most striking characteristic of DS in a newborn is hypotonia (Weijerman and de Winter, 2010). Others include the presence of a transverse line across the palm of the hand called the ‘Simian fold’, upward slant to the eyes (epicanthic folds), depressed nasal bridge creating flat facial features and a short neck (Bosch, 2003; Roizen and Patterson, 2003; Kava et al, 2004; Sherman et al, 2007; Weijerman and de Winter; Prows et al, 2013)

Symptoms include the presence of a coronary heart defect, problems feeding, congenital defect of the GI tract including Hirschsprung’s disease and hearing loss (Bosch, 2003; Roizen and Patterson, 2003; Sherman et al, 2007; Weijerman and de Winter, 2010).

Diagnosis should be made through chromosomal karyotyping on suspicion of DS.

### 2.3.2 Health problems in DS

Children with DS are reported as having many health issues. It is well reported that they are at increased risk of cardiac disorders, leukaemia, hearing problems, sight problems, thyroid disorders, respiratory problems and orthopaedic issues such as hip dysplasia and atlantoaxial instability. A few of the most common are discussed below.

#### 2.3.2.1 Coronary defects

Approximately half of children with DS are reported as having congenital cardiac defects at birth with atrioventricular septal defects and ventricular septal defects being the most commonly reported (Howells, 1989; Pueschel et al, 1995; Roizen, 1996; Roizen, 2001; Bosch, 2003; Roizen and Patterson, 2003; Kava et al, 2004; Sherman et al, 2007; Prows et al, 2013; Weijerman and de Winter, 2010). This statistic of approximately 50% appears to be unchanged from Howells paper in 1989 to Prows et al in 2013.

#### 2.3.2.2 Thyroid disorders

Congenital hypothyroidism has been widely reported in DS (Howells, 1989; Pueschel et al, 1995; Roizen, 1996; Roizen, 2001; Bosch, 2003; Roizen and Patterson, 2003; Weijerman and de Winter, 2010) and children are screened at birth, then generally screened annually for thyroid problems. One of the sources for our population was the Glasgow Thyroid Register.



### 2.3.2.3 Sensory problems

Auditory and visual problems are observed in children with DS such as congenital cataracts, nystagmus, blepharitis, glaucoma, middle ear effusions and distortion of the tympanic membrane (Howells, 1989; Pueschel et al, 1995; Roizen, 1996; Roizen, 2001; Roizen and Patterson, 2003; Kava et al, 2004; Weijerman and de Winter, 2010; Prows et al, 2013).

### 2.3.2.4 Gastrointestinal problems

Gastrointestinal problems are documented in DS and can be found in approximately 10% of the population (Pueschel et al, 1995; Bosch, 2003; Sherman et al, 2007; Weijerman and de Winter, 2010). These conditions include Hirschsprung's disease, perforations and duodenal stenosis.

### 2.3.2.5 Leukaemia

Children with DS are known to have a higher risk of developing acute myeloid and lymphoblastic leukaemia and may also present with other haematological disorders such as thrombocytopenia and polycythaemia (Bosch, 2003; Weijerman and de Winter, 2010).

### 2.3.3 Prognosis and Life Expectancy

Life expectancy has increased greatly over the years for individuals with DS as screening and newer treatments improve their recovery from associated medical disorders, especially in the first year of life as early diagnosis and intervention in coronary defects and gastrointestinal disorders have improved mortality rates (Weijerman and de Winter, 2010). Yang et al (2002) examined data from death certificates between 1983 and 1997 and discovered that the median age of life expectancy rose from 25 years in 1983 to 49 years in 1997. Life expectancy in the early part of the 20<sup>th</sup> century was approximately 9 years but more recent figures have suggested that median life expectancy is now approximately 60 years of age (Bittles and Glasson, 2004; Bittles et al, 2006).

#### 2.4 Recognised associated health problems in Down's syndrome

John Langdon Down studied facial features, head circumference and brain size in these children. He took numerous photographs of these children (Picture 2.4, Picture 2.5) to assist his research. The only physical condition he mentions is that 'the circulation is feeble' (Down, 1866). Other physical conditions are not considered in his paper. Despite this, it is very interesting to note that the girl in John Langdon Down's photograph on the frontispiece shows marked arthritis in her hands (Picture 2.6). However, his interest in their wellbeing was a huge leap forward for people with DS.

Many different medical conditions have been described in children with Down's syndrome as in section 2.3.2. In the articles discussing the various associated medical conditions, the authors mention atlantoaxial instability, hip instability, patellofemoral instability, hypermobility and hypotonia under musculoskeletal disorders but for the purposes of this study it is important to note that they fail to mention inflammatory arthritis except for Roizen and Patterson who mention it briefly and suggest vigilance is required. This will be explored fully later in this chapter.

Cardiac, respiratory and thyroid problems are well documented in DS as are higher risks of leukaemia and Alzheimer's disease. Certain orthopaedic disorders are also well documented such as atlanto-axial instability, hip dysplasia, patellofemoral instability and hypermobility. Inflammatory arthritis is not so well researched other than a small number of studies looking at case reports of children already diagnosed with inflammatory arthritis.



Picture 2.4 - pictures of girls with DS taken by John Langdon Down in the 1800s  
 (www.intellectualdisability.info)  
 (picture quality poor as old photos)



Picture 2.5 6 pictures of girls with DS taken by John Langdon Down in the 1800s  
 ([www.intellectualdisability.info](http://www.intellectualdisability.info))

## 2.5 Musculoskeletal disorders in DS

### 2.5.1 Arthritis in Down's syndrome

Literature on the prevalence of inflammatory arthritis in children with DS is notably limited despite evidence of arthritis in the hands of the girl in John Langdon Down's photograph on the frontispiece. (Picture 2.6).

In a letter to the British Journal of Radiology in 1984, H G Kinnell commented that neither he, nor his colleagues, had seen cases of rheumatoid arthritis in children with DS. His letter speculated that rheumatoid arthritis might be less common in these children than in the general population.

However, in the same year, Yancey, Zmijewski, Athreya and Doughty (1984) published a paper on their observations of a number of children with DS who had attended the rheumatology department. JIA was termed JRA (juvenile rheumatoid arthritis) at this time. Seven children were described with arthropathy. In 1 patient, hypermobility of the joints could account for the arthropathy. In the other 6 children, the arthropathy of Down's syndrome resembled JRA (Yancey et al, 1984). They estimated that the prevalence of arthritis was much higher in the Down's population. Four of the children had symptoms for some time prior to attending and three didn't appear to respond to treatment. They concluded that this could not be called JRA due to the higher prevalence of immune disorders in this population. As JRA was diagnosed following exclusions of other diagnoses they classified it as arthropathy of Down syndrome. Subsequent papers, therefore, referred to the condition as the arthropathy of Down's syndrome following this classification.



Picture 2.6 ó girl's hand showing arthritic change from photo taken  
by John Langdon Down in the 1800s (picture quality poor as old photo)  
([www.intellectualdisability.info](http://www.intellectualdisability.info))

In a similar study in 1990 Olson, Bender, Levinson, Oestreich and Lovell described nine children with the arthropathy of DS. All but one had delay from symptom onset to appointment and Olson et al calculated a mean time of 3.3 years in comparison with 0.7 years in the general population. Behavioural problems were mistakenly given as the main reason for changes in activities of living causing delayed diagnosis of arthritis and they recognised that earlier diagnosis would improve with increased awareness of arthritis in this population group. Eight of the nine children either did not respond to treatment or had complications resulting from the treatment which led them to query whether these patients are more prone to drug toxicities. All the children were treated prior to methotrexate therapy being available. All were commenced on non steroidal anti-inflammatories with three also on gold therapy and one commenced on hydroxychloroquine.

By 2002 a letter to Rheumatology by Padmakumar, Evans-Jones and Sills (2002) asked 'Is arthritis more common in children with Down's syndrome?' They wished to estimate how common arthritis was in their population of children with DS. They concluded that the numbers of arthritis in children with DS could be three times higher than the general population. However, they only identified a small case series of four children and made very generalised estimates of the population of DS recognising that their figure could be an underestimate, possibly due to misdiagnosis, and a larger study would be required to confirm their findings. They suggested that inexperienced examiners might miss arthropathy in these children due to hypermobility and unusual hand shape. This would support the suggestion that these children have a delayed time to diagnosis for arthritis.

The poster presentation of the pilot study carried out by Cruikshank, Tunc, Walsh, Galea, Davidson and Gardner-Medwin (2008) described eight children with DS and arthritis, a similar number of cases described by Yancey et al, (1984) and Olson et al, (1990). This looked mainly at the delay to diagnosis of inflammatory arthritis. 'Diagnosis of arthritis in children with Down's syndrome is still significantly delayed compared to other children presenting with inflammatory arthritis' (Cruikshank et al, 2008). The children had attended other health professionals during the course of routine screening and review of this population, or for other health reasons, and been given a number of misdiagnoses before attending rheumatology despite often documenting of MSK symptomatology and in some cases accurate descriptions of synovitis. This would support the idea that developing an education package for other health professionals involved in the care of these children might facilitate earlier diagnosis. It would also be beneficial to educate the parents who had often identified the MSK concerns to help prevent delay in accessing appropriate services. 'Many of this cohort had significant joint damage and disability by time of diagnosis' (Cruikshank et al, 2008). In contrast to previous studies, where treatments were less sophisticated, all but one of the children responded well to modern treatment with DMARDs and biologics. Earlier diagnosis of

inflammatory arthritis would be likely to significantly improve outcome as it would optimise treatment response.

Investigation into delayed diagnosis and response to treatment was continued by Juj and Emery (2009) who identified nine children at their hospital who had DS and fulfilled the criteria for JIA. They also identified a delay to correct referral and significant joint damage and remarked that lack of awareness of inflammatory arthritis in this population led to diagnosis delay and unnecessary procedures. Diagnosis delay meant the children presented late and led to irreversible damage to joints and functional damage. This study is very recent and, in comparison to the previous studies, all of their cases were started on disease modifying therapy, responding well to treatment, with four children maintained on methotrexate, one on methotrexate and infliximab, one on hydroxychloroquine and one on infliximab. One other child is maintained with anti-inflammatories and the ninth child is off all medication. This evidence concurs with Cruickshank et al (2008) findings that arthritis in DS responds well to modern treatments including biologics. Juj et al (2009) linked their findings with Padmakumar (2008) but suggested that their numbers estimate that arthritis is six times more common in DS than in the general population.

All these studies have small and very similar numbers but the fact that they have discovered comparable results suggests a trend and gives them more significance than a single study. All examined children already diagnosed with JIA and none of them screened populations of children with DS which may give a more accurate representation of the prevalence of arthritis. . All support the introduction of a musculoskeletal screening tool that would be beneficial to this population. These and previous studies suggest that the incorporation of arthritis into routine health surveillance practices may benefit children with Down's syndrome (Juj and Emery, 2009). Despite these conclusions, an MSK examination is still not included in the routine annual review of these children.

#### 2.5.1.1 Psoriatic arthritis

Perlman (1984) and Sharma and Dogra (2010) commented that the association between arthritis and psoriasis was first reported in the early 1900s but this classification of arthritis may have been present as early as the fifth century. Zias and Mitchell (1996) discussed the 1983 excavation of a Judean monastery which had been destroyed in 614 AD. Human remains discovered in a tomb were examined and, following exclusion of other conditions, two of the remains were diagnosed with psoriatic arthritis (PsA). They discussed that it has been agreed that psoriasis was one of the more common dermatological conditions regarded as biblical leprosy and by this period of history people with these dermatological conditions were housed in monasteries and cared for. Previously they had been shunned and expelled.

Cruickshank et al (2008) found that the majority of the children reviewed displayed characteristics of psoriatic arthritis which is not evident in other literature and queried whether this may be a feature in arthritis in DS children.

### 2.5.2 Atlanto-axial instability

From the literature reviewed for this study the most frequently recognised and serious MSK problem in children with Down's syndrome is atlanto-axial instability (AAI). This is excessive mobility in the first and second cervical vertebrae (the atlantoaxial joint) and is caused by the laxity of the transverse atlantal ligament. People with DS can be prone to cervical spine instability due to lax ligaments and literature seems to suggest it could be present in approximately 10-20% of them. (Collacott, 1987; Roy, 1990; King, 2005; Ali et al, 2006). Of these 10-20% approximately 1-2% will develop symptoms (Ali et al, 2006). However AAI is generally asymptomatic and mainly diagnosed by radiography. The main concern with AAI in children with DS is spinal cord compression causing paralysis although placing restriction on activities in this population to prevent complications of AAI can then impact on their obesity levels which places pressure on the MSK system in general.

Ali, Al-Bustan, Al-Busairi, Al-Mulla and Esbaita (2006) looked at 44 Kuwaiti subjects with Down's syndrome who were identified because they received primary health care through the two state run institutes. The subjects were all adult over the age of 15. A study history was taken, physical examination carried out and radiological views of the cervical spine taken in neutral and flexion positions looking at anterior atlanto-odontoid distance (AAOD) and posterior atlanto-odontoid distance (PAOD). Two researchers separately carried out the physical exam and read the X-rays, each blind to the others results.

Their results showed eight out of the 44 subjects showed AAI on radiology (18%) and all were asymptomatic. This is consistent with the above references suggesting 10-20% of individuals may be affected and that AAI is generally asymptomatic (Roy, 1990; King, 2005).

The study by Ali et al had a small number of participants but the authors acknowledged by discussing that lacking controls is a possible drawback as a control group would give more evidence for any radiological findings in the DS group. Their thorough review of all the evidence and previous literature made a good case for imaging the PAOD as well as AAOD as it indicates the space available for the cord. They discussed that patients diagnosed with AAI on X-ray may not have symptoms if the PAOD is ample as cord compression may not occur.

This study looked at the diagnosis of AAI quite thoroughly but would have benefit of a higher number of subjects and a control group to compare the radiographic results. They made very valid



points about positioning of cervical spine for X-ray and areas of the spine to image which confirms previous study outcomes as this has been very widely researched.

As AAI is generally asymptomatic it does not have a great impact on the health of the majority of children with DS. However these children can be restricted in the types of activities they can participate in due to the risk of AAI. Sports considered high risk can include diving, martial arts, high jump, football, rugby and gymnastics but other situations such as road traffic accidents are also considered high risk for AAI.

The Special Olympics Committee instigated a screening policy for atlantoaxial subluxation in all athletes with DS (Tassone and Duey-Holtz, 2008). Athletes with DS must have a radiological exam prior to taking part in sporting activities considered high risk. If X-rays show any sign of instability, the athlete is restricted from participating in any of these activities. Similarly to Ali et al (2006), Tassone and Duey-Holtz discussed the importance of taking X-rays in flexion and extension and also the importance of consideration of cord space as it increases the significance of using X-ray to predict the level of risk.

Cremers, Bol, de Roos and van Gijn (1993) studied AAI and sports risk in children with DS. A total of 282 children were examined radiographically and 91 were identified as having an increased atlantoaxial distance. These 91 children were divided into two groups to assess the effect of sporting activities on the atlantoaxial joint. Group A consisted of 44 children (33 boys) whose sporting activities were restricted and Group B consisted of 47 children (32 boys) who were allowed to continue normal sporting activities. A third control group of 44 children (25 boys) with no evidence of AAI were also included. The study concluded that there was no change to the atlantoaxial distance of individual subjects ( $p=0.99$ ) and that restricting activities actually impacted on functional performance.

Although this appeared to be a thorough study and all aspects are described in detail, the tables in this study do not show clear numerical results for atlantoaxial distance between groups A and B after a year although they state there was no difference and the p value of 0.99 is given in the text. They do provide a table for groups B and C and the results show that the difference in atlantoaxial distance between these groups was no longer significant after a year ( $p=0.19$ ).

Collacott (1987) and Roy et al (1990) both agreed that guidelines and recommendations should be in place regarding AAI in Down syndrome. However, this remains a complicated issue with lifestyle and neurological signs and symptoms to consider instead of the single assumption that an AAOD greater than 3mm leads to dislocation as it suggests that approximately one sixth of the DS

population would have their activity levels restricted when the benefits would be greater than the risk.

### 2.5.3 Hypermobility

The late Dr Barbara Ansell frequently stated that hypermobility is tricky in children (Bird, 2005). Joint hypermobility (JH) describes lax ligaments around the joint allowing the joint a wider range of movement (ROM) than is considered normal in an asymptomatic individual. Joint hypermobility syndrome (JHS) describes this condition but with symptoms which can include joint pain, foot pain and joint dislocation. Kirk, Ansell and Bywaters (1967) used the name 'Hypermobility Syndrome' to describe the situation where joint laxity is linked to musculoskeletal symptoms. From review of the literature this is described as the first time the term is used. Hypermobility is measured using the Beighton scale (Table 3.3) and hypermobility syndrome diagnosed by the Brighton criteria (Table 3.4)

The majority of the literature reviewed described hypermobility and lax ligaments present in DS which can precipitate instability problems such as hip and patellar instability and foot deformities. (Caird et al, 2006). Despite this, literature that looked at generalised hypermobility in children with DS was very limited. The majority of literature looked at hypermobility in relation to joint instability, particularly instability of the atlantoaxial joint.

Livingstone and Hirst (1986) examined 39 children (16 girls) with DS identified from a register in their local health district and examined their joints for hypermobility. They followed a criteria developed by Carter and Wilkinson in 1964 which described a diagnosis based on (1) Hyperextension of the elbows beyond 10°. (2) Ability to touch the forearm with the thumb on wrist flexion. (3) Hyperextension of the wrist and metacarpal joints so that the fingers lie parallel to the forearm. (4) Dorsiflexion of the ankles to 45° or more, from plantigrade. (5) Hyperextension of the knees beyond 10°. Abnormal generalized joint laxity was diagnosed if three of these features were found bilaterally with both upper and lower limbs being involved (Livingstone and Hirst, 1986). Livingstone and Hirst found signs of joint laxity in 23 children but showed that only three children showed pairs of joints with upper and lower involvement. They, therefore, concluded that the orthopaedic problems found in DS were related to hypotonia rather than hypermobility.

The results of this study showed that the strict criteria given by Carter and Wilkinson were inappropriate for diagnosing hypermobility and may have been one of the reasons that they were revised and the Beighton criteria produced in 1973. These are now accepted internationally and are used widely for diagnosis of general joint hypermobility. (Juul-Kristensen et al, 2007).

## 2.6 Hypotonia

Hypotonia is mentioned in much of the literature examining DS, particularly in newborns and. Infants with DS are described as floppy at birth (Picture 2.7) and it is one of the most common reasons for considering a genetic disorder (Patterson and Lott, 2011; Prows et al, 2013).

Shumway-Cook and Woollacott (1985) studied the dynamics of postural control in the child with Down syndrome and discussed that few studies have explored the specific motor control deficits that could underlie postural instability and subsequent developmental delay in motor coordination. They compared temporal delay between distal and proximal muscles in a small cohort of 11 children from the general population and 6 children with DS. They then compared the results from the children with results from adults in a previous study. All the children showed a significant difference from the adults but although the children with DS showed a delay compared to the non DS children it was not a significant difference. They did find that the organisation of postural patterns between the control cohort and the DS cohort was considerably different in children under three years of age. This is a very small cohort on which to base any conclusions and they do suggest that more research is needed to examine whether these results show a difference in development in control of posture and not delayed development. This study opens up the question that hypotonia may not be the only factor in motor development in DS children and further studies would be advantageous in examining this theory.

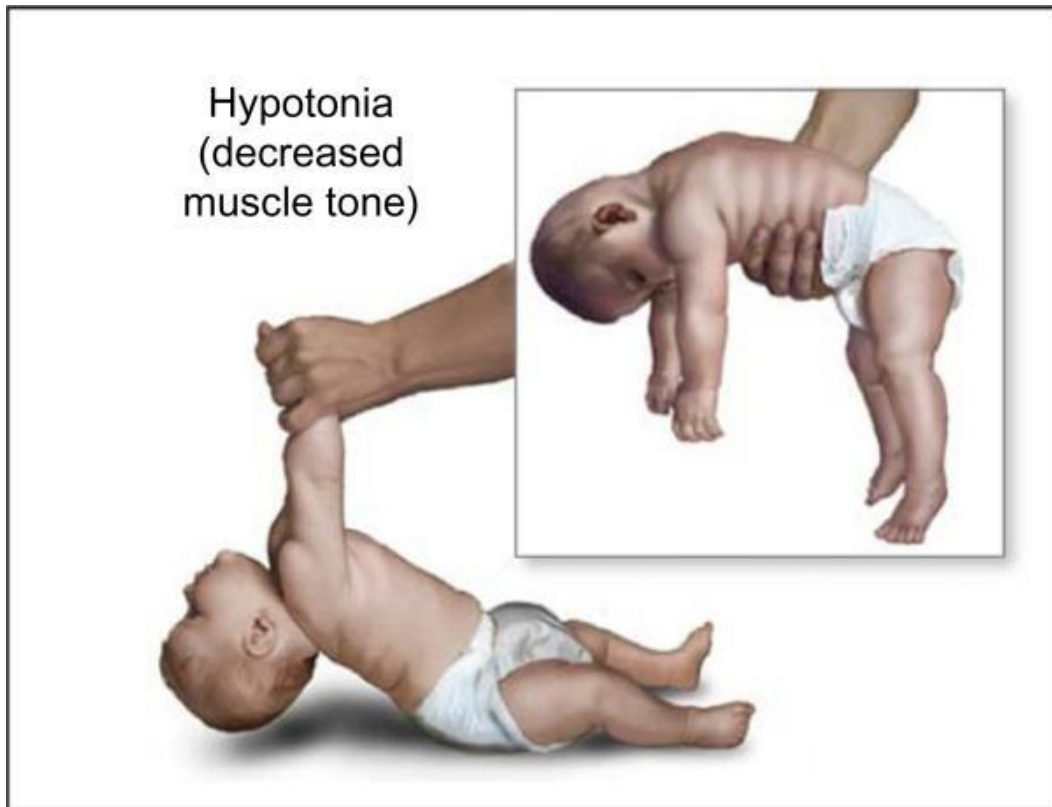
Latash, Wood and Ulrich (2008) discussed the fact that the majority of literature on motor studies in DS mention that hypotonia is a large factor in differences between movement in people with and without DS. Their paper examines what is currently known about hypotonia, motor skill development and physical activity in DS and interestingly starts with a discussion on muscle tone being a frequently used clinical term that has no clear definition and introduce a definition of hypotonia for their discussion which is -an examiner moves a joint of a person smoothly and slowly, while the person is instructed to relax and not to resist the motion. The examiner compares the feeling of resistance to his or her internal gauge based on previous experience what he or she associates with being normal and lower than expected resistance is called hypotonia (Latash, Wood and Ulrich, 2008). This definition is not ideal as it relies on the examiner's perception of what is normal and they suggested that more objective assessment and further research is needed to study the relationship between hypotonia and muscle development in children with DS. This paper gives the reader some very interesting perspectives and thought provoking questions about hypotonia and motor problems in children with DS.

Chang, Kubo and Ulrich (2009) examined muscle activation patterns of eight non DS children compared with eight DS children from walking onset for six months. They discovered that both

sets of children improved their muscle activation patterns after six months but the DS group did not display the same level of stability as their peers and the timing of their muscle bursts was more inconsistent. They summarised that both groups demonstrated the need for a prolonged period of practice to develop rhythmic and stable muscle activation during gait. Again this is a very small cohort and a larger cohort may produce more specific results in differences between the two groups.

The majority of the literature mentions hypotonia as a feature of DS without exploring it further. Weijerman and de Winter (2010) discussed the care of children with DS and observed that the level of hypotonia is directly related to motor developmental delay. Rigoldi et al (2011) examining gait development during lifespan in DS mention lax ligaments and hypotonia are typical DS features.

Hypotonia is a well reported and recognised diagnostic sign in DS at birth and some of these studies show that postural control in DS children displays deficiencies but hypotonia may not be the sole cause of this and further studies are required to explore the issues surrounding motor development and hypotonia.



*Picture 2.7: Hypotonia in a newborn displaying head lag on pull to sitting and inability to support posture in ventral suspension (Lott, 2012)*

## 2.7 Other orthopaedic and musculoskeletal disorders

There are various additional orthopaedic and musculoskeletal disorders recognised in DS, primarily hip instability, slipped upper femoral epiphysis, knee problems, particularly patella-femoral instability, and scoliosis. Most of these conditions are linked to hypermobility and lax ligaments. Jacobsen and Hansson (2000) reviewed orthopaedic disorders in DS. This paper looked at DS in general and then sections on the recognised orthopaedic disorders. Each disorder is discussed in a fairly brief paragraph but it is noted that arthritis in DS is not mentioned. Interestingly, though, they summarised that the DS patients' lack of communication and lack of awareness of the frequency of orthopaedic problems leads to these problems being overlooked.

A similar review highlighting orthopaedic disorders by Caird, Wills and Dormans (2006) looked at the role of the orthopaedic surgeon. In comparison to Jacobsen and Hansson they emphasised AAI and hip instability but also included a short paragraph on arthropathy of DS. However their description of this arthropathy in DS is based only on Olson et al (1990) when there were other published articles available to reference (Yancey et al, 1984; Padmakumar, 2002).

Dugdale and Renshaw (1986) researched patellofemoral instability. They examined 210 institutionalised patients with DS and reviewed the notes of all patients with DS hospitalised in a 28 year period at a children's hospital in Connecticut. Seven children were identified with a reported patellofemoral instability from hospital notes and interviewed with their families. They were not included in the analysis for prevalence as could not be considered a random group. The remaining 210 institutionalised patients (132 male) were examined for instability and 22.4% were found to have bilateral patellofemoral instability which was a similar finding to a previous study by Diamond, Lynne and Sigman (1981). Dugdale and Renshaw concluded that patellofemoral instability can be common in DS but commented on the fact that it is often overlooked.

## 2.8 Pain response in DS

Lind, Vuorenkoski, Rosberg, Partanen and Wasz-Höckert performed varied studies into pain stimuli in infants including a study in infants with DS (1970). Forty seven children were identified from two hospitals in Sweden. Seventeen were excluded from the study; three failed to give a cry response despite repeated stimuli and 14 due to an underlying medical condition. The pain cries of the 30 remaining children were compared with 120 infants without DS. Eight attributes of cry were examined; latency, length, minimum pitch, maximum pitch, flat melody form, bi-phonation, stuttering voice and nasality. Seven of the eight attributes showed a statistical difference ( $p < 0.001$ ) with latency showing a  $p$  value of 0.05. Lind et al showed that the pitch of the cry is lower in DS but also acknowledged that this change in pitch can be altered in infants with other serious

diseases, not only in infants with DS. Pitch alone is not the only attribute in infants DS and other attributes alongside pitch determine the differences. Lind et al did not mention response time in early infancy but discussed that many of the children over a year produced no response to pain such as grimacing or limb movement showing reduced cry response. They also commented that, at this stage, the cry was particularly short.

The authors direct the reader to previous studies for methods and analysis rather than describe how they collected the data in this paper. This leads to the results and discussion appearing disjointed and confusing without access to these studies as they were not available within the literature search.

Hennequin et al (2000) looked at pain expression and localisation of stimulus in DS. This was based on the conclusion of previous studies by Lind et al (1970) and Biersdorff (1994) which suggested that patients with learning difficulties displayed behaviour suggesting a decreased response to pain. Hennequin et al identified 26 people with DS and 75 controls. They were recruited based on attendance at a dental unit within a period of 12 months. Two clinicians were trained and calibrated to apply cold stimulus in the form of ice cubes to the skin until sensation of pain was first felt and then cold stimulus applied to different points to establish localisation.

The study showed that the individuals with DS took longer to express pain and made more errors in localising the stimulus. In the test showing length of time to report pain a Mann-Whitney test showed a significant difference between the individuals with DS and the controls ( $p=0.0005$ ). In the localisation test a Fisher's exact test showed a significant difference for localising cold stimulus on the hand ( $p=0.0005$ ), the face ( $p=0.0005$ ) and the mouth ( $p=0.0005$ ). The authors acknowledged that the study was a pilot and further investigations should be carried out. However, despite the small sample size of DS patients, this is a thorough and well explained project.

In letters to the Lancet in 2001 both Jessop and Brandt wrote to comment on the paper by Hennequin et al (2000). Jessop suggested that the decreased perception of pain may be due to raised opioid peptides in the frontal cortex of this group of individuals. Brandt suggested that there might be a link between Down's syndrome and impaired peripheral somatosensory nerve function.

The literature suggests that there may be reduced perception of pain in children with Down's syndrome (Lind et al, 1970; Martínez-Cué et al, 1999; Hennequin et al, 2000) which concurs with the clinical observations of the RHSC Yorkhill pilot study that children with DS do not feel or express the same level of pain as the general population (Cruikshank et al, 2008). The mean delay from symptom onset to the diagnosis of arthritis in children with DS was 2.9 years compared to 0.3 years in JIA and a factor in the delay was felt to be the lack of expression of pain (Cruikshank et al, 2008). A number of these patients had not complained of joint pain when seen by a health

professional. It is also interesting to note that, in the 25 cases described by Yancey et al (1984), Olson et al (1990) and Juj et al (2009), only two of the children presented complaining of pain whereas the majority of patients presenting with JIA in the general population will complain of pain.

### 2.9 Growth retardation

Growth retardation and delayed bone age are important in MSK development and related disorders.

There have been numerous studies into growth retardation in children with DS. Cronk, Crocker, Pueschel, Shea, Zackai et al (1988) examined 730 children with DS aged from one month to 18 years to create DS specific growth charts in America. The children were divided into five groups which makes the study more robust as each group had a different age range and were measured at different intervals. Comparison of the five groups showed no statistical significance so all results were analysed together. There were no exclusions but complicating medical disorders were recorded because of their potential impact on growth.

Myrelid, Gustafsson, Olars and Annerén (2002) carried out a similar study to create DS specific growth charts in Swedish children. They examined 354 children between birth and 18 years monthly until aged 2, quarterly until aged 3 and thereafter annually. Their only exclusion was individuals who had received growth hormone previously. Their results showed that children with DS were shorter in stature than the general population (-2.5 SD, Swedish standard). Myrelid et al (2002) compared their results with Cronk et al (1988) commenting on the fact that there were differences between the mean final heights of the Swedish and American children which they couldn't explain but which could be down to ethnic differences or size of the study population.

Myrelid et al and Cronk et al both agreed that there is a reduction in height in children with DS compared with the general population. Both studies correlated that the period of the largest impairment in growth velocity is between six months and three years. Similar studies carried out by Cremers, van der Tweel, Boersma, Wit and Zonderland (1996) in Dutch children and Kimura, Tachibana, Imaizumi, Kurosawa and Kuroki (2003) in Japanese children showed comparable results indicating a trend and, therefore, more validity to the results.

Various studies looked at growth hormone (GH) deficiency in children with DS and the use of GH to improve height outcome in these children. Castells, Torrado, Bastian and Wisniewski (1992) carried out a study on 20 children with DS measuring serum GH levels over 24 hours. Serum GH response to levodopa and clonidine stimulation was also recorded. Results showed reduced GH concentration in response to levodopa and clonidine stimulation. A study with a control group is



required for more conclusive results, but this study suggests growth hormone deficiency may be an important factor in growth retardation in DS.

Castells, Beaulieu, Torrado, Wisniewski, Zarny and Gelato (1996) followed the 1992 study up with a further study this time including a control group. Their aim was to determine whether hypothalamic or pituitary dysfunction was the cause of growth retardation. Three groups were involved. These were a group of 14 children with DS, a group of seven children who were small in stature but had normal GH serum levels and a group of 25 children with normal heights and weights. The results showed no significant difference in GH levels following GH releasing hormone between the groups but a significantly lower response to levodopa and clonidine in the DS group. Maximum response to levodopa stimulation in controls was  $12.3 \pm 11.1$  and in the children with DS was  $5.7 \pm 6.3$ ;  $p < 0.0003$ ). These results suggested a hypothalamic link to reduced GH levels in DS. Although the number of children with DS is smaller in this study compared to the 1992 study, these results are more conclusive due to a comparison with control groups. Both studies showed retardation in bone age in the children with DS.

#### 2.10 Podiatric disorders and gait

Specific foot problems are described in DS such as pes planus, syndactyly and hallux valgus and, due to the frequency of other severe pathologies in DS, these problems can be overlooked in their importance. (Concolino et al, 2006).

Prasher, Robinson, Krishnan and Chung (1995) performed a podiatric exam on three groups of children, also examining footwear. The first group was 50 children (29 males) with DS, the second was 50 children (32 males) with a learning disability (LD) other than DS and the third group of 50 children (20 males) had no learning disability. This study showed an increase in foot pathology within the DS group and the non DS group with LD compared to the non LD group ( $p < 0.05$ ). The DS group had greater incidence of pes planus (58% versus 20% for the other groups). Footwear was generally good in all the groups although the children with an LD were more likely to wear ill fitting footwear. This study, however, displayed drawbacks in that the children were selected by their school so recruitment may have been biased but it does highlight the need for correct footwear and vigilance regarding pedal problems to prevent the development of more serious conditions.

Concolino, Pasquzzi, Capalbo, Sinopoli and Strisciuglio (2006) examined 50 children (19 males) with DS and a control group of 100 children (32 males) without DS in Italy. Full orthopaedic examination of the lower limbs and podiatric examination was carried out by the authors. Results showed an increased incidence of bony deformities of the forefoot in the children with DS (90% compared to 10% in the controls) and also an increase in joint laxity (20% showed severe laxity

and 80% moderate laxity compared to 20% showing slight laxity and 80% with no laxity in the control group). It was concluded that podiatric examination is important when these children are reviewed as early detection and treatment will improve quality of life. This study showed a very thorough examination of each child and concluded that podiatric exam is an important inclusion as treating pedal problems can improve posture and improve quality of life for children with DS.

A number of studies have investigated gait and posture in children with DS (Shumway-Cook et al, 1985; Selby-Silverstein et al, 2001; Galli et al, 2008; Chang et al, 2009; Rigoldi et al, 2010).

Selby-Silverstein, Hillstrom and Palisano (2001) concentrated on the effect that using foot orthoses (FO) had on posture and gait in DS. The investigator examined 16 children with DS and 10 controls. The DS children were examined at three separate visits where they were casted for FOs at the first, examined in sneakers at the second and then examined with sneakers and FOs at the third. The control children were examined twice and not casted for FOs. The mean resting stance position in children with DS changed from 11 degrees everted barefoot to 3 degrees everted in FOs (73% change;  $p < 0.001$ ) and the mean transverse plane foot angle for children with DS 7 degrees walking in sneakers and 0 degrees walking in sneakers and orthosis ( $p < 0.001$ ). This study is of a very small group of children and may benefit from a higher population with a wider range across the learning disability spectrum. A larger number may be more conclusive about the appropriate use of FOs. The authors concluded that their findings warranted further investigation particularly around the use of FOs affecting the development of external tibial torsion and the effect on the knees. They acknowledged that, to ensure the appropriate alignment, foot orthoses and shoes should be evaluated correctly before provided to the wearer.

Galli, Rigoldi, Brunner, Virji-Babul and Giorgio (2008) and Rigoldi, Galli and Albertini (2010) both examined gait development and pattern in children with DS in Rome, with the latter also examining joint stiffness. Both studies carried out kinetic studies using a gait walkway. Galli et al examined 98 children with DS and 30 control children and Rigoldi et al followed 32 children with DS and studied them in childhood, teenage years and adulthood. Both studies found that the children with DS showed a statistically significant lower step length than controls ( $p < 0.05$  in both studies), statistically significant lower velocity ( $p < 0.05$  in both studies) and Rigoldi et al also showed a statistically significant higher step width ( $p < 0.05$ ). Both studies concluded that reduced step length and lower velocity are due to compensation to increase stability while walking as movement is unstable due to lax ligaments and hypotonia.

Chang, Kubo and Ulrich (2009) studied development of walking from walking onset over a six month period in children with DS compared to children with typical development. They examined eight toddlers with DS (three female) and eight toddlers with typical development (four females) walking across a gait walkway. Although their main focus was muscle burst duration and

frequency as well as timing, they also found that the toddlers with DS showed a statistically significant higher step width and lower velocity ( $p < 0.05$ ). This correlates with Galli et al (2008) and Rigoldi et al (2010). The step length variation was not consistent over this six month period. This may be because of the age and stage of the children and the fact that it is a very small study of eight children in each group. Rigoldi et al (2008) do not mention the age range of the children examined but the youngest child examined by Galli et al was five years. This suggests that a longitudinal study covering a number of years from walking onset with a higher number of children may produce data to show if step length decreases consistently over a period of time.

### 2.11 General care and screening

Pueschel, Annerén, Durlach, Flores, Sustrová and Verma (1995) published a committee report for the International League of Societies for Persons with Mental Handicap on guidelines for the optimal care of people with DS. They advised when screening by health professionals for particular medical conditions related to Down's syndrome should be carried out, divided into four age categories – neonatal, infancy, childhood and adolescence and adulthood. Each condition is discussed fairly briefly as they acknowledge that it is not possible to discuss all related conditions within the paper. However, some of the screening is advised into adulthood, particularly weight, eye screening, hearing exam and thyroid screening supporting the reasoning that people with DS should have regular assessment. In relation to MSK disorders, atlantoaxial, hip and patellar instability, foot disorders and scoliosis are mentioned within the screening. There is no mention of arthritis in DS.

Roizen and Patterson (2003) discussed the genetics, assessment and management of DS. They divided the various health problems associated with DS into three categories – those to prevent; those to monitor and those that require vigilance. Arthritis was in the last category. They agreed that arthritis occurs more frequently in the Down's population – but not frequently enough to warrant routine monitoring procedures (Roizen and Patterson, 2003). They mentioned the delay to diagnosis and used it as the reason why arthritis requires vigilance. However, the evidence base behind their comments is weak due to the use of only two references (Olson et al, 1990; Ihnat et al, 1993) despite others being available (Yancey et al, 1984; Padmakumar et al, 2002). Incorporating a routine monitoring procedure would help diagnose multiple MSK problems within this population.

Harrison, Plant and Berry investigated regular screening for people with learning disabilities within a primary care centre. All patients with learning disabilities were identified and records checked for last contact with a health professional. They discovered that only 22% of the 60 patients identified had attended in the last year. One patient hadn't attended for 14 years. Invitation letters were sent to invite the patients in for screening and by the end of the year 92% of the 60

patients had attended for health screening. This appears to have been a very well run and executed study. The improvement in numbers for screening was extremely high. The authors took the patients' individual needs into consideration as well as general screening and also took time to discuss and consider the needs of the carers also. They also offered a choice of clinic or home for the assessment to allow flexibility for the carers.

Weijerman and de Winter (2010) investigated the care of children with DS. They also discussed the background to DS and assessment involved and the different related health problems. Arthritis is discussed under the orthopaedic heading in one sentence that a rare arthropathy can develop in children with DS.

### 2.12 MSK screening in DS

It is obvious that MSK disorders are still not considered important within the care or screening of children with DS. The papers, looking specifically at arthritis in DS, concur that arthritis is misdiagnosed and these delays can lead to significant damage to the joints and, therefore, a great reduction in mobility. This then makes a significant impact on the quality of life of these children.

An MSK exam can be done quickly and efficiently following the pGALS (paediatric gait arms legs spine) (Figure 2.1) criteria. GALS is a screening process suggested by Doherty et al (1992) as a practical tool for health professionals to follow. Foster et al (2006) revised this tool to create a similar process for children.

Goff et al (2010) researched the addition of pGALS to routine assessment on presentation at an acute paediatric unit. Presenting complaint, diagnosis, time taken in completing pGALS and a patient scale on acceptability were recorded. The examining doctor had no previous rheumatology training. He was given the video teaching tool of pGALS being performed and then observed in the rheumatology clinic performing the assessment prior to the study. The authors conclude that using pGALS does not make a large impact on general assessment and can be carried out in just three to four minutes which is a favourable comparison with the rheumatology specialists. This means it can be carried out completely at initial assessment.

Annual reviews are recommended for children with DS due to their greater health requirements. (McGrath, 2010) At present these reviews are not mandatory but are generally carried out. The importance of this screening is summed up by a parent that took part in the study carried out by Harrison et al (2005). An elderly carer claimed, 'I have been waiting years for my son to be called for the type of screening I take for granted' (Harrison et al, 2005).

There are many various health problems linked to DS making screening a difficult and, possibly, prolonged exercise. However, the addition of an MSK screen should not extend this greatly and its addition is extremely important in this group of patients. This will lead to earlier diagnosis, reduced incidence of joint damage, improved prognosis and continued quality of life for these children.

### 2.13 Summary:

A wide range of MSK problems occur in DS during childhood. These have been identified in a significant body of literature over a number of years, however their true prevalence in the population is not known, nor the impact in terms of disability. This study aims to screen a population of children under the age of 16 years with DS to identify the prevalence of MSK problems, to identify their nature and impact on this group of children.

pGALS Musculoskeletal Screening Examination

*Screening Questions:*

Do you have any pain or stiffness in your joints, muscles or your back?

Do you have any difficulty getting yourself dressed without any help?

Do you have any difficulty going up and down stairs?

*Gait:*

Observe the child walking

-Walk on tip-toes/walk on your heelsø

*Arms:*

-Put your hands out in front of youø

-Turn your hands over and make a fistø

-Touch the tips of your fingersø

Squeeze metacarpal joints

-put your hands together/put your hands back to backø

-reach up and touch the skyø

-look at the ceilingø

-put your hands behind your neckø

*Legs:*

Feel for effusion at the knee

Active movement of knees and feel for crepitus

Passive movement ( full flexion, internal and external rotation) of hip

*Spine:*

-Open your mouth and put three( *child's own*) fingers in your mouthø

Lateral flexion of cervical spine -try and touch your shoulder with your earø

Observe spine from behind

-Can you bend and touch your toes?ø-observe curve of spine from side and behind

*Figure 2.1 pGALS exam (Foster and Cabral, 2006)*

## **CHAPTER 3**

### **MATERIALS AND METHODOLOGY**

This chapter will look at the evidence base behind the equipment and methods used in this study. This will include ethics in medical research and the examinations, measurements and equipment involved in the study.

#### **3.1 Ethics**

This study submitted an ethics application which was approved by the West of Scotland Research Ethics Committee (Appendix 1). Medical research must be approved by a medical ethics committee prior to commencement. Medical ethics is in place to protect the participants and those conducting the study. Ethical committees were created to allow assessment of research proposals from different viewpoints. Committees consist of representatives from clinical, research and community groups (Davidson and O'Brien, 2009). Community involvement is particularly important as these representatives are likely to digest the information in a similar manner to the patients.

Literature on history of research shows experiments performed over centuries with no regard for the subjects. Queen Cleopatra carried out research into the development time period of male and female foetuses. This was done by the insemination of servants who were then executed and the foetus examined post mortem for development status (Kottek, 1981; Cohen, 1990). In 1796 Edward Jenner exposed a boy to the cowpox virus and then inoculated him with smallpox to see if it would develop (Gross and Sepkowitz, 1998) and numerous medical experiments were carried out by the Nazis during World War II in the concentration camps. Many of these experiments resulted in the torture and, in the majority of cases, death of the prisoners involved (Cohen, 1990).

Following the Nazi trial at Nuremberg in 1947, the Nuremberg code was developed to protect people from unethical research and, most importantly, introduced the necessity for informed consent (<http://ohsr.od.nih.gov/guidelines/nuremberg.html>). In 1964 the Declaration of Helsinki was developed by the World Medical Association to provide ethical principles for research involving human subjects ([www.wma.net](http://www.wma.net)). This is regularly updated with the most recent update in 2008.

In 1979 Beauchamp and Childress formulated the four main principles in ethics. These are now the standard model for teaching ethics. (Gillon, 1994; Lawson, 2011)

### 3.1.1 Autonomy

Autonomy describes each individual's ability to make their own decisions which should be respected in research. All relevant information involved in the proposed research should be given to the individual to allow them to make a full, informed decision about participation. Respecting autonomy also includes ensuring good communication, maintaining confidentiality and avoiding deception.

### 3.1.2 Beneficence and non-maleficence

The principles of beneficence and non-maleficence describe decisions made in the best interests of each individual. Beneficence describes a decision that will cause no harm whereas non-maleficence describes decision making intended not to cause harm to the individual despite possible risks involved or where the benefits surpass any involved risk.

### 3.1.3 Justice

The principle of justice involves treating all individuals in an equal manner and allowing fair distribution of resources. In medical care this means allowing each individual the same access to treatment and relevant information although treatment patterns will be different for each person. In research it means ensuring each participant receives the same information regarding the study, the same experience throughout the study and the same opportunities that result from the research.

These principles all combine in individual decision making as each can conflict. An individual can be given all information regarding treatment that is in their best interest which may or may not have side effects (beneficence and non-maleficence) but they may decide to refuse the treatment despite having all the information and, if considered competent, their autonomy in making that decision must be respected.

Nurses involved in research are bound by the Nursing and Midwifery Council Code of Professional Conduct which includes treating the client as an individual, respecting their dignity and upholding their right to be fully involved in decisions about their care ([www.nmc.org/Nurses-and-midwives/The-code/The-code-in-full](http://www.nmc.org/Nurses-and-midwives/The-code/The-code-in-full)). It also states that you must respect and support people's rights to accept or decline treatment and care. All these take the principles of ethics into account. The nursing code of conduct was originally developed by the United Kingdom Central Council for Nursing and Midwifery in 1983 and is reviewed regularly ([www.nmc.org](http://www.nmc.org)).



### 3.1.4 Informed consent

All relevant information must be given to participants in medical research to allow them to make a full informed decision to consent to taking part. Research cannot proceed without participants signing a consent form. The Nuremburg Code states 'The voluntary consent of the human subject is absolutely essential' (<http://ohsr.od.nih.gov/guidelines/nuremburg.html>). Participants cannot be coerced into signing consent and must be allowed time to consider all the information prior to consent being signed and the research commenced.

### 3.1.5 Ethics in research involving children

With respect to this study our main consideration was that it required consent for children being involved and, in particular, the ethical issues surrounding research involving individuals with learning disabilities and this was examined fully. Several issues have to be considered in these cases such as whether the individual is able to give informed consent, how their level of understanding can be tested and, even if unable to give informed consent, can they give assent to the research.

Research involving children is given more ethical consideration to ensure the child is not being exploited or coerced into the research. Ethics committees may scrutinise paediatric research projects more closely than an adult project (Davidson and O'Brien, 2009). At present parental consent is required for children up to the age of 16. If the child is considered mature enough to understand the information and make an informed decision, they may sign assent as an agreement to take part, although parental consent is still required. Information sheets should, therefore, be designed to allow an understanding level in accordance with the age of the child in addition to parent information. It is important to respect the child by involving them in the decisions (Davidson and O'Brien, 2009). Information sheets for this study were designed using three levels of understanding for the children as well as information sheets for parents. The parents were then given the decision to choose which level of information sheet was appropriate for their child. (Appendix 2)

In 2002 the Royal College of Paediatrics and Child Health (RCPCH) outlined six key principles (Table 3.1) when revising the 1992 document on guidance on the conduct of medical research with children (Neill, 2005).

A decision was made to involve children between the ages of two and fifteen in this study as, over 16, the child is considered an adult with learning disabilities at which point the ethical

considerations become very complicated, particularly in the issue of informed consent. The adult has to be deemed incompetent to make an informed decision before the parent or surrogate makes the decision for them. The surrogate must fully consider the benefits and risks to the participant before signing consent on their behalf. Researchers prefer not to use surrogates unless absolutely necessary as it is considered inappropriate by many and would require a strong justification for the ethics committee (Wiles et al, 2005). Even if surrogate consent has been given, the individual's wishes still have to be considered as their rights to decide to participate requires to be recognised (Lewis and Porter, 2004).

Although parental consent was given for the study, the rights of all the children involved were considered at all times as they were given the right to refuse to allow any examination involved in the study visit.

### Six Key Principles

1. Research involving children is important to benefit all children and should be conducted in an ethical manner.
2. Children are not small adults; they have an additional unique set of interests.
3. Research on children should only be done if comparable research cannot be done on adults.
4. Research not of direct benefit to the child is not necessarily unethical or illegal.
5. All proposals involving medical research on children should be referred to a research ethics committee.
6. Legally valid consent should be obtained from the child, parent or guardian as appropriate. Parental consent for school children should also have the child's agreement.

*Figure 3.1: Six principles for research involving children; RCPH Ethics Advisory Committee, 2000 (Neill, 2005)*

### 3.2 Subject identification and recruitment

The Glasgow thyroid register and the community paediatrician's register were assessed to identify children with Down's syndrome aged between 2 and 15 resident in Glasgow. 147 children were identified from these registers. Five children were excluded due to serious illness and 142 children invited to participate in the study. Study packs including an invitation letter and parent's information sheet were sent out. These packs also included three separate children's information sheets which aimed at three different levels of understanding to allow the parents to decide which sheet was most appropriate for their child to understand. These were then followed up with a phone call. To avoid parents feeling they were being harassed, it was considered a non response after three unsuccessful contact attempts.

### 3.3 Inclusion criteria

Children identified to have DS and resident in Glasgow and aged between two and sixteen years.

### 3.4 Exclusion criteria

The exclusion criteria were:

1. Children with co-morbidities and too unwell to take part or considered unsuitable by the community paediatrician or GP.
2. Children under two or over sixteen.
3. Children who declined or were unable to participate.

### 3.5 Study visit examinations

This study was designed to examine a variety of measurements related to MSK disorders and anthropometric measurements in Down's syndrome including a full joint examination assessing for joint limitation, hypermobility and evidence of synovitis, assessment of entheses and podiatric examination. Height, weight, head circumference and arm span were measured and questionnaires were completed by the parents.

Participants were invited to attend a one off study visit at their community paediatrician annual review appointment, at RHSC Yorkhill or as a home visit to allow flexibility and choice. All study participants were examined by the same research nurse and the same podiatrist to allow for consistency and the same equipment was used for each study visit. Each study visit lasted approximately 45-60 minutes depending on the ease of co-operation of individual children.

### 3.5.1 MSK examination

The main component within the study visit was a complete MSK and podiatric examination of each child. An adapted version of the pREMS (Paediatric Regional Examination of the Musculoskeletal System) assessment (Appendix 3), developed by Foster et al (2011) from the adult REMS assessment developed by Coady et al (2004), suitable for this population of children was carried out during the study visit.

The shorter pGALS method of examination (Figure 2.1) has been shown to be sensitive and acceptable to school age children and parents (Foster et al, 2006). However, it is a screening tool to identify active and limited joints and the pREMS gives a more thorough examination of each anatomic region although younger children may require a different approach depending on compliance. This was more suitable for identifying hypermobile joints. Foster et al (2011) developed pREMS to work with pGALS as a thorough method of examination with an aim to incorporate both assessments into routine practice to improve outcome.

For this study, examination did not completely adhere to the full pREMS procedure due to the compliance of children with learning difficulties. Each child was considered on an individual basis and examined accordingly. Children who were non compliant with certain parts of the examination had a reduced exam carried out to their level of tolerance. Often observation of children's functioning was supportive evidence, for example sitting posture with feet behind head strongly suggested hypermobile hips even if examination was not possible. In general the children were very compliant with the study process. pREMS was shown to be a reliable method of examination and well tolerated as a screening tool for MSK problems in this population.

MSK examination was carried out to determine the presence of arthritis, hypermobility, enthesitis, signs of joint instability, scoliosis of the spine, limb length discrepancy and genu valgum (knock knees).

### 3.5.2 Arthritis

All joints were examined for signs of arthritis including pain, heat, swelling and limitation of movement. The number of active and limited joints found on examination was noted as per the core outcome variables for arthritis disease activity. The core outcome variables incorporate patient or parent global assessment, physician's global assessment, the childhood health assessment questionnaire and the number of active and limited joints present on examination (Giannini et al, 1997; Gardner-Medwin and Southwood, 2005).

The Childhood Health Assessment Questionnaire (CHAQ) (Appendix 4) is a disease specific health instrument that measures functional ability in daily living activities in children with juvenile idiopathic arthritis (Nugent et al, 2001). This questionnaire asks how the child's activities have been limited by their condition over the last seven days. Parents are asked to complete the child form for children up to 11 years and the child completes the adolescent form (Appendix 5) after this age. For this study level of understanding and learning disability was ascertained and parents asked to complete the child form for all children even if they were over 11 if they felt it more appropriate for their child's level of learning disability. It has been shown to be reliable and sensitive in measuring how children function with arthritis (Dempster et al, 2001).

The Child Health Questionnaire (CHQ) has been designed to assess the well being of children with underlying disease (Nugent et al, 2001). This questionnaire asks how the child's illness affects them in different areas such as physical, emotional, general well being and also how it affects the family as a whole. (Appendix 6)

The CHAQ also incorporates a parent/child and physician global assessment. This involves the completion of an analogue scale 10cm long to determine level of pain and wellness over the last 7 days.

### 3.5.3 Hypermobility

The number of hypermobile joints was also recorded and general hypermobility was assessed by the use of the Beighton scoring system (Figure 3.2) and Brighton criteria (Figure 3.3).

The Beighton scoring system shows limitations as it only includes 9 joints. Joint hypermobility syndrome is a complex condition to diagnose as there is no current gold standard in place for normal joint mobility (Remvig et al, 2007). Simmonds and Keer (2007) acknowledged that the Beighton score on its own has been criticised for only sampling a few joints but incorporating it into the Brighton criteria makes it stronger as it links joint hypermobility with other symptoms and characteristics of connective tissue laxity.

Smits-Engelsman, Klerks and Kirby (2011) examined the use of the Beighton score in children and concluded that the Beighton score was a valid instrument to calculate generalised joint mobility in children but recommended increasing the threshold to 7/9 instead of 5 as they believed that having the threshold at 5/9 classified too many children as hypermobile incorrectly.

Juul-Kristensen, Røgind, Jensen and Remvig (2007) showed that reproducibility for the Beighton tests and Brighton criteria was good ( kappa values mostly above 0.80 and 0.73 respectively) but suggested further research is required.

In a letter to the British Journal of Rheumatology Silman and Day (1987) wrote “we believe, however, it is preferable to measure the actual range of movement at one or more joint sites rather than relying on fairly arbitrary cut off levels”. This was in response to a study comparing the mean Beighton scores in population groups. Silman and Day considered this inappropriate as individuals with the same Beighton score cannot be assumed to be the same in relation to their mobility.

The Beighton scoring system was developed for epidemiological studies as opposed to a diagnostic test but is used in conjunction with the Brighton criteria to diagnose joint hypermobility syndrome. It has received criticism and researchers have attempted to create more updated systems but it remains the universal assessment for studies in hypermobility (Grahame 1990). The Beighton score still continues to be used today.

The Beighton score has been used in previous population studies and we have used Clinch et al, 2011 specifically to compare results which is described in Chapter 5.

In this study the Beighton scores and Brighton criteria were used in conjunction with range of movement examination of all joints to provide a more complete assessment of the level of hypermobility of each child with the hypermobility of all joints being specifically charted to avoid incorrect assessment from the scoring systems alone.

#### 3.5.4 Enthesitis

Enthesitis is inflammation at the site that a tendon, ligament, fascia or joint capsule is attached to the bone. Inflammation at these sites occurs in the related group of conditions known as seronegative arthropathies in adults, which include ankylosing spondylitis (inflammation of the spinal column), psoriatic arthritis (arthritis related to psoriasis) and reactive arthritis (arthritis following infection) (McGonagle and Benjamin, 2009), and in JIA enthesitis related arthritis, but currently not psoriatic arthritis, as the classification stands, although in adult disease this association is well described. It can also include arthritis related to inflammatory bowel disease. Spondyloarthropathies are an adult group of inflammatory disorders that can all include inflammation of the spine and have a negative rheumatoid factor (Keat, 2008). They were first described as associated with a positive HLAB27 (Human leucocyte antigen B27), 95% of ankylosing spondylitis and 75% of reactive arthritis cases are HLA B27 positive with lower percentages in psoriatic arthritis. A positive HLAB27 can also aid a diagnosis of early psoriatic arthritis (Stafford and Youssef, 2002).

Only a certain number of entheses are routinely palpated and, in children, the commonest sites of enthesitis to be examined are the insertion points of the plantar fascia on the base of the foot and the Achilles tendon insertion at the heel (Gardner-Medwin and Southwood, 2005). The entheses

points are pressed to elicit signs of tenderness which indicates enthesitis and several scoring systems have been devised to assess this. (McGonagle and Benjamin, 2009).

The scale used in the study is based on the Mander enthesitis index where intensity of pain is graded on a 0-3 scale - 0 = no pain; 1=mild tenderness; 2=moderate tenderness; 3=wince or withdraw (Mander et al, 1987; Heuft-Dorenbosch et al, 2003). This scale covered a 0-2 scale: 0=no pain; 1=tender; 2= tender + grimace. (Appendix 7)

#### 3.5.5 Podiatric examination

A foot examination standardised for the study was devised and carried out by a single consultant podiatrist, very experienced in paediatric podiatry, based on current examination standards and techniques (Goel and Watt, 2010) looking at foot type and posture, characteristics of the foot, shoe type, gait and nail conditions. (Appendix 8) All subjects were examined by the same researcher using the same methodology for each in order to maintain consistency.

The main joint complexes in the foot were assessed physically for range of motion.

Foot type was recorded as shape of the foot, foot length and arch height. Posture was examined in relaxed and dynamic stance. Gait was examined with particular attention to hypotonic gait, genu valgum or varum (knock knees or bow legs), pelvic tilt or limp. Any deformities were recorded and also skin changes. Examination of nails and entheses were included.

Footwear was examined with regard to correct sizing, type and suitability of footwear, use of orthoses (eg insoles) and wear marks. Wear marks should correlate with foot posture during walking and can indicate any issues with gait such as walking with over pronation or over supination (feet rolling inwards or outwards). Incorrect footwear can lead to disorders such as flat feet, hallux valgus (bunions), toe deformities and calluses (Prasher et al, 1995; Menz and Morris, 2005).



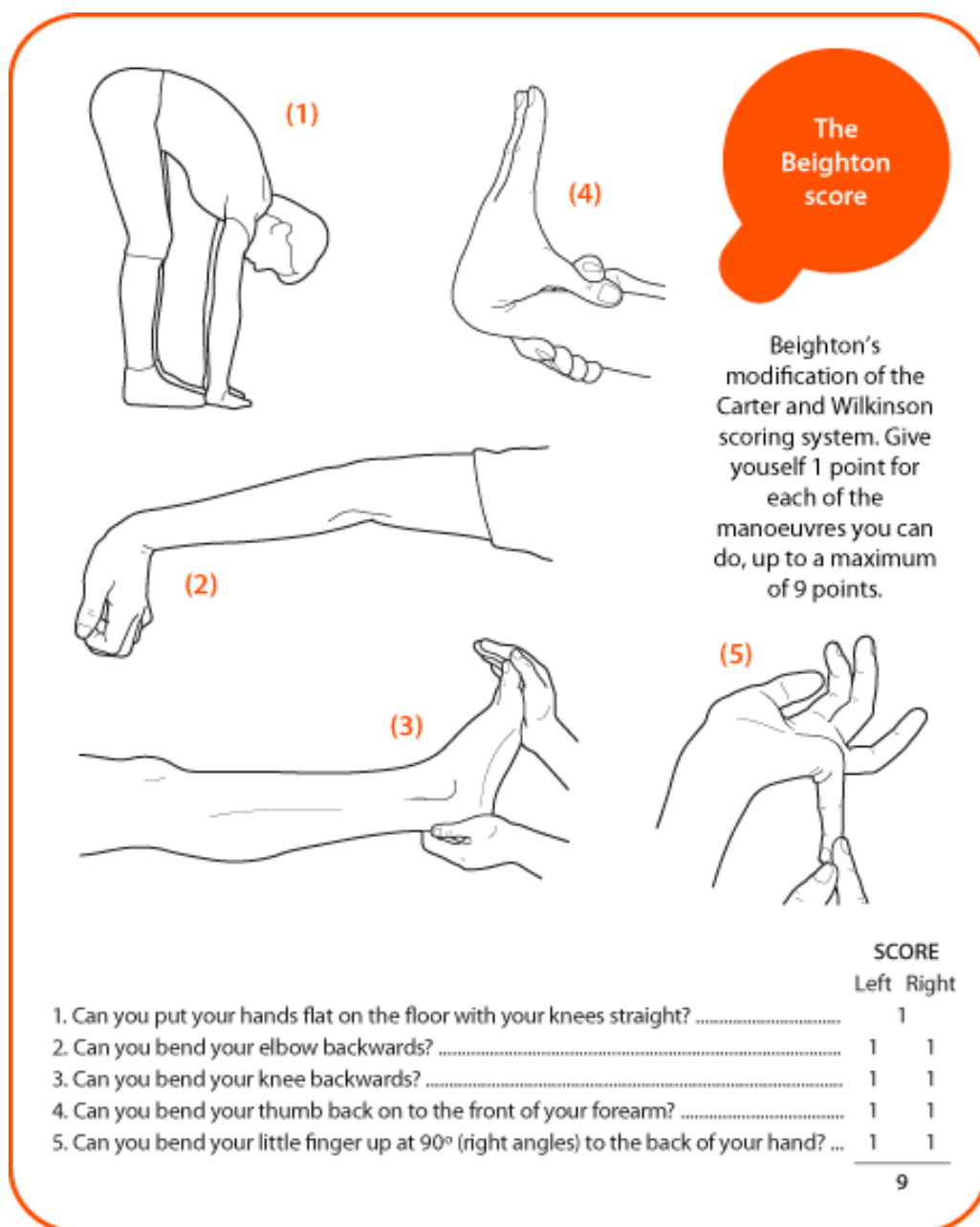


Figure 3.2: Beighton score ([www.arthritisresearchuk.org](http://www.arthritisresearchuk.org))

## REVISED DIAGNOSTIC CRITERIA FOR THE BENIGN JOINT HYPERMOBILITY SYNDROME (BJHS)

### Major Criteria

- A Beighton score of 4/9 or greater (either currently or historically)
- Arthralgia for longer than 3 months in 4 or more joints

### Minor Criteria

- A Beighton score of 1, 2 or 3/9 (0, 1, 2 or 3 if aged 50+)
- Arthralgia (> 3 months) in one to three joints or back pain (> 3 months), spondylosis, spondylolysis/spondylolisthesis.
- Dislocation/subluxation in more than one joint, or in one joint on more than one occasion.
- Soft tissue rheumatism. > 3 lesions (e.g. epicondylitis, tenosynovitis, bursitis).
- Marfanoid habitus (tall, slim, span/height ratio >1.03, upper: lower segment ratio less than 0.89, arachnodactyly [positive Steinberg/wrist signs]).
- Abnormal skin: striae, hyperextensibility, thin skin, papyraceous scarring.
- Eye signs: drooping eyelids or myopia or antimongoloid slant.
- Varicose veins or hernia or uterine/rectal prolapse.

The BJHS is diagnosed in the presence two major criteria, or one major and two minor criteria, or four minor criteria. Two minor criteria will suffice where there is an unequivocally affected first-degree relative.

BJHS is excluded by presence of Marfan or Ehlers-Danlos syndromes (other than the EDS Hypermobility type (formerly EDS III) as defined by the Ghent 1996 (8) and the Villefranche 1998 (9) criteria respectively). Criteria Major 1 and Minor 1 are mutually exclusive as are Major 2 and Minor 2.

*Figure 3.3: Brighton criteria ([www.hypermobility.org](http://www.hypermobility.org))*

### 3.5.6 Psoriasis and psoriatic arthritis

The case series of children with DS arthritis (Cruickshanks et al, 2008) showed that the majority of the children displayed characteristics of psoriatic arthritis. PsA belongs to the group of spondyloarthropathies. Although linked to psoriasis, the child may not have any history of psoriasis or current psoriatic lesions. Joint symptoms can occur prior to any evidence of the skin condition appearing in approximately 15% of patients (Southwood et al, 1989; Duran-McKinster et al, 2000; Veale and Fitzgerald, 2002; Stoll et al, 2006; Leung and Lim, 2007; Taniguchi and Kamatani, 2007; Stoll et al, 2008; Prignano et al, 2010).

Parents were asked if the child had a history of psoriasis or if there was a family history of psoriasis in accordance with the ILAR (International League Against Rheumatism) classification of psoriatic arthritis (Gardner-Medwin and Southwood, 2005) (Table 3.5)

Other clinical features of PsA include nail changes such as pitting, ridging and onycholysis (Tudor, 1976; Southwood et al, 1989; Duran-McKinster et al, 2000; Veale and Fitzgerald, 2002; Leung and Lim, 2007; Taniguchi and Kamatani, 2007; Maejima et al, 2010; Natarajan et al, 2010; Prignano et al, 2010).

Nails were examined for the above conditions and presence recorded. Number of nail pits was also recorded.

Fingers and toes were examined for dactylitis which is common in PsA. This appears as swelling of the entire digit, mainly caused by inflammation and swelling in the flexor tendon sheaths and is referred to as a sausage digit (Leung and Lim, 2007). This dactylitis has been observed regularly in children with psoriatic arthritis as compared to children with JIA and often without evidence of psoriasis (Stoll and Punaro, 2011).

### 3.5.7 Spine

The movement level of the lumbar spine was recorded using the modified Schober's test. An anchor point is identified at the L5-S1 level of the lumbar spine (dimples of Venus), a 10cm mark above and a 5cm mark below are marked while the patient is upright. They are asked to bend forward and the measured segment should increase from 15cm to 21cm. (Gladman et al, 2004). Schober's test is one of the clinical tests used in population studies examining lumbar mobility in ankylosing spondylitis (Macrae and Wright, 1969; Gran et al, 1985; Mitra et al, 2000) and is a quick test to carry out. However this test displays limitations in this study cohort as accuracy may have been affected by the children's level of understanding and level of compliance.

### 3.5.8 Anthropometric measurements

Standing and sitting height were measured using a Leicester Height measure. Sitting height was measured to establish trunk and leg length (Gerver and Bruin, 1995; Fredriks et al, 2005). The Leicester height measure was chosen due to its portability as it was easily carried to various locations where study visits were carried out. It is also relatively inexpensive and is comparable in accuracy as the more expensive models (Voss and Bailey, 1994).

Weight and body composition including bioelectrical impedance analysis (BIA) were recorded using Tanita scales. This is measured in Ohms and works on the fact that lean muscle will act as a conductor of electricity due to the high level of water and electrolytes it contains as oppose to fat tissue. A higher impedance value is indicative of a higher amount of body fat. ([www.tanita.com](http://www.tanita.com)). The reproducibility of anthropometrical and BIA Tanita measurements of fat mass are comparable in children and are convenient for epidemiological studies ( Sun et al, 2003; Kettaneh et al, 2005). Because the Tanita scales use an electrical signal, it was checked that none of the study participants had a pacemaker in situ due to the high risk of cardiovascular problems in this population. It was considered safer to avoid any risk that the electrical signal might have interfered with the function of the pacemaker. However it was also limited in this study cohort due to restlessness as the children have to stay still on the scales for a few seconds to obtain a BIA measurement.

Head circumference and arm span were also measured as they are indicators of normal growth and development (Smith, 1981; Ishikawa et al, 1987; Hoey and Cox, 1990; Palmer et al, 1992; Mohanty et al, 2001; Gnanavel et al, 2007). Palmer, Cronk, Pueschel, Wisniewski, Laxova, Crocker and Pauli (1992) carried out a study to develop head circumference reference curves for children with DS. Their results showed that males and females with DS have parallel growth and that head growth velocity appears to be similar to that of the general population until 5-6 months of age. Gnanavel, Parkash, Vishnu, Ramachandra and Rajesh (2007) found decreased head circumference in children with Down's syndrome from birth contradicting the findings of Palmer et al. Despite contradictions in results head circumference remains one of several useful indices of a child's development and is commonly used to screen for macro or microcephaly as even small deviations from the normal could be related to various diseases (Ishikawa et al, 1987; Hoey and Cox, 1990; Palmer et al, 1992; Schienkiewitz et al, 2010).

### 3.5.9 Hypotonia

There is no recognised standardised measure of hypotonia other than clinical judgement. Elements of the childhood myositis assessment scale (CMAS) were used as a crude proxy to assess weakness. Core muscle strength was estimated using the CMAS scale (Lovell et al, 1999). This scale determines ease of certain movements such as sitting to standing, steadiness on all fours, rolling from supine to prone and picking up from floor to determine presence of hypotonia. A number of the measurements included in the CMAS score involved a measurement of duration. These measurements were removed from the analysis for the study due to the poor quality and uncertain value of the measurements due to the level of learning disability of the children and their ability to comply with the study measurements.

The CMAS scale is a valid and reliable tool for assessing muscle strength and endurance in children (Lovell et al, 1999; Huber et al, 2004). It was developed by Lovell, Lindsley, Renebohm, Ballinger, Bowyer et al (1999) as a scoring system for juvenile idiopathic inflammatory myopathies, such as juvenile dermatomyositis, to complement manual muscle testing in determining the severity of muscle weakness. It aims to assess the degree of weakness in the proximal myopathy associated with dermatomyositis, but is much more sensitive to small changes than manual muscle testing. They compared the CMAS scores, in children with a myopathy, with the physician's global assessments, manual muscle strength testing (which is unreliable in children under 5), creatine kinase levels and the Juvenile Arthritis Functional Assessment Report (JAFAR) scores, which is a functional assessment questionnaire, and concluded that the CMAS was a valid and reliable scoring system. CMAS scores from morning and afternoon showed  $P < 0.001$  and interrater reliability showed  $P < 0.001$  for each of the 14 items on the CMAS and for the overall score. However they did find that the scores did not correlate with the age at the time of evaluation ( $P = 0.86$ ).

### 3.5.10 General

These examinations were carried out to allow a complete evaluation of each child's musculoskeletal system and development to assess for any underlying or undiagnosed issues. The visit was also utilised as a chance to educate the parents on signs of joint problems such as heat, swelling and inflammation. They were also advised that change of movement could be a sign of possible joint issues such as change in gait or change in use of a joint.

All the children involved in the study were offered a referral to a consultant rheumatologist as a follow up to the study visit. The study personnel understood that the study visit may raise some concerns in the parents who may then prefer an appointment to reassure them. For children who

displayed any limitation in joint movement, the parents were encouraged to attend the rheumatology clinic. Any parents who did not wish referral at that time were advised that they could contact the service at any point up to their child's 18<sup>th</sup> birthday.

The majority of the children who participated in the study were very compliant with the examinations carried out, with the less compliant tending to have a higher level of learning disability. The parents were all very keen to be involved with the study and learn more about their children's joints making the study visits successful and enjoyable.

### 3.6 Validity of measurements and limitations

The above examinations and measurement techniques are shown by literature to be valid and reliable tools in their own areas but this is the first population study of this kind within the DS population so there was no reference to aid whether they would be reliable within this group of children.

The CMAS scoring system had to be amended prior to the study commencing as the aspects that included duration measurements were considered unsuitable for this group of children and, although, the majority of the children were compliant with the tests, the scoring of this was not useful to assess hypotonia.

## **CHAPTER 4**

### **FOCUS GROUPS**

#### *4.1 Introduction*

Concerns arising from a pilot study carried out in The Royal Hospital for Sick Children (RHSC), Glasgow (Cruickshanks et al, 2008) about the delay in diagnosis of arthritis in DS led to a decision to run focus groups to identify any barriers to care for these children with regard to MSK disorders.

Cruickshanks et al (2008) identified 10 children with DS arthritis who had attended the rheumatology department. A number of these children presented late despite numerous contacts with health professionals, including annual review by community paediatricians, regular contact with physiotherapists and school nurses and appointments with orthopaedic consultants. Figures showed a median age at symptom onset of 5.9 (2.6-13.3) years but a median age at diagnosis of 8.1 (4.2-15.6) years. This corresponded with the median time from symptom onset to first paediatric rheumatology appointment of 2.9 (0.1-8.7) years in comparison with 0.3 (0.1-9.9) years for a comparable cohort of 325 children with JIA from the same general population. This delay contributed to very destructive disease at presentation and four of the children were non-weight bearing at first appointment. This correlates with previous literature describing children presenting late with destructive disease (Olsen et al, 1990; Juj and Emery, 2009). However the children in the RHSC pilot study responded well to modern standard treatment for JIA, which is in contrast to previous literature which commented that children with DS didn't appear to respond to treatment (Yancey et al, 1984; Olsen et al, 1990). This may suggest modern treatments, including biologic agents, are more effective.

The pilot study raised concerns that these children were attending multiple medical appointments but signs and symptoms of arthritis were not being recognised until significant joint damage had already occurred. It also suggested that these children were responding well to treatment, contrary to the current literature.

On the basis of these concerns it was considered important to conduct focus groups with the following three groups.

1. Parents of children, who had already been diagnosed with arthritis and were attending RHSC, to discover what their journey to diagnosis had involved and the length of time taken.

2. Community paediatricians who lead the care of children in the community with DS, particularly their annual reviews, and are the gatekeepers to other allied health professionals (AHP) and other services to determine knowledge of MSK disorders and assessments carried out in the DS population.
3. Paediatric rheumatology specialists involved with the care of these children to ascertain their experiences of level of disease, late presentation, prognosis at presentation and also response to treatment.

#### 4.2 Case study

A 15 year old boy was referred to the rheumatology department by orthopaedics at RHSC with marked crepitus in his knee asking if an intra-articular steroid would help. It was discovered on presentation that he had at least a five year history of joint complaints.

- At age 10 he was referred to orthopaedics with a rather an odd gait but received no intervention at that point.
- At age 12 he was referred to physio with flexion in his knee. He was then referred back to orthopaedics by general paediatrics with a marked lumbar lordosis, crepitus in his knees but displaying no apparent pain. His knees were x-rayed at that point. His walking became very limited and he was found to have a full flexion deformity in his right knee which was warm and synovitic. The x-rays were reported as being consistent with multiple epiphyseal dysplasia (MED) and his parents were advised that his mobility would deteriorate gradually.
- At age 13 he was re-referred to physio as he complained of being tired walking short distances.
- At age 14 his hips, knees and elbows were found to be restricted but he did not complain of pain. His knees were crepitus and his gait was described as awful. He was unable to walk short distances and was unable to partake in physical activities at school. His mother thought that he was in pain but was dismissed as over-anxious and advised that his symptoms were the natural progression of MED and he was referred back to physio.
- At age 15 he was referred to rheumatology asking if an intra-articular steroid injection would help as his knee had been synovitic for some time with crepitus present

All these investigation were valid for the complaints this child presented with but all the features of arthritis were not pulled together to make the correct diagnosis for him.

On presentation at rheumatology this child was wheelchair bound. He was found to have widespread polyarthritis with florid synovitis and widespread hypermobility and he presented



with extensive joint damage. His gait was dreadful, he had fixed flexion deformities and swelling in both knees (Picture 4.1 and 4.2), had restricted elbows, shoulders, wrists, neck and temporomandibular joints and subluxation at the wrists (Pictures 4.3). He was also found not to vocalise pain, but had obviously adapted his movement to minimize pain.

This boy responded well to intra-articular and oral steroids and, despite side effects to initial disease modifying rheumatology drugs he responded well to treatment and was able to walk again fairly quickly. This boy is continuing to respond quite well to treatment but is limited in function due to joint damage sustained prior to treatment commencing. He still does not complain of pain and has described his joints as feeling ticklish.

This delay to correct diagnosis caused concern regarding knowledge of MSK disorders in this population of children within other health professionals as particular signs and symptoms of arthritis such as complaints of pain may not be evident. However, in this case, signs of arthritis such as synovitis and crepitus were overlooked or misdiagnosed. If this boy had been referred to rheumatology much sooner his prognosis and outcome would have been much improved.

This case study in conjunction with the concerns raised in the pilot study led to the decision to run these focus groups to establish level of joint damage and concerns at rheumatology presentation and level of knowledge of MSK disorders within the community and how this may be a barrier to early diagnosis.



*Picture 4.1 Swelling and deformity shown in front of knees in DS child with delayed diagnosis of arthritis*



*Picture 4.2: Swelling and deformity shown in back of knees in DS child with delayed diagnosis of arthritis*



*Picture 4.3: Wrist deformity and swelling in hands shown in DS child with delayed diagnosis of arthritis*

### 4.3 Methods

#### 4.3.1 Focus group planning

It was planned to hold all three focus groups within RHSC Yorkhill. It was known that the community paediatricians and paediatric rheumatology specialists held regular educational meetings and each group was approached through a convener to organise the focus group during one of their meetings. Subjects were given information and signed consent forms agreeing to being recorded. It was planned to approach the parents and arrange a convenient and suitable time for those happy to participate to attend RHSC Yorkhill.

The topics for each group were formulated from discussions around the literature and the pilot study, from which the facilitator and supervisor derived a panel of four open ended questions given in the sections below

The planned analysis by the facilitator was around themes highlighted manually within the transcription and extracting relevant quotes for the discussion.

#### 4.3.2 Subject recruitment:

Three focus groups were planned to take participants from three select groups: parents of children with DS who had developed arthritis who already attended the rheumatology department at RHSC, Glasgow; a group of community paediatricians who provided annual review of children with DS; and a group of paediatric rheumatology specialists with experience of the arthritis associated with DS.

Ethics were obtained for the focus groups and participants were invited to take part.

Parents or guardians of children with DS who already attended the rheumatology department at RHSC were identified through the rheumatology department and contacted by telephone to ask if they would be happy to participate and the telephone call followed up with the information sheets and invitation letter.

The community paediatricians were identified through the education meeting facilitator and invited by email to participate in the focus group as part of an educational meeting. The community paediatrician focus group was carried out at RHSC Yorkhill, was facilitated by the author and lasted approximately 60 minutes. It was audio recorded and minuted by an administrator. The transcription was analysed by the author, themes extracted manually and

relevant quotes selected. Participants had given their consent to being recorded. This was a large group consisting of 20 consultant community paediatricians and associated registrars.

The rheumatology specialists were identified through the rheumatology department at RHSC Yorkhill and invited by email to participate in the focus group as part of an educational meeting. Participants gave their consent to be interviewed and recorded. The paediatric rheumatology specialists' focus group was carried out at RHSC, Yorkhill, was facilitated by the author and lasted approximately 60 minutes. It was audio recorded, transcribed verbatim and then analysed by the author, themes extracted manually and relevant quotes selected. Participants gave their consent to be recorded.

Key open questions were identified prior to the sessions. Focus groups were recorded and transcribed. The author facilitated all focus groups.

#### 4.4 Parents

##### 4.4.1 Inclusion criteria

Parents or guardians of children with DS attending the rheumatology department at RHSC, Glasgow

##### 4.4.2 Exclusion criteria

Parents or guardians of children with DS not already attending rheumatology.  
Parents or guardians of study participants.

##### 4.4.3 Questions

The intended questions for the parents' focus group were to ask about any delays from symptom onset to attending paediatric rheumatology and what were their experiences within the health care setting.

##### 4.4.4 Results

Recruitment to the parents' focus group was unsuccessful as the parents approached were unable to commit to being involved or were reluctant to be involved mostly voicing concerns about offering any criticism about the quality of care their children had received. Therefore, no results were obtained

However, after the study commenced, the mother of one of the children who had attended rheumatology at RHSC was interviewed by Arthritis Today magazine, the quarterly magazine produced by Arthritis Research UK, and the comments she made were considered relevant and important in the absence of the focus group data. This parent had not had a good experience and complained about a delay to diagnosis saying that her son had experienced symptoms for approximately four years prior to diagnosis. She had an excellent relationship with her community paediatrician but felt she wasn't taken seriously while trying to find out a reason for her son's symptoms and commented 'if we hadn't been his parents, pushing all the time, he wouldn't be diagnosed yet'. She expressed frustration due to the implication that she had to expect issues with her son's health due to his DS. 'The older doctors in particular took the view that we had to lower our expectations for him because he had Down's syndrome'. This parent has been quite happy with her son's treatment since diagnosis but wishes he had been diagnosed earlier as he has significant joint damage.

#### 4.5 Paediatric rheumatology specialists

The paediatric rheumatology specialist's focus group was asked about delay to diagnosis, response to treatment and education requirements. This group comprised of three consultant paediatric rheumatologists and a paediatric rheumatology specialist nurse.

##### 4.5.1 Inclusion criteria

Paediatric rheumatologists working within RHSC, Glasgow

Paediatric rheumatology nurse specialists working within RHSC, Glasgow

##### 4.5.2 Exclusion criteria

Paediatric rheumatology clinicians not directly managing inflammatory arthritis in children, including children with DS

##### 4.5.3 Questions

Q1. How often have you seen children with Down's syndrome attend with arthritis?

Q2. Were you aware there may be a link between DS and arthritis?

Q3. What have your experiences been with regard to symptom onset to referral time and involvement of other specialties?

Q4. Do you think there is any specific education needed within rheumatology for arthritis in DS?

#### 4.5.4 Results

The main themes extracted from the transcription of this focus group were that these children present with severe disease, they do respond to treatment contrary to literature and that education is recommended for health professionals to improve identification of MSK disorders in children with DS

With regard to the theme of first presentation all the paediatric rheumatologists commented that a large number of the children with DS they had seen over the years with arthritis had been seen quite late in the process. These are a number of the comments made: 'I think we do see a lot of them late because they have other joint problems and are often hypermobile and if their mobility drops people assume it's due to their DS or hypermobility' 'One had been told by a series of health professionals that her mobility was deteriorated due to her associated cardiac disease which had been stable so why her mobility should be getting worse I don't know' 'Similar experience. Cases seen presented late for the same sort of reasons ó symptoms not put down to arthritis' The consensus of opinion was that these children present late with those presenting early in the disease process being a small minority. This concurs with the findings of previous literature that this group of children present late ( Yancey et al, 1984; Olson et al, 1990; Juj et al, 2009).

Previous literature has suggested that these children do not respond well to treatment (Yancey et al, 1984; Olson et al, 1990) but all the rheumatologists agreed that the response to treatment was good despite this suggestion. 'Ones I've seen tend to respond to quite a low dose of methotrexate and joint injections as standard JIA' 'First went to a hospital there were a number of children with DS around the clinic and there was undoubtedly a feeling that you shouldn't use methotrexate and they didn't respond to treatment therefore you didn't treat them and I had quite a battle to get 3 of them on methotrexate ó about 1995' 'Methotrexate had been around for a number of years (about 7) and people were using in other JIAs but I think there was still this thing about DS arthritis was different and they won't respond to treatment and therefore you don't give them this nasty drug but once we'd treated a few and clearly they had responded people shifted their thinking' 'When I started in paediatric rheumatology they were considered different and they weren't given methotrexate because they didn't respond but we now know they do respond' Again the consensus was that these children respond well to modern

treatments for JIA and should be treated accordingly concurring with the RHSC pilot study (Cruickshank et al, 2008) and the case studies described by Juj et al (2009).

Following on from the discussion about delay to diagnosis there was also a consensus that other healthcare professionals would benefit from education on musculoskeletal problems in DS, particularly arthritis as it does not appear to be getting recognised at other health care appointments, possibly because these children present in an atypical manner. -One seen by multiple people and was under orthopaedics because of her hypermobility and unstable ankles and had repeatedly been pointed out by physios that she had joint swelling and it was just said that it was because she's got very flexible joints -Interesting that people have actually documented in the notes swollen joints, synovitis and somehow the penny hasn't dropped -It's in a different box from DS in people's heads. Or that pain and stiffness are what you expect in arthritis and you don't get that history even though you've got all the rest of it

The main conclusions drawn from the themes obtained from this group were that this population of children tend to present late to rheumatology and, therefore, education of health professionals who review these children regularly would be beneficial but, once seen, these children do respond well to treatment.

#### 4.6 Community paediatricians

The community paediatricians' focus group was asked about their awareness of musculoskeletal problems in children with DS and any training needs they thought might be useful.

##### 4.6.1 Inclusion criteria

Community paediatricians based in Glasgow performing annual reviews in children with DS.

##### 4.6.2 Exclusion criteria

Community paediatricians not performing annual reviews in children with DS.

##### 4.6.3 Questions

Q1. Do you all have much involvement with children with Down's syndrome?

Q2. What are the main focuses of your annual review of these children? (Or regular review if non Drs present?)



What kind of physical examination would it involve?

Q3. Do you think these children are prone to musculoskeletal problems? ----- what MSK conditions would you consider to be a problem in these children?

Q4. We are looking to evaluate and improve the recognition and diagnosis of arthritis and other musculoskeletal problems in these children ó can you make any suggestions how we can go about this and can you recognise any training needs?

#### 4.6.4 Results

Unfortunately the recording equipment failed during this focus group so only the minuted version was transcribed.

The main themes from this focus group were that this group of health professionals were not aware of certain MSK disorders in children with DS, they considered MSK problems to be an acute issue they would not discover and MSK examination is not part of the annual review process.

When asked about MSK disorders in these children a number commented that they examine the children for atlanto-axial instability and hip instability but none suggested arthritis as a possible condition. One commented -I didn't realise arthritis was a problem in DS

When asked if the annual review could be useful in recognising arthritis and other MSK problems in this population the general consensus was that any musculoskeletal problems would be picked up by another healthcare professional outwith the annual review process. -Joint problems would be picked up by the GP or school physiotherapists between annual review appointments

This theme continued with the discussion on education as the general impression was that they did not consider education was an important issue at present as they wouldn't have to deal with these conditions at the annual review. It was considered that arthritis would present as an acute condition and the parents would attend their GP with any concerns.

Time constraints also appeared to be an issue with the annual review appointment and one paediatrician suggested that we could share data collected from the study visits for their annual review visit which would save them time.

#### 4.7 Discussion

The main themes from the focus groups were that children with DS do appear to be referred late to rheumatology despite numerous healthcare contacts, these children do respond to current treatments in contrast to the literature, that community paediatricians consider arthritis to be an acute presentation of pain or joint swelling that they would not have to diagnose and that education is required to increase awareness and improve diagnosis and prognosis.

The paediatric rheumatologists had all seen children who had been referred late which meant that joint damage was worse due to prolonged inflammation before appropriate referral. Some of these children had been seen by numerous departments including community paediatrics, school nurses, physiotherapists, general practitioner and orthopaedics. One had been told that her mobility problems were due to her cardiac condition and another was told that her joint swelling were due to her very flexible joints. Arthritis hadn't been considered as a diagnosis.

There also seemed to be an expectation that these children should have lower levels of mobility because of their DS. These children do tend to be hypermobile with podiatric conditions such as pes plano valgus but this should not necessarily have an impact on their mobility.

The parent interviewed by Arthritis Today complained about a delay to diagnosis despite a number of healthcare appointments. However as other parents were unable to participate in a focus group this does not give an all round view of parents experiences and the pilot study does identify three children who were seen by a General Practitioner or Accident and Emergency and referred promptly to rheumatology.

Previous literature has described children who did not appear to respond to treatment (Yancey et al, 1984; Olson et al, 1990) but the paediatric rheumatologists experience was that these children were treatment responsive concurring with the more recent case studies presented by Juj et al (2009). Early diagnosis is vital to allow treatment to commence before any joint damage has occurred. Unfortunately for a lot of these children their joints are badly damaged before they are referred to rheumatology. One rheumatologist said of a former patient who was referred after a long period of time 'He's sad because he's completely wrecked all his joints and actually he's very treatment responsive'.

The community paediatricians appeared to think that arthritis was something that they would not have to diagnose as it would present as an acute complaint of pain or joint swelling and would be seen by a GP or school nurse. This may not be the case as these children may not display an acute presentation. As discussed in Chapter 2, literature suggests that these children do not

appear to express pain in the same way as the general population (Lind et al, 1990; Biersdorff et al, 1994; Martinez-Cué et al, 1999; Hennequin et al, 2000) and, in her interview with Arthritis Today, our parent said that her son never complains of pain but says that his joints are tickly. Also, anecdotally, a large number of parents involved in the study commented that their children didn't generally complain of pain. If a child doesn't complain of pain, their parents may not pick up on a warm or slightly swollen joint immediately. These children may develop a change of gait or movement or even a change in mood due to pain or discomfort in a joint which the parent may not consider to be an acute problem. Most parents would not consider a change of mood to be caused by pain or discomfort but may query this at the child's next annual review with their community paediatrician.

The pilot study at RHSC, Glasgow raised concerns over the delayed diagnosis of this population of children and the results suggested that there may be issues with diagnosing MSK disorders in this population.

These focus groups show that education is vitally important for other health professionals to have better awareness of joint problems in this group of children, and their unique presentations, to allow earlier and better diagnosis. As the paediatric rheumatology specialists discussed, children had seen multiple healthcare professionals and still had been misdiagnosed but the community paediatricians felt education wasn't an important issue as they thought what they considered to be an acute problem would be dealt with by another health professional. However if a parent comes to annual review and mentions a change of gait or mood, the community paediatrician needs to be aware that arthritis should be considered. School nurses, physiotherapists and other healthcare professionals who attend to these children regularly should be included in education so they would be able to pick up a possible arthritis when seeing the child. One child mentioned by the paediatric rheumatologists had been seen by multiple people and was only referred because an occupational therapist was asked to give a school hand assessment and phoned the GP to ask for a rheumatology referral. An issue with this child's hand had been identified but not recognised as arthritis. Education of these health professionals would also help improve expectations of these children and allow understanding that their mobility shouldn't be any different from the general population. Education of parents would also improve their awareness of signs and symptoms and allow them to be confident about querying symptoms with their GP or community paediatrician.

Since holding the focus group with the community paediatricians, awareness in musculoskeletal conditions has improved and a number of referrals have been received at RHSC Yorkhill following annual review consultations. Also a number of community paediatricians have attended an annual study day run by one of the consultant rheumatologists at RHSC Yorkhill on

paediatric musculoskeletal conditions (although not specifically in DS) which includes recognition of symptoms, diagnosis, examination and treatment. Other specialties are involved including podiatry, occupational therapy and orthopaedics.

It is hoped that in conjunction with Arthritis Research UK educational material for health professionals and parents can be produced to raise awareness of symptoms to look out for. It would also be beneficial if a musculoskeletal examination could be included in the annual review of children with DS. As discussed in Chapter 2 the short pGALS examination with some minor adaptations could be added to a general appointment with minor time disruption. This would, hopefully, lead to earlier diagnosis and referral, earlier treatment initiation, faster remission and less joint destruction to allow these children to get back to normal mobility across a range of MSK disorders including arthritis.

#### 4.8 Limitations and clinical implications

The main limitation of these focus groups was the inability to recruit a parent group to understand parent experiences of their healthcare pathway and diagnosis.

With regard to the community paediatricians' group a major limitation was the lack of a recording as the equipment failed and an administrator's transcript was all that was available. Also this was a large group as it was part of an educational meeting and not all the participants entered into the discussion and we may have had a better in depth discussion with more concise themes from a smaller group.

The facilitator was new to focus groups and it may have been more beneficial to have a facilitator who was experienced with focus groups or a co-facilitator to lead the groups to obtain better discussion and a more robust data analysis from the groups.

If the study had had a longer time frame we would have liked to have added focus groups involving other health professionals involved in the care of these children such as physiotherapists and occupational therapists regarding their experience and knowledge of MSK disorders in this population as they may be just as likely to discover a problem in these children. This may also have given more robust data from the groups.

From the results obtained, the clinical implications for the future are that, although the community paediatricians were reluctant about including MSK examination and felt that MSK disorders were something a GP or other health professional would diagnose, awareness has now

been raised regarding MSK problems in this population which is hopeful for referral in these children in the future.

Also, the pilot study at RHSC, Glasgow (Cruickshank et al, 2008) and the case studies presented by Juj et al (2009) showed that these children respond to treatment in comparison to previous literature and the comments from the rheumatology specialists back this up, so children diagnosed with arthritis in future can be prescribed rheumatology medication early allowing better prognosis.

## **CHAPTER 5**

### **HYPERMOBILITY**

#### **5.1 Introduction**

Joint hypermobility (JH) describes lax ligaments around the joint allowing the joint a wider range of movement (ROM) than is considered normal in an asymptomatic individual. Joint hypermobility syndrome (JHS) describes this condition but involves symptoms which can include joint pain, foot pain and joint dislocation. Hypermobility may pose no problems, but in some individuals it predisposes to a wide variety of soft tissue injuries and internal joint derangements, arthritis, arthralgias or myalgias, which lead sufferers to seek medical attention (Simmonds and Keer, 2007).

The majority of literature describing Down's syndrome mentioned hypermobility, lax ligaments and muscle hypotonia present in these individuals which can cause mobility and instability problems. Despite this, literature that examined generalised hypermobility in children with DS is very limited. The majority of the literature examining JH within the DS population looked at hypermobility in relation to joint instability, particularly instability of the atlantoaxial joint. Clinch et al (2011) examined hypermobility within the general population of fourteen year old children but acknowledged that JH can be present within other genetic disorders and syndromes such as osteogenesis imperfect, Marfan syndrome, trisomy 21 and bony dysplasia.

JH is recorded by using the Beighton scoring system (Beighton and Horan, 1969) (Table 3.3) and JHS diagnosed using the 1998 revised Brighton criteria (Grahame, Bird and Child, 2000) (Table 3.4). Beighton score gives a whole number score ranging from zero to nine. A Beighton score of over four is considered to be a sign to identify hypermobility and counts as a major criteria in the Brighton scoring system. The Brighton scoring system uses 2 major criteria and 8 minor criteria with a diagnosis of JHS depending on a certain amount of these scores being fulfilled (Table 3.4). The BJHS is diagnosed in the presence two major criteria, or one major and two minor criteria, or four minor criteria. Two minor criteria will suffice where there is an unequivocally affected first-degree relative (<http://hypermobility.org/hypermobility/do-i-have-hms/the-brighton-score/>).

Hypotonia is described in DS particularly in newborns and may be a factor in delayed motor response in these children. Infants with DS are floppy at birth and start walking later than the general population. They display a gait with shorter steps and a longer stance time and delayed developmental motor responses compared to children without DS (Shumway-Cook and

Woollacott, 1985; Selby-Silverstein et al, 2001; Gontijo et al, 2008; Chang et al, 2009, Rigoldi et al, 2011).

### 5.2 Methods

73 children (28 boys; 45 girls) aged between 2.4 and 15.9 (median 8.94) were recruited from an identified population of 142 children with DS resident in Glasgow and examined as described in Chapter 3.

A complete musculoskeletal examination based on the pREMS procedure (Appendix 3: Foster et al, 2011) and a podiatric examination by a senior podiatrist were carried out.

Joints were examined and recorded as hypermobile if an MCP, MTP, wrist, ankle, hip or shoulder joint fulfilled the criteria of hyperextending over 90 degrees or an elbow or knee joint fulfilled the criteria of hyperextending more than 10 degrees. The Beighton and Brighton scoring systems were used as part of the examination. Parents were asked to complete questionnaires about their child's past medical history, family history and to identify any musculoskeletal concerns.

In order to make some comparison with the degree of hypermobility in the normal paediatric population some comparisons were made with the numbers by Clinch et al (2011) who analysed a cross section of the population based cohort from the ALSPAC study ([www.alspac.bris.ac.uk](http://www.alspac.bris.ac.uk)). 6032 14 year old children attended the research centre and hypermobility data was collected using the Beighton scale. This study was used as a comparison as they were closest in the literature although this was a poor match as the Clinch et al cohort were all 14 years old and the DS study cohort ages ranged from 2 to 15.

As there is no way of measuring hypotonia a revised version of the CMAS score (Lovell et al, 1999) was used to assess weakness. A number of the measurements included in the CMAS score involved a measurement of duration. It was decided prior to the study commencing that these measurements would be removed from the scoring due to the level of learning disability of these children and their ability to comply with the study measurements.

### 5.3 Results

73 children (28 boys; 45 girls) aged between 2.4 and 15.9 (median 8.94) were recruited from this cohort and examined according to the study protocol Appendix 1). 51 children did not respond to the invitation, 18 declined, cancelled or did not attend appointments and these 69 children (35 boys; 24 girls) not seen were aged between 2.2 and 15.9 (median 9.77). Deprivation category by postcode was not documented in the study.

#### 5.3.1 Joint examination

71 (97%) children demonstrated hypermobility from the criteria in at least one joint. Hip joints were the most commonly hypermobile with 56 (77%) children demonstrating at least one hypermobile hip joint and 111 hip joints out of the 146 examined demonstrating hypermobility. Figure 5.1 and Tables 5.1 to 5.3 below show the breakdown of joints which fulfilled criteria for hypermobility. The majority of hypermobile joints in this cohort of children were in the lower limbs.



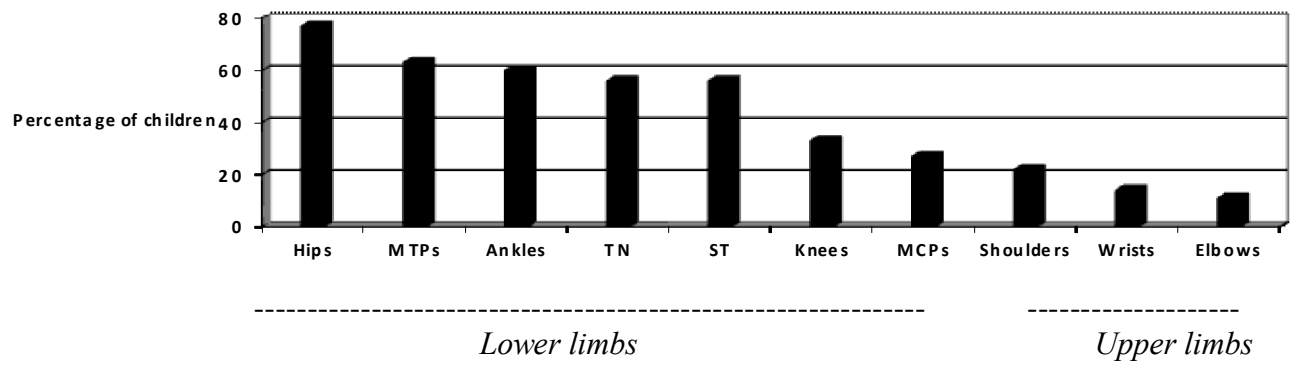


Figure 5.1: The distribution of hypermobile joints in 73 study children: MTPs; metatarsophalangeal joints: TN; talonavicular: ST; subtalar: MCPs; metacarpophalangeal joints

<b>Lower limbs</b>	<b>Joints</b>	<b>Number/73 (%)</b>
Hips	111/146 (76%)	56 (77%)
Knees	47/146 (32%)	24 (33%)
Ankles	80/146 (55%)	41 (56%)
Subtalar	82/146 (56%)	41 (56%)
Talonavicular	88/146 (60%)	44 (60%)

*Table 5.1: The distribution of hypermobility in lower limbs of this DS study cohort*

<b>Upper limbs</b>	<b>Joints</b>	<b>Children/73 (%)</b>
Shoulders	32/146 (22%)	16 (22%)
Elbows	16/146 (11%)	8 (11%)
Wrists	20/146 (14%)	10 (14%)

*Table 5.2: The distribution of hypermobility in upper limbs of this DS study cohort*

<b>Small joints</b>	<b>Joints (730)</b>	<b>No. of children (%)</b>
MTPS	459 (63%)	46 (63%)
MCPS	239 (33%)	20 All MCPS (27%) 44 MCP5 (60%)
PIPS	30 (4%)	3 (4%)
Neck	1 (1.4%)	1 (1.4%)

*Table 5.3: The distribution of hypermobility in small joints and the neck joint in this DS study cohort: MTPs; metatarsophalangeal joints: MCPs; metacarpophalangeal joints: PIPs; proximal interphalangeal joints (20 (27%) children showed hypermobility in all MCPs and 44 (60%) children showed hypermobility in their MCP5 joint which is one of the joints checked on the Beighton scoring system)*

### 5.3.2 Beighton scores

The breakdown of Beighton joint scores from the study cohort showed a prevalence of generalised joint laxity in 39 (53%) of the children as defined using a Beighton score over or equal to 4.

The cohort from this study showed higher numbers of children with Beighton scores  $>4$  and  $>6$  (Table 5.5) as compared with Clinch et al scores and a comparison of 13-16 year olds in this study also showed this age group displayed higher levels of hypermobility (Table 5.7). Clinch et al's cohort showed hypermobility to be more prevalent in girls. The DS study cohort showed similar levels of hypermobility between the two sexes (Table 5.6).

Comparison was made between the distribution of joints in the DS study cohort and the Beighton scale. Only 1 joint was found to correspond in both - the fifth metacarpal joint (Figure 5.2)

Beighton Score	Number of children
1	16
2	10
3	8
4	16
5	5
6	8
7	9
8	0
9	1

*Table 5.4: The distribution of Beighton scores in the study cohort of DS children (n=73)*

<b>Beighton Score (0-9)</b>	<b>DS study results population prevalence n/73 (%)</b>	<b>Clinch et al population prevalence n/6022 as a percentage</b>	<b>DS study 13-16 year olds prevalence n/21 (%)</b>
<b>&gt;4</b>	39 (53%)	19.2%	10 (48%)
<b>&gt;6</b>	18 (25%)	4.2%	3 (14%)

*Table 5.5: The comparison of Beighton scores from the DS study cohort with Beighton scores from Clinch et al (2011)*

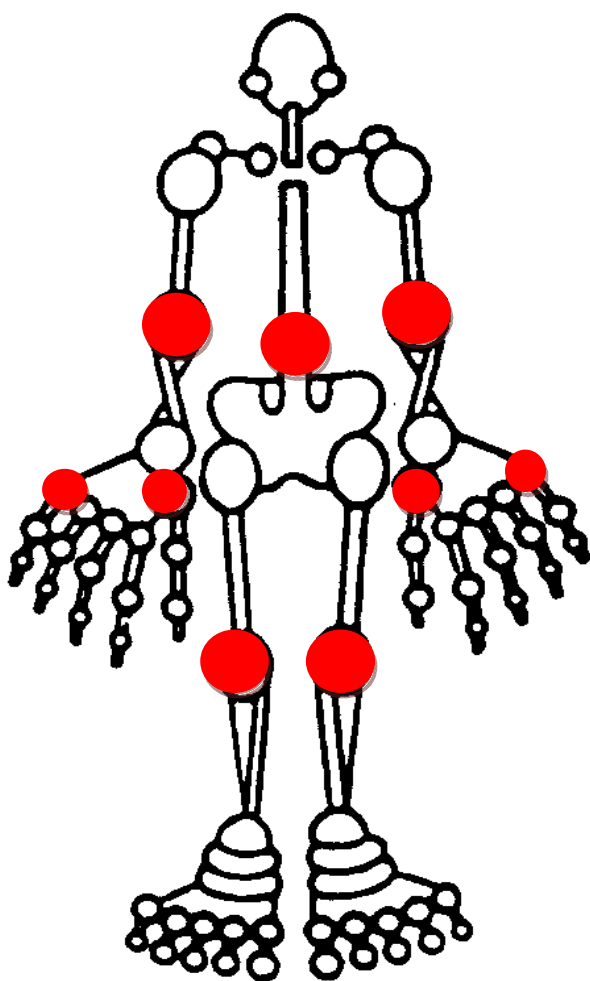
<b>Children</b>	<b>Our results Beighton &gt;4</b>	<b>Clinch et al Beighton &gt;4</b>	<b>Our results Beighton &gt;6</b>	<b>Clinch et al Beighton &gt;6</b>
<b>Boys</b>	57%	10.6%	25%	1.3%
<b>Girls</b>	51%	27.5%	24%	7%

*Table 5.6: The comparison of Beighton scores between the sexes in Beighton scores  $\leq 4$  and  $\leq 6$  in the DS study cohort and Clinch et al (2011) cohort*



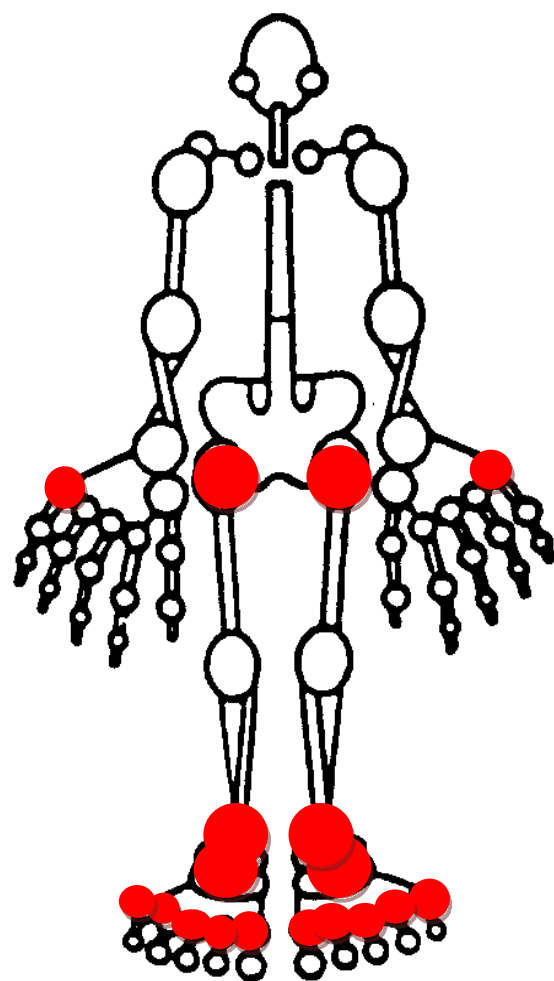
<b>Beighton Score</b>	<b>Number of Children / 21</b>	<b>%</b>
<b>0</b>	<b>6</b>	<b>29%</b>
<b>2</b>	<b>2</b>	<b>9%</b>
<b>3</b>	<b>3</b>	<b>14%</b>
<b>4</b>	<b>6</b>	<b>29%</b>
<b>5</b>	<b>1</b>	<b>5%</b>
<b>6</b>	<b>2</b>	<b>9%</b>
<b>7</b>	<b>1</b>	<b>5%</b>

*Table 5.7: Table showing Beighton scores for 13-16 year olds within the DS study cohort*



*Figure 5.2*

*The joints examined in the Beighton hypermobility scoring criteria showing carpo-metacarpal joints; 5<sup>th</sup> metacarpal joints; elbows; knees and lower back*



*The joints found to be hypermobile within the DS study cohort showing 5<sup>th</sup> metacarpal joint, hip, subtalar joints, talonavicular joints and all metatarsal joints*

### 5.3.3 Brighton scores

The DS cohort of children displayed high levels of individual joint hypermobility but Brighton scores were low in this cohort with only 11 (15%) children fulfilling the criteria for a diagnosis of JHS.

### 5.3.4 Hypotonia

The children generally scored highly using the revised CMAS scoring system for the study. (Table 5.9)

### 5.3.5 Anecdotal results

A number of parents whose children participated in the study, and no other pathology was found, commented that their children would stop suddenly while walking and refuse to walk any further. Some of them would sit down where they stopped and a number of mothers travelled with a buggy for older children. This may be related to discomfort due to hypermobility in the lower limbs. Another common comment within the parents of the study cohort was that the children were most comfortable with their legs in the lotus position or wrapped around their neck as illustrated by one of the boys in the study cohort in Picture 5.1. One parent even commented that their child regularly ate in that position causing some comment when eating out.

<b>Brighton Major Score</b>	<b>Number of Children</b>
<b>0</b>	<b>33</b>
<b>1</b>	<b>40</b>

*Table 5.8 The distribution of Brighton major score criteria in this DS study cohort*

<b>Brighton Minor Score</b>	<b>Number of Children</b>
<b>0</b>	<b>0</b>
<b>1</b>	<b>45</b>
<b>2</b>	<b>20</b>
<b>3</b>	<b>6</b>
<b>4</b>	<b>2</b>

*Table 5.9 The distribution of Brighton minor criteria in this DS study cohort*

<b>CMAS scores</b>	<b>Number of Children / 73</b>	<b>%</b>
<b>18</b>	1	1%
<b>20</b>	1	1%
<b>23</b>	1	1%
<b>24</b>	5	7%
<b>25</b>	4	5.5%
<b>26</b>	6	8%
<b>27</b>	4	5.5%
<b>28</b>	7	10%
<b>29</b>	6	8%
<b>30</b>	10	14%
<b>31</b>	9	12%
<b>32</b>	12	16%
<b>Non Compliant</b>	7	10%

*Table 5.10: Table showing distribution of CMAS scores within the study cohort*

#### 5.4 Discussion

A high level of hypermobility was expected in this cohort of children in accordance with DS literature and our study showed 97% of children fulfilling criteria for hypermobility in at least one joint. However the pattern of hypermobility found in DS does not correlate with the Beighton and Brighton scoring systems.

Although the Beighton scores showed 53% of the study cohort appeared to be hypermobile, the Beighton scoring system uses 9 specific joints and the results from study joint exam discovered that the pattern of hypermobile joints in the study cohort were mainly in the lower limbs and did not correlate with the joints examined within the Beighton scoring system as illustrated in Figure 3.2. The only joint that occurred in both the Beighton scale and was frequently hypermobile in DS was the fifth metacarpal phalangeal joint . This suggests that the Beighton and Brighton scores underestimate the level of hypermobility in DS and that a disease specific score is needed.

The Beighton scoring system was not developed as a diagnostic test ([www.hypermobility.org](http://www.hypermobility.org)) due to its limited sample of joints but the joint pattern found within this cohort of children suggests that the Beighton scoring system is not useful in this population and a complete joint examination focusing particularly on the lower limbs would be more useful in determining level of hypermobility. Because the majority of hypermobile joints are lower limb joints this then impacts on mobility levels and weightbearing for this population, particularly with other compounding risk factors such as obesity.

The comparison between the DS study cohort and Clinch et al<sup>8</sup> (2011) cohort showed a higher percentage of children fulfilling the criteria for hypermobile joints in the DS cohort which would suggest higher levels of hypermobility in this population of children and a direct comparison of 13-16 year olds showed higher levels of hypermobility in this study cohort. However the age range of the DS cohort between two and sixteen was considerably different with Clinch et al<sup>8</sup> cohort all aged 14 and the DS cohort population of aged 13 -16 was only 21 and therefore is not a large enough representative number to draw an accurate comparison . This suggests the difference in hypermobility could be due to different ages and would be a more accurate representation if the DS study cohort had been all of a similar age to the Clinch et al cohort.

The hypermobility levels were high in the DS cohort of children but the Brighton scores did not suggest a high level of joint hypermobility syndrome. The Brighton scoring system uses the Beighton scale and takes other clinical factors into account for diagnosis. (Figure 3.3)

One of the minor Brighton criteria is the -anti-mongoloid<sup>8</sup> slant of the eyes which is present in all children with Down<sup>8</sup> syndrome and, therefore, gave all the children in the study cohort one minor

score automatically. Another minor Brighton score is complaining of pain in one or more joints for 3 months or longer. Literature suggests that this population of children appear to display reduced perception of pain as discussed in Chapter 2. A reduced perception of pain would make this minor score difficult to judge. A large number of parents commented anecdotally that their child did not complain of pain, particularly in comparison to their siblings.

There is also debate within literature about the level of Beighton score that should be applied to the Brighton criteria. The current major criteria is a Beighton score of four or more out of nine but Smits-Engelsman, Klerks and Kirby (2011) recommended a score of seven out of nine after concluding that their threshold of five out of nine classified children as hypermobile incorrectly. The limitations to the Brighton scoring system suggest that it may not necessarily be suitable as a diagnosis tool for this population of children.

The CMAS scores obtained were generally high and the exercises carried out well by the children. The lower scores obtained were mainly by children who were not completely compliant with the exercises. The most useful exercises for measuring weakness within the CMAS were the sustaining exercises but these were not used as it was considered these children would not have the concentration to sustain the exercise. This suggests that this scoring system is not useful in this population, and was a poor proxy for hypotonia. Developing an alternative method of measuring hypotonia in children with DS would be of value.

In conclusion, this population of children displays a high level of hypermobility which is underestimated using the Beighton and Brighton scores because it affects a different set of joints than used in these scoring systems. Introducing a general joint examination with focus on the lower limbs to the annual review process of these children would help to understand mobility issues caused by hypermobility. It would also screen this population of children for other musculoskeletal complaints. We were unable to make objective assessments of hypotonia.



*Picture 5.1: Picture of study participant showing hypermobile hips*



## **CHAPTER 6**

### **MUSCULOSKELETAL RESULTS**

#### **6.1 Introduction**

Published case reports of children with DS presenting with an inflammatory arthritis (Yancey et al, 1984; Juj et al, 2009, Padmakumar et al, 2002, Olsen et al, 1990) showed that most of these children presented late with significant disease and did not appear to respond to the treatments given.

A pilot study carried out in The Royal Hospital for Sick Children, Glasgow (Cruickshanks et al, 2008) identified 12 children who had attended the paediatric rheumatology service in Scotland. A number of these children presented late despite numerous contacts with health professionals, including annual review by community paediatricians, regular contact with physiotherapists and school nurses and appointments with orthopaedic consultants. Figures showed a median age at symptom onset of 5.9 (2-13.3) years but a median age at diagnosis of 8.1(4.2-15.6) years. This corresponded with the median time from symptom onset to first paediatric rheumatology appointment of 2.9 (0.1-8.7) years. This contributed to already established, destructive disease at presentation and four of the children were non weight bearing at first appointment. However these children responded well to treatments offered. This is in contrast to previous literature which may suggest modern treatments are more effective. This pilot study identified five children resident in Glasgow with DS and juvenile arthritis in a DS population of 174 identified from three separate registers available. This gave a prevalence of 2.87% and a relative risk of 3.38 of developing JIA in DS compared to children without DS, assuming a prevalence of JIA in 1 in 1000 children (Andersson-Gare, 1999).

An ongoing study being carried out in Ireland performing a screening MSK examination on children with DS from birth to 18 years has diagnosed 10 new cases of arthritis (from a population of 164 examined to date) compared to 11 already known from a ten-fold larger population of children with DS (personal communication O Killeen 2013). In contrast to the RHSC study, however, their anecdotal evidence suggests methotrexate intolerance as 24% of their current cohort were commenced on methotrexate and all have been discontinued due to lack of tolerance and failure to respond so it will be very interesting to compare their final study results with evidence from the RHSC pilot study.

Studies have also showed that children with DS appear to display higher levels of pain tolerance or express pain differently (Lind et al, 1970; Hennequin et al, 2000) which was considered a factor in misdiagnoses as joint pain would generally be one of the first signs of inflammatory arthritis.

This late presentation led to the hypothesis that there may be undiagnosed arthritis within the community of DS children as the children identified had lived with their arthritis for a median of 3 years without diagnosis.

## 6.2 Methods

73 children (28 boys; 45 girls) aged between 2.4 and 15.9 (median 8.94) were recruited from an identified population of 142 children with DS resident in Glasgow and examined as described in Chapter 3.

All joints were examined for the range of movement, heat, swelling and pain or tenderness and any findings documented. All children were offered referral to paediatric rheumatology following the study visit whether the study personnel had concerns or not as it was considered that inviting the children to take part in the study may have raised concerns or questions with the parents.

A full podiatry examination was carried out by the same consultant podiatrist and is discussed fully in Chapter 7.

Schobers test was carried out to determine any limitations in spine movement.

Parents were asked to complete questionnaires involving past medical history, family history and any musculoskeletal concerns. Pain threshold was recorded within the study questionnaires as a visual analogue scale (VAS) within the CHAQ form where parents were asked to record their child's pain level at its worst over the last seven days on a 100mm line and the pain score is recorded as a measurement of  $x/100\text{mm}$ .

In this study we undertook anthropometric measurements including height, weight, sitting height, arm span and head circumference of the study population of children with Down's syndrome which will allow comparison to previous populations, particularly in a time of worldwide concern about increasing levels of obesity, and to consider whether there was a relationships with their MSK findings and mobility levels. Normative values for height and weight were taken for comparison with this cohort from two sources. Height and weight data were compared to the Down's normative LMS data compiled by Styles et al (2002) who collated data from a cohort of 1089 children and young adults with DS to develop more up to date centile charts for the DS population. Measurements of height, weight and head circumference were recorded from health records,

cleaned and studied. Centile charts were then fitted to data using the LMS method (Cole et al, 1998). Previous studies referred to as the UK90 data collected measurements from birth to 70 years old was assessed across seven studies in the UK and the results from these led to the development of growth centile charts from birth to 20 years old (Freeman et al, 1995). As Styles et al failed to report normative values for BMI in the DS population despite measuring height and weight we were unable to compare this cohort to the Down's data and were forced to make the less appropriate comparison to the BMI for the normative population from the UK90 data, and only to height and weight individually from Styles data.

### 6.3 Results

73 children (28 boys; 45 girls) aged between 2.4 and 15.9 (median 8.94) were recruited from this cohort and examined according to the study protocol Appendix 1). 51 children did not respond to the invitation, 18 declined, cancelled or did not attend appointments and these 69 children (35 boys; 24 girls) not seen were aged between 2.2 and 15.9 (median 9.77). Deprivation category by postcode was not documented in the study.

#### 6.3.1 Joint exam

In the 73 children screened none had active synovitis but 22 children (30%) showed joint limitations in at least one joint. This limitation may have been only on one movement within the joint such as inversion only or eversion only. In four children hip joints showed hypermobility on external rotation but appeared limited on internal rotation. Sixteen children (22%) displayed limitations in two or more joints. The majority of limited joints were discovered in lower limb joints as shown in Table 6.1. Three children were completely non compliant with the joint exam and one only allowed upper joints to be examined. Of the three non compliant children, two were severely autistic. However, in these children, some results were obtained by observation, particularly evidence of hypermobility.

#### 6.3.2 Referral

A total of 28 (38%) children from a total cohort of 73 were referred to the paediatric rheumatologist. All referred children had displayed some joint limitation at study visit. 1 child failed to attend for appointment. None of the children who attended had any evidence of active synovitis on examination by the paediatric rheumatologist. Two children displayed ongoing hip limitation with corresponding mobility changes. These children underwent MRI scanning. Neither showed joint abnormalities, however, one child was discovered to have an undescended testicle.

### 6.3.3 Pain response

Pain was recorded as a visual analogue scale (VAS) within the CHAQ as a measurement of x/100mm. Anecdotally, a large number of parents commented that their children did not complain of pain and were more likely to complain of tiredness and just stop walking and sit down. There were also a number of comments about how their children didn't complain of pain when they fell or bumped themselves. The VAS scores ranged from 1mm to 47mm with a median of 10.6mm.

### 6.3.4 Anthropometric results

There was no statistically significant difference for height or weight when compared to the Down's normative data (Styles (2002)). There was no statistical difference between the sexes in comparison to Styles (2002) (Table 6.2). Comparison with the UK90 data showed that the children with DS were shorter and heavier than the general population as would be expected.

Only seven children (10%) were found to be obese (weight > 95<sup>th</sup> centile) (Table 6.4). Centile value was depicted in weight as Styles et al had failed to report normative values for BMI and we were unable to compare for normative DS data.

18 (25%) of the children were non-compliant with standing on the Tanita scales for BIA and scores ranged from 383 to 797 (median 566). However this data was not used for analysis as there were no comparable studies to compare results with for this population.

### 6.3.5 CHAQ form results

58 CHAQ questionnaires were returned following the study visits. CHAQ forms are scored from 0 (no disability) to 3 (severe disability). CHAQ forms are scored from 0 (no disability) to 3 (severe disability) (Groen et al, 2010). Study CHAQ scores ranged from 0 to 2.5 with a mean of 1.39 and a median of 1.56. 18 questionnaires scored under one (31%), 25 (43%) scored between one and two and 15 (26%) scored over 2.

### 6.3.6 Schober's test results

18 (23%) of the children were non compliant with the Schober's test, 21 (30%) had a result above 15 but below 21 and 34 (47%) had a result above 21

<b>Joints</b>	<b>Limited joints</b>	<b>Total children</b>
<b>Ankles</b>	19 (13%)	10 (14%)
<b>Hips</b>	11 (8%)	6 (8%)
<b>Knees</b>	9 (6%)	6 (8%)
<b>ST</b>	4 (3%)	3
<b>TN</b>	0	0
<b>Shoulders</b>	2	1
<b>Elbows</b>	1	1
<b>Wrists</b>	1	1
<b>MCP</b>	1	1
<b>PIP</b>	1	1
<b>MTP</b>	0	0
<b>Neck</b>	3 (4%)	3
<b>Enthesitis</b>	0	0

*Table 6.1: Table showing limited joints found on examination, expressed as joint number and by child. ST; subtalar; TN; talonavicular; MCP; metacarpophalangeal joints; PIP; proximal interphalangeal joints; MTP; metatarsophalangeal joints*

<b>Variable</b>	<b>N</b>	<b>Mean</b>	<b>StDev</b>	<b>SE</b>	<b>Mean 95% CI</b>	<b>T</b>	<b>P</b>
<b>Height</b>	<b>70</b>	<b>-0.155</b>	<b>1.119</b>	<b>0.134</b>	<b>(-0.422, 0.111)</b>	<b>-1.16</b>	<b>0.249</b>
<b>Weight</b>	<b>70</b>	<b>-0.012</b>	<b>1.267</b>	<b>0.151</b>	<b>(-0.314, 0.291)</b>	<b>-0.08</b>	<b>0.939</b>
<b>Head circumference</b>	<b>67</b>	<b>0.645</b>	<b>1.221</b>	<b>0.149</b>	<b>( 0.347, 0.943)</b>	<b>4.33</b>	<b>&lt;0.001</b>

*Table 6.2: Table showing the mean group comparisons between study cohort data for height, weight and head circumference against the Down's normative data given as standard deviation scores (Styles et al, 2002)*

<b>Variable</b>	<b>N</b>	<b>Mean</b>	<b>StDev</b>	<b>SE</b>	<b>Mean 95% CI</b>	<b>T</b>	<b>P</b>
<b>Height</b>	<b>70</b>	<b>-2.340</b>	<b>1.236</b>	<b>0.148</b>	<b>(-2.635, -2.045)</b>	<b>-15.83</b>	<b>&lt;0.001</b>
<b>Weight</b>	<b>70</b>	<b>-0.485</b>	<b>1.598</b>	<b>0.191</b>	<b>(-0.866, 0.104)</b>	<b>-2.54</b>	<b>0.013</b>
<b>Head circumference</b>	<b>70</b>	<b>1.117</b>	<b>1.322</b>	<b>0.158</b>	<b>( 0.802, 1.432)</b>	<b>7.07</b>	<b>&lt;0.001</b>

*Table 6.3: Table showing the mean group comparisons between study cohort data for height, weight and head circumference against the UK90 data given as standard deviation scores*

<b>Weight</b>	<b>Number of children n= 73</b>	<b>%</b>
<b>Obese ( weight &gt;95<sup>th</sup> centile)</b>	<b>7</b>	<b>10</b>
<b>Overweight ( weight &gt;85<sup>th</sup>-95<sup>th</sup> centile)</b>	<b>7</b>	<b>10</b>
<b>Underweight (weight &lt;2<sup>nd</sup> centile)</b>	<b>3</b>	<b>4</b>

*Table 6.4: Table showing number of children with weight results outside normal values*



#### 6.4 Discussion

No new arthritis cases were discovered by the study and this means the ten year prevalence from 2008 of 2.87% is unchanged. However the study cohort represented 51% of the DS population and future studies would be advisable to try and capture a higher percentage of the population although one theory for non response to contact for the study was that these parents already have a number of hospital appointments and they may not have appreciated another one. This is why it is so important that the health professionals that see these children on a regular basis are educated to examine for and detect musculoskeletal abnormalities in this population of children.

Approximately a third of these children showed joint limitations on examination but no signs of active inflammatory arthritis. The mechanism for the limitation is unclear but possible explanations may be compliance, pain or responses to hypermobility. One child had appeared to show neck limitation on extension at the study visit but gave full extension when reviewed by a paediatric rheumatologist.

Another possibility is that limitation was considered because the joints in these children are expected to be hypermobile. At the beginning of the study, the study staff thought these children were showing limitations in elbows as they were not giving a positive Beighton score but very quickly came to the conclusion that this was the normal range of movement in these children. Only 8 children in the study displayed hypermobile elbows.

All the children in the study were offered referral to paediatric rheumatology as it was considered that the study visit may have raised anxieties within some parents and they may prefer to see a rheumatologist to address those anxieties. The majority of parents were very enthusiastic about the study and happy to take the advice of the study team but only a small number were keen to take up the offer of a referral. All children who had displayed joint limitation were referred to paediatric rheumatology for follow up and parents encouraged to attend the appointment. No children were found to have evidence of arthritis. However the discovery of an undescended testicle in one of the children was an important medical finding for a 14 year old boy.

The anecdotal evidence from the parents that these children do not complain of pain and the VAS scores support the RHSC Yorkhill pilot study theory that children with DS have a higher pain threshold. One of the study participants was resident in a care facility and had been displaying a limp and adjusted walking patterns for a number of months but, while the staff thought this child had injured himself when this presented, after several weeks with no complaints of pain they considered him to be attention seeking. They did not appreciate that for a child, particularly one with learning difficulties, it would not be possible to continue to display the same pattern for a

lengthy period of time. A child would change walking patterns and possibly which leg the limp was presenting if no discomfort or pain was present. It would be advantageous in a future study to add specific questions about pain levels to study questionnaires to examine this. The VAS scores themselves may not be relevant as none of the children were discovered to have arthritis and the score is therefore a general score by the parents and more relevant questions would be beneficial to exploring this topic.

Our main consideration regarding the anthropometric measurements was whether this population of children was overweight which would further compound any MSK issues and put added pressure on the lower limb joints which have already proven to be considerably hypermobile as discussed in Chapter 5. Obesity in children with DS places more strain on the MSK system which makes screening for MSK disorders in this population imperative to prevent injury (Murray and Ryan-Krause, 2010). We anticipated that the study cohort would prove to have an overrepresentation of obese patients compared to the Down's cohort of a decade ago given current health trends, but results show that they are not. Although the DS population is described as being shorter and heavier than the general population (Cronk et al, 1988; Pueschel, 1995; Cremers et al, 1996; Bosch 2003; Roizen, 2003; Murray and Ryan-Krause, 2010; Myrelid et al, 2011), and this is shown in the comparison between this DS study data and the UK90 data, only seven children in the study were shown to be obese and the comparison between this study data and the Down's normative data (Styles et al, 2002) showed no significant difference compared with this cohort reported a decade earlier. They do not calculate body mass index (BMI) for this cohort of DS so we had to compare height and weight only. This suggests that this study cohort does not appear to show any increase in obesity levels within the DS population over the last 10 years but does still appear to show that DS children are shorter with higher BMIs than the general population.

Pubertal status was not documented in the study population but may have been a useful consideration with regards to growth and development especially as 37 (51%) of the study cohort was over the age of 10.

CHAQ forms are based on limitations due to musculoskeletal problems and CHQ forms are based on well being in children with underlying disease and were therefore considered to be irrelevant to the study results as it was unclear if they had been completed from a musculoskeletal or Down's syndrome point of view. Results from CHAQ forms were unclear regarding any musculoskeletal issues as 26% of the forms returned suggested moderate disability and showed the limitations of using this form for a population study in this cohort. It was decided not to analyse the CHQ data following this conclusion as there was no further funding available to cover the cost of the analysis.

Schober's test in this study cohort was inconclusive as it was unclear if lower values were due to lack of understanding of the test and non compliance rather than any spinal limitation.

This population of children is seen regularly by health professionals including community paediatricians, physiotherapists and school nurses. Despite this, the pilot study showed that musculoskeletal disorders were not being picked up and part of this study was to help raise awareness of musculoskeletal disorders in health professionals for children with DS. One intention from the study is to educate these health professionals in musculoskeletal examination with an aim to developing an education leaflet.

## **CHAPTER 7**

### **PODIATRY**

#### *7.1 Introduction*

Specific foot problems are described in DS such as pes planus, syndactyly and hallux valgus which can be overlooked in children with DS as more severe problems are frequently (Concolino et al, 2006).

A number of studies have examined foot pathologies, footwear, gait development and pattern and posture (Shumway-Cook et al, 1985; Prasher et al, 1995; Concolino et al, 2006; Selby-Silverstein et al, 2001; Galli et al. 2008; Chang et al. 2009; Rigoldi et al, 2010).

Examining for podiatric conditions such as pes plano valgus and deformities such as leg length discrepancy is important because early intervention can be made to prevent pain and discomfort developing from hypermobility and hypotonia, and limit long term deformity. This intervention can be in the use of orthoses such as implants for inside footwear or specially made footwear to support the foot and ankle joint and encourage a more normal foot posture.

#### *7.2 Methods*

73 children (28 boys; 45 girls) aged between 2.4 and 15.9 (median 8.94) were recruited from an identified population of 142 children with DS resident in Glasgow and examined as described in Chapter 3.

66 of the 73 children were examined by a consultant podiatrist for foot size to shoe size ratio, adequacy of footwear, use of orthoses, range of movement, foot type, foot posture in relaxed and dynamic phase of gait, lower limb posture, leg length discrepancy, intrinsic foot biomechanics, enthesitis, digital and metatarsal formula, digital deformity, skin type and pathologies and nail features and pathologies. All these examinations were devised and carried out by a consultant podiatrist following current standards and techniques (Goel and Watt, 2010).

66 children of the study cohort were examined by the podiatrist as, due to his retirement, he was unable to examine the final 7 children of the cohort and they had MSK assessment only.

### 7.3 Podiatry examination

Shoe size to foot size ratio was examined to assess whether the children were wearing the correct size of footwear. This difference was expressed in number of feet rather than children as 16 of the children had feet of different sizes and the results compared with the recognised foot health and industry standard two size difference (Walther et al, 2008) as it allows for elongation and growth within the shoe during gait and prevents the restriction of the feet and toes which could cause trauma and deformity (Figure 7.1).

Foot type was assessed as different foot types can have implications for shoe fitting and therefore trauma and deformity and also to compare with the description of the Downø foot in current literature. Foot type can be determined by the digital formula which is the relative length of the toes to one another. Different foot types include square forefoot (all toes of relatively equal length), Egyptian foot (big toe longest tapering to little toe), Greek foot (second toe longer than big toe) short/broad foot (very broad in relation to length), long slender foot, triangular foot, hypermobile foot and low and high arched foot. Shoe type was assessed as an inappropriate shoe can cause trauma and deformity to the foot.

Foot and lower limb posture were examined, as postural disorders such as pes plano valgus and sub-talar joint pronation can cause discomfort, pain and disability. Orthotic usage was assessed to discover how many children were being treated appropriately for postural foot disorders. The addition of an orthosis can improve the posture of the foot and improve and correct gait.

Digits, skin conditions and nails were examined as part of the routine podiatric screen although nails were specifically examined for nail pitting and striations with regard to a possible link to psoriatic arthritis as considered by Cruickshank et al (2008).

Metatarsal formula shows the relative length of metatarsals to one another and the positioning of the first metatarsal head. Metatarsal heads are numbered one to five with the relative length from longest to shortest displayed within the formula. 21345 known as the index minus formula (second metatarsal head sits highest down to fifth sitting lowest) is the most prevalent formula with the index plus formula 12345 also considered within normal parameters (Gottschalk et al, 1980; Dominguez et al, 2006; Morandi et al, 2009). A metatarsal formula of 23415 could cause a pronated foot caused by the first metatarsal head being too short.

## 7.4 Results

30 (45%) feet examined displayed the 2 size differential between foot size and shoe size as described above. (Table 7.1).

### 7.4.1 Footwear

42 (64%) children had footwear with adequate foot support and 23 (35%) had footwear with inadequate support with no data on one child. 48 (73%) wore shoes with appropriate heel height and 17 (26%) had shoes with too low a heel height. Appropriate heel height was considered to be between ½cm and 1½cm as a slight heel height gives a mechanical advantage during locomotion. Types of footwear are shown in Table 7.2. 42 (64%) children had had their feet measured. The shoes which had inadequate counter and low heel height tended to be plimsolls or converse trainers and the material for these shoes were generally canvas or plastic.

### 7.4.2 Orthotic usage

26 (39%) children had attended orthotics and had foot orthoses fitted for their shoes.

### 7.4.3 Foot type

25 (36%) of the study population displayed a square forefoot, 27 (41%) a short broad foot and 46 (70%) a triangular foot which can all have implications for shoe fitting which could lead to deformity (Table 7.3). 39 (59%) of the study population displayed hypermobility in the feet.

### 7.4.4 Foot posture

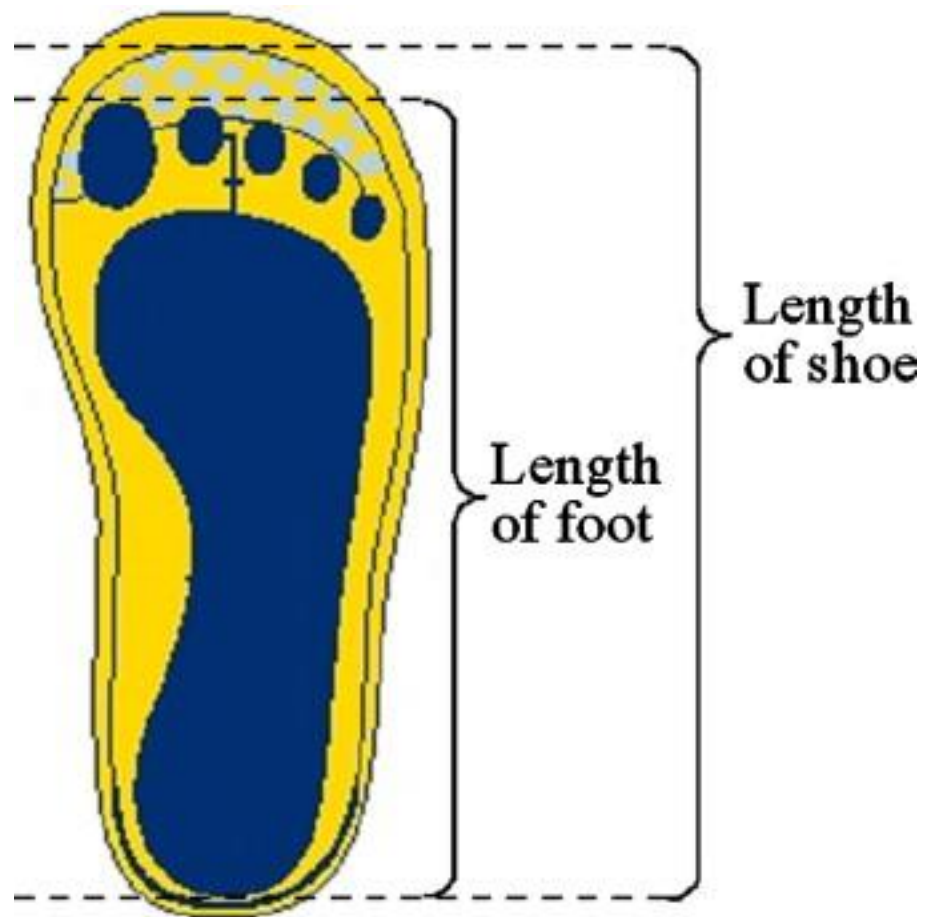
32 of the children displayed a pes plano valgus which is just under half of the study population. 55 (83%) showed sub-talar joint pronation in relaxed stance and 49 (74%) showed this during gait. (Table 7.5).

### 7.4.5 Metatarsal formula

32 (48%) children displayed a metatarsal formula of 21345 with another 9 (14%) displaying the index plus formula of 12345. 11 children (17%) displayed a formula of 23415 which could lead to pronation. 12 children displayed the formula 23145 with the remaining 2 children non-compliant to examination (Table 7.4) .

<b>Foot size to shoe size difference</b>	<b>Number of feet /132 (%)</b>
<b>No data</b>	14 (21%)
<b>0</b>	10 (15%)
<b>+ 1</b>	17 (26%)
<b>+ 1½</b>	18 (27%)
<b>+ 2</b>	30 (45%)
<b>+ 2½</b>	14 (21%)
<b>+ 3</b>	22 (33%)
<b>+ 3½</b>	3 (4.5%)
<b>+ 4</b>	2 (3%)
<b>+ 4½</b>	1 (1.5%)
<b>+ 5</b>	1 (1.5%)

*Table 7.1: Table showing difference between foot size and shoe size*



*Figure 7.1: Figure showing foot size to shoe size normal standard (Walther et al, 2008)*



<b>Shoe type</b>	<b>Number of children (%)</b>
<b>Lacing</b>	11 (17%)
<b>Strap</b>	5 (8%)
<b>Velcro</b>	47 (71%)
<b>Slip-on</b>	1 (1.5%)
<b>Pointed</b>	7 (11%)
<b>Square</b>	7 (11%)
<b>Round</b>	51 (77%)
<b>Adequate Counter</b>	42 (64%)

*Table 7.2: Table showing types of footwear worn*

<b>Foot type</b>	<b>Number of children (%)</b>
<b>Square Forefoot</b>	25 (36%)
<b>Short Broad</b>	27 (41%)
<b>Long Slender</b>	20 (30%)
<b>Triangular</b>	46 (70%)
<b>Hypermobile</b>	39 (59%)
<b>High Arched</b>	15 (23%)
<b>Low Arched</b>	40 (61%)

*Table 7.3: Table showing foot types in study cohort*

<b>Metatarsal formula</b>	<b>Number of children (%)</b>
<b>21345</b>	32 (48%)
<b>12345</b>	9 (14%)
<b>23415</b>	11 (17%)
<b>23145</b>	12 (18%)
<b>No data</b>	2 (3%)

*Table 7.4 Table showing metatarsal formula in study cohort*

<b>Posture</b>	<b>Number of children (%)</b>	<b>Posture during Gait / Dynamic</b>
<b>Sub-talar joint pronation</b>	55 (83%)	49 (74%)
<b>Pes Plano Valgus</b>	-	32 (48%)
<b>Neutral</b>	7 (11%)	13 (20%)
<b>Supination</b>	1 (1.5%)	1 (1.5%)
<b>No data</b>	3 (4.5%)	3 (4.5%)

*Table 7.5 Table showing differing foot postures in study cohort*



*Picture 7.1 Picture showing sub-talar pronation with hypermobility*

#### 7.4.6 Leg length discrepancy

48 (73%) children displayed no leg length differential. 11 (17%) children displayed a leg length differential of half centimetre and 7 (11%) children displayed a differential of 1cm .

#### 7.4.7 Nail features and pathologies

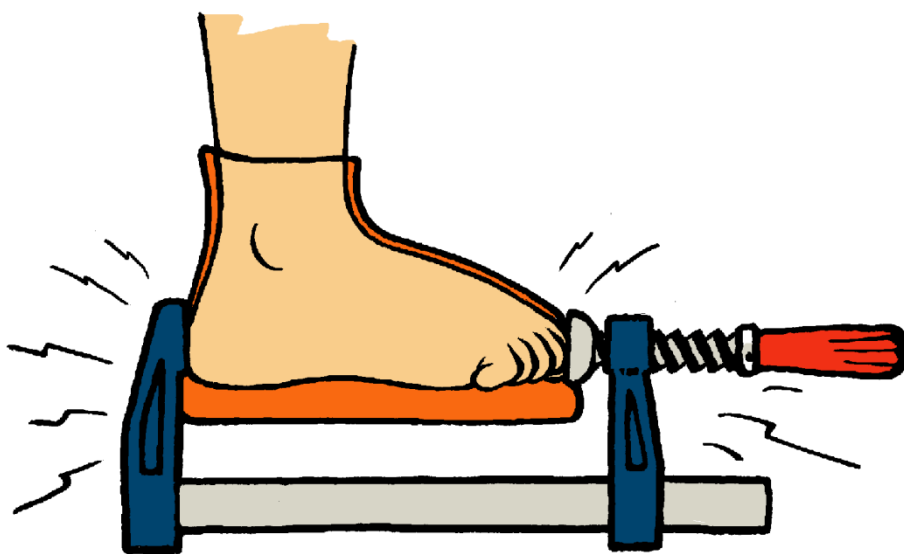
Longitudinal and transverse striations were the most common nail changes found with 39 children showing longitudinal nail striations (Table 7.6).

#### 7.4.8 Skin pathologies

18 children displayed syndactyly with the majority between 2<sup>nd</sup> and 3<sup>rd</sup> toes. 14 children displayed anhydrosis and 4 displayed tinea pedis.

<b>Nail changes</b>	<b>% of children</b>
<b>Longitudinal striations</b>	39 (59%)
<b>Transverse Ridging</b>	9 (14%)
<b>Involution</b>	5 (8%)

*Table 7.6: Table showing nail changes discovered in the study cohort*



*Figure 7.2: Figure showing effect too tight shoes can have on toes  
(an initiative of the 'Kids: Healthy feet – healthy life' research team: Appendix 9)*



### 7.5 Discussion

Foot size to shoe size ration was examined as shoes that are too short can cause deformity to the feet and children are especially at risk as their feet are growing, are softer than adult feet and can be affected more easily by footwear that is too tight or short as expressed in Figure 7.2. Children with DS are especially vulnerable as they are more likely to display a pes plano valgus and a sub-talar joint pronation which would require a broader shoe to accommodate the altered physiology. However 45 of the feet displayed a difference that was shorter than the recommended standard with 10 showing a 0 size difference and 17 showing a +1 size difference which means these children were in shoes too small for their feet. One child had one foot showing a +2½ size difference and the other a +3 size difference but in this case the larger shoe size was required due to the broadness of the feet. 32 of the feet examined displayed a two size difference between shoe size and foot size taking account of growth, elongation during gait, particularly with hypermobile feet, and accommodation for style.

Footwear was assessed for style, retaining medium (how the footwear is held on the foot), toe box shape, counter (support in the heel area, particularly medially), material, heel height and base of heel. Deformity can arise from poor design in any of these features. In general the footwear was very good with round or square toe boxes, adequate counters, velcro retaining mediums, leather uppers and an appropriate heel height and base of heel. The style of shoe was typically 'school shoe' or trainer. A small proportion of footwear was plastic and 'cheap' which may reflect the current economic climate rather than ignorance or negligence. Most of the parents appeared to be making an effort to have good quality footwear and a good fit but educating parents regarding the importance of good fitting, suitable footwear is recommended.

Orthotic usage was examined as it is well known that pes plano valgus is an overt feature in DS but only a very small proportion of children with this deformity had management with foot orthosis and less than 5% had access to a podiatrist or had specialist podiatric assessment. Prescribed foot orthotic usage was present in 39% and it appeared to be a lottery as to whether children had been referred to orthotics or podiatry or not. Many children with gross deformity had no orthotics whereas children with marginal or no deformity were being managed by orthotics. This is an area that needs to be addressed urgently with appropriate protocols and specialist assessment.

As discussed in Chapter 5 the feet of this group of children displayed generalised hypermobility, especially in the ankles, subtalar and talonavicular joints which did not correlate with the joints examined in the Beighton hypermobility scoring system.

A considerable number of foot configurations were identified in this population. The DS foot has been described as short and broad with a larger space between the 1<sup>st</sup> and 2<sup>nd</sup> metatarsophalangeal

joint (Kava et al, 2003; Roizen, 2003; Weijerman and de Winter, 2010; <http://www.nichd.nih.gov/health/topics/down/conditioninfo/Pages/symptoms.aspx>; <http://www.downsyn.com/joomla/index.php/questions-articles/what-are-the-physical-characteristics>) (Picture 7.1). This was a pattern identified in this population but the space was only obvious in a small number of cases. This study showed that the majority of the feet were short and broad with an adducted first ray, hypermobile and a low arch suggesting pes plano valgus but 30% displayed long, slender feet demonstrating considerable variation in foot type and structure, which is not clear in the existing literature.

Foot and lower limb posture were examined to determine the number of children with postural defects. The majority demonstrated excessive sub-talar joint pronation and 48% displayed pes plano valgus. With pes plano valgus the foot is always flat but with sub-talar joint pronation the foot collapses in which could be developmental or pathological and may also be secondary to hypermobility, hypotonia and lower limb posture. This is particularly relevant with regard to orthotic usage as orthoses can correct sub-talar joint pronation and highlights the need for podiatric review of these children.

Eighteen (27%) children displayed syndactyly with the majority occurring between the 2<sup>nd</sup> and 3<sup>rd</sup> toe. All showed partial syndactyly with the fusion extending only to the proximal inter phalangeal joint. This is a large percentage compared to a prevalence found in a study of congenital limb defects in Finland of 0.03% (Aro et al, 1982) and an estimated prevalence of 0.04% in the general population (Malik, 2012) The location of the syndactyly is the most common pattern and is classified as syndactyly type 1. Type 1 syndactyly is one of the most common types demonstrating fusion of third and fourth fingers and/or second and third toes (Malik, 2012). Syndactyly may, therefore, be more prevalent in DS. Concolino et al (2006) found syndactyly in 10% of their DS population compared to 2% in the control population.

Leg length discrepancy was examined in order to determine the possible association with mobility problems. All the children displayed a leg length discrepancy of 1cm or under which is considered to be within the normal parameters. The literature is conflicting as to when a leg length discrepancy becomes a problem but the general consensus is that corrective treatment would not be considered in a difference under 2cm (Gibson et al, 1983; McCaw and Bates, 1991; Gurney, 2002; Perttunen et al, 2004; Defrin et al, 2005; [www.childreorthopaedics.com/llcd/html](http://www.childreorthopaedics.com/llcd/html)).

A large number (39) of the children displayed longitudinal ridging on their toe nails with a smaller number (nine) displaying transverse ridging. Nail morphology was documented because of interest in determining whether psoriasis or nail features were over represented in the population, and any relation to psoriatic arthritis following the RHSC Yorkhill pilot study (Cruickshank et al, 2008)

which found two of the 12 children who attended had psoriatic arthritis and eight displayed features of psoriatic arthritis. Parents of seven of the children in this cohort had described a family history of psoriasis in a first degree relative. However this ridging was not clinically typical of psoriasis, and it was considered that this may be a peculiarity to toenails in DS rather than a link to psoriatic nail changes. A small number (four) displayed nail pitting but this may be due to trauma of the nail instead of due to underlying psoriasis.

Many of the foot and lower limb features concur with the literature descriptions in DS but do not appear as obvious as would be expected. Foot posture and gait are an issue mainly due to sub-talar pronation and hypermobility. Each case should be managed on its own merit and children should be screened by a paediatric podiatric specialist experienced in children with DS particularly with regard to orthotic management.



*Picture 7.2: Down's foot showing wide gap between first and second metacarpal joints*  
*<http://newborns.stanford.edu/PhotoGallery/Downs4.html>*

## **CHAPTER 8**

### **DISCUSSION**

The research objective for this study was to determine the frequency of musculoskeletal disorders in children with Down's syndrome and the levels of associated physical disability with particular attention to hypermobility, foot disorders, arthritis and obesity. This is the first population survey to examine MSK disorders in children with DS and the main finding of the study was the level of hypermobility within this population of children, particularly in the lower limbs, with associated podiatric disorders.

Recognising MSK issues in this population of children is complicated by the fact that they do not appear to express pain in the same way as the general population. Studies by Lind et al (1970), Martínez-Cué et al (1999), Hennequin et al (2000) examined the reduced pain perception within the DS population and many of our parents gave us anecdotal evidence that their children did not appear to complain of pain, including one boy with extensive joint damage whose functional loss was indicative of adaption to pain, but who had never expressed pain. This apparent lack of pain causes difficulty in diagnosis, as joint pain is generally one of the key symptoms in arthritis and hypermobility in the general population. If pain is not described on presentation arthritis or hypermobility may not be considered by the health professional first seen despite other symptoms being present such as synovitis, crepitus and over extending joints. This lack of pain expression is evident in the original case series by Yancey et al, 1984; Olson et al, 1990 and Juj et al, 2009 as presentation included morning stiffness, limited motion, gait change, fatigue, inability to feed or dress and an increasing desire to be carried. Only two of these 25 patients are described as presenting with pain which correlates with the findings of the RHSC Yorkhill pilot study (Cruickshank et al, 2008). In a study of hypermobility in children with DS by Livingstone and Hirst (1986) pain is not mentioned in the presentation whereas a study of 125 non DS children with recorded hypermobility by Adib et al (2005) mentioned joint pain as one of the most common presenting features. Lack of pain could cause major implications regarding joint damage and complications from undiagnosed MSK disorders such as hip dysplasia and arthritis and also good joint function within hypermobility.

The majority of literature describing MSK features in DS describe general hypermobility and hypotonia but these are mainly specified as causing hip dysplasia, atlanto-axial instability and sub-talar joint pronation. There are no descriptions of hypermobility

examining separate joints so our findings that certain joints, particularly the lower limb joints, appear to be more hypermobile than others is an important finding.

The main finding of this study that the children in the study cohort were found to be particularly hypermobile in the lower limbs had two implications. Firstly these are the weight bearing joints that are most likely to be associated with altered mobility, and secondly that the pattern of joints found to be most hypermobile did not correlate with the joints examined using the Beighton (Figure 3.1) or Brighton scales (Figure 3.2). Only 11 children displayed a Brighton score (Figure 3.2) that would diagnose benign joint hypermobility syndrome despite all the children displaying at least one hypermobile joint, and some very extreme ranges of hypermobility within the affected joints. The lower limbs were found to be most hypermobile with the hips being the most common. Anecdotally many of the children immediately sat in the lotus position and a large number were able to put their feet behind their heads like the boy in Picture 4.1 displaying these extreme ranges of joint mobility. Feet were also particularly hypermobile with a large number displaying sub-talar joint pronation and pes plano valgus. Other literature does not appear to have examined individual joints, instead using the Carter/Wilkinson score (Livingstone and Hirst, 1986) or the Beighton score (Clinch et al, 2011). Livingstone and Hirst (1986) followed the Carter/Wilkinson method as described in Chapter 2, examining only particular joints. One of their patients presented with a dislocatable hip but hips are not mentioned within their results regarding hypermobility. Their conclusions that general joint laxity is not present in DS, following a criteria that upper and lower limb involvement must be present, does not correlate with the results from this study showing a high number of hypermobile joints in these children. Although this is an older scoring system the current scoring systems still only look to diagnose the presence of hypermobility. There is no system to grade levels of hypermobility and the development of a DS specific scoring system would be extremely useful within this population as there was a large variability of hypermobility levels in these children, not only in the number of joints affected, but the degree of laxity in the joints.

Only 53% of the children had Beighton scores over four which gives one of the Brighton major criteria. Debate over whether a higher threshold for defining hypermobility may be more discriminatory in children is ongoing. Smits-Engelsman, Klerks and Kirby (2011) suggested that their threshold of five appeared to be classifying children as hypermobile incorrectly and recommended raising the level to seven. A Beighton score of over seven would only have given 10 (14%) of these children a Brighton major criteria, which was a considerable underestimate and mismatch with the level and number of joints that were hypermobile documented in this population. However this is still a higher incidence than

Clinch et al (2011) incidence of 4.2% of their population displaying Beighton scores higher than six suggesting that this population of children appears to be more hypermobile than the general population, albeit the mismatch in ages made by this comparison. These results also support the development of a DS specific system scoring levels of hypermobility.

Interestingly, Adib et al (2005) examined 125 non DS rheumatology patients with recorded hypermobility and found that the knees had the highest rate for increased range of movement and, although the hips and ankles had high rates also, elbows, metacarpal joints and wrists had very similar rates unlike this population where the lower limbs were found to be considerably more hypermobile than the upper limbs. They also found more than 30% of their study population to have Beighton scores of 8 or 9 in stark contrast to 1 child in the DS study cohort which, again, suggests that these scoring systems are not suitable for the DS population.

Hand and feet joints appear to be the most common joints to display synovitis and deformity in this population (Cruickshank et al, 2008; personal communication O Killeen, 2013) and a new hypothesis around the relationship between extreme hypermobility, lack of pain and the pattern and rapidity of deformity from arthritis in the hands suggested that the areas of highest hypermobility would be more susceptible to deformity. However hands did not display as high a level of hypermobility as feet. A significant and varied number of problems were also identified in the feet of these children, many with the potential to lead to progressive problems and become more difficult to remedy so we would recommend that they should all be seen by a specialist podiatrist who understands this population and can refer appropriately for orthotic usage on a regular basis.

The pattern of hypermobility in lower limb joints is particularly concerning in this population of children as it affects weight bearing joints which may lead to increased pain and discomfort or mobility problems. This was quite evident in some of the anecdotal comments from the parents who said that their children would suddenly sit down after walking a distance and refuse to walk any further. Some of the parents thought this was due to mood or disobedience but were interested in the findings of the lower limb hypermobility, particularly feet and hips, and how this may be contributing to discomfort from the hypermobile joints.

Hypermobility may also be linked to other issues that are described in DS such as urinary tract disorders and voiding disturbances (Bosch, 2003; Mercer et al, 2004; Weijerman and de Winter, 2010). Adib et al (2005) commented that urinary incontinence and infections

were more prevalent in girls with generalised joint hypermobility. Although specific urinary tract disorders are described in DS such as renal malformation, cysts and posterior urethral valves (Bosch 2003; Mercer et al, 2004; Weijerman and de Winter, 2010) it may be worth considering a link between delayed toilet training and urinary incontinence with hypermobility in this population.

Use of a modified CMAS score within the study suggested that this was not useful as a proxy for making any assessment of muscle function in this population. The lack of a reproducible method to assess hypotonia in contrast to hypermobility was a limitation. It was clear examining these children that both problems often co-exist and together have an additive effect on function, but developing robust data on this was not possible without development of a robust tool. Hip joints are heavily supported by a strong musculature. Hypotonia may be very important in contributing to the extreme hypermobility found at the hips in these children with DS.

Livingstone and Hirst (1986) concluded that the orthopaedic problems that occur in children with DS was related to hypotonia rather than hypermobility in comparison to this study's findings that suggest that joint problems may be linked to hypermobility and therefore development of a DS specific tool for measuring hypotonia would be of value with regard to joint problems.

Mobility issues may also arise from weight problems as obesity can affect mobility levels. The current worldwide epidemic of obesity led to the inclusion of an anthropometric component to the study. Obesity will put pressure on the lower limbs and compound any issues already caused by hypermobility in these joints. The unexpected finding of the study was that this population of children, usually considered at risk for obesity, had no higher levels of obesity than the reference population from a decade ago. Whilst only 10% of this study cohort was shown to be obese it is still an important issue to monitor the weight and BMI of DS children to prevent weight increase contributing to mobility problems.

This study did not find any additional cases of inflammatory arthritis within the children examined as part of the study so the RHSC Yorkhill pilot study prevalence of 2.87% remains unchanged. A study in Ireland, currently in progress, of a ten-fold larger population of children with DS arising despite a remarkably similar total population size (both Scotland and Ireland have about 1 million children) has identified undiagnosed cases of arthritis at a high rate (21 cases identified from a population of 164 examined to date), and suggests a higher prevalence of arthritis is anticipated to be calculated at



completion of the study (personal communication Charlene Foley and O Killeen September 2013). It is unclear why the Irish population should appear to have a much higher prevalence rate than previous reported rates (Padmakumar et al, 2002; Cruickshank et al, 2008; Jui et al, 2009) and it will be interesting to see their final figures.

One of the barriers to correct diagnosis of MSK disorders may be that attitudes towards these children can vary as comments from a parent of a DS child with arthritis suggests. She was advised by doctors that she should expect mobility issues as he had Down's syndrome but as one of the focus group rheumatologists said 'I don't know why their expectation is that their mobility should be so poor'. Attitudes to prenatal testing for DS and people with DS was examined by Bryant, Green and Hewison (2006) and they commented that 'there was strong agreement that the biggest obstacle to people with Down's syndrome having a good quality of life was a society that struggled to include people with disabilities'.

One of the children seen as part of the study had displayed a change of gait for a number of months. The care home staff thought he had hurt his hip originally but felt that the limp was put on as time went on. Children would be unable to continue displaying a limp on the same leg if there was nothing wrong, especially children with a learning difficulty so, if this child was limping continually, it was suggestive there was definitely a problem. This child was seen as having mood issues which probably led to this attitude and, although no MSK disorder was diagnosed, he was found to have an undescended testicle, which was a very important diagnosis in a teenage boy. This is an example of an altered perception or expectations of the physical abilities in this population which may be a major contributor to late diagnoses. In a review of literature in palliative care in learning disabilities, Tuffrey-Wijne (2003) discussed studies that concluded that in some cases diagnosis was delayed because symptom complaints were attributed to learning disability which supports this theory and suggests that rheumatology is not the only area where this is a problem.

A number of the children seen by the consultant rheumatologists and identified from the RHSC Yorkhill pilot study were given various misdiagnoses which included maternal anxiety and developmental issues. This is also present in the previous case studies described by Olson et al (1990). 'Very frequently, pain behavior and changes in activities of daily living were attributed to behavioural problems associated with the Down syndrome' (Olson et al, 1990). It appears that the attitude towards these children, particularly with regard to MSK disorders, needs to be addressed to allow correct and timely diagnosis and early intervention before joint damage can occur. 'While the impairment associated with the condition is real, affected individuals have frequently

exceeded expectations and limitations set for them by health professionals (Bryant et al, 2006).

The recurring theme and most important outcome of this study is the recognition of the need for education. In the first instance parents require to be educated on the possibility of MSK problems in their children and the requirement to remain vigilant to change of function and mood as these should not be dismissed as developmental or behavioural problems related to DS. The majority of the parents involved in the study were aware that neck and hip problems were possible in their children as checking for atlanto-axial instability and hip instability are part of the annual review exam by the community paediatricians. Many parents were also aware that their children were particularly hypermobile but were not necessarily aware that hypermobility could cause pain and discomfort leading to reduced levels of mobility. Those that said their children sat down suddenly after walking a distance appeared interested in possible alternative explanations such as pain and hypermobility.

An education leaflet giving parents information on various possible MSK disorders such as hypermobility, arthritis and joint instability, including signs and symptoms would be an extremely useful tool as it would give parents the confidence to query symptoms with their health professional and, hopefully encourage the health professional to complete an MSK assessment or refer, if unsure. This leaflet should also include information about changes in mood or gait, loss of function and adaptations of movement as these children may not complain of pain but adapt round any discomfort they may be experiencing. Including foot problems and why correct shoe fitting is extremely important in this population of children is also vital for parents as keeping their child's feet healthy will help reduce mobility problems. Encouraging the parents to seek podiatric advice would also be recommended.

Education on healthy diet and weight management would also be very important for the parents as trying to maintain their child at a healthy weight would prevent mobility issues occurring or worsening if already present. Information about regular exercise and activities should be included. It is recognised that this may not be possible for all children with DS as some children may have a deeper learning disability or other problems such as autism and it may be more difficult to maintain these children at a healthy weight.

Education will also help address the incorrect impression that these children should have mobility issues because of their DS and that regular exercise will help weight management and allow them to socialise. Many children with DS participate in exercise such as football, athletics, swimming and dance classes and should be encouraged to

become involved with sports and exercise alongside children in the general population. This will help improve the attitudes towards mobility levels and issues in these children. Indeed good work in raising expectation for the sporting achievements is seen in the petitions and campaigns for people with DS to compete in the Paralympics as the categories between physical disabilities and learning disabilities excludes them at present.

Education of the various health professionals who see these children regularly is also vital to prevent mobility problems and allow timely diagnosis of any disorders present. This would include general practitioners, community paediatricians, physiotherapists, occupational therapists and school nurses. This should include information on general mobility in this population of children to remove the attitude that these children will have mobility issues due to their DS and raise awareness that children in this population are more likely to present with a gradual decrease in function or a change in behavior rather than an acute painful presentation. The annual health checks would be the ideal opportunity to identify any of these issues and refer where appropriate. Discussing palliative care in learning disabilities Tuffrey-Wijne (2003) commented that a particularly under researched area was how people with learning disabilities express and experience their symptoms which needs to be addressed.

General practitioners (GPs) and community paediatricians should be educated in how to undertake an MSK examination in children to identify multiple MSK disorders which would benefit the general population of children as well as the DS population. Education for GPs and community paediatricians should also include information about pain perception in this population as this is an extremely important factor in recognising arthritis and other MSK disorders. Pain in the joint is usually one of the first symptoms a child will complain about which may lead the parent to notice other symptoms, if present. Reduced pain perception in the DS population make identifying MSK problems harder and these health professionals will require extremely well developed examination techniques.

One of the focus group rheumatologists thought that the lack of complaints of pain may be why arthritis was not considered as a diagnosis in some of the children who presented late with joint destruction. It is, therefore, very important that the health professionals who see these children regularly are aware that a child presenting with reduced mobility, change in gait or mood, swollen or stiff joints or crepitus in a joint are most likely to be presenting with inflammatory arthritis or other significant MSK disorder even if the child is not complaining of any pain.

The rheumatology department at RHSC Yorkhill run an annual educational meeting which provides education on MSK examination techniques, orthopaedic problems, diagnosing MSK and connective tissue disorders and reading Xrays. GPs and community paediatricians should be encouraged to attend such educational meetings to improve their knowledge of rheumatological and orthopaedic disorders. Education can also be given in the form of educational leaflets, DVDs and on site training.

While we would recommend educating in MSK disorders, our focus group suggested that community paediatricians may not welcome an additional examination within the annual review process, in addition the identification of MSK problems appears from the study to be particularly challenging, and require high quality MSK examination skills that are well developed and well maintained. Whilst education of community paediatricians to use existing MSK examination tools such as pGALS would be a useful way forward, we also consider that this might still lead to difficulties in identifying pathology. This study recommends the creation of a DS specialist nurse who can liaise with the families regarding all aspects of their care and could also be trained in MSK examination. They could facilitate coordination of appointments between specialties to the same day, if possible, to prevent too many separate appointments taking up the family's time, shared general anaesthetics for more than one procedure, and many other organisational skills that would be of benefit. One parent taking part in the study declined the referral to paediatric rheumatology because she already had enough appointments to attend. A nurse specialist would be able to help educate the parents and support them with any concerns. In her interview with *Arthritis Today* magazine one parent commented 'if we hadn't been his parents, pushing all the time, he wouldn't be diagnosed yet' (Tadman, 2012). Some parents may not know that there is something wrong and to push for a correct diagnosis but a nurse specialist could liaise with the health professionals to ensure the child's healthcare journey is thorough and appropriate. The nurse could also facilitate correct podiatric referral to ensure ongoing footcare and appropriate orthotic usage. This nurse working with one group of patients over a wider geographic area would become more skilled at making these assessments, would not be working with large numbers of neuromuscular disability which requires different skills, and would develop relationships with relevant specialist services, such as paediatric rheumatology, podiatry, cardiology and haematology, becoming very skilled in identifying the specific needs for these children and families. Sloper et al (2006) examined the use of key workers in children with disabled children which included 15 children with DS. They commented that research into the use of key workers suggested that these families are better informed, have higher morale and have a better involvement and relationship with the services they use.

Development of a DS specific MSK examination tool, equivalent to pGALS, taking into account the differences this study has identified in the MSK pathologies and their presentations in this population, is a key development to facilitate early and confident MSK assessment where MSK presentations are difficult and different in this population.

### 8.1 Study limitations

The main study limitation was performing a population study in children with learning difficulties as we were unaware how co-operative the children would be. Generally the majority of the children were compliant with the study visit, however, there were some children who were only compliant with certain aspects of the visit and a complete assessment was not obtained.

Recruitment was an issue for the study with 36% not responding to the study invitation. It was considered, though, that this group of children already have a large number of clinic and hospital appointments and the parents may have decided they already had enough appointments without involving themselves in another. Deprivation category was not documented for the study population but would have been a useful tool to assess any difference between the parents who agreed to participate and those who did not respond.

As discussed in Chapter 3 a number of the various tests used in this study were found to be unsuitable for this population of children. However, this gave us interesting results to compare to the tests such as the comparison of hypermobile joints within the Beighton scoring system.

It was discovered that the CHAQ questionnaire was not useful within this population as it is aimed at scoring for function limitations in arthritis and it was unclear if parents were scoring around their children's DS rather than any MSK issues. This meant the scoring was not valid for assessing for MSK problems in these children.

The CHQ questionnaire was also considered not to be useful for the same reasons as it is a well-being questionnaire for children with an underlying disease and, again, was unclear if completed around the child's DS rather than any MSK problems.

The Beighton score proved to be unreliable in this population as the majority of joints found to be hypermobile did not correlate with the ones examined within the Beighton score. Similarly the Brighton score, used in conjunction with the Beighton score was not useful in diagnosing hypermobility syndrome as discussed in Chapter 5.

Bioelectrical impedance measurements were taken but there was no data to compare them with to assess the significance of impedance values in this population and 25% of the children did not stand still long enough on the Tanita scales to allow for an impedance measurement.

The Schober's test had limitations in this population due to compliance and understanding of instructions. 16 children were non-compliant with the test and it was difficult to ascertain if the children who showed a result under 21 had understood the instructions and the lower result was due to a limitation or non compliance.

The patient questionnaires were devised to receive answers to issues we wished to address within the study. However, if the study were to be repeated, we would include more open ended questions and supplementary questions as a small number of parents answered yes to a question regarding any MSK concerns without giving any further details.

Pubertal status was not documented within the study but would be considered in a further study as it is an important consideration in growth and development.

The focus groups were limited for a number of reasons previously discussed in Chapter 4.

If the study was to be repeated various changes would be made to improve the data outcome such as improved questionnaires, assessing an alternative method of recruitment to improve participant numbers, improving the facilitation of any focus groups and using the study to try and identify suitable tools for this population of children.

## 8.2 Recommendations and future work

We would recommend the development of education tools on MSK disorders and examination such as information leaflets and study days for health professionals involved with the care of these children to allow better understanding and awareness of MSK issues and information leaflets for parents to allow them to understand what symptoms to be aware of. This will facilitate early diagnosis and greatly improve the prognosis for these children on presentation at rheumatology. It may be possible to develop information leaflets in collaboration with Arthritis UK.

We would also recommend the inclusion of an MSK examination such as pREMS to be incorporated into the annual review of children with DS.

Appropriate podiatric examination would be recommended for this population by a senior paediatric podiatrist, preferably one who is experienced in this population of children and can assess for appropriate orthotic referral.

Following on from this study, it would be advantageous to compare our results with the results of the population study in Ireland (personal communication O Killeen and C Foley), although they appear to have a much higher DS population which may be a result of Irish anti-abortion laws, and then consider repeating this study with a larger population group to try and establish a more definitive conclusion on MSK disorders in this population.

### 8.3 Summary and Clinical Implications

In conclusion this study did not discover any new cases of arthritis among the cohort and the RHSC Yorkhill pilot study prevalence of 2.87% remains unchanged. This percentage suggests that arthritis may be more prevalent in the DS population but further studies with a larger cohort or covering a wider area are underway and may establish a much higher prevalence (personal communication O Killeen and C Foley, 2013).

This population of children is shown to be extremely hypermobile but mainly in lower limbs leading to mobility problems, which does not correlate with the Beighton scoring system. A full examination of all joints in these children is recommended to establish level of hypermobility, and a specific DS hypermobility tool would be very valuable as the Beighton and Brighton scoring systems do not appear to be compatible with the joints found to be hypermobile in this study cohort.

Regular contact with a podiatrist experienced in children and especially DS children is highly recommended to improve quality of foot care and appropriate orthotic usage.

One positive outcome from the study is that referral rates to rheumatology from community paediatrics has increased and, therefore raised awareness regarding MSK problems in children with DS as we believe that the most important message from the study is that education of parents and health professionals is vital to improve knowledge and awareness of the signs and symptoms of MSK disorders and MSK complications within the DS population to ensure early diagnosis and appropriate management.

This group of children are found to be at risk of mobility problems due to MSK disorders but, if awareness is improved following this study and it is possible to create DS specific tools to examine and assess for MSK problems, the risk can be reduced and mobility problems can be minimised to allow good quality of life and improvement in outcome and prognosis.



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## **APPENDIX 1: ETHICS APPLICATION; SSI FORM AND NOTICE OF AMENDMENT**

NHS R&amp;D Form

IRAS Version 3.1

### Welcome to the Integrated Research Application System

### IRAS Project Filter

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

**Please enter a short title for this project** (maximum 70 characters)  
Prevalence of Musculoskeletal Disability in Down's syndrome

#### 1. Is your project research?

☒ Yes ☐ No

#### 2. Select one category from the list below:

- ☐ Clinical trial of an investigational medicinal product
- ☐ Clinical investigation or other study of a medical device
- ☐ Combined trial of an investigational medicinal product and an investigational medical device
- ☒ Other clinical trial or clinical investigation
- ☐ Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
- ☐ Study involving qualitative methods only
- ☐ Study limited to working with human tissue samples, other human biological samples and/or data (*specific project only*)
- ☐ Research tissue bank
- ☐ Research database

**If your work does not fit any of these categories, select the option below:**

☐ Other study

#### 2a. Please answer the following question(s):

- a) Does the study involve the use of any ionising radiation? ☐ Yes ☒ No
- b) Will you be taking new human tissue samples (or other human biological samples)? ☐ Yes ☒ No
- c) Will you be using existing human tissue samples (or other human biological samples)? ☐ Yes ☒ No

#### 3. In which countries of the UK will the research sites be located? (Tick all that apply)

- ☐ England
- ☒ Scotland
- ☐ Wales
- ☐ Northern Ireland

#### 3a. In which country of the UK will the lead NHS R&D office be located:

- ☐ England
- ☒ Scotland

NHS R&amp;D Form

IRAS Version 3.1

- ☐ Wales
- ☐ Northern Ireland
- ☐ This study does not involve the NHS

**4. Which review bodies are you applying to?**

- ☒ NHS/HSC Research and Development offices
- ☒ Research Ethics Committee
- ☐ National Information Governance Board for Health and Social Care (NIGB)
- ☐ Ministry of Justice (MoJ)
- ☐ National Offender Management System (NOMS)

**5. Will any research sites in this study be NHS organisations?**

- ☒ Yes ☐ No

**6. Do you plan to include any participants who are children?**

- ☒ Yes ☐ No

**7. Do you plan to include any participants who are adults unable to consent for themselves through physical or mental incapacity?** *The guidance notes explain how an adult is defined for this purpose.*

- ☐ Yes ☒ No

**8. Do you plan to include any participants who are prisoners or young offenders in the custody of HM Prison Service or who are offenders supervised by the probation service in England or Wales?**

- ☐ Yes ☒ No

**9. Is the study, or any part of the study, being undertaken as an educational project?**

- ☒ Yes ☐ No

**9a. Is the project being undertaken in part fulfilment of a PhD or other doctorate?**

- ☐ Yes ☒ No

**10. Is this project financially supported by the United States Department for Health and Human Services?**

- ☐ Yes ☒ No

**Integrated Research Application System**  
**Application Form for Other clinical trial or investigation**

**NHS/HSC R&D Form (project information)**

Please refer to the *Submission* and *Checklist* tabs for instructions on submitting R&D applications.

The student should complete this form on behalf of the Chief Investigator. Guidance on the questions is available wherever you see this symbol displayed. We recommend reading the guidance first. The complete guidance and a glossary are available by selecting [Help](#).

**Short title and version number:** (maximum 70 characters - this will be inserted as header on all forms)  
 Prevalence of Musculoskeletal Disability in Down's syndrome

**PART A: Core study information**

**1. ADMINISTRATIVE DETAILS**

**A1. Full title of the research:**

Study of the prevalence of musculoskeletal abnormalities in children with Down's syndrome in the Glasgow population

**A2-1. Give details of the educational course or degree for which this research is being undertaken:**

Name and level of course/ degree:

MSc in Research

Name of educational establishment:

University of Glasgow

Name and contact details of academic supervisor:

	Title	Forename/Initials	Surname
	Dr	Janet	Gardner-Medwin
Address	Department of Child Health		
	RHSC Yorkhill		
	Dalnair Street, Glasgow		
Post Code	G3 8SJ		
E-mail	Janet.Gardner-Medwin@glasgow.ac.uk		
Telephone	01412010867		
Fax	01412010837		

Name and contact details of student:

	Title	Forename/Initials	Surname
	Mrs	Maureen	Todd
Address	Dept of Child Health		
	RHSC Yorkhill, Dalnair Street		
	Glasgow		
Post Code	G3 8SJ		

E-mail	maureen.todd2@nhs.net
Telephone	01412321836
Fax	01412010837

A copy of a current CV for the student (maximum 2 pages of A4) must be submitted with the application.

**A2-2. Who will act as Chief Investigator for this study?**

- ☐ Student  
☒ Academic supervisor  
☐ Other

**A3-1. Chief Investigator:**

	Title Forename/Initials Surname
	Dr Janet Gardner-Medwin
Post	Senior Lecturer in Paediatric Rheumatology
Qualifications	MBChB FRCPCH PhD
Employer	University of Glasgow
Work Address	Dept of Child Health
	RHSC Yorkhill, Dalnair Street
	Glasgow
Post Code	G3 8SJ
Work E-mail	Janet.Gardner-Medwin@glasgow.ac.uk
* Personal E-mail	Janet.Gardner-Medwin@glasgow.ac.uk
Work Telephone	01412010867
* Personal Telephone/Mobile	
Fax	01412010837

*\* This information is optional. It will not be placed in the public domain or disclosed to any other third party without prior consent.*

A copy of a current CV (maximum 2 pages of A4) for the Chief Investigator must be submitted with the application.

**A4. Who is the contact on behalf of the sponsor for all correspondence relating to applications for this project?**

*This contact will receive copies of all correspondence from REC and R&D reviewers that is sent to the CI.*

	Title Forename/Initials Surname
	Dr Michael Barber
Address	R&D Management Office
	The Tennent Institute,
	Western Infirmary, Glasgow.
Post Code	G11 6NT
E-mail	Michael.Barber@ggc.scot.nhs.uk
Telephone	01412118548
Fax	

**A5-1. Research reference numbers.** Please give any relevant references for your study:

Applicant's/organisation's own reference number, e.g. R & D (if available):



Sponsor's/protocol number:  
 Protocol Version:  
 Protocol Date:  
 Funder's reference number:  
 International Standard Randomised Controlled Trial Number (ISRCTN):  
 ClinicalTrials.gov Identifier (NCT number):  
 European Clinical Trials Database (EudraCT) number:  
 Project website:

Ref.Number Description	Reference Number
REC reference number	11/AL/0032

**A5-2. Is this application linked to a previous study or another current application?**

☒ Yes ☐ No

*Please give brief details and reference numbers.*

REC No 08/S0709/89. This study was previously given ethical approval in August 2008 but we have, unfortunately, been unable to commence it until now so we are resubmitting the application again, as advised, as over the 24 month period. The project is unchanged but now has funding secured to start 1/1/11

**2. OVERVIEW OF THE RESEARCH**

*To provide all the information required by review bodies and research information systems, we ask a number of specific questions. This section invites you to give an overview using language comprehensible to lay reviewers and members of the public. Please read the guidance notes for advice on this section.*

**A6-1. Summary of the study.** *Please provide a brief summary of the research (maximum 300 words) using language easily understood by lay reviewers and members of the public. This summary will be published on the website of the National Research Ethics Service following the ethical review.*

Case reports have described chronic inflammatory arthritis (CIA) in children with Down's syndrome (DS) which is characteristically polyarticular, aggressive and unresponsive to treatment. The prevalence is unknown, but crude estimates suggest this may affect 1-2% of DS. Other musculoskeletal problems, especially those related to ligamentous laxity (LL) are well reported, but their prevalence and the associated level of musculoskeletal disability is unknown. Our pilot cases of DS CIA were characterised by late presentation, extensive joint involvement and significant disability. We saw clinical and functional improvement in response to standard treatments for CIA, and documented a particularly strong association with psoriatic arthropathy. We propose to screen the population of children with DS resident in Glasgow to determine for the first time the prevalence of CIA, other musculoskeletal pathology including LL and foot problems, and the levels of musculoskeletal disability in this population. This one year project will act as a pilot study for development of a larger UK wide project.

**A6-2. Summary of main issues.** *Please summarise the main ethical and design issues arising from the study and say how you have addressed them.*

The main issues for the participants is that they are giving of their time - this will be made clear in the patient information sheet. The study visit can be arranged at the subject's home, their school or their visit at the community paediatrician, so that they do not miss additional school or parent's miss work. There is potential to identify undiagnosed musculoskeletal problems or to raise concerns for the parents during these examinations. We will always inform the parents of our findings at the end of the study visit, and with their consent inform their GP and community paediatrician. Additionally we will offer the subjects and their parents rapid access to the Rheumatology clinic at the RHSC for any families with concerns, but we will suggest that they discuss this with their own doctor(s) before they decide whether they wish to take up this offer. If any child is unhappy and distressed with any elements of the examination we will stop. We will also be sensitive to them getting tired.

**3. PURPOSE AND DESIGN OF THE RESEARCH**



**A7. Select the appropriate methodology description for this research. Please tick all that apply.**

- ☐ Case series/ case note review
- ☐ Case control
- ☒ Cohort observation
- ☐ Controlled trial without randomisation
- ☐ Cross-sectional study
- ☐ Database analysis
- ☐ Epidemiology
- ☐ Feasibility/ pilot study
- ☐ Laboratory study
- ☐ Metanalysis
- ☐ Qualitative research
- ☐ Questionnaire, interview or observation study
- ☐ Randomised controlled trial
- ☐ Other (please specify)

**A10. What is the principal research question/objective? Please put this in language comprehensible to a lay person.**

How frequent are musculoskeletal disorders in children with Down's syndrome and what is the level of physical disability associated with these?

**A11. What are the secondary research questions/objectives if applicable? Please put this in language comprehensible to a lay person.**

The research objectives are specifically to identify musculoskeletal disorders in four areas:  
 What proportion of children with Down's syndrome  
 1. are hypermobile and what are the levels of impairment and disability associated with it?  
 2. have significant foot abnormalities, and associated disability?  
 3. have arthritis and what are the levels of disability associated with it?  
 4. are significantly overweight, contributing to their musculoskeletal disability?

**A12. What is the scientific justification for the research? Please put this in language comprehensible to a lay person.**

Children with Down's syndrome (DS) are described as developing a chronic inflammatory arthritis (CIA) resembling juvenile idiopathic arthritis (JIA) in a number of short case series. The reports describe these children as developing polyarticular, aggressive, destructive and untreatable arthritis of unknown aetiology occurring more frequently than expected in the general population. The true prevalence of this problem has not been described, although crude estimates have been attempted suggesting CIA may affect 1-2% of cases of DS. Confounding musculoskeletal features, particularly severe ligamentous laxity are well recognised as common features in DS, with a large number of associated problems, especially in the hip such as SUFE, hip dislocation and cervical and lower spine abnormalities. Many have bony deformity of the foot and other foot problems which are associated with poor biomechanical functioning. Increased body mass has been documented as contributing to disability, particularly in relation to foot pathologies and ligamentous laxity. Skeletal dysplasia has been described but may be diagnosed more frequently than this single report suggests (personal communication Down's Syndrome Medical Special Interest Group (DSMIG) 2007). These additional musculoskeletal problems may mask or mimic arthritis, and compound disability. The aetiology of this inflammatory arthritis is not understood, but repeated documentation of the association of psoriatic arthritis in children with Down's syndrome suggest this is significantly more common than expected. In contrast although a few case reports of psoriasis in DS exist an increased incidence of psoriasis alone in DS is not suggested by the available literature, but DS is associated with increased reports of immunological/ autoimmune problems.

Case study of eight children currently attending our clinical service with Down's arthritis identified two key features. The first related to late diagnosis and outcome. These children had median age 8.7(4.2-15.6) years at presentation to rheumatology services, took a median of 2.2(0.9-8.7) years from symptom onset to diagnosis in stark contrast to a median of 0.3(0.01-9.9) years in a comparable cohort of 325 children with JIA over the same time period to the same clinical service. This delay for DS children occurred despite repeated contacts with a median of 5(1-16) health



professionals who documented features of arthritis, including persistently raised acute phase response, swollen joints and synovitis, but failed to make the diagnosis of arthritis. Alternative diagnoses offered included soft tissue injury, skeletal dysplasia and behavioural problems. All eight had severe polyarthritis with disabling irreversible joint damage and significant levels of musculoskeletal disability at diagnosis, including being wheelchair bound. In contrast only 41% of the cohort of JIA and 22% with psoriatic arthritis presented with polyarthritis, and with much lower levels of disability. All eight DS children had LL which was clinically contributing to their level of disability but disguised loss of range of movement secondary to arthritis. Both LL and the failure of these patients to vocalise pain, despite demonstrable adaptations or loss of function secondary to pain, appeared to have contributed to the difficulties of the health professionals to recognise arthritis.

The second area of interest relates to clinical associations, and therapeutic responses. Of the 325 children with JIA, 18(5.5%) fulfilled Eular classification criteria (Petty) for psoriatic arthritis, and a further one case had psoriatic features but did not fulfill criteria (possible psoriatic arthritis). From the same population five of the eight children with CIA and DS fulfilled the criteria for psoriatic arthritis, and a further 2 had first degree relatives with seronegative, psoriatic arthritis or psoriasis. Standard therapeutic approaches for JIA were offered to all DS children. Five of eight offered methotrexate had a clinically significant improvement. Two failed to respond to methotrexate, and were offered etanercept showing clinically significant improvement. All eight had residual joint damage and disability relating to late diagnosis but were supported by appropriate physiotherapy, occupational therapy and podiatry interventions from the rheumatological multidisciplinary team. These cases suggest that:

- There is likely to be undiagnosed inflammatory arthritis in the childhood population of Down's syndrome, with a prevalence significantly higher than other inflammatory arthritis of childhood, including a group of children with less extensive joint involvement than the eight cases presented here.
- The arthritis of DS in our group does respond to treatment, unlike earlier published reports which predate modern therapies, suggesting early diagnosis and therapeutic intervention can improve outcome. Developing diagnostic musculoskeletal skills in health professionals is key to improving early diagnosis and access to care.
- The CIA of DS mimics psoriatic arthritis in both the pre-existing literature and our pilot work. Elucidating this further would support future work towards understanding the aetiology of DS CIA, and would guide therapeutic approaches.

**A13. Please give a full summary of your design and methodology.** It should be clear exactly what will happen to the research participant, how many times and in what order. Please complete this section in language comprehensible to the lay person. Do not simply reproduce or refer to the protocol. Further guidance is available in the guidance notes.

**Purpose:**

This is a pilot study with the purpose of demonstrating the prevalence, the range and level of musculoskeletal disorders including arthritis in children with Down's syndrome and demonstrating the impact of changes on function and the level of disability.

The study is a cross sectional survey of children resident in Glasgow with Down's syndrome: participants will be offered a single assessment of full musculoskeletal examination including a joint assessment, documenting arthritis by a paediatric rheumatology research nurse, and a foot assessment by a podiatrist.

**Methods:**

**Subjects**

**Inclusions and the approach to the child**

Subjects must have Down's syndrome and must be resident in Glasgow, as defined by their current residential postcode, and be between the age of 2 and 16. Patients on the Scottish Down's syndrome thyroid screening group and community databases will be approached through their community or other paediatric services to enrol in the study. Identified children unknown to paediatric services will be sought and approached through their GP. No family will be directly approached by study staff.

**Exclusions**

Children who are too unwell, are unable to cooperate with the measurements, if parents or children decline or are unable to take part, or children who are considered unsuitable by their community paediatrician or own doctor will be excluded.

**Study visit**

Subjects will have one study visit, with examination of the musculoskeletal system, in their home or school, or at the time of a routine visit at their community paediatrician, depending on their preference.

The musculoskeletal examination including the joint assessment will be made by the research nurse. The measurements of the foot will be made by a trained podiatrist.

Pilot suggests the visit will last about 60 minutes.

Musculoskeletal examination will consist of simple clinical examination and simple measurements.

**Study protocol**

In a cross sectional survey participants will receive a single clinical assessment within the community setting. This



will involve a full musculoskeletal assessment documenting:

- a) The presence and severity of inflammatory arthritis by nurse assessment, and quantified using the validated tool of the Core Outcome Variables (Giannini). This consists of physician documentation of active and limited joints. Global assessments of well being made by physician, parents and, where able, the child. An assessment of pain made by the parents and, where able, the child. Parental and, where able, child completion of the CHAQ questionnaire to identify the level of musculoskeletal functioning at the time of the assessment.
- b) The level of hypermobility will be assessed using the Brighton criteria (Grahame), a physician led clinical assessment tool.
- c) A clinical foot assessment made by a podiatrist, who will also assess walking speed.
- d) Measurement of height, weight and BMI calculation, relating these to DS specific normal values (Cronk, Styles). Body composition will be further assessed using bioelectrical impedance estimating the ratio of body fat to muscle.
- e) Nurse assessment of psoriasis in skin and nails.
- f) Ultrasound scan of joints suspected of having arthritis to confirm presence of inflammation if considered necessary by research nurse who is a qualified MSK sonographer.
- g) Assessment of disability using CHQ and CHAQ questionnaires completed by parents and, where appropriate, the child.
- h) Nurse led assessment of muscle strength using key elements of the CMAS score (Lovell)
- i) Screening for limb growth abnormalities including skeletal dysplasia, scoliosis, genu valgum, patellofemoral instability and growth abnormalities will be made by measuring sitting height, arm span, upper to lower segment ratio (U/L) and head circumference, and documentation of features such as micrognathia, limb or digit length discrepancies, and scoliosis.
- j) Structured interview of the parents by the nurse to identify history in the patient or family of autoimmune disease, psoriasis and related disorders such as seronegative arthropathy. To identify any musculoskeletal concerns from the family, and any previous musculoskeletal assessments and diagnoses. To document other medical problems such as developmental dysplasia of the hip, floppy larynx, cardiac and gastrointestinal abnormalities which might be associated with LL.

Two researchers will be present at the study visit. This will facilitate a number of areas. It will: allow efficient and relaxed visits because recording of data, with one person measuring and the other scribing will be quick; one researcher interviewing parents, asking questions, obtaining consent etc whilst the other is able to engage with the child and keep them amused and relaxed, allowing the parents to be relaxed. The researchers will also act as chaperones and improve the safety of community visits for themselves.

**A14-1. In which aspects of the research process have you actively involved, or will you involve, patients, service users, and/or their carers, or members of the public?**

- ☒ Design of the research
- ☐ Management of the research
- ☐ Undertaking the research
- ☐ Analysis of results
- ☐ Dissemination of findings
- ☐ None of the above

*Give details of involvement, or if none please justify the absence of involvement.*

We asked parents of children with Down's syndrome about the importance of this project to them, and the feasibility and practicality of what we propose for their children. Parents of children with Down's syndrome with arthritis were very enthusiastic as they had experienced delay in diagnosis and significant disability in their children. They thought the project was practical in terms of what we wanted to do with individual children. They also commented on the appropriateness and usability of the PIS

**4. RISKS AND ETHICAL ISSUES**

**RESEARCH PARTICIPANTS**

**A15. What is the sample group or cohort to be studied in this research?**

Select all that apply:

- ☐ Blood
- ☐ Cancer
- ☐ Cardiovascular
- ☐ Congenital Disorders
- ☐ Dementias and Neurodegenerative Diseases
- ☐ Diabetes
- ☐ Ear
- ☐ Eye
- ☐ Generic Health Relevance
- ☐ Infection
- ☐ Inflammatory and Immune System
- ☐ Injuries and Accidents
- ☐ Mental Health
- ☐ Metabolic and Endocrine
- ☐ Musculoskeletal
- ☐ Neurological
- ☐ Oral and Gastrointestinal
- ☒ Paediatrics
- ☐ Renal and Urogenital
- ☐ Reproductive Health and Childbirth
- ☐ Respiratory
- ☐ Skin
- ☐ Stroke

Gender: Male and female participants

Lower age limit: 2 Years

Upper age limit: 16 Years

**A17-1. Please list the principal inclusion criteria (list the most important, max 5000 characters).**

To be suitable for recruitment subjects must have been diagnosed with Down's syndrome, be between 2 and 16 years old and must be resident in Glasgow, as defined by their current residential postcode.

**A17-2. Please list the principal exclusion criteria (list the most important, max 5000 characters).**

Children who are too unwell, who are unable to cooperate with the measurements, where parents or children decline or are unable to take part or children who are considered unsuitable by their community paediatrician or other medical practitioner will be excluded. A note of their age, sex and first three digits of postcode will be recorded for all those not recruited to facilitate the quality of the final analysis.

**RESEARCH PROCEDURES, RISKS AND BENEFITS**

**A18. Give details of all non-clinical intervention(s) or procedure(s) that will be received by participants as part of the research protocol. These include seeking consent, interviews, non-clinical observations and use of questionnaires.**

Please complete the columns for each intervention/procedure as follows:

1. Total number of interventions/procedures to be received by each participant as part of the research protocol.
2. If this intervention/procedure would be routinely given to participants as part of their care outside the research, how many of the total would be routine?
3. Average time taken per intervention/procedure (minutes, hours or days)



## 4. Details of who will conduct the intervention/procedure, and where it will take place.

Intervention or procedure	1	2	3	4
Other questionnaire	1	10	CHQ questionnaire will be completed by the accompanying parent and, dependant on the level of learning difficulties in individual child/young person with Down's, they will be given an opportunity to contribute to the answers. This questionnaire covers psychological and physical well being.	
Other questionnaire	1	5	CHAQ questionnaire will be completed by the accompanying parent and, dependant on the level of learning difficulties in individual child/young person with Down's, they will be given an opportunity to contribute to the answers. This questionnaire covers physical abilities.	
Face to face interview	1	10	A structured interview with the parents will be performed by the researchers who will take the parents through the questions.	

**A19. Give details of any clinical intervention(s) or procedure(s) to be received by participants as part of the research protocol.** These include uses of medicinal products or devices, other medical treatments or assessments, mental health interventions, imaging investigations and taking samples of human biological material. Include procedures which might be received as routine clinical care outside of the research.

Please complete the columns for each intervention/procedure as follows:

1. Total number of interventions/procedures to be received by each participant as part of the research protocol.
2. If this intervention/procedure would be routinely given to participants as part of their care outside the research, how many of the total would be routine?
3. Average time taken per intervention/procedure (minutes, hours or days).
4. Details of who will conduct the intervention/procedure, and where it will take place.

Intervention or procedure	1	2	3	4
Clinical examination	1	25	Detailed clinical examination of the musculoskeletal system to allow the examiner to score the Beighton hypermobility score, to document any joints with arthritis or limitation of movement, assessment of muscle strength and detailed examination of the foot to document abnormalities of structure, function and gait.	
Other	1	15	Measurements of height, weight, arm span, sitting height, head circumference.	
Other	1	3	Tanita measurement of bioelectrical impedance. the subject stands on the bioelectrical impedance machine in bare feet. This resembles bathroom scales. Much like an ECG the Tanita measures electrical resistance which is dependant on body fat and gives an estimate of body composition. It is quite painless and takes only a few minutes.	
Ultrasound scan (if required)	1	10	Ultrasound scan of any joints suspected of having inflammatory arthritis to confirm the presence of inflammation if judged to be necessary by the research nurse who holds a PG Cert in Medical Ultrasound specialising in MSK.	

**A20. Will you withhold an intervention or procedure, which would normally be considered a part of routine care?**

☐ Yes ☒ No

**A21. How long do you expect each participant to be in the study in total?**

One hour. Less if the child is very easy to examine. In a cooperative confident child this would take about 30 minutes.

**A22. What are the potential risks and burdens for research participants and how will you minimise them?**

*For all studies, describe any potential adverse effects, pain, discomfort, distress, intrusion, inconvenience or changes to lifestyle. Only describe risks or burdens that could occur as a result of participation in the research. Say what steps would be taken to minimise risks and burdens as far as possible.*

The two examiners are experienced in musculoskeletal examination and this should not be uncomfortable or distressing in any way. This group of children with learning difficulties may unexpectedly become distressed or not engage in the examination, and we will be sensitive to these responses and accept that not all patients will manage the examination on the day. We would discuss sensitively with the parent whether they felt it right to try on another occasion or whether this response was likely to be repeated and we should abandon that child's involvement in the study. We have built in extra time so these children can take their time and two examiners will be present so that one can engage the child in play whilst the parents do the questionnaires and one will act as a scribe to make measurements as quick as possible. We have piloted the examinations to ensure they are simple, quick, effective to ensure the protocol is as simple and uninvasive for the children as possible.

**A23. Will interviews/ questionnaires or group discussions include topics that might be sensitive, embarrassing or upsetting, or is it possible that criminal or other disclosures requiring action could occur during the study?**

☒ Yes ☐ No

*If Yes, please give details of procedures in place to deal with these issues:*

Yes, potentially we may identify new physical, musculoskeletal problems of which the child/young person and parents were unaware. We plan to give feedback at the end of each subject visit to the parents and child/young person telling them what we found. We will also, with their permission, inform the GP and their community paediatrician. We will offer rapid access to the paediatric rheumatology service at Yorkhill to all families who would like this after the assessment, regardless of the findings in the study. (We anticipate some children with mild musculoskeletal features may choose to attend the rheumatology service for reassurance, whilst others decline an appointment despite significant musculoskeletal findings.) We will suggest they discuss referral with their GP or community paediatrician who can support each family in what is most appropriate for them. We will also take referrals from the GP/community paediatric services up to the child's 18th birthday if they decide after the study they would like an appointment after all.

**A24. What is the potential for benefit to research participants?**

They may be reassured that their child does not have musculoskeletal difficulties; they will receive information on the possibility that musculoskeletal problems can occur in DS, and that services exist to deal with this, and their primary carers will also receive this education raising awareness of the potential of musculoskeletal problems; participants may have musculoskeletal problems identified earlier than if the study did not occur giving them an opportunity to take up additional health care earlier; they are offered direct access to a formal medical musculoskeletal opinion should they choose to take up the offer.

**A25. What arrangements are being made for continued provision of the intervention for participants, if appropriate, once the research has finished? May apply to any clinical intervention, including a drug, medical device, mental health intervention, complementary therapy, physiotherapy, dietary manipulation, lifestyle change, etc.**

We plan to give feedback at the end of each subject visit to the parents and child/young person telling them what we found. We will also, with their permission, inform the GP and their community paediatrician. We will offer rapid access to the paediatric rheumatology service at Yorkhill to all families who would like this after the assessment, regardless of the findings in the study. (We anticipate some children with mild musculoskeletal features may choose to attend the rheumatology service for reassurance, whilst others decline an appointment despite significant musculoskeletal findings.) We will suggest they discuss referral with their GP or community paediatrician who can support each family in what is most appropriate for them. We will also take referrals from the GP/community paediatric services up to the child's 18th birthday if they decide after the study they would like an appointment after all.

**A26. What are the potential risks for the researchers themselves? (if any)**

The presence of two examiners will ensure they act as chaperones for each other whilst visiting families in the community improving safety in this setting. Should they 'uncover' distress in families about musculoskeletal concerns or actual pathology they have the support and expertise of the clinical paediatric rheumatology service to support these families. They have regular supervision and support for the work they are doing in the community and by the university, should unexpected difficulties arise.



## RECRUITMENT AND INFORMED CONSENT

*In this section we ask you to describe the recruitment procedures for the study. Please give separate details for different study groups where appropriate.*

**A27-1. How will potential participants, records or samples be identified? Who will carry this out and what resources will be used?** For example, identification may involve a disease register, computerised search of GP records, or review of medical records. Indicate whether this will be done by the direct healthcare team or by researchers acting under arrangements with the responsible care organisation(s).

Information on current patients with Down's syndrome under the care of the consultant community paediatrician is kept in the database of the Scottish thyroid screening. We will ask the community paediatricians who know these children to indicate any families who may be inappropriate to approach and to guide us to the educational level of these children as well as their learning abilities regarding the patient information sheet. Only families identified through their community paediatrician, GP or other medical practitioner will be asked to participate in the study visits, and the invitation will come from the medical staff known to them. This is to ensure we do not cause distress by approaching families with children who are seriously ill, recently deceased or any other circumstances which would cause distress. In order to assess the completeness of the cohort obtained by this method a capture recapture analysis will be performed. Therefore children with Down's syndrome will be identified by two other methods and the overlap between the three data sets will be compared by statistical analysis.

We will ask the cytogenetic and genetics department for registered patients and search the community database for all children with the diagnosis of Down's syndrome, who are living in Glasgow.

We will estimate the number of patients captured by the Scottish thyroid screening database, and the number of children with Down's syndrome resident in Glasgow missed using this database. These additional patients will not be approached for the study, but only used to estimate the size of the population of DS children resident in Glasgow.

**A27-2. Will the identification of potential participants involve reviewing or screening the identifiable personal information of patients, service users or any other person?**

☒ Yes ☐ No

*Please give details below:*

The information gathered about the patients (name, date of birth, postcode, CHI number) will be used to compare the databases and will not be retained afterwards.

**A27-3. Describe what measures will be taken to ensure there is no breach of any duty of confidentiality owed to patients, service users or any other person in the process of identifying potential participants.** Indicate what steps have been or will be taken to inform patients and service users of the potential use of their records for this purpose. Describe the arrangements to ensure that the wishes of patients and service users regarding access to their records are respected. Please consult the guidance notes on this topic.

Patient data will be recorded with a unique study number. The child's date of birth, sex and full postcode will be recorded. The written information will be kept in a locked filing cabinet in a locked office. Information transferred to computer will be kept on a University computer which is password protected. The postcodes or other personal information will not be kept in the same database as other information.

**A27-4. Will researchers or individuals other than the direct care team have access to identifiable personal information of any potential participants?**

☐ Yes ☒ No

**A28. Will any participants be recruited by publicity through posters, leaflets, adverts or websites?**

☐ Yes ☒ No

**A29. How and by whom will potential participants first be approached?**

Subjects identified by their community paediatricians, GP or other medical practitioner who knows them well will then

be approached by that doctor who is known to them. That doctor will send out an invitation letter to the subjects and parents including a flyer/summary information sheet (example enclosed is addressed from an example community paediatrician which is likely to be the most common scenario). After sending out the information sheet we will obtain contact details from the doctor caring for the child, telephone no sooner than 24 hours later or write to the parents as appropriate. During that call we will answer any questions about the study and ask if the subjects and parents are interested in participating. If the families agree a study visit will be arranged, and the full information sheet and children's information sheet posted after discussion with the parents of the appropriate level of information for the child. On the day of the study, and after a final opportunity to ask questions, we will take parents informed consent and, as appropriate, the child's assent before proceeding with the study measurements

**A30-1. Will you obtain informed consent from or on behalf of research participants?**

☒ Yes ☐ No

*If you will be obtaining consent from adult participants, please give details of who will take consent and how it will be done, with details of any steps to provide information (a written information sheet, videos, or interactive material). Arrangements for adults unable to consent for themselves should be described separately in Part B Section 6, and for children in Part B Section 7.*

*If you plan to seek informed consent from vulnerable groups, say how you will ensure that consent is voluntary and fully informed.*

Informed consent will be taken from the parents by the researcher at face to face interview at the time of their study visit. At the same time assent will be taken from the children as appropriate, depending on their level of ability. The subjects will have had the opportunity to discuss the study with their own doctor before this, and will have had adequate time to read the subject information sheets appropriate to the child's level of learning ability.

*If you are not obtaining consent, please explain why not.*

Please enclose a copy of the information sheet(s) and consent form(s).

**A30-2. Will you record informed consent (or advice from consultees) in writing?**

☒ Yes ☐ No

**A31. How long will you allow potential participants to decide whether or not to take part?**

A minimum of 24 hours, but it will usually be longer. After this time we will telephone or write to the parents, as appropriate the subject, to ask whether they are interested to participate or not.

**A32. Will you recruit any participants who are involved in current research or have recently been involved in any research prior to recruitment?**

☒ Yes  
☐ No  
☐ Not Known

*If Yes, please give details and justify their inclusion. If Not Known, what steps will you take to find out?*

There are a number of observational studies in paediatric rheumatology. Children in this cohort who are already known to have arthritis may be invited to join more than one observational study. There may be other observational studies involving children with Down's syndrome we are unaware of which would not preclude them from taking part but we will be sensitive to overburdening them with studies.

**A33-1. What arrangements have been made for persons who might not adequately understand verbal explanations or written information given in English, or who have special communication needs?(e.g. translation, use of interpreters)**

These children with learning difficulties are known to the community paediatricians. They are divided into three groups: mainstream school children, children attending the moderate learning difficulty schools and the children attending the complex learning difficulty schools. Patient information sheets, including information for parents to read to their



children for all these levels of learning difficulty are provided. Some children may not be able to understand the nature of the study, but they will be used to medical consultations and the study will be very similar to a routine medical consultation. In this case the parents may decide to consent for their child knowing they do not understand. We are going to see these children in an environment they are familiar with and we will take advice from their parents and community paediatricians on their level of understanding. This screening examination will be held as simple and as child friendly as possible. It is no more complex than the clinical examination the child receives in a normal paediatric rheumatology consultation. Translators can be provided if required at the routine community paediatrician visit. In this situation we would not be able to see the child in their own home.

**A34. What arrangements will you make to ensure participants receive any information that becomes available during the course of the research that may be relevant to their continued participation?**

The patients will be seen once for a single assessment. Should any important information relating to the whole study become available during the course of the study we would let the families know through their community paediatrician. We will also feedback the results at the end of the study to both patients and medical staff in the form of a short summary.

**A35. What steps would you take if a participant, who has given informed consent, loses capacity to consent during the study? Tick one option only.**

- ☐ The participant and all identifiable data or tissue collected would be withdrawn from the study. Data or tissue which is not identifiable to the research team may be retained.
- ☒ The participant would be withdrawn from the study. Identifiable data or tissue already collected with consent would be retained and used in the study. No further data or tissue would be collected or any other research procedures carried out on or in relation to the participant.
- ☐ The participant would continue to be included in the study.
- ☐ Not applicable – informed consent will not be sought from any participants in this research.

*Further details:*

*If you plan to retain and make further use of identifiable data/tissue following loss of capacity, you should inform participants about this when seeking their consent initially.*

**CONFIDENTIALITY**

**In this section, personal data means any data relating to a participant who could potentially be identified. It includes pseudonymised data capable of being linked to a participant through a unique code number.**

**Storage and use of personal data during the study**

**A36. Will you be undertaking any of the following activities at any stage (including in the identification of potential participants)? (Tick as appropriate)**

- ☐ Access to medical records by those outside the direct healthcare team
- ☐ Electronic transfer by magnetic or optical media, email or computer networks
- ☐ Sharing of personal data with other organisations
- ☐ Export of personal data outside the EEA
- ☒ Use of personal addresses, postcodes, faxes, emails or telephone numbers
- ☐ Publication of direct quotations from respondents
- ☐ Publication of data that might allow identification of individuals
- ☐ Use of audio/visual recording devices
- ☒ Storage of personal data on any of the following:
- ☐ Manual files including X-rays

- ☐ NHS computers  
☐ Home or other personal computers  
☒ University computers  
☐ Private company computers  
☐ Laptop computers

*Further details:*

This will be password protected and anonymous, kept by study number only.

Personal details for the purposes of contacting the patients will be kept in a separate database, also password protected.

**A37. Please describe the physical security arrangements for storage of personal data during the study?**

The written information will be kept in a locked filing cabinet in a locked office. Information transferred to computer will be kept on a University computer which is password protected. The postcodes or other personal information will not be kept in the same database as other information.

**A38. How will you ensure the confidentiality of personal data?** Please provide a general statement of the policy and procedures for ensuring confidentiality, e.g. anonymisation or pseudonymisation of data.

Patient data will be recorded with a unique study number. The child's date of birth, sex and full postcode will be recorded. The written information will be kept in a locked filing cabinet in a locked office. Information transferred to computer will be kept on a University computer which is password protected. The postcodes or other personal information will not be kept in the same database as other information.

**A40. Who will have access to participants' personal data during the study?** Where access is by individuals outside the direct care team, please justify and say whether consent will be sought.

The research personnel only

**Storage and use of data after the end of the study**

**A41. Where will the data generated by the study be analysed and by whom?**

Analysis will take place in the Department of Child Health, within the Royal Hospital for Sick Children, Yorkhill, Glasgow. The analysis will be done by members of the research team only

**A42. Who will have control of and act as the custodian for the data generated by the study?**

	Title Forename/Initials Surname
	Dr Janet Gardner-Medwin
Post	Arthritis Research UK Senior Lecturer in Paediatric Rheumatology
Qualifications	MBChB FRCPCH PhD
Work Address	Dept of Child Health
	RHSC, Yorkhill, Dalnair Street
	Glasgow
Post Code	G3 8SJ
Work Email	Janet.Gardner-Medwin@glasgow.ac.uk
Work Telephone	01412010867
Fax	01412010837

**A43. How long will personal data be stored or accessed after the study has ended?**

- ☒ Less than 3 months  
☐ 3 – 6 months  
☐ 6 – 12 months  
☐ 12 months – 3 years  
☐ Over 3 years

**A44. For how long will you store research data generated by the study?**

Years: 20

Months:

**A45. Please give details of the long term arrangements for storage of research data after the study has ended. Say where data will be stored, who will have access and the arrangements to ensure security.**

Data will be stored according to GGC archiving policy

**INCENTIVES AND PAYMENTS****A46. Will research participants receive any payments, reimbursement of expenses or any other benefits or incentives for taking part in this research?**

- ☒ Yes   ☐ No

*If Yes, please give details. For monetary payments, indicate how much and on what basis this has been determined.*  
 Yes, should the families have to travel we will need to reimburse their expenses. However we intend to see patients at the time of their routine community clinic appointment, or in their own homes/schools if the family prefer.

**A47. Will individual researchers receive any personal payment over and above normal salary, or any other benefits or incentives, for taking part in this research?**

- ☐ Yes   ☒ No

**A48. Does the Chief Investigator or any other investigator/collaborator have any direct personal involvement (e.g. financial, share holding, personal relationship etc.) in the organisations sponsoring or funding the research that may give rise to a possible conflict of interest?**

- ☐ Yes   ☒ No

**NOTIFICATION OF OTHER PROFESSIONALS****A49-1. Will you inform the participants' General Practitioners (and/or any other health or care professional responsible for their care) that they are taking part in the study?**

- ☒ Yes   ☐ No

*If Yes, please enclose a copy of the information sheet/letter for the GP/health professional with a version number and date.*

**A49-2. Will you seek permission from the research participants to inform their GP or other health/ care professional?**



☒ Yes ☐ No

*It should be made clear in the participant's information sheet if the GP/health professional will be informed.*

#### PUBLICATION AND DISSEMINATION

##### A50. Will the research be registered on a public database?

☒ Yes ☐ No

*Please give details, or justify if not registering the research.*  
NHS Greater Glasgow & Clyde Research database

##### A51. How do you intend to report and disseminate the results of the study? Tick as appropriate:

- ☒ Peer reviewed scientific journals
- ☐ Internal report
- ☒ Conference presentation
- ☐ Publication on website
- ☐ Other publication
- ☐ Submission to regulatory authorities
- ☐ Access to raw data and right to publish freely by all investigators in study or by Independent Steering Committee on behalf of all investigators
- ☐ No plans to report or disseminate the results
- ☒ Other (please specify)

Development of an educational resource pack to improve awareness of musculoskeletal problems in Down's arthritis for medical professionals.

##### A52. If you will be using identifiable personal data, how will you ensure that anonymity will be maintained when publishing the results?

The data will be discussed in general terms and relate to the whole cohort. No individual data will be identifiable.

##### A53. Will you inform participants of the results?

☒ Yes ☐ No

*Please give details of how you will inform participants or justify if not doing so.*  
At the end of the study a letter outlining the results will be sent to all participants. All participants will receive individual feedback about the study findings on their child immediately on the day of the study visit.

#### 5. Scientific and Statistical Review

##### A54. How has the scientific quality of the research been assessed? Tick as appropriate:

- ☒ Independent external review
- ☐ Review within a company
- ☐ Review within a multi-centre research group
- ☐ Review within the Chief Investigator's institution or host organisation
- ☒ Review within the research team
- ☐ Review by educational supervisor
- ☒ Other

*Justify and describe the review process and outcome. If the review has been undertaken but not seen by the researcher, give details of the body which has undertaken the review:*

The UK Down's syndrome Medical Special Interest Group has reviewed this project, and is fully supportive of its importance. The project has received funding from Arthritis Research UK after independent external review.

*For all studies except non-doctoral student research, please enclose a copy of any available scientific critique reports, together with any related correspondence.*

*For non-doctoral student research, please enclose a copy of the assessment from your educational supervisor/ institution.*

**A56. How have the statistical aspects of the research been reviewed?** *Tick as appropriate:*

- ☐ Review by independent statistician commissioned by funder or sponsor
- ☐ Other review by independent statistician
- ☐ Review by company statistician
- ☐ Review by a statistician within the Chief Investigator's institution
- ☒ Review by a statistician within the research team or multi-centre group
- ☐ Review by educational supervisor
- ☐ Other review by individual with relevant statistical expertise
- ☐ No review necessary as only frequencies and associations will be assessed – details of statistical input not required

*In all cases please give details below of the individual responsible for reviewing the statistical aspects. If advice has been provided in confidence, give details of the department and institution concerned.*

	Title	Forename/Initials	Surname
	Professor	John	McColl
Department	School of Mathematics and Statistics		
Institution	University of Glasgow		
Work Address	Room 233		
	15 University Gardens		
	Glasgow		
Post Code			
Telephone	01413304749		
Fax	01413304814		
Mobile			
E-mail	John.McColl@glasgow.ac.uk		

*Please enclose a copy of any available comments or reports from a statistician.*

**A57. What is the primary outcome measure for the study?**

Any abnormality of the musculoskeletal system - in particular:  
i) hypermobility  
ii) inflammatory arthritis

**A58. What are the secondary outcome measures? (if any)**

The level of physical disability associated with these findings

**A59. What is the sample size for the research?** *How many participants/samples/data records do you plan to study in total? If there is more than one group, please give further details below.*

Total UK sample size: 170

Total international sample size (including UK):

Total in European Economic Area:

*Further details:*

The Glasgow School Age Children with Down's syndrome Thyroid Screening database currently has 170 children who are eligible for this study between 1/1/11 and 31/12/11 (Jez Jones personal communication). We aim to recruit as many of these as possible, and estimate a minimum recruitment rate of 60% (= 102 cases)

**A60. How was the sample size decided upon?** *If a formal sample size calculation was used, indicate how this was done, giving sufficient information to justify and reproduce the calculation.*

There is no published literature from which to estimate the prevalence of musculoskeletal disability in these children. Case series of under 10 cases of children with Down's syndrome with arthritis exist but with little reference to the population from which they were drawn. There is insufficient data existing to develop formally a power calculation. Our own clinical experience is of 8 children with Down's syndrome from the Glasgow area have been referred with arthritis, all with significant delay, and all those children are very hypermobile adding to the level of deformity and disability. This is a pilot study to determine the level of problems in the population of children with Down's syndrome. This pilot study would be the first survey for arthritis in the literature, and would allow a power calculation to be done for future study. A precise calculation estimating CIA in the cohort of DS has been made using a prevalence of JIA of 1 in 1000 children (Gare). 5/8 pilot cases with DS CIA fulfilled criteria for entry to the study by residence and age on 1/5/08 giving a conservative estimate of 5/170 cases with CIA, or 2.87% prevalence, and a relative risk of 3.38 should no further cases be found in the survey. However the severity and late presentation of these cases suggests it is likely we will find additional cases. LL and disability are likely to be significantly more common than CIA.

**A61. Will participants be allocated to groups at random?**

☐ Yes ☒ No

**A62. Please describe the methods of analysis (statistical or other appropriate methods, e.g. for qualitative research) by which the data will be evaluated to meet the study objectives.**

The information will be used to give a prevalence rate of musculoskeletal problems in children with Down's arthritis. Capture recapture analysis will be used to estimate the true size of the population from which index cases were drawn.

## 6. MANAGEMENT OF THE RESEARCH

**A63. Other key investigators/collaborators.** *Please include all grant co-applicants, protocol co-authors and other key members of the Chief Investigator's team, including non-doctoral student researchers.*

	Title	Forename/Initials	Surname
	Sister	Maureen	Todd
Post	Research Nurse		
Qualifications	RGN PG Cert in MSKUS		
Employer	NHS Greater Glasgow & Clyde		
Work Address	Department of Child Health		
	RHSC Yorkhill, Dalnair Street		
	Glasgow		
Post Code	G3 8SJ		
Telephone	01412321836		
Fax	01412010837		
Mobile			
Work Email	maureen.todd2@nhs.net		



	Title Forename/Initials Surname
	Dr Katherine Leyland
Post	Consultant Community Paediatrician
Qualifications	MBChB DCH MRCPCH
Employer	SE Community Health and Care Partnership, Greater Glasgow & Clyde
Work Address	Community Child Health Services
	Southbank Child Centre
	207 Old Rutherglen Road, Glasgow
Post Code	G5 0RE
Telephone	01412010908
Fax	
Mobile	
Work Email	kath.leyland@ggc.scot.nhs.uk

	Title Forename/Initials Surname
	Mr Jez Jones
Post	Research Assistant
Qualifications	BSc (Biological Sciences) MSc DMS
Employer	University of Glasgow
Work Address	Department of Child Health
	RHSC Yorkhill, Dalnair Street
	Glasgow
Post Code	G3 8SJ
Telephone	0141201236
Fax	01412010837
Mobile	
Work Email	jjones@clinmed.gla.ac.uk

	Title Forename/Initials Surname
	Dr Gordon Watt
Post	Lecturer in Podiatry
Qualifications	MChS, DPodM, FCPodM, Cert AdEd
Employer	Glasgow Caledonian University
Work Address	School of Health and Social Care
	Glasgow Caledonian University
	Cowcaddens Road, Glasgow
Post Code	G4 0BA
Telephone	01413313237
Fax	
Mobile	
Work Email	g.f.watt@gcal.ac.uk

	Title Forename/Initials Surname
	Prof James Woodburn
Post	Professor of Rehabilitation Studies
Qualifications	BSc MPhil PhD
Employer	Glasgow Caledonian University
Work Address	School of Health and Social Care
	Glasgow Caledonian University

	Cowcaddens Road, Glasgow
Post Code	G4 0BA
Telephone	01413318483
Fax	
Mobile	
Work Email	jim.woodburn@gcal.ac.uk
	Title Forename/Initials Surname
	Dr Malcolm Donaldson
Post	Senior Lecturer in Paediatric Endocrinology
Qualifications	MBChB, MD, MRCP
Employer	University of Glasgow
Work Address	Department of Child Health
	RHSC Yorkhill
	Dalnair Street, Glasgow
Post Code	G3 8SJ
Telephone	01412010236
Fax	01412010837
Mobile	
Work Email	Malcolm.Donaldson@glasgow.ac.uk

#### A64. Details of research sponsor(s)

##### A64-1. Sponsor

###### Lead Sponsor

Status: ☒ NHS or HSC care organisation

Commercial status:

☐ Academic

☐ Pharmaceutical industry

☐ Medical device industry

☐ Local Authority

☐ Other social care provider (including voluntary sector or private organisation)

☐ Other

*If Other, please specify:*

###### Contact person

Name of organisation NHS Greater Glasgow & Clyde

Given name Michael

Family name Barber

Address R&D Management Office, Tennent Institute

Town/city Glasgow

Post code G11 6NT

Country UNITED KINGDOM

Telephone 01412118548

Fax

E-mail michael.barber@ggc.scot.nhs.uk



**Is the sponsor based outside the UK?**

☐ Yes ☒ No

*Where the lead sponsor is not established within the UK, a legal representative in the UK may need to be appointed. Please consult the guidance notes.*

**A65. Has external funding for the research been secured?**

- ☒ Funding secured from one or more funders  
☐ External funding application to one or more funders in progress  
☐ No application for external funding will be made

**Please give details of funding applications.**

Organisation      Arthritis Research UK  
Address            Copeman House, St Mary's Gate  
                         Chesterfield  
                         Derbyshire  
Post Code         S41 7TD  
Telephone        03007900400  
Fax                 03007900401  
Mobile  
Email               enquiries@arthritisresearchuk.org

Funding Application Status: ☒ Secured ☐ In progress

Amount:          46,214

**Duration**

Years:

Months:          12

*If applicable, please specify the programme/ funding stream:*

What is the funding stream/ programme for this research project?

University held grant to support salary of Maureen Todd

What type of research project is this?

- ☐ Standalone project  
☐ Project that is part of a programme grant  
☒ Project that is part of a fellowship/ personal award/ research training award  
☐ Other

Other – please state:

**A66. Has responsibility for any specific research activities or procedures been delegated to a subcontractor (other than a co-sponsor listed in A64-1) ? Please give details of subcontractors if applicable.**

☐ Yes ☒ No

**A67. Has this or a similar application been previously rejected by a Research Ethics Committee in the UK or another country?**

☐ Yes ☒ No

*Please provide a copy of the unfavourable opinion letter(s). You should explain in your answer to question A6-2 how the reasons for the unfavourable opinion have been addressed in this application.*

**A68. Give details of the lead NHS R&D contact for this research:**

	Title Forename/Initials Surname
	Dr Michael Barber
Organisation	Research and Development
Address	R&D Management Office
	Tennent Institute
	Western Infirmary, Glasgow
Post Code	G11 6NT
Work Email	michael.barber@ggc.scot.nhs.uk
Telephone	01412118548
Fax	
Mobile	

*Details can be obtained from the NHS R&D Forum website: <http://www.rdforum.nhs.uk>*

**A69-1. How long do you expect the study to last in the UK?**

Planned start date: 01/01/2011

Planned end date: 31/12/2011

Total duration:

Years: Months: 12 Days:

**A71-1. Is this study?**

☒ Single centre  
☐ Multicentre

**A71-2. Where will the research take place? (Tick as appropriate)**

☐ England  
☒ Scotland  
☐ Wales  
☐ Northern Ireland  
☐ Other countries in European Economic Area

Total UK sites in study

**Does this trial involve countries outside the EU?**

☐ Yes ☒ No

**A72. What host organisations (NHS or other) in the UK will be responsible for the research sites? Please indicate the type of organisation by ticking the box and give approximate numbers of planned research sites:**

- ☐ NHS organisations in England  
☐ NHS organisations in Wales  
☒ NHS organisations in Scotland 1  
☐ HSC organisations in Northern Ireland  
☐ GP practices in England  
☐ GP practices in Wales  
☐ GP practices in Scotland  
☐ GP practices in Northern Ireland  
☐ Social care organisations  
☐ Phase 1 trial units  
☐ Prison establishments  
☐ Probation areas  
☐ Independent hospitals  
☐ Educational establishments  
☐ Independent research units  
☐ Other (give details)

Total UK sites in study:

**A73-1. Will potential participants be identified through any organisations other than the research sites listed above?**

☐ Yes ☒ No

**A74. What arrangements are in place for monitoring and auditing the conduct of the research?**

Regular research meetings are proposed during the period of the pilot study to ensure recruitment, data quality and appropriate conduct of research. The research nurse is trained in musculoskeletal examination and is a qualified musculoskeletal sonographer. A consultant podiatrist will perform the foot assessment. There will always be two people going out to see the children, providing security for the investigators and 'chaperones' for each other. In the community setting the research nurse and podiatrist will be supported by the community paediatricians.

**A75-1. Will a data monitoring committee (DMC) be convened?**

☐ Yes ☒ No

*If Yes, please forward details of the membership of the DMC, its standard operating procedures and summary reports of interim analyses to the Research Ethics Committee which gives a favourable opinion of the study (or to GTAC if applicable).*

**A75-2. What are the criteria for electively stopping the trial or other research prematurely?**

None - observational study.

**A76. Insurance/ indemnity to meet potential legal liabilities**

**Note: in this question to NHS indemnity schemes include equivalent schemes provided by Health and Social Care (HSC) in Northern Ireland**

**A76-1. What arrangements will be made for insurance and/or indemnity to meet the potential legal liability of the sponsor(s) for harm to participants arising from the management of the research? Please tick box(es) as applicable.**

**Note:** Where a NHS organisation has agreed to act as sponsor or co-sponsor, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For all other sponsors, please describe the

arrangements and provide evidence.

- ☒ NHS indemnity scheme will apply (NHS sponsors only)  
☐ Other insurance or indemnity arrangements will apply (give details below)

Please enclose a copy of relevant documents.

**A76-2. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of the sponsor(s) or employer(s) for harm to participants arising from the design of the research?** Please tick box(es) as applicable.

*Note: Where researchers with substantive NHS employment contracts have designed the research, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For other protocol authors (e.g. company employees, university members), please describe the arrangements and provide evidence.*

- ☒ NHS indemnity scheme will apply (protocol authors with NHS contracts only)  
☐ Other insurance or indemnity arrangements will apply (give details below)

Please enclose a copy of relevant documents.

**A76-3. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of investigators/collaborators arising from harm to participants in the conduct of the research?**

*Note: Where the participants are NHS patients, indemnity is provided through the NHS schemes or through professional indemnity. Indicate if this applies to the whole study (there is no need to provide documentary evidence). Where non-NHS sites are to be included in the research, including private practices, please describe the arrangements which will be made at these sites and provide evidence.*

- ☒ NHS indemnity scheme or professional indemnity will apply (participants recruited at NHS sites only)  
☐ Research includes non-NHS sites (give details of insurance/ indemnity arrangements for these sites below)

Please enclose a copy of relevant documents.

**A77. Has the sponsor(s) made arrangements for payment of compensation in the event of harm to the research participants where no legal liability arises?**

- ☐ Yes ☒ No

Please enclose a copy of relevant documents.

**A78. Could the research lead to the development of a new product/process or the generation of intellectual property?**

- ☒ Yes ☐ No ☐ Not sure

## PART B: Section 7 - Children

**1. Please specify the potential age range of children under 16 who will be included and give reasons for carrying out the research in this age group.**

Age range from aged 2 to aged 16. This study is a paediatric study looking at the prevalence of juvenile arthritis in



children with Down's syndrome. All staff are paediatrically trained and all assessments will be undertaken in a paediatric environment.

**2. Indicate whether any children under 16 will be recruited as controls and give further details.**

No children will be recruited as controls

**3-2. Please describe the arrangements for seeking informed consent from a person with parental responsibility and/or from children able to give consent for themselves.**

On the day of the study, and after a final opportunity to ask questions, we will take parents' informed consent and, where appropriate, the child's assent before proceeding with the study measurements.

**4. If you intend to provide children under 16 with information about the research and seek their consent or agreement, please outline how this process will vary according to their age and level of understanding.**

We will ask the community paediatricians who know these children best, and the parents, to guide us to the educational level of these children as well as their learning abilities regarding the patient information sheet. We will obtain the child's assent, if appropriate.

*Copies of written information sheet(s) for parents and children, consent/assent form(s) and any other explanatory material should be enclosed with the application.*

**PART C: Overview of research sites**

**Please enter details of the host organisations (Local Authority, NHS or other) in the UK that will be responsible for the research sites.** For NHS sites, the host organisation is the Trust or Health Board. Where the research site is a primary care site, e.g. GP practice, please insert the host organisation (PCT or Health Board) in the Institution row and insert the research site (e.g. GP practice) in the Department row.

Research site		Investigator/ Collaborator/ Contact	
Institution name	Royal Hospital for Sick Children	Title	Dr
Department name	Child Health	First name/ Initials	Janet
Street address	Dalnair Street	Surname	Gardner-Medwin
Town/city	Glasgow		
Post Code	G3 8SJ		

## PART D: Declarations

### D1. Declaration by Chief Investigator

1. The information in this form is accurate to the best of my knowledge and belief and I take full responsibility for it.
2. I undertake to abide by the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research.
3. If the research is approved I undertake to adhere to the study protocol, the terms of the full application as approved and any conditions set out by review bodies in giving approval.
4. I undertake to notify review bodies of substantial amendments to the protocol or the terms of the approved application, and to seek a favourable opinion from the main REC before implementing the amendment.
5. I undertake to submit annual progress reports setting out the progress of the research, as required by review bodies.
6. I am aware of my responsibility to be up to date and comply with the requirements of the law and relevant guidelines relating to security and confidentiality of patient or other personal data, including the need to register when necessary with the appropriate Data Protection Officer. I understand that I am not permitted to disclose identifiable data to third parties unless the disclosure has the consent of the data subject or, in the case of patient data in England and Wales, the disclosure is covered by the terms of an approval under Section 251 of the NHS Act 2006.
7. I understand that research records/data may be subject to inspection by review bodies for audit purposes if required.
8. I understand that any personal data in this application will be held by review bodies and their operational managers and that this will be managed according to the principles established in the Data Protection Act 1998.
9. I understand that the information contained in this application, any supporting documentation and all correspondence with review bodies or their operational managers relating to the application:
  - Will be held by the main REC or the GTAC (as applicable) until at least 3 years after the end of the study; and by NHS R&D offices (where the research requires NHS management permission) in accordance with the NHS Code of Practice on Records Management.
  - May be disclosed to the operational managers of review bodies, or the appointing authority for the main REC, in order to check that the application has been processed correctly or to investigate any complaint.
  - May be seen by auditors appointed to undertake accreditation of RECs.
  - Will be subject to the provisions of the Freedom of Information Acts and may be disclosed in response to requests made under the Acts except where statutory exemptions apply.
10. I understand that information relating to this research, including the contact details on this application, may be held on national research information systems, and that this will be managed according to the principles established in the Data Protection Act 1998.
11. I understand that the main REC or its operational managers may share information in this application or supporting documentation with the Medicines and Healthcare products Regulatory Agency (MHRA) where it is relevant to the Agency's statutory responsibilities.
12. I understand that the summary of this study will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named below. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.

#### Contact point for publication(Not applicable for R&D Forms)

NRES would like to include a contact point with the published summary of the study for those wishing to seek further information. We would be grateful if you would indicate one of the contact points below.

- ☒ Chief Investigator  
☐ Sponsor  
☐ Study co-ordinator  
☐ Student  
☐ Other – please give details  
☐ None

**Access to application for training purposes** *(Not applicable for R&D Forms)*

*Optional – please tick as appropriate:*

☒ I would be content for members of other RECs to have access to the information in the application in confidence for training purposes. All personal identifiers and references to sponsors, funders and research units would be removed.

Signature: .....

Print Name: Janet Gardner-Medwin

Date: 26/01/2011 (dd/mm/yyyy)



**D2. Declaration by the sponsor's representative**

*If there is more than one sponsor, this declaration should be signed on behalf of the co-sponsors by a representative of the lead sponsor named at A64-1.*

I confirm that:

1. This research proposal has been discussed with the Chief Investigator and agreement in principle to sponsor the research is in place.
2. Any necessary indemnity or insurance arrangements, as described in question A76, will be in place before this research starts. Insurance or indemnity policies will be renewed for the duration of the study where necessary.
3. Arrangements will be in place before the study starts for the research team to access resources and support to deliver the research as proposed.
4. Arrangements to allocate responsibilities for the management, monitoring and reporting of the research will be in place before the research starts.
5. The duties of sponsors set out in the Research Governance Framework for Health and Social Care will be undertaken in relation to this research.
6. I understand that the summary of this study will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named in this application. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.

Signature: .....

Print Name: Dr Michael Barber

Post: Academic Research Co-ordinator

Organisation: NHS Greater Glasgow & Clyde Research and Development

Date: 26/01/2011 (dd/mm/yyyy)

**D3. Declaration for student projects by academic supervisor**

1. I have read and approved both the research proposal and this application. I am satisfied that the scientific content of the research is satisfactory for an educational qualification at this level.
2. I undertake to fulfil the responsibilities of the Chief Investigator and the supervisor for this study as set out in the Research Governance Framework for Health and Social Care.
3. I take responsibility for ensuring that this study is conducted in accordance with the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research, in conjunction with clinical supervisors as appropriate.
4. I take responsibility for ensuring that the applicant is up to date and complies with the requirements of the law and relevant guidelines relating to security and confidentiality of patient and other personal data, in conjunction with clinical supervisors as appropriate.

Signature: .....

Print Name: Janet Gardner-Medwin

Post: Senior Lecturer in Paediatric Rheumatology

Organisation: University of Glasgow

Date: 26/01/2011 (dd/mm/yyyy)

### Welcome to the Integrated Research Application System

### IRAS Project Filter

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

**Please enter a short title for this project** (maximum 70 characters)

Prevalence of Musculoskeletal Disability in Down's syndrome

#### 1. Is your project research?

☒ Yes ☐ No

#### 2. Select one category from the list below:

- ☐ Clinical trial of an investigational medicinal product
- ☐ Clinical investigation or other study of a medical device
- ☐ Combined trial of an investigational medicinal product and an investigational medical device
- ☒ Other clinical trial or clinical investigation
- ☐ Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
- ☐ Study involving qualitative methods only
- ☐ Study limited to working with human tissue samples, other human biological samples and/or data (*specific project only*)
- ☐ Research tissue bank
- ☐ Research database

**If your work does not fit any of these categories, select the option below:**

☐ Other study

#### 2a. Please answer the following question(s):

- a) Does the study involve the use of any ionising radiation? ☐ Yes ☒ No
- b) Will you be taking new human tissue samples (or other human biological samples)? ☐ Yes ☒ No
- c) Will you be using existing human tissue samples (or other human biological samples)? ☐ Yes ☒ No

#### 3. In which countries of the UK will the research sites be located? (Tick all that apply)

- ☐ England
- ☒ Scotland
- ☐ Wales
- ☐ Northern Ireland

#### 3a. In which country of the UK will the lead NHS R&D office be located:

- ☐ England
- ☒ Scotland

- ☐ Wales
- ☐ Northern Ireland
- ☐ This study does not involve the NHS

**4. Which review bodies are you applying to?**

- ☒ NHS/HSC Research and Development offices
- ☒ Research Ethics Committee
- ☐ National Information Governance Board for Health and Social Care (NIGB)
- ☐ Ministry of Justice (MoJ)
- ☐ National Offender Management System (NOMS)

**5. Will any research sites in this study be NHS organisations?**

- ☒ Yes ☐ No

**6. Do you plan to include any participants who are children?**

- ☒ Yes ☐ No

**7. Do you plan to include any participants who are adults unable to consent for themselves through physical or mental incapacity?** *The guidance notes explain how an adult is defined for this purpose.*

- ☐ Yes ☒ No

**8. Do you plan to include any participants who are prisoners or young offenders in the custody of HM Prison Service or who are offenders supervised by the probation service in England or Wales?**

- ☐ Yes ☒ No

**9. Is the study, or any part of the study, being undertaken as an educational project?**

- ☒ Yes ☐ No

**9a. Is the project being undertaken in part fulfilment of a PhD or other doctorate?**

- ☐ Yes ☒ No

**10. Is this project financially supported by the United States Department for Health and Human Services?**

- ☐ Yes ☒ No

### Site-Specific Information Form

**Is the site hosting this research a NHS site or a non-NHS site?** NHS sites include Health and Social Care organisations in Northern Ireland. The sites hosting the research are the sites in which or through which research procedures are conducted. For NHS sites, this includes sites where NHS staff are participants.

- ☒ NHS site  
☐ Non-NHS site

*This question must be completed before proceeding. The filter will customise the form, disabling questions which are not relevant to this application.*

*One Site-Specific Information Form should be completed for each research site and submitted to the relevant R&D office with the documents in the checklist. See guidance notes.*

*The data in this box is populated from Part A:*

Title of research:  
 Study of the prevalence of musculoskeletal abnormalities in children with Down's syndrome in the Glasgow population

Short title: Prevalence of Musculoskeletal Disability in Down's syndrome

Chief Investigator:	Title	Forename/Initials	Surname
	Dr	Janet	Gardner-Medwin

Name of NHS Research Ethics Committee to which application for ethical review is being made:  
 Glasgow West

Project reference number from above REC: 11/AL/0032

#### 1-1. Give the name of the NHS organisation responsible for this research site

NHS Greater Glasgow & Clyde

#### 1-2. In which country is the research site located?

- ☐ England  
☐ Wales  
☒ Scotland  
☐ Northern Ireland

#### 1-3. Is the research site a GP practice or other Primary Care Organisation?

- ☐ Yes ☒ No

#### 2. Who is the Principal Investigator or Local Collaborator for this research at this site?



Select the appropriate title: ☒ Principal Investigator  
☐ Local Collaborator

Title Forename/Initials Surname  
 Dr Janet Gardner-Medwin  
 Post Senior Lecturer in Paediatric Rheumatology  
 Qualifications MBChB FRCPCH PhD  
 Organisation University of Glasgow  
 Work Address Dept of Child Health  
 RHSC Yorkhill  
 Dalnair Street  
 PostCode G3 8SJ  
 Work E-mail Janet.Gardner-Medwin@glasgow.ac.uk  
 Work Telephone 01412010867  
 Mobile  
 Fax 01412010837

a) Approximately how much time will this person allocate to conducting this research? *Please provide your response in terms of Whole Time Equivalents (WTE).*  
 0.1

b) Does this person hold a current substantive employment contract, Honorary Clinical Contract or Honorary Research Contract with the NHS organisation or accepted by the NHS organisation? ☒ Yes ☐ No

A copy of a current CV for the Principal Investigator (maximum 2 pages of A4) must be submitted with this form.

**3. Please give details of all locations, departments, groups or units at which or through which research procedures will be conducted at this site and describe the activity that will take place.**

*Please list all locations/departments etc where research procedures will be conducted within the NHS organisation, describing the involvement in a few words. Where access to specific facilities will be required these should also be listed for each location.*

*Name the main location/department first. Give details of any research procedures to be carried out off site, for example in participants' homes.*

	Location	Activity/facilities
1	RHSC Yorkhill Dalnair Street, Glasgow G3 8SJ	Clinic provided for those children to whom a follow up appointment is recommended and those wishing a follow up appointment if concerned.
2	Southbank Child Health Centre 207 Old Rutherglen Road Gorbals, Glasgow G5 0RE	Study visits carried out alongside visit to community paediatrician
3	Bridgeton Child Development Centre Bridgeton HC, 201 Abercromby St, Glasgow G40 2DA	Study visits carried out alongside visit to community paediatrician
4	Glenfarg Suite Child Development Centre, Possilpark HC, 85 Denmark Street, Glasgow G22 5EG	Study visits carried out alongside visit to community paediatrician

Achamore Child Development Centre  
Study visits carried out alongside visit to community paediatrician

5 Drumchapel HC,  
80-90 Kinfauns Drive, Glasgow  
G15 7PS

6

**5. Please give details of all other members of the research team at this site.**

1

	Title Forename/Initials Surname
	Mrs Maureen Todd
Work E-mail	maureen.todd2@nhs.net
Employing organisation	NHS Greater Glasgow and Clyde
Post	Research Nurse
Qualifications	RGN PG Cert MSK US
Role in research team:	research nurse

a) Approximately how much time (approximately) will this person allocate to conducting this research? *Please provide your response in terms of Whole Time Equivalents (WTE).*

1.0

b) Does this person hold a current substantive employment contract, Honorary Clinical Contract or Honorary Research Contract with the NHS organisation or accepted by the NHS organisation? ☒ Yes ☐ No

*A copy of a current CV for the research team member (maximum 2 pages of A4) must be submitted to the R&D office.*

2

	Title Forename/Initials Surname
	Mr Gordon Watt
Work E-mail	g.f.watt@gcu.ac.uk
Employing organisation	Glasgow Caledonian University
Post	Lecturer in Podiatry
Qualifications	MChS, DPodM, FCPodM, Cert AdEd
Role in research team:	other (please specify) podiatrist

a) Approximately how much time (approximately) will this person allocate to conducting this research? *Please provide your response in terms of Whole Time Equivalents (WTE).*

0.2

b) Does this person hold a current substantive employment contract, Honorary Clinical Contract or Honorary Research Contract with the NHS organisation or accepted by the NHS organisation? ☒ Yes ☐ No

**6. Does the Principal Investigator or any other member of the site research team have any direct personal involvement (e.g. financial, share-holding, personal relationship etc) in the organisation sponsoring or funding the research that may**

give rise to a possible conflict of interest?

☐ Yes ☒ No

**7. What is the proposed local start and end date for the research at this site?**

Start date: 01/01/2011

End date: 31/12/2011

Duration (Months): 12

**8-1. Give details of all non-clinical intervention(s) or procedure(s) that will be received by participants as part of the research protocol. (These include seeking consent, interviews, non-clinical observations and use of questionnaires.)**

Columns 1-4 have been completed with information from A18 as below:

1. Total number of interventions/procedures to be received by each participant as part of the research protocol.
2. If this intervention would have been routinely given to participants as part of their care, how many of the total would have been routine?
3. Average time taken per intervention (minutes, hours or days)
4. Details of who will conduct the procedure, and where it will take place

Please complete Column 5 with details of the names of individuals or names of staff groups who will conduct the procedure at this site.

Intervention or procedure	1	2	3	4	5
Other questionnaire	1		10	CHQ questionnaire will be completed by the accompanying parent and, dependant of the level of learning difficulties in individual child/young person with Down's, they will be given an opportunity to contribute to the answers. This questionnaire covers psychological and physical well being.	Maureen Todd Gordon Watt
Other questionnaire	1	5		CHAQ questionnaire will be completed by the accompanying parent and, dependant on the level of learning difficulties in individual child/young person with Down's, they will be given an opportunity to contribute to the answers. This questionnaire covers physical abilities.	Maureen Todd Gordon Watt
Face to face interview	1		10	A structured interview with the parents will be performed by the researchers who will take the parents through the questions.	Maureen Todd Gordon Watt

**8-2. Will any aspects of the research at this site be conducted in a different way to that described in Part A or the protocol?**

☐ Yes ☒ No

If Yes, please note any relevant changes to the information in the above table.

Are there any changes other than those noted in the table?



**9-1. Give details of any clinical intervention(s) or procedure(s) to be received by participants as part of the research protocol.** (These include uses of medicinal products or devices, other medical treatments or assessments, mental health interventions, imaging investigations and taking samples of human biological material. Include procedures which might be received as routine clinical care outside of the research.)

Columns 1-4 have been completed with information from A19 as below:

1. Total number of interventions to be received by each participant as part of the research protocol
2. If this intervention would have been routinely given to participants as part of their care, how many of the total would have been routine?
3. Average time taken per intervention (minutes, hours or days)
4. Details of who will conduct the procedure, and where it will take place

Please complete Column 5 with details of the names of individuals or names of staff groups who will conduct the procedure at this site.

Intervention or procedure	1	2	3	4	5
Clinical examination	1		25	Detailed clinical examination of the musculoskeletal system to allow the examiner to score the Beighton hypermobility score, to document any joints with arthritis or limitation of movement, assessment of muscle strength and detailed examination of the foot to document abnormalities of structure, function and gait.	Maureen Todd Gordon Watt
Other	1		15	Measurements of height, weight, arm span, sitting height, head circumference.	Maureen Todd Gordon Watt
Other	1		3	Tanita measurement of bioelectrical impedance. the subject stands on the bioelectrical impedance machine in bare feet. This resembles bathroom scales. Much	Maureen Todd Gordon Watt

			like an ECG the Tanita measures electrical resistance which is dependant on body fat and gives an estimate of body composition. It is quite painless and takes only a few minutes.	
Ultrasound scan (if required)	1	10	Ultrasound scan of any joints suspected of having inflammatory arthritis to confirm the presence of inflammation if judged to be necessary by the research nurse who holds a PG Cert in Medical Ultrasound specialising in MSK.	Maureen Todd

**9-2. Will any aspects of the research at this site be conducted in a different way to that described in Part A or the protocol?**

☐ Yes ☒ No

*If Yes, please note any relevant changes to the information in the above table.*

*Are there any changes other than those noted in the table?*

**10. How many research participants/samples is it expected will be recruited/obtained from this site?**

All patients are identified through community paediatric services in these outreach child health centres.

**11. Give details of how potential participants will be identified locally and who will be making the first approach to them to take part in the study.**

Children with Down's children will be identified through the thyroid register. However the approach will be made by their own community paediatrician who knows their case and can confirm it is appropriate to approach them.

**12. Who will be responsible for obtaining informed consent at this site? What expertise and training do these persons have in obtaining consent for research purposes?**

Name	Expertise/training
Dr Janet Gardner Medwin	17 years research experience GCP and informed consent trained
Mrs Maureen Todd	2 years research experience GCP and informed consent trained

**15-1. Is there an independent contact point where potential participants can seek general advice about taking part in research?**

Consultant community paediatrician Kath Leyland knows the patients well and will act as an independent patient advocate.

**15-2. Is there a contact point where potential participants can seek further details about this specific research project?**

The patient information sheets will have a phone number for potential participants to contact Dr Gardner Medwin and phone number, mobile number and email address to contact research nurse Maureen Todd.

**16. Are there any changes that should be made to the generic content of the information sheet to reflect site-specific issues in the conduct of the study? A substantial amendment may need to be discussed with the Chief Investigator and submitted to the main REC.**

No

*Please provide a copy on headed paper of the participant information sheet and consent form that will be used locally. Unless indicated above, this must be the same generic version submitted to/approved by the main REC for the study while including relevant local information about the site, investigator and contact points for participants (see guidance notes).*

**17. What local arrangements have been made for participants who might not adequately understand verbal explanations or written information given in English, or who have special communication needs? (e.g. translation, use of interpreters etc.)**

These children with learning difficulties are known to the community paediatricians. They are divided into three groups: mainstream school children, children attending the moderate learning difficulty schools and the children attending the complex learning difficulty schools. Patient information sheets, including information for the parents to read to their children for all these levels of learning disability are provided. Some children may not be able to understand the nature of the study, but they will be used to medical consultations and the study will be very similar to a routine medical consultation. In this case the parents may decide to consent for their child knowing they do not understand. We are going to see these children in an environment they are familiar with and we will take advice from their parents and community paediatricians on their level of understanding. This screening examination will be held as simply and as child friendly as possible. It is no more complex than the clinical examination the child receives in a normal paediatric rheumatology consultation. Translators can be provided if required at the routine community paediatrician visit. In this situation we would not be able to see a child in their own home.

**18. What local arrangements will be made to inform the GP or other health care professionals responsible for the care of the participants?**

As main application

**19. What arrangements (e.g. facilities, staffing, psychosocial support, emergency procedures) will be in place at the site, where appropriate, to minimise the risks to participants and staff and deal with the consequences of any harm?**

We have the support of the clinical team who know the patients well.

**20. What are the arrangements for the supervision of the conduct of the research at this site? Please give the name and contact details of any supervisor not already listed in the application.**

Research nurse is supervised by Dr Gardner-Medwin and is appropriately trained. Two clinically experienced members of staff will be present at all consultations.

**21. What external funding will be provided for the research at this site?**

☐ Funded by commercial sponsor



- ☒ Other funding  
☐ No external funding

Please give details of the funding:

Barbara Ansell Fellowship grant provided by Arthritis Research UK

Type of funding	Details (including breakdown over years if appropriate)
(i) Block grant	£46,214 for 12 months to pay salary and research expenses for the duration of the study
(ii) Per participant	
(iii) Other (give details)	

Which organisation will receive and manage this funding?  
 University of Glasgow

### 23. Authorisations required prior to R&D approval

This section deals with authorisations by managers within the NHS organisation. It should be signed in accordance with the guidance provided by the NHS organisation. This may include authorisation by clinical supervisors, line managers, service managers, support department managers, pharmacy, data protection officers or finance managers, depending on the nature of the research. Managers completing this section should confirm in the text what the authorisation means, in accordance with the guidance provided by the NHS organisation.

This section may also be used by university employers or research support staff to provide authorisation to NHS organisations, in accordance with guidance from the university.

#### 1. Type of authorisation:

To carry out the study within the Child Health Centres

	Title Forename/Initials Surname
	Dr Katherine Leyland
Post	Consultant Community Paediatrician
Qualifications	MBChB DCH MRCPCH
Organisation	SE Community Health and Care Partnership, Greater Glasgow & Clyde
Work Address	Southbank Child Centre 207 Old Rutherglen Road, Glasgow
PostCode	G5 0RE
Work E-mail	kath.leyland@ggc.scot.nhs.uk
Work Telephone	01412010908
Mobile	
Fax	

Signature: .....

Date: .....

### Declaration by Principal Investigator or Local Collaborator

- The information in this form is accurate to the best of my knowledge and I take full responsibility for it.

2. I undertake to abide by the ethical principles underpinning the World Medical Association's Declaration of Helsinki and relevant good practice guidelines in the conduct of research.
3. If the research is approved by the main REC and NHS organisation, I undertake to adhere to the study protocol, the terms of the application of which the main REC has given a favourable opinion and the conditions requested by the NHS organisation, and to inform the NHS organisation within local timelines of any subsequent amendments to the protocol.
4. If the research is approved, I undertake to abide by the principles of the Research Governance Framework for Health and Social Care.
5. I am aware of my responsibility to be up to date and comply with the requirements of the law and relevant guidelines relating to the conduct of research.
6. I undertake to disclose any conflicts of interest that may arise during the course of this research, and take responsibility for ensuring that all staff involved in the research are aware of their responsibilities to disclose conflicts of interest.
7. I understand and agree that study files, documents, research records and data may be subject to inspection by the NHS organisation, the sponsor or an independent body for monitoring, audit and inspection purposes.
8. I take responsibility for ensuring that staff involved in the research at this site hold appropriate contracts for the duration of the research, are familiar with the Research Governance Framework, the NHS organisation's Data Protection Policy and all other relevant policies and guidelines, and are appropriately trained and experienced.
9. I undertake to complete any progress and/or final reports as requested by the NHS organisation and understand that continuation of permission to conduct research within the NHS organisation is dependent on satisfactory completion of such reports.
10. I undertake to maintain a project file for this research in accordance with the NHS organisation's policy.
11. I take responsibility for ensuring that all serious adverse events are handled within the NHS organisation's policy for reporting and handling of adverse events.
12. I understand that information relating to this research, including the contact details on this application, will be held by the R&D office and may be held on national research information systems, and that this will be managed according to the principles established in the Data Protection Act 1998.
13. I understand that the information contained in this application, any supporting documentation and all correspondence with the R&D office and/or the REC system relating to the application will be subject to the provisions of the Freedom of Information Acts and may be disclosed in response to requests made under the Acts except where statutory exemptions apply.

Signature of Principal Investigator  
or Local Collaborator: .....

Print Name:

Dr Janet Gardner-Medwin

Date:

26/01/2011

Welcome to the Integrated Research Application System

IRAS Project Filter

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

**Please enter a short title for this project** (maximum 70 characters)  
Prevalence of Musculoskeletal Disability in Down's syndrome

**1. Is your project research?**

☒ Yes ☐ No

**2. Select one category from the list below:**

- ☐ Clinical trial of an investigational medicinal product
- ☐ Clinical investigation or other study of a medical device
- ☐ Combined trial of an investigational medicinal product and an investigational medical device
- ☒ Other clinical trial or clinical investigation
- ☐ Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
- ☐ Study involving qualitative methods only
- ☐ Study limited to working with human tissue samples, other human biological samples and/or data (*specific project only*)
- ☐ Research tissue bank
- ☐ Research database

**If your work does not fit any of these categories, select the option below:**

☐ Other study

**2a. Please answer the following question(s):**

- a) Does the study involve the use of any ionising radiation? ☐ Yes ☒ No
- b) Will you be taking new human tissue samples (or other human biological samples)? ☐ Yes ☒ No
- c) Will you be using existing human tissue samples (or other human biological samples)? ☐ Yes ☒ No

**3. In which countries of the UK will the research sites be located?** (*Tick all that apply*)

- ☐ England
- ☒ Scotland
- ☐ Wales
- ☐ Northern Ireland

**3a. In which country of the UK will the lead NHS R&D office be located:**

- ☐ England
- ☒ Scotland



- ☐ Wales  
☐ Northern Ireland  
☐ This study does not involve the NHS

**4. Which review bodies are you applying to?**

- ☒ NHS/HSC Research and Development offices  
☒ Research Ethics Committee  
☐ National Information Governance Board for Health and Social Care (NIGB)  
☐ Ministry of Justice (MoJ)  
☐ National Offender Management Service (NOMS) (Prisons & Probation)

**5. Will any research sites in this study be NHS organisations?**

- ☒ Yes   ☐ No

**6. Do you plan to include any participants who are children?**

- ☒ Yes   ☐ No

**7. Do you plan at any stage of the project to undertake intrusive research involving adults lacking capacity to consent for themselves?**

- ☐ Yes   ☒ No

*Answer Yes if you plan to recruit participants aged 16 or over who lack capacity, or to retain them in the study following loss of capacity. Intrusive research means any research requiring consent in law. This includes use of identifiable tissue samples or personal information, except where application is being made to the NIGB Ethics and Confidentiality Committee to set aside the common law duty of confidentiality in England and Wales. Please consult the guidance notes for further information on the legal frameworks for research involving adults lacking capacity in the UK.*

**8. Do you plan to include any participants who are prisoners or young offenders in the custody of HM Prison Service or who are offenders supervised by the probation service in England or Wales?**

- ☐ Yes   ☒ No

**9. Is the study, or any part of the study, being undertaken as an educational project?**

- ☒ Yes   ☐ No

**9a. Is the project being undertaken in part fulfilment of a PhD or other doctorate?**

- ☐ Yes   ☒ No

**10. Will this research be financially supported by the United States Department of Health and Human Services or any of its divisions, agencies or programs?**

- ☐ Yes   ☒ No

**NOTICE OF SUBSTANTIAL AMENDMENT**

*Please use this form to notify the main REC of substantial amendments to all research other than clinical trials of investigational medicinal products (CTIMPs). For CTIMPs, please use the European Commission notice of substantial amendment form at <http://eudract.emea.europa.eu/document.html>. The form should be completed by the Chief Investigator using language comprehensible to a lay person. Support in principle should be sought from the study sponsor before the amendment is submitted.*

**Details of Chief Investigator:**

	Title Forename/Initials Surname
	Dr Janet Gardner-Medwin
Work Address	Dept of Child Health RHSC Yorkhill, Dalnair Street Glasgow
PostCode	G3 8SJ
Email	Janet.Gardner-Medwin@glasgow.ac.uk
Telephone	01412010867
Fax	01412010837

<b>Full title of study:</b>	Study of the prevalence of musculoskeletal abnormalities in children with Down's syndrome in the Glasgow population
<b>Lead sponsor:</b>	NHS Greater Glasgow & Clyde
<b>Name of REC:</b>	Glasgow West
<b>REC reference number:</b>	11/AL/0032
<b>Name of lead R&amp;D office:</b>	Research and Development
<b>Date study commenced:</b>	07/03/2011
<b>Protocol reference (if applicable), current version and date:</b>	
<b>Amendment number and date:</b>	Substantial amendment 1. 05/11

**Type of amendment**

(a) Amendment to information previously given in IRAS

☒ Yes ☐ No

If yes, please refer to relevant sections of IRAS in the "summary of changes" below.

(b) Amendment to the protocol

☒ Yes ☐ No

If yes, please submit either the revised protocol with a new version number and date, highlighting changes in bold, or a document listing the changes and giving both the previous and revised text.



(c) Amendment to the information sheet(s) and consent form(s) for participants, or to any other supporting documentation for the study

☒ Yes ☐ No

If yes, please submit all revised documents with new version numbers and dates, highlighting new text in bold.

Community Paediatrician invite letter

Parent Information Sheet and Flyer

Parent advert

Is this a modified version of an amendment previously notified and not approved?

☐ Yes ☒ No

### Summary of changes

Briefly summarise the main changes proposed in this amendment. Explain the purpose of the changes and their significance for the study.

If this is a modified amendment, please explain how the modifications address the concerns raised previously by the ethics committee.

If the amendment significantly alters the research design or methodology, or could otherwise affect the scientific value of the study, supporting scientific information should be given (or enclosed separately). Indicate whether or not additional scientific critique has been obtained.

We originally asked to perform the study visits alongside the annual review appointment with the community paediatrician. However, the two visits combined then takes over an hour and some parents have expressed a preference to come in at a separate time. This could be because a grandparent is bringing them for their paediatrician appointment and, therefore, cannot sign consent for the study or the parent doesn't want to be there for so long an appointment - they may need to be back at work. Our study is taking less time than we thought originally so a separate appointment would only require the child and parent to be there for approx 30 - 45 minutes depending on how co-operative the child is. With a co-operative child it takes approx 30 mins.

There is also an issue with room availability in the child development centres and we would like to give the parents the option of coming up to the Paediatric Clinical Research Facility at RHSC Yorkhill as an alternative. We are already offering to carry out the study visits within the home setting, if that is their preference, but this would give the parents more choice regarding their participation. This would also allow us to offer more appointments over holiday periods when it would suit the parents better, as many of the community paediatrician reviews take place within the school setting during term time.

The main significance for the study will be an improvement in recruitment numbers over a shorter time as it will allow us to see more participants in one session and increase the option of venue for study visits. This will, ultimately, allow the parents more choice regarding their appointment time and venue.

### Any other relevant information

Applicants may indicate any specific issues relating to the amendment, on which the opinion of a reviewing body is sought.

### List of enclosed documents

Document	Version	Date
Community Paediatrician invite letter	3	17/05/2011
Parent information sheet and flyer	3	17/05/2011
Revised protocol	3	17/05/2011

### Declaration by Chief Investigator

1. I confirm that the information in this form is accurate to the best of my knowledge and I take full responsibility for it.
2. I confirm that the study sponsor has been notified of the proposed amendment.

## Notice of Amendment

IRAS Version 3.1

3. *I consider that it would be reasonable for the proposed amendment to be implemented.*

**Date:**.....

## **APPENDIX 2: PARENT AND PATIENT INFORMATION SHEETS**

### **AND INVITATION**

**NHS Greater Glasgow &**

**Clyde**

Royal Hospital for Sick Children  
Dalnair Street  
Glasgow G3 8SJ



### **Can you help us?**

We are inviting you and your child to take part in a research study



### **What is the study about?**

Children and young people with Down's Syndrome often have very bendy joints that get sore, and sometimes the joints are swollen because of arthritis. We don't know how often this happens, but we know some children with Down's syndrome have these problems for a long time without anyone knowing. If we knew we could help prevent damage to the joints. We want to check the joints of all children with Down's syndrome in Glasgow to find out how common these problems really are.

### **What will happen?**

We would like to come to see your child once. You can choose for the visit to be in your home, at school, at your next clinic visit to your community paediatrician or at the Clinical Research Facility at Yorkhill Hospital. We will look, feel and move your child's muscles, bones and joints and feet, and measure your child's height and weight. It will be friendly and relaxed for your child, and easy for them to do. All we ask is that you bring shorts and a T shirt for your child to wear so they feel comfortable.

### **Who is organising the research?**

The paediatric rheumatology team at Yorkhill is organising the study. You can contact Sr. Maureen Todd, the research nurse on the telephone 0141-232 1836; mobile 07760 240415 or e-mail [maureen.todd2@nhs.net](mailto:maureen.todd2@nhs.net). Dr Gardner-Medwin is the consultant in charge of the study. You can contact her on telephone number 0141 232 1836/1837 or email [Janet.Gardner-Medwin@glasgow.ac.uk](mailto:Janet.Gardner-Medwin@glasgow.ac.uk). Your child's own community doctor also knows about this study, and you can ask them questions if you prefer.

We will ring you in the next day or so to answer any questions, and find out if you would be happy to help us.

**Thank you very much for taking the time to read this sheet.**

**NHS Greater Glasgow & Clyde**

Royal Hospital for Sick Children  
Dalnair Street  
Glasgow G3 8SJ

**Parent/Guardian Information Sheet**

**Study Title: Study of incidence of musculoskeletal abnormalities in children with Down's syndrome in the Glasgow population**

**Study Staff:** Sr. Maureen Todd, Prof. Jim Woodburn, Dr Malcolm Donaldson, Jez Jones, Dr Kath Leyland, Mr Gordon Watt, Prof. John McColl and Dr Janet Gardner-Medwin

Your child is being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read this information carefully. Please ask us if there anything is not clear. Take time to decide whether you wish your child to take part.

**What is the purpose of the study?**

Children with Down's syndrome can get problems with their bones, joints and muscles. Many children with Down's syndrome are very flexible, and some get arthritis. We want to find out how common these problems are, and whether they cause serious physical problems. We are concerned they are often overlooked leaving children in pain or with difficulty getting about which adds to their difficulties. Finding these problems early would improve the well-being of these children.

**Why has my child been chosen?**

We are inviting all children with Down's syndrome, who are between 2 and 16 years old, and who live in Glasgow to take part.

**Do we have to take part?**

No. It is up to you to decide whether or not your child takes part. We have designed the study to be easy for children with learning difficulties and other physical problems to take part, and we are happy to talk to you about how we can make the visit as easy for your child as possible. If you think that your child cannot take part at the moment we would be happy to invite you at a better time for your family. If you do decide to take part, you will be given this information sheet to keep and asked to sign a consent form. You are free to withdraw at any time without giving a reason. A decision not to take part will not affect the standard of care your child receives.

**What will happen to my child if he/she takes part?**

We would like to come to see your child once. This can either be at your home, at school, at your next routine visit to your community paediatrician or you can come to the Clinical Research Facility at Yorkhill Hospital. You can let us know what would be most suitable for you. We are very happy to answer any further questions before you decide to join the study. Once you have decided to take part we will ask you to sign a consent form. With your help the research nurse will learn about your child's medical story, your child's daily activities, physical abilities and whether you think they get any pain or discomfort. We will ask about anyone in the family with arthritis or similar conditions. Then the research nurse

will do a simple examination of your child's muscles, bones and joints. This involves looking, feeling and moving the bones and joints. A foot expert will look at your child's feet. We will measure your child's height and weight

### **What do we have to do?**

**Getting in touch:** We will already have contacted you to ask if you would like to take part. We are happy to answer any further questions you have, find out what arrangements will suit you and

your child best, and arrange a visit. You can contact us if you prefer, our details are at the end of this sheet.

**Explaining to your child:** We enclose different information, and ask you to choose which one best suits your child. You are the best person to choose whether this information suits your child's level of understanding. It may be you feel it best to explain the study in your own words.

**The visit:** On the day of the visit please bring shorts and T-shirt for your child to wear. At the visit you will meet Maureen Todd, the research nurse, and Gordon Watt, the foot expert. We will make sure you and your child are happy to take part, and you will be asked to sign a consent form. Children who would like and are able can sign an assent form.

All the measurements are very simple. We want your child to be comfortable, relaxed and to enjoy the visit. We know children with Down's syndrome sometimes need a little extra encouragement and time, and might even decide not to cooperate so please don't worry. We have allowed an hour for the study which is plenty of time. If things go very quickly it won't take that long. We will be sensitive to how your child feels on the day, and stop if they don't want to go on.

Maureen will measure your child's height and weight. Then she will look at your child's bones, muscles and joints in detail. Gordon will examine your child's feet and watch them walk. We will ask you some general questions about your child and your family's health. One of the study staff will be free to play or care for your child while you answer questions, or ask us questions. Your child can rest, have a snack or play whilst we answer your questions and tell you the results of the visit. You will then have finished your part in the trial, thank you.

### **Is there any disadvantage in taking part?**

We will tell you everything we found during the visit. With your permission, we will tell your family doctor and community / school doctor. If we find a problem you didn't already know about, or if you wish for a further medical opinion we can arrange an outpatient clinic appointment for your child at Yorkhill. It is entirely up to you to decide if you would like an appointment. You can discuss this with your child's own doctors before making up your mind, and you can ask for an appointment later. We would be happy to see your child anytime up to their 18<sup>th</sup> birthday. You are of course able to arrange with your own doctor for a referral elsewhere if you prefer.

### **What will happen to the results of the research study?**

Any information collected during this study will be kept strictly confidential. Each participant will be given a code number so that they cannot be identified. All data will be stored on a secure database that can only be accessed by authorised individuals. The results will be published in a medical journal. It will not be able possible to identify your child in this publication. It will say general things like '150 children aged 2 to 17 were examined'. We would like to tell you the overall results of the whole study after it is finished. However this will take some time, so it will probably be 2012 by the time the study is finished and we write to you.

**Who is organising the research?**

The paediatric rheumatology team at Yorkhill is organising the study. If you have any questions, problems or difficulties with the study, please contact Sr. Maureen Todd, the research nurse, on the telephone 0141-232 1836; mobile 07760 240415 or e-mail [maureen.todd2@nhs.net](mailto:maureen.todd2@nhs.net). Dr. Janet Gardner-Medwin, Consultant and Senior Lecturer in paediatric Rheumatology is in charge of the study. You can contact her on telephone number 0141 232 1836/1837. This study has been approved by a medical ethics research committee. They are happy that this study is of a good standard. This information sheet is yours to keep. We are very grateful to children and their families for helping with research. **Thank you very much for taking the time to read this information sheet.**



NHS Greater Glasgow & Clyde  
 Royal Hospital for Sick Children  
 Dalnair Street  
 Glasgow G3 8SJ



## Patient Information Sheet No. 1

**Study Title: Study of incidence of musculoskeletal abnormalities in children with Down's syndrome in the Glasgow population**

**Study Staff:** Sr. Maureen Todd, Prof. Jim Woodburn, Dr Malcolm Donaldson, Jez Jones, Dr Kath Leyland, Mr Gordon Watt, Prof. John McColl and Dr Janet Gardner-Medwin

We are inviting you to take part in a research study. This is to tell you about the research. Please take time and discuss it with your parents before you decide to take part. Please ask if you have any questions.

### **What is the study about?**

Children and young people with Down's Syndrome can have very bendy joints that get sore, and sometimes they can get sore swollen joints. We don't know how often this happens, but we think some children may have these problems without anyone knowing. If we knew we could help. This study is to find out how often these problems happen.

### **Why have I been chosen?**

We are inviting all children and young people with Down's syndrome who live in Glasgow to help us.

### **Do I have to take part?**

No. It is up to you to decide whether or not you take part. If you do decide to take part, you can keep this information and if you wish you can sign to say you are happy to take part. You can stop whenever you want.

### **What will happen to me if I take part?**

We will see you just once. This can be at your home, at school, at your next routine visit to the school doctor or at the Clinical Research Facility at Yorkhill Hospital. We are very happy to answer any questions before you start. We will ask you and your parents about your health. Then the nurse will look, feel and move your muscles, bones and joints. A foot expert will look at your feet. We will measure your height and weight. You can help us with the questions we ask you and your parents about your health.

### **What do I have to do?**

Talk to your Mum or Dad and if you want to do the study they will let us know. On the day it is best to wear shorts and T-shirt so we can see your arms and legs. You will meet Maureen Todd, the nurse, and Gordon Watt, the foot expert. After we have done the measurements you will then have finished, thank you.

### **Will you tell me what you found?**

Yes, we will tell you, your parents and your doctor everything we found. However, no one else will know you took part.

**Thank you**

**NHS Greater Glasgow &**

**Clyde**

Royal Hospital for Sick Children  
Dalnair Street  
Glasgow G3 8SJ



**Study Title: Study of incidence of musculoskeletal abnormalities in children with Down's syndrome in the Glasgow population** Study Staff: Sr. Maureen Todd, Prof. Jim Woodburn, Dr Malcolm Donaldson, Jez Jones, Dr Kath Leyland, Mr Gordon Watt, Prof. John McColl and Dr Janet Gardner-Medwin

## Patient Information Sheet No. 2

We are doctors and nurses who care for children who have difficulties in moving. We would like to see children like yourself and check out your movement. We would like to come and visit you and your parents to do this, if you and your Mum and Dad say it is OK. You don't have to help if you don't want to.

### What will happen?

My name is Maureen, I am a nurse and here is a picture of me.



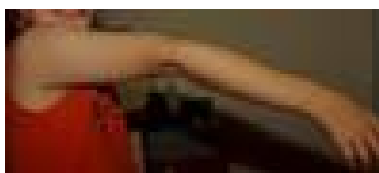
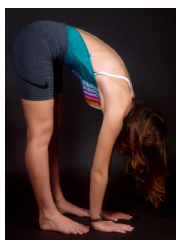
I will measure how tall you are



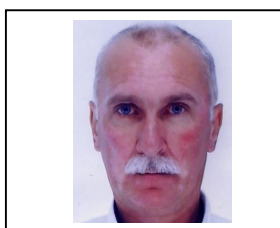
and weigh you



I will have a look at your hands, arms, legs and feet to see how you move. These pictures show some of the movements. I will ask you to copy them.



This is Gordon Watt.



He will have a look at your feet.



Then you can have a snack or play, while we talk to your parents.  
Then it will be time to go home. Thank you very much for helping us. 🧡



**NHS Greater Glasgow & Clyde**

Royal Hospital for Sick Children  
Dalnair Street  
Glasgow G3 8SJ



**Study Title: Study of incidence of musculoskeletal abnormalities in children with Down's syndrome in the Glasgow population** Study Staff: Sr. Maureen Todd, Prof. Jim Woodburn, Dr Malcolm Donaldson, Jez Jones, Dr Kath Leyland, Mr Gordon Watt, Prof. John McColl and Dr Janet Gardner-Medwin

### Patient Information Sheet No. 3

This is what will happen when we visit.

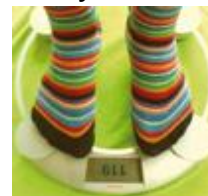
My name is  
Maureen, I am a  
nurse



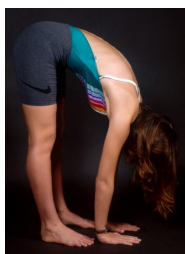
How tall are you



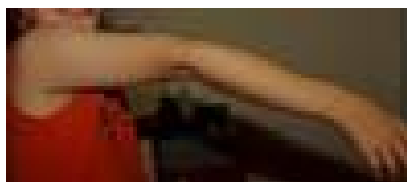
How heavy are  
you?



Can you do this?



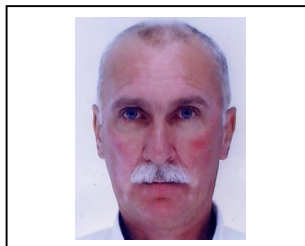
Or this?



Or this?



My name is Gordon Watt.



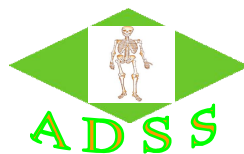
Can I look at your feet?



Time for a snack before you go  
home. Thank you



Community Child Health  
Services  
Southbank Child Centre  
207 Old Rutherglen Road  
Glasgow  
G5 0RE



{Date}

Dear Parents of {child's name}

I am writing to ask if you might be able to help us with a research study. This would involve a one off short study visit lasting approximately 30 - 45 minutes.

Children and young people with Down's Syndrome often have very bendy joints that get sore, and sometimes the joints are swollen because of arthritis. We don't know how often they get these problems and would like you to help us learn more by taking part in a study.

In the study we will look at your child just once, by looking at your child's arms and legs. There are no tests, just a gentle look at your child. We will tell you everything we find so that it can be used to help your child. This can be done at the same time as your review appointment here at the clinic or it can be done at the clinic on another day that suits you better, at the Clinical Research Facility at Yorkhill Hospital or in your own home.

I enclose a flyer telling you a bit more. I, or the study staff, would be happy to answer any questions you have.

I hope you will feel able to take part so we can learn more about this, and get better at helping the children who have these problems

Many thanks

Yours sincerely

Dr K Leyland  
Consultant Community Paediatrician

## **APPENDIX 3: pREMS**

### **Supplementary Appendix 1: pediatric Regional Examination of the Musculoskeletal System (pREMS)**

#### **General Principles**

##### ***Introduction***

- ◆ Introduction of assessor to child and parent / carer
- ◆ Explanation of what to be examined, Gain verbal consent to examine
- ◆ Be aware of normal variants in leg alignment, joint range, gait, developmental milestones

##### ***Look for:***

- ◆ Swellings, Rashes , Muscle wasting , Scars
- ◆ Deformity / Dysmorphism / Discomfort (nonverbal) / “Disproportions”

##### ***Feel for:***

- ◆ Temperature, Swelling, Tenderness

##### ***Move***

- ◆ Full range of movement – active and passive
- ◆ Restriction – mild, moderate or severe

##### ***Function and measure***

- ◆ Functional assessment of joint / anatomic region to include power of muscles and stability
- ◆ Measurement of height / leg length

##### ***Additional Options pending clinical scenario***

**Examination schedules by anatomical region** (note - the components underlined are those additional to adult REMS and the components *in italics* are those deemed to be appropriate for the specialist trainee in pediatric rheumatology to be aware of but not necessarily competent)

#### **Examination of the hand and wrist**

- ◆ Look at the hands (palms and backs) for muscle wasting, joint swelling, skin and nail changes
- ◆ Feel for radial pulse, tendon thickening and bulk of thenar and hypothenar eminences
- ◆ Feel for skin temperature
- ◆ Squeeze metacarpophalangeal joints (MCPJs)
- ◆ Bimanually feel /palpate small joints of the hands including wrists and especially if there are swollen or painful joints or restricted movement noted)
- ◆ Look and feel along ulnar border
- ◆ Assess full finger extension and full finger tuck
- ◆ Assess wrist flexion and extension, abduction and adduction – active and passive
- ◆ Assess function: grip and pinch, picking up small object, writing / drawing
- ◆ Option – hypermobility syndromes, muscle power, capillaroscopy, peripheral nerves

### **Examination of the elbow**

- ◆ Look for carrying angle, scars, swellings or rashes, deformity
- ◆ Feel for skin temperature
- ◆ Feel over head of radius, joint line, medial and lateral epicondyles
- ◆ Assess full flexion and extension, pronation and supination – actively and passively
- ◆ Assess function – e.g. hand to nose or mouth, hands behind head
- ◆ Option – hypermobility syndromes, muscle power, entheses, instability tests

### **Examination of the shoulder**

#### **With the patient standing or sitting:**

- ◆ Look at the shoulders , clavicles and sternoclavicular joints from the front, side and behind and assess shoulder height
- ◆ Look at the skin in axillae and palpate for lymphadenopathy
- ◆ Assess skin temperature
- ◆ Feel bony landmarks and surrounding muscles
- ◆ Assess movement and function: hands behind head, hands behind back
- ◆ Assess (actively and passively) external rotation, flexion, extension and abduction
- ◆ Observe scapular movement
- ◆ Options – hypermobility syndromes, muscle power, instability

### **Examination of the hip**

#### **With the patient supine lying on couch:**

- ◆ Look for flexion deformity and leg length disparity
- ◆ Check for scars, rashes
- ◆ Feel the greater trochanter for tenderness
  - Assess full hip flexion, internal and external rotation, abduction and adduction
  - Perform Thomas' test
  - Hip abduction (lying on side)

#### **Patient lying prone on couch**

- SIJ palpation
- Hip internal (and external) rotation

#### ***With the patient standing:***

- ◆ Assess posture and leg alignment
- ◆ Look for gluteal muscle bulk
- ◆ Perform the Trendelenburg test
- ◆ Assess function (gait with turning and running, ancillary movements)
- ◆ Options – hypermobility, muscle power, entheses, thigh foot angle (child with intoeing)

## **Examination of the knee**

### **With the patient standing:**

- ◆ Look for varus/valgus deformity, hyperextension and popliteal swellings
- ◆ Look at the skin for pattern of bruising and rashes
- ◆ Assess gait (see hip)

### **With the patient lying on couch:**

- ◆ Look from the end of the couch for varus/valgus deformity, muscle wasting, scars and swellings
- ◆ Look from the side for fixed flexion deformity
- ◆ Check for passive hyperextension and leg length discrepancy
- ◆ Feel skin temperature
- ◆ With the knee slightly flexed feel/palpate the joint line and the borders of the patella
- ◆ Feel the popliteal fossa
- ◆ Perform a patellar tap and cross fluctuation (bulge sign)
- ◆ Assess full flexion and extension (actively and passively)
- ◆ Option - Assess stability of knee ligaments – medial and lateral collateral – and perform anterior draw test
- ◆ Option – tests for ant knee pain / patellar maltracking / apprehension / patella glide
- ◆ Option – hypermobility, muscle power, entheses, hamstring tightness, iliotibial band tightness, thigh-foot angle

## ***Examination of the foot and ankle***

### ***With the patient lying supine on couch:***

- ◆ Look at dorsal and plantar surfaces of the foot
- ◆ Feel the skin temperature
- ◆ Feel/palpate for peripheral pulses
- ◆ Squeeze the MTPJs
- ◆ Feel/palpate the mid-foot, ankle joint line and subtalar joint
- ◆ Assess movement (actively and passively) at the subtalar joint (inversion and eversion), the big toe (dorsi- and plantar flexion), the ankle joint (dorsi- and plantar flexion) and mid-tarsal joints (passive rotation)
- ◆ Look at the patient's footwear
- ◆ Option – hypermobility, muscle power, entheses, capillaroscopy, thigh foot angle

### ***With the patient standing:***

- ◆ Look at the forefoot, mid-foot (foot arch) and the hindfoot
- ◆ Assess gait cycle (heel strike, stance, toe off), running and turning
- ◆ Assess muscle bulk (calves)

### ***Examination of the spine***

#### ***With the patient standing:***

- ◆ Look at the spine from the side and from behind
- ◆ Look at the skin and natal cleft
- ◆ Look at limb and trunk proportions
- ◆ Look at the face and jaw profile
- ◆ Feel the spinal processes and paraspinal muscles and Temporomandibular joints (TMJs)
- ◆ Assess movement: lumbar flexion and extension and lateral flexion; cervical flexion, extension, rotation and lateral flexion, thoracic rotation
- ◆ Assess TMJ opening
- ◆ Options – Schober’s test, “stork test”

#### ***With the patient sitting on couch (standing in younger child):***

- ◆ Assess thoracic rotation

#### ***With the patient lying on couch:***

- ◆ Perform straight leg raising and dorsi-flexion of the big toe
- ◆ Assess limb reflexes
- ◆ Option – leg length, hypermobility, sacroiliac joint palpation (Faber’s / Patrick’s test)

## APPENDIX 4: CHAQ FORM

### CHILDHOOD HEALTH ASSESSMENT QUESTIONNAIRE

1990 © Original version Singh G et al. 1998 © Cross-cultural version Woo p, Murray P, Nugent J

Child's Name

Hospital No

Date  /  /

Chi (4 digits)

DOB  /  /

We are interested in learning how your child's illness affects his/her ability to function in daily life. Please feel free to add any comments on the back of this page. In the following questions please mark the one response which best describes your usual activities OVER THE PAST WEEK. ☒ ONLY NOTE THOSE DIFFICULTIES OR LIMITATIONS WHICH ARE DUE TO ILLNESS. If most children at your child's age are not expected to do a certain activity, please mark it as 'not applicable'. For example, if your child has difficulty in doing a certain activity or is unable to do it because he/she is too young, but not because he/she is RESTRICTED BY ILLNESS, please remember to mark it as 'not applicable'

	Without ANY difficulty	With SOME difficulty	With MUCH difficulty	UNABLE to do	Not applicable
<b>Dressing and personal care</b> - Is your child able to:					
- dress including tying shoe laces and doing buttons?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- shampoo his/her hair?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- remove socks?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- cut fingernails?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>Getting Up</b> - Is your child able to:					
- stand up from a low chair or floor?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- get in and out of bed?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>Eating</b> - Is your child able to:					
- cut his/her own meal?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- lift a cup or glass to mouth?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- open a new cereal box?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>Walking</b> - Is your child able to:					
- walk outside on flat ground?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- climb up five steps?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Please tick any AIDS or DEVICES that your child usually uses for any of the above activities:

Walking stick <input type="checkbox"/>	Walking frame <input type="checkbox"/>	Crutches <input type="checkbox"/>
Wheelchair <input type="checkbox"/>	Devices used for dressing <input type="checkbox"/>	Built up pencil or utensils <input type="checkbox"/>
Special built up chair <input type="checkbox"/>	Other (specify) <input type="checkbox"/>	<input type="text"/>

Please tick any categories for which your child usually needs help from another person BECAUSE OF PAIN OR ILLNESS

Dressing and personal care <input type="checkbox"/>	Getting up <input type="checkbox"/>	Eating <input type="checkbox"/>	Walking <input type="checkbox"/>
---	-------------------------------------	---------------------------------	----------------------------------

Survey : 9024



Serial : 50



Page : 1



	Without ANY difficulty	With SOME difficulty	With MUCH difficulty	UNABLE to do	Not applicable
<b>Hygiene</b> - Is your child able to:					
- wash and dry entire body?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- take a bath (get in and out)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- get on and off toilet?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- brush teeth?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- comb/brush hair?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>Reach</b> - Is your child able to:					
- reach and get down a heavy object such as a large game or book from just above his/her head?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- bend down to pick up clothing or a piece of paper from the floor?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- pull on a jumper over his/her head?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- turn neck to look back over shoulder?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>Grip</b> - Is your child able to:					
- write with pen or pencil?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- open car doors?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- open jars which have previously been opened?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- turn taps on and off?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- push open a door when you have to turn a door knob?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>Activities</b> - Is your child able to:					
- run errands and shop?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- get in and out of a car or school bus?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- ride bike or tricycle?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- do household chores (e.g. wash dishes, take out rubbish, hoovering, gardening, make bed, clean room)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- run?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Please tick any **AIDS** or **DEVICES** that your child usually uses for any of the above activities:

Raised toilet seat ☐      Bath seat ☐      Jar opener ☐  
 Bath rail ☐      Long-handled appliances for reach ☐      Long-handled appliances in bathroom ☐

Please tick any **ACTIVITIES** that your child usually uses any of the above **AIDS** or **DEVICES** for:

Hygiene ☐      Gripping and opening things ☐      Reach ☐      Errands and chores ☐

**PAIN:** We are also interested in learning whether or not your child has been affected by pain because of his/her illness. How much pain do you think your child has had **IN THE PAST WEEK**? Place a mark on the line below to indicate the severity of the pain:

No pain |-----| Very severe pain

**GENERAL EVALUATION:** Considering all the ways that arthritis affects your child, rate how he/she is doing by placing a single mark on the line below:

Parent/Child      Very well |-----| Very poor

Physician      Very well |-----| Very poor





## **APPENDIX 5: CHAQ ADOLESCENT FORM**

Name:	Surname:	Unit No:
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### ***CHILDHOOD HEALTH ASSESSMENT QUESTIONNAIRE***

#### **Adolescent Version**

**THIS FORM IS FOR ADOLESCENTS OLDER THAN 11 YEARS OF AGE**

**We are interested in learning how your illness affects your ability to function in daily life. Please feel free to add any comments on the back of this page. In the following questions, please tick the one response which best describes your usual activities OVER THE PAST WEEK. ONLY NOTE THOSE DIFFICULTIES OR LIMITATIONS WHICH ARE DUE TO ILLNESS.**

*In the end, please go back and check once again that every item has been answered.*

	<b><u>UNABLE</u> To do</b>	<b><u>Without</u> <u>ANY</u> Difficulty</b>	<b><u>With</u> <u>SOME</u> difficulty</b>	<b><u>With</u> <u>MUCH</u> difficulty</b>
<b>DRESSING &amp; PERSONAL CARE</b>				
Are you able to:				
- Dress, including tying shoelaces and doing buttons?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Shampoo your hair?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Remove socks?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Cut fingernails?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>GETTING UP</b>				
Are you able to:				
- stand up from a low chair or floor?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Get in and out of bed ?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>EATING</b>				
Are you able to:				
- Cut your own meat?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Lift a cup or glass to mouth?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Open a new cereal box?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>WALKING</b>				
Are you able to:				
- Walk outside on flat ground?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Climb up five steps?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

**\* Please tick any AIDS or DEVICES that you usually use for any of the above activities:**

Devices used for dressing	<input type="checkbox"/>	(eg. button hook, zip pull, long-handled shoe horn)
Walking stick	<input type="checkbox"/>	
Walking frame	<input type="checkbox"/>	Built up pencil or special utensils
Crutches	<input type="checkbox"/>	Special or built up chair
Wheelchair	<input type="checkbox"/>	

Other

---

☐

**\* Please tick any categories for which you usually need help from another person  
BECAUSE OF PAIN OR ILLNESS:**

Dressing and personal care

☐

Eating

☐

Getting up

☐

Walking

☐

	<b><u>UNABLE</u> TO DO</b>	<b><u>Without</u> <u>ANY</u> Difficulty</b>	<b><u>With</u> <u>SOME</u> Difficulty</b>	<b><u>With</u> <u>MUCH</u> Difficulty</b>
<b>HYGIENE</b>				
Are you able to:				
- Wash and dry your entire body?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Take a bath (get in and get out)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Get on and off the toilet?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Brush teeth?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Comb/brush hair?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>REACH</b>				
Are you able to:				
- Reach and get down a heavy object such as a large game or books from just above your head	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Bend down to pick up clothing or a piece of paper from the floor?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Pull on a jumper over your head?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Turn neck to look back over shoulder?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>GRIP</b>				
Are you able to:				
- Write with pen or pencil?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Open car doors?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Open jars which have been previously opened?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Turn taps on and off?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Push open a door when you have to turn a door knob?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>ACTIVITIES</b>				
Are you able to:				
- Run errands and shop?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Get in and out of a car or school bus?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Ride bike or tricycle?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Do household chores (e.g. wash dishes, take out rubbish, hovering, gardening, make bed, clean room)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Run?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

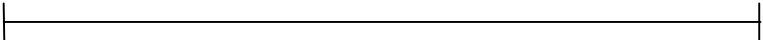
\* Please tick any AIDS or DEVICES that you usually use for any of the above activities:

Raised toilet seat	<input type="checkbox"/>
Bath rail	<input type="checkbox"/>
Bath seat	<input type="checkbox"/>
Long-handled appliances for reach	<input type="checkbox"/>
Jar opener (for jars previously opened)	<input type="checkbox"/>
Long-handled appliances in bathroom	<input type="checkbox"/>

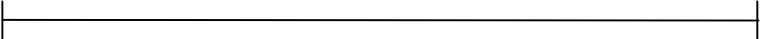
**\* Please tick any categories for which you usually need help from another person BECAUSE OF PAIN OR ILLNESS:**

Hygiene	<input type="checkbox"/>
Gripping and opening things	<input type="checkbox"/>
Reach	<input type="checkbox"/>
Errands and chores	<input type="checkbox"/>

**PAIN :** How much pain do you think you have had IN THE PAST WEEK? Place a mark on the line below,  
to indicate the severity of the pain

No pain      0            100      Very  
severe pain

**GENERAL EVALUATION:** Considering all the ways that arthritis affects you, rate how you are doing by  
placing a single mark on the line below.

Very well      0            100      Very poor

**Please tell us the date on which you completed this form**

**Date:**.....

## **APPENDIX 6: CHQ FORM**

### **CHILD HEALTH QUESTIONNAIRE (CHQ) (For children five years or older)**

Child's Name

Hospital No

Chi (4 digits)

Date   /   /

DOB   /   /

This booklet asks about your child's health and well-being. Your individual answers will not be shared with anyone. If you choose not to participate it will not affect the care your child receives.

Answer the questions by marking one of the appropriate boxes with a check mark as shown. ☒

Certain questions may look alike, but each one is different. Some questions ask about problems your child may not have, but it is important for us to know that too.

Please answer every question. There are no right or wrong answers, just choose the response that you think fits your situation best.

If you are unsure how to answer a question, please give the best answer you can and make a comment in the margin. All comments will be read, so please feel free to make as many as you wish.

At the end, please go back and check once again that every item has been answered.

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## SECTION 1: YOUR CHILD'S GENERAL HEALTH

1.1 In general, would you say your child's health is

Excellent ☐

Very good ☐

Good ☐

Fair ☐

Poor ☐

## SECTION 2: YOUR CHILD'S PHYSICAL ACTIVITIES

The following questions ask about physical activities your child might do during a day.

2.1 During the past 4 weeks has your child been limited in any of the following activities due to health problems?

	Yes, limited a lot	Yes, limited somewhat	Yes, limited a little	No, not limited
a. Doing things that take a lot of energy, such as playing football or netball, running?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Doing things that take some energy, such as riding a bike or roller skating?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Ability (physically) to get around the neighbourhood, playground or school?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Walking 100 metres or climbing one flight of stairs?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. Bending, lifting or stooping?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f. Taking care of themselves, that is, eating, drinking, dressing, bathing or going to the toilet?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

## SECTION 3: YOUR CHILD'S EVERYDAY ACTIVITIES

3.1 During the past 4 weeks has your child's schoolwork or activities with friends been limited in any of the following ways due to EMOTIONAL difficulties or problems with his/her behaviour?

	Yes, limited a lot	Yes, limited somewhat	Yes, limited a little	No, not limited
a. Limited in the <u>KIND</u> of schoolwork or activities with friends he/she could do?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Limited in the <u>AMOUNT</u> of time he/she could spend on schoolwork or activities with friends?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Limited in <u>PERFORMING</u> schoolwork or activities with friends (it took extra effort)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

3.2 During the past 4 weeks has your child's schoolwork or activities with friends been limited in any of the following ways due to problems with his/her PHYSICAL health?

	Yes, limited a lot	Yes, limited somewhat	Yes, limited a little	No, not limited
a. Limited in the <u>KIND</u> of schoolwork or activities with friends he/she could do?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Limited in the <u>AMOUNT</u> of time he/she could spend on schoolwork or activities with friends?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

## SECTION 4: PAIN

4.1 During the past 4 weeks how much bodily pain or discomfort has your child had?

None ☐

Very mild ☐

Mild ☐

Moderate ☐

Severe ☐

Very severe ☐

4.2 During the past 4 weeks how often has your child had bodily pain or discomfort?

None of the time ☐

Once or twice ☐

A few times ☐

Fairly often ☐

Very often ☐

Every/almost  
every day ☐



## SECTION 5: BEHAVIOUR

Below is a list of items that describe children's behaviour or problems they sometimes have.  
5.1 How often during the past 4 weeks did each of the following statements describe your child?

	Very often	Fairly often	Sometimes	Almost never	Never
a. Argued a lot?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Had difficulty in concentrating or paying attention?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Not told the truth?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Taken things which didn't belong to them?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. Had tantrums or a hot temper?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

5.2 Compared to other children your child's age, in general would you say his/her behaviour is

Excellent ☐ Very good ☐ Good ☐ Fair ☐ Poor ☐

## SECTION 6: WELL-BEING

The following are about children's moods  
6.1 During the past 4 weeks how much time do you think your child:

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Felt like crying?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Felt lonely?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Acted nervous?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Acted bothered or upset?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. Acted cheerful?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

## SECTION 7: SELF ESTEEM

The following ask about your child's satisfaction with self, school and others. It may be helpful if you keep in mind how other children your child's age might feel about these areas.

7.1 During the past 4 weeks how satisfied do you think your child has felt about:

	Very satisfied	Somewhat satisfied	Neither satisfied nor dissatisfied	Somewhat dissatisfied	Very dissatisfied
a. His/her school ability?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. His/her athletic ability?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. His/her friendships?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. His/her looks/appearance?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. His/her family relationships?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f. His/her life overall?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

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## SECTION 8: YOUR CHILD'S HEALTH

The following statements are about health in general.

8.1 How true or false is each of these statements for your child?

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a. My child seems to be less healthy than other children I know	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. My child has never been seriously ill	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. When there is something going around my child usually catches it	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. I expect my child will have a very healthy life	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. I worry more about my child's health than other people worry about their children's health	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

8.2 Compared to one year ago, how would you rate your child's health now?

Much better now than one year ago <input type="checkbox"/>	Somewhat better now than one year ago <input type="checkbox"/>	About the same now as one year ago <input type="checkbox"/>	Somewhat worse now than one year ago <input type="checkbox"/>	Much worse now than one year ago <input type="checkbox"/>
--	--	---	---	---

## SECTION 9: YOU AND YOUR FAMILY

9.1 During the past 4 weeks how MUCH emotional worry or concern did each of the following cause YOU?

	None at all	A little bit	Somewhat	A lot	A great deal
a. Your child's physical health?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Your child's emotional well-being or behaviour?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Your child's attention or learning difficulties?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

9.2 During the past 4 weeks were you limited in the amount of time YOU had for your own needs because of:

	Yes, limited a lot	Yes, limited somewhat	Yes, limited a little	No, not limited
a. Your child's physical health?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Your child's emotional well-being or behaviour?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Your child's attention or learning difficulties?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

9.3 During the past 4 weeks how often has your child's health or behaviour:

	Very often	Fairly often	Sometimes	Almost never	Never
a. Limited the types of activities you could do as a family?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Limited various everyday family activities (eating meals, watching TV)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Limited your ability as a family to 'get up and go' on a moment's notice?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Caused tension or conflict in your home?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. Been a source of disagreements or arguments in your family?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f. Caused you to cancel or change plans (personal or work) at the last minute?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

9.4 Sometimes families may have difficulty in getting along with one another. They do not always agree and they get angry. In general, how would you rate your family's ability to get along with one another?

Excellent <input type="checkbox"/>	Very good <input type="checkbox"/>	Good <input type="checkbox"/>	Fair <input type="checkbox"/>	Poor <input type="checkbox"/>
------------------------------------	------------------------------------	-------------------------------	-------------------------------	-------------------------------





## APPENDIX 7: GLASGOW ENTHESITIS SCALE

### Clinical Examination (Form 1)

page 3 of 5

Study Number 

#### ENTHESITIS FORM

**This patient has no enthesitis** ☐

**Please tick if blank boxes = 0** ☐

0 = no pain, 1 = tender, 2 = tender + grimace

#### UPPER LIMB ENTHESES

##### LEFT

##### RIGHT

	0	1	2		0	1	2
Coracoid process	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Manubriosternal joint	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
1 <sup>st</sup> Costochondral joint	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7 <sup>th</sup> Costochondral joint	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Medial epicondyle of humerus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Lateral epicondyle of humerus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

#### LOWER LIMB ENTHESES

	0	1	2		0	1	2
Superior pole of patella	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Inferior pole of patella	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Tibial tuberosity	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Achilles origin (sup.pole calcaneus)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Plantar fascia (inf.pole calcaneus)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

## APPENDIX 8: PODIATRY EXAMINATION FORM

### Down's Syndrome Study

#### Podiatry

Subject \_\_\_\_\_ Gender M/F \_\_\_\_\_ Age \_\_\_\_\_

FS R \_\_\_\_\_ L \_\_\_\_\_ SS R \_\_\_\_\_ L \_\_\_\_\_ Difference R \_\_\_\_\_ L \_\_\_\_\_

**ROM** (R – Restricted M – “Normal” H – Hypermobile)

Ankle Jt \_\_\_\_\_ STJt \_\_\_\_\_ Mid-Tarsal Jt \_\_\_\_\_ 1st MTPJ \_\_\_\_\_ Lesser MTPJs \_\_\_\_\_ IPJs \_\_\_\_\_

#### Foot Type

Square Forefoot \_\_\_\_\_ Short/Broad \_\_\_\_\_ Long/Slender \_\_\_\_\_ Triangular \_\_\_\_\_

Hypermobile \_\_\_\_\_ High Arched \_\_\_\_\_ Low Arched \_\_\_\_\_

#### Foot Posture (Relaxed Stance)

STJt Pronation \_\_\_\_\_ Supinated \_\_\_\_\_ Neutral \_\_\_\_\_

#### Foot Posture (Gait/Dynamic)

STJt Pronation \_\_\_\_\_ Supinated \_\_\_\_\_ Neutral \_\_\_\_\_ PPV \_\_\_\_\_

#### Tibial Torsion

Internal \_\_\_\_\_ External \_\_\_\_\_

LLD \_\_\_\_\_

#### FF/RF

FF Varus \_\_\_\_\_ FF Valgus \_\_\_\_\_ RF Varus \_\_\_\_\_ RF Valgus \_\_\_\_\_ Equinus \_\_\_\_\_

#### Gait

Hypotonic \_\_\_\_\_ Genu Valgum \_\_\_\_\_ Genu Varum \_\_\_\_\_ Pelvic Tilt \_\_\_\_\_ O/W \_\_\_\_\_ Limp \_\_\_\_\_

**Met Formula** \_\_\_\_\_

**Digital Formula** \_\_\_\_\_

**Deformity**

Claw Toe \_\_\_\_ Retracted Toe \_\_\_\_ Hammer Toe \_\_\_\_ Mallet Toe \_\_\_\_

Curly Toe \_\_\_\_ Burrowing Toe \_\_\_\_ DQMV \_\_\_\_

HAV \_\_\_\_ HA \_\_\_\_ HV \_\_\_\_ TPA \_\_\_\_ Met Adductus \_\_\_\_

Syndactyly \_\_\_\_ Site \_\_\_\_ Other \_\_\_\_

Dysmorphism \_\_\_\_

**Skin**

Anhidrosis \_\_\_\_ Hyperidrosis \_\_\_\_ Eczema \_\_\_\_ Psoriasis \_\_\_\_ Other \_\_\_\_

TP \_\_\_\_ Site \_\_\_\_

**Skin Lesions**

HD \_\_\_\_ Site \_\_\_\_

Call \_\_\_\_ Site \_\_\_\_

**Nails**

Involuted \_\_\_\_ O/X \_\_\_\_ O/Ph \_\_\_\_ O/G \_\_\_\_ O/C \_\_\_\_ O/M \_\_\_\_

Psoriatic \_\_\_\_ Pitting \_\_\_\_

Other \_\_\_\_

**Enthesitis**

PI Fascia \_\_\_\_ TA \_\_\_\_ Other \_\_\_\_

**Footwear**

Feet Measured? Yes \_\_\_\_ No \_\_\_\_

Style : "School Shoe" \_\_\_\_ Boot \_\_\_\_ Fashion \_\_\_\_ Ugg Type \_\_\_\_ Trainer \_\_\_\_ "Converse"  
\_\_\_\_

Retaining Medium: Lace \_\_\_\_ Strap \_\_\_\_ Velcro \_\_\_\_ Slip-on

Toe Box: Pointed \_\_\_\_ Square \_\_\_\_ Round \_\_\_\_

Counter: Adequate \_\_\_\_ Inadequate \_\_\_\_

Material: Leather \_\_\_\_ Suede \_\_\_\_ Gore-Tex \_\_\_\_ Plastic \_\_\_\_ Rubber \_\_\_\_ Canvas \_\_\_\_

Heel Height: Too low \_\_\_\_ Adequate \_\_\_\_ Too High \_\_\_\_

Wear Marks \_\_\_\_\_

**Subjective Foot Comments:**

## APPENDIX 9: KIDS SHOE FITTING

**MORE THAN 50% OF ALL CHILDREN WEAR SHOES THAT ARE TOO SHORT IN LENGTH**

**SHOES THAT ARE TOO SHORT CAUSE DAMAGE TO CHILDREN'S FEET**

**HELPFUL TIPS FOR CHOOSING KIDS' SHOES AND KEEPING KIDS' FEET HEALTHY**

**RESEARCH PROJECT:**  
**KIDS**  
 HEALTHY FEET  
 HEALTHY LIFE

**BUNDESMINISTERIUM FÜR  
GESUNDHEIT UND PRÄVENTION**

An initiative of the "Kids: Healthy feet – healthy life" research team  
 Commissioned by the Austrian Federal Ministry of Health and the Fonds Gesundes Österreich (Fund for a Healthy Austria)

### ONCE UPON A TIME... (AND EVEN STILL TODAY)

- Recent studies have shown that over 50% of all children wear shoes that are too small.\*
- Ill-fitting shoes are seriously detrimental to the health of children's feet.\*
- Too-tight shoes can also cause further physical damage (for example to the knees, hips and spine), and lead to a reduced motivation to exercise.

### CHILDREN'S FEET ARE SPECIAL

- Kids' feet are very soft and elastic can be compressed and deformed all too easily (for example by wearing shoes that are too tight or too short).
- Going barefoot is the best training for children's feet: Going barefoot exercises and strengthens the muscles of the foot in many different ways. It's also the best way to recover from wearing shoes!
- Kids' feet grow very fast: Between the ages of 3 and 6, children's feet grow at an average rate of about 1 mm (0.04") every month.\*
- Children's feet aren't fully developed until about the age of 16.
- Kids can't tell if their shoes are too small. Even shoes that are markedly shorter than the foot itself are often judged by their little wearers to fit just fine.\*
- That's why it's important to check the fit of your kids' shoes every 3 – 4 months.

### WHY IS IT IMPORTANT FOR KIDS' SHOES TO FIT PROPERLY?

- Healthy feet in childhood are fundamental for a further well-balanced development. Not only that, healthy feet make exercise fun!
- Shoes that are too short can permanently deform children's feet.
- Many kids already have markedly crooked big toes, caused by wearing poorly-fitting shoes.\*
- Shoes that are too short in length stunt and delay the healthy development of children's feet.\*

shoes that are too short deform children's feet

\* Results of the research projects "Children's Feet – Children's Shoes" (2001 – 2003) and "Kids: healthy feet – healthy shoes" (2005 – 2006)

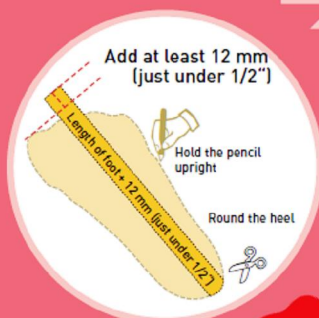


## → THE RIGHT FIT FOR KIDS' SHOES



- Feet can be quite moody: Usually the right and left feet are different lengths, they are shorter and narrower in the morning than in the evening, and they're longer when you're standing than when you're sitting or lying down. Feet need the most room when they're in motion: The toes slide forwards with every step.
- Children's feet need at least 12 mm (just under 1/2") of extra space in the toe of the shoe to be able to move unrestrictedly. New shoes can have up to 17 mm (not quite 3/4") extra "wiggle room". This way, they should fit well for quite a few months.
- The ideal shoe for children should be soft and pliable.

## → TWO WAYS TO FIND OUT IF THE SHOE FITS



### CARDBOARD TEMPLATE

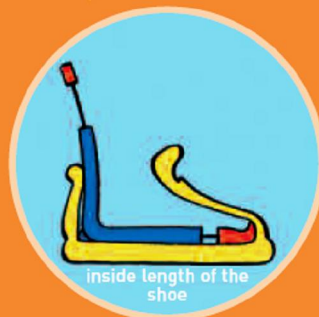
- Have the child stand on a piece of cardboard and trace the outline of each foot.
- Add at least 12 mm (just under 1/2") to the length of the longest toe (for new shoes, add 17 mm, or not quite 3/4").
- You don't have to cut out the whole template, a strip the width of two fingers is sufficient (see illustration). If the cardboard strip fits inside the shoe, then the shoe is long enough.



If the cardboard strip fits, so does the shoe.



If the cardboard strip buckles, the shoe is too short.



### plus12

- With this handy tool, you can measure both the length of the child's foot and the inside length of the shoe.
- Convenient: The plus12 automatically adds the necessary 12 mm of extra space when measuring the length of the foot.

## → QUESTIONS, QUESTIONS...

- **IS IT ALRIGHT FOR MY CHILD TO WEAR SECOND-HAND SHOES?**  
Of course it is. And over 50% of all parents hand down shoes from older children to younger ones. Just make sure the "new" shoes aren't worn down unevenly and that they are long enough.
- **ARE EXPENSIVE SHOES NECESSARILY BETTER THAN CHEAPER MODELS?**  
No. A high price does not guarantee high quality children's shoes.

- **SLIPPERS, HOUSE SHOES OR BAREFOOT - WHICH IS BETTER?**  
Going barefoot is the best option for children's feet. If your child does need to wear house shoes or slippers, make sure they fit well (over 80% of all children wear house shoes that are too short in length...). Our advice: Try non-skid socks. They're better because the foot has more freedom of movement and it's easier to see if the socks fit properly.
- **DO CHILDREN'S SHOES HAVE TO BE STIFF AND PROVIDE A LOT OF SUPPORT?** No. If kids' feet are healthy, they don't need any extra support. The ideal shoe for children is soft and pliable, so that the foot has plenty of freedom of movement.