Risk factors for knee injuries in children 8-15 years
– the impact of Generalised Joint Hypermobility
The CHAMPS Study-DK

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Content

Preface

This thesis was accomplished at the Faculty of Health Sciences, Institute of Regional Health Research, University of Southern Denmark, in the period 2011-2015. Both the main supervisor, clinical Professor, MD, Ph.D. Niels Wedderkopp from the Institute of Regional Health Research, University of Southern Denmark and the co-supervisor Associate Professor, Ph.D. Birgit Juul-Kristensen from the Department of Sports Science and Clinical Biomechanics, University of Southern Denmark, provided supervision.

This Ph.D. thesis presents results obtained from The Childhood Health, Activity and Motor Performance School Study, Denmark – The CHAMPS Study-DK. The study is on-going since August 2008 and has the overall aim to investigate children's health, including musculoskeletal injuries. The studies of this thesis have focus on knee injuries and hypermobility in children and adolescents in the period August 2011 to June 2014.

Funding

The CHAMPS-Study DK, in which this thesis is comprised, was supported by grants from the Department of Physiotherapy, University College Lillebaelt, The Nordea Foundation, The TRYG Foundation, The IMK Foundation, The Region of Southern Denmark, The Egmont Foundation, The A.J. Andersen Foundation, The Danish Rheumatism Association, The Østifternes Foundation, The Brd. Hartmanns Foundation, Team Danmark, The University of Southern Denmark and The Danish Chiropractic Research Foundation.

List of papers

This thesis is based on the following four studies, which will be referred to by their roman numerals in the text:

I. Junge T, Jespersen E, Wedderkopp N, Juul-Kristensen B. Inter-tester reproducibility and inter-method agreement of the Beighton test for determining Generalised Joint Hypermobility in primary school children. *BMC Pediatrics* 2013, 13:214

II. Junge T, Larsen LR, Juul-Kristensen B, Wedderkopp N. Risk factors for traumatic and overuse knee injuries in children aged 8-15 years: A substudy of the CHAMPS-study Denmark. *Medicine & Science in Sports & Exercise,* 2015, Nov

III. Junge T, Larsen LR, Juul-Kristensen B, Wedderkopp N. The extent and risk of knee injuries in children aged 9-14 with Generalised Joint Hypermobility and knee joint hypermobility - the CHAMPS-study Denmark. *BMC Musculoskeletal Disorders* 2015, 16:143

IV. Junge T, Wedderkopp N, Thorlund JB, Søgaard K, Juul-Kristensen B. Altered knee joint neuromuscular control during landing from a jump in 10-15 year old children with Generalised Joint Hypermobility. A sub study of the CHAMPS-study Denmark. *J Electromyogr Kinesiol.* 2015 Jun; 25(3):501-7.

Thesis at a glance

Paper	Objectives	Study design and participants	Methods	Conclusions
I	1) To determine the inter-tester reproducibility of tests and criteria for two different test batteries (A+B) for performing the BT in a standardised protocol format. 2) To determine the inter-method agreement of the prevalence of Generalised Joint Hypermobility (GJH) of Methods A and B, using the criterion of a positive BT ≥5 for GJH.	Methodological study. 1) 38 children for Method A and 32 children for Method B, (57% boys) mean age 7.4 years. 2) 62 children (60%) represented 7-8 year olds and 41 children (40%) 10-12 year olds.	Beighton Tests (BT) for joint hypermobility.	The inter-tester reproducibility of both Methods A and B was moderate to substantial, when following a standardised study protocol. The described BT and criteria for classification of GJH are reproducible for children and therefore suitable for comparative studies of children, when using a GJH criterion of ≥5/9. No significant difference in prevalence was found when using the two test batteries.
II	1) To report the distribution and incidence of traumatic and overuse knee injuries in children aged 8-15 years old. 2) To examine risk factors of traumatic and overuse knee injuries, focusing at the intrinsic factors of sex, age, height, BMI, GJH, previous knee injury, and the extrinsic factors of amount of organised sport participation and sports type.	Cohort study with 2 yearly follow-ups. Baseline: 1326 children, mean age: 10 (8-14) years.	SMS survey (weekly automated text messaging) reports on: • Musculoskeletal pain • Sports type • Amount of organised sports participation Telephone consultation identifying injuries and a clinical examination diagnosing knee injuries. Baseline clinical test and two yearly follow-ups for anthropometrics and BT for joint hypermobility.	Growth-related overuse knee injuries were the main injury type. Children participating in tumbling gymnastics had an increased risk for traumatic knee injuries. Significant intrinsic risk factors for overuse knee injuries were being a girl and previous knee injury. Extrinsic factors were children participating in soccer, handball, basketball, rhythmic and tumbling gymnastic. Further extrinsic risk factor for both types of injury was participation in sports more than two times/week.

III	1) To report the extent of knee injuries in children with GJH versus controls. 2) To estimate the risk of knee injuries, when looking at GJH as a risk factor, adjusting for sex, age, BMI and amount of organised sport.	Cohort study with one-year follow-up. Baseline: 999 children (36 (4%) GJH), mean age: 11.2 (8-14).	SMS survey (weekly automated text messaging) reports on: • Musculoskeletal pain • Sports type • Amount of organised sports participation Telephone consultation identifying injuries and a clinical examination diagnosing knee injuries. Baseline clinical test and one yearly follow-up for anthropometrics and BT for joint hypermobility.	Traction apophysitis, distortions and contusions were the most frequent knee injuries in both groups. The number of children with a constant status of GJH in both test rounds was low, with no significant increased risk for knee injuries in children with GJH.
IV	1) To identify potential differences in knee joint neuromuscular control, defined as muscle activity, time of onset and co-contraction, in children with GJH and knee hypermobility compared with controls before and after landing from the Single Leg Hop for Distance test (SLHD).	Case-control study. 54 children, 25 with GJH and knee hypermobility and 29 controls, mean age 11.5 (10-15 years).	Surface electromyography (EMG) of the knee flexor and knee extensor muscles during landing in the SLHD test. Clinical test for anthropometrics and BT for joint hypermobility.	Although equal jump lengths, children with GJH had a Gastrocnemius Medialis-dominated neuromuscular strategy before landing, but without compensatory Gastrocnemius Medialis activity for the reduced Semitendinosus activity seen before and after landing. Reduced pre and post-activation of the ST may present a risk factor for future traumatic knee injury in participants with GJH and knee hypermobility.

Description of contributions

Paper I

Study design:	Tina Junge, Eva Jespersen, Birgit Juul-Kristensen
Data collection:	Tina Junge, Eva Jespersen
Data analysis:	Tina Junge, Eva Jespersen, Niels Wedderkopp, Birgit Juul-Kristensen
Manuscript writing:	Tina Junge, Eva Jespersen
Manuscript revision:	Eva Jespersen, Niels Wedderkopp, Birgit Juul-Kristensen

Paper II

Study design:	Tina Junge, Lisbeth Runge Larsen, Niels Wedderkopp
Data collection:	Tina Junge, Kristina Dissing, Signe Fuglkjær, Lisbeth Runge Larsen
Data analysis:	Tina Junge, Niels Wedderkopp
Manuscript writing:	Tina Junge
Manuscript revision:	Lisbeth Runge Larsen, Birgit Juul-Kristensen, Niels Wedderkopp

Paper III

Study design:	Tina Junge, Lisbeth Runge Larsen, Niels Wedderkopp
Data collection:	Tina Junge, Kristina Dissing, Signe Fuglkjær, Lisbeth Runge Larsen
Data analysis:	Tina Junge, Birgit Juul-Kristensen, Niels Wedderkopp
Manuscript writing:	Tina Junge
Manuscript revision:	Lisbeth Runge Larsen, Birgit Juul-Kristensen, Niels Wedderkopp

Paper IV

Study design:	Tina Junge, Jonas Bloch Thorlund, Henrik B. Olsen, Karen Søgaard, Birgit Juul-Kristensen
Data collection:	Tina Junge
Data analysis:	Tina Junge, Henrik B. Olsen, Niels Wedderkopp, Birgit Juul-Kristensen
Manuscript writing:	Tina Junge
Manuscript revision:	Niels Wedderkopp, Jonas Bloch Thorlund, Karen Søgaard, Birgit Juul-Kristensen

Abbreviations

ACL	Anterior Cruciate Ligament
CCI	Co-Contraction Index
BF	m. Biceps Femoris
BMI	Body Mass Index
BT	Beighton Tests
CHAMPS	The Childhood Health, Activity and Motor Performance School study Denmark
EMG	Electromyography
GJH	Generalised Joint Hypermobility
GL	m. Gastrocnemius Lateralis
GM	m. Gastrocnemius Medialis
MVC	Maximal Voluntary Contraction
MVE	Maximal Voluntary Electrical activity
OR	Odds Ratios
PFT	Posterior Femoral Translation
PPV	Positive Predictive Value
RMS	Root Mean Square
SLHD	Single Leg Hop for Distance test
SMS	Short Message Service
ST	m. Semitendinosus
VL	m. Vastus Lateralis
VM	m. Vastus Medialis

Introduction

Epidemiology of knee injuries in children

Engaging in sport and physical activity has beneficial effects for children, such as physical, cognitive and mental health (1-4), but participation also involves a risk of musculoskeletal injuries (5-11). Sports-related injuries account for 10-27% of all injury presentations in children 6-18 years in hospital emergency departments in northern European countries (12-15). Correspondingly, 25% of all Danish children 10-19 years are treated each year in hospital emergency departments because of sports-related injuries, typically being traumatic injuries to the lower extremities (16). In epidemiological studies, a traumatic injury is often defined as a macro trauma resulting from a specific, identifiable event, and an overuse injury as caused by repeated micro trauma without a single, identifiable event responsible for that injury (17).

Knee injuries are frequent in children (18-20); yet, most epidemiological studies either report traumatic knee injuries from specific settings, e.g. hospital emergency departments, report specific diagnoses e.g. Anterior Cruciate Ligament (ACL) ruptures or are being sports-specific, often for participants at high school or elite level (18, 21-23). Information of epidemiologic data on knee injuries in a general paediatric population is scarce.

Traumatic injuries may reflect only one part of the overall injury representation in children, illustrated in a recent study with 2.5 times more overuse (growth-related) than traumatic injuries of the lower extremities (24). Injuries occur as the maturing child and adolescent is more vulnerable to physical and physiological stress than adults (25, 26), yet, overuse injuries including growth-related injuries, such as apophyseal injuries, may be underestimated since these injuries are not registered in specific settings like hospital emergency departments or orthopaedic sport clinics (20, 26, 27). Recording overuse injuries may be complicated by the fact, that there is no clearly identified onset and not necessarily a time loss from sport participation (28).

In order to describe the extent of knee injuries in a general population of children, both traumatic and overuse knee injuries must be included.

The consequences of knee injuries are a significant cause of concern for the individual and society (29). Short and long-term consequences for the individual child could be considerable, as both traumatic and overuse knee injuries may result in pain, reduced levels of physical activity, absence from sport, and loss of enthusiasm for participating in physical activity of any kind (30-34). Although apophyseal injuries most often resolve without growth complication, there is a risk of stress related premature partial or complete physeal closure (25). Traumatic knee injuries may increase the risk of accelerated development of (secondary) osteoarthritis in young adults (35).

Although knee injuries may be more or less unavoidable among children and adolescents through the years of growth, it is important to establish evidence on how to predict, prevent and/or reduce the number of these injuries (18), from an individual and a public health point of view. Therefore, it seems critical to evaluate the extent and risk of both traumatic and overuse knee injuries to ensure that the benefits of sport and physical activity are not outweighed by potential harms as knee injuries (36).

In order to prevent knee injuries, van Mechelen has previously outlined a four step sequence for injury prevention, where (i) the extent of the knee injury problem is established, (ii) the risk factors or mechanisms of knee injuries are identified, (iii) preventive measures are introduced and (iv) the effectiveness of prevention is measured by repeating the first step (37). In this thesis, focus will be at the first and second step, estimating the extent of knee injuries in children and examining risk factors and mechanisms of these injuries.

Risk factors for knee injuries in children – an epidemiological model

Knee injuries result from a complex interaction of multiple non-modifiable and modifiable, intrinsic and extrinsic risk factors and inciting events (29). This complexity may be one of the reasons, why the knowledge of risk factors of knee injuries is inconclusive, also in children and adolescents, besides methodological and study differences (29). Nevertheless, in injury prevention research, investigating components that may form or be part of causes to injuries is important (38).

Risk factors for knee injuries may be associated with injury risk, but not necessarily causal related, as a statistical association is no proof of causation. To establish a causal relationship between two events, Hills´ Criteria (39) of strength, consistency, specificity, temporality, biological gradient, plausibility, coherence, experiment, and analogy, must be considered as a background framework. In a human dynamic and changing system, establishing a meaningful and statistically valid connection between exposure and outcome may fulfil some of these criteria. Injuries may be formed by, and not caused by specific risk factors or mechanisms, why chance findings, bias and confounding must be considered (38).

The risk of knee injury is dynamic and can change frequently over time (29). In order to describe the nature of the risk of knee injuries, a dynamic model as proposed by Meeuwisse (40) (Figure 1) may illustrate the complex aetiology of sports injuries. The model exemplifies the multifactorial nature of sports injuries, and in addition, takes into account the sequence of events eventually leading to an injury.

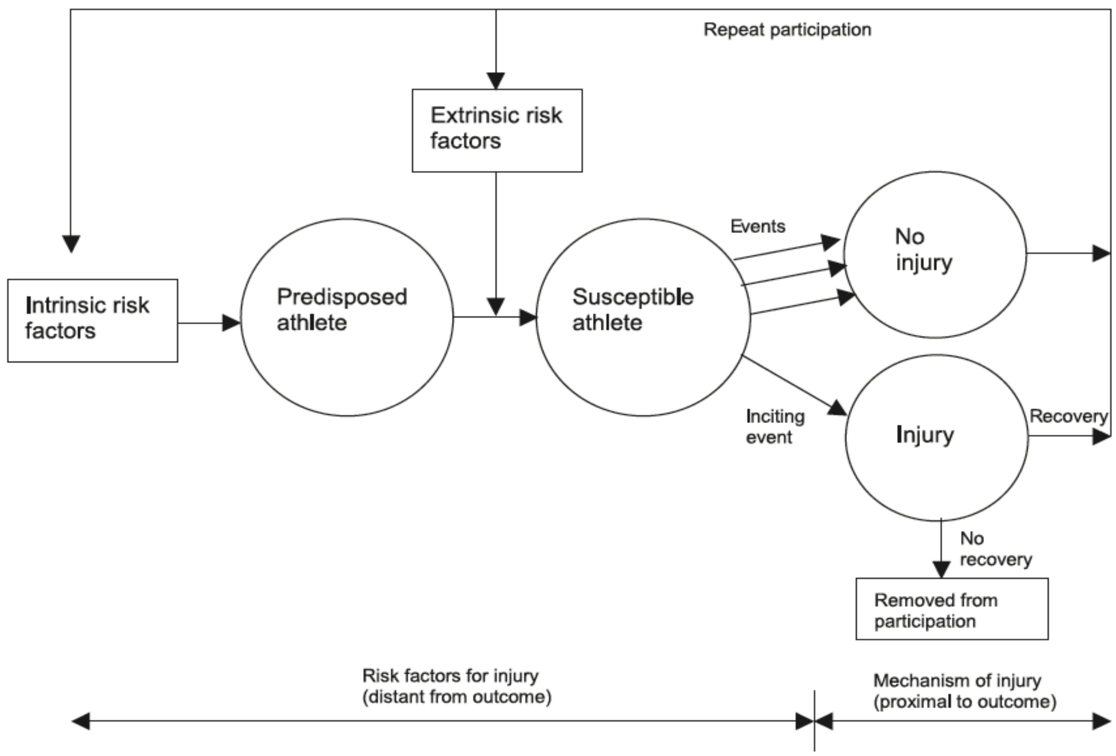

Figure 1. A dynamic model of aetiology in sport injury (40).

Intrinsic risk factors suggested to predispose children to knee injuries are e.g. sex, age, maturational status, body composition, previous injuries and flexibility, e.g. Generalised Joint Hypermobility (GJH) (18, 22, 29, 41, 42). Extrinsic risk factors are e.g. sports level, items characterising the specific sports type such as rules, playing time and equipment, and also the amount of sports participation, making the child more or less susceptible to injury (22, 38). An inciting event may or may not imply a knee injury within this dynamic system with a changing risk profile over time (40). When applying the dynamic model of injury aetiology, it may be appropriate to measure conditions repeatedly to account for changes over time (38, 40). As most evidence concerns risk factors for traumatic knee injuries in children, this is reflected in the following sections, but may hypothetically be transferred to overuse knee injuries as well.

Extrinsic risk factors for knee injuries in children

Sport participation

Through the last decade, a polarization in physical activity has been observed in children and adolescents (43, 44). Although inactivity and obesity are on the rise, a high number of active children across all sports are observed (18). In Denmark, 31% of 7-15 year olds report participation in sport 1-2 times a week, 41% respond 3-4 times a week and 21% answer more than five times a week (2000 respondents, response rate 50%) (45). The risk of injury is suggested to increase with an increasing amount of time spent doing sporting activity (22), but on the other side, low habitual physical activity level is also found to be associated to lower extremity injuries in children (46).

To accommodate for variations in the time exposure of individual athletes and sports, incidence rate is a preferred measure of incidence of injuries, although different units of time-at-risk, varying in precision, are used to calculate incidence rates (18). Expressing injury rates using hourly exposure to sports participation account for the potential variance in exposure of participants to risk of injury, which may improve comparison between sports (23). Incidence rates may well be compared within multiple sports in the same study, as study differences may restrict the interpretation and comparison of findings across specific sport studies (18).

Sports type

For Danish children in general, soccer is by far the most popular organised sport, followed by swimming, gymnastics and handball (45). The risk of injury is suggested to increase with organised sport versus unorganised sport (22), although assessment of time spent in unorganised sport and play seems challenging. The sport type itself may not constitute a risk factor, but children participating in a specific sport and items related to the specific sport may constitute an extrinsic risk for knee injuries, interacting with intrinsic risk factors and inciting events.
The highest rates of knee injuries, mostly traumatic injuries, are in international studies reported for boys participating in sports as hockey, basketball, rugby and soccer, and for girls participating in sports as gymnastics, basketball and soccer (18, 22, 41). The aforementioned sports involve both player-to-player contact, a high rate of jumping, pivoting and high impact landings, all situations often involved in the mechanisms of traumatic knee injury (22).

The existing sports specific knee injury rates may vary considerably by the definition of injury used, the age of the participating children, and with a geographically, cultural and climatically diversity (23).

Knowledge of extrinsic risk factors for knee injuries in children is inconclusive, but may involve increasing amount of time in sports and participation in organised sport, especially high-load sports.

Intrinsic risk factors for knee injuries in children

Sex

In identifying non-modifiable, intrinsic risk factors for injury in child and adolescent sport, there is evidence that boys have a higher risk for injury in general (OR 1.16-2.4), as boys are more likely to participate in vigorous activities and sport, have a higher risk-taking attitude and a larger body mass leading to greater forces generated on contact (22, 47). An exception is seen soccer, baseball and basketball, in which girls appear to be at greater risk (22, 23), plausibly due to the increased physical and physiological demands of these specific sports.

With respect to knee injuries, higher incidence rates for girls have been reported in several sports specific studies as soccer, basketball and running (18). For specific clinical conditions, the risk of sustaining a knee injury, especially ACL injuries, is known to be higher for females than males, however, contradictory results exist regarding other knee injuries (18, 42, 48). Girls may be more predisposed to severe knee injuries than boys, as seen with ACL injuries, which plausibly is mediated by intrinsic factors such as anatomical variation, hormonal influences and neuromuscular factors, although controversy exists on the relative importance of the different factors (42, 49).

Age

Maturation can be expressed by e.g. age, growth or puberty status. In sport-specific studies, it is known that older children, especially adolescents from the age of 13 years, experience higher rates of knee injuries than younger (18, 22, 41), plausibly as the child by maturation becomes faster, heavier and stronger, typically increase sport participation, have higher levels of competition and generated more force on contact (18, 22). Contradictory results was obtained from a hospital emergency department, with a decrease in incidence rate seen for both sexes after growth spurt (50).

Although same chronologic age, children may vary substantially in biologic age, and these individual differences in maturity status may influence functional capacity and injury profile during childhood and adolescence (51). Thus, when children are grouped by age, variation is associated with chronological age per se and also with differences in biological maturity (51).

Body Mass Index

Increased Body Mass Index (BMI) is suggested as a risk factor for lower extremity injuries in children and adolescents, due to a proportional increase in the forces that joint, ligaments, tendons and muscular structures must resist or endure to overweight (42, 52-54). Still, the relation between body size and injury is unclear and inconclusive, as different measures are used to represent body size such as height and weight, lean muscle mass, body fat content and most commonly body mass index (42). Also, BMI appears to be injury and sports specific (22, 46, 52, 53, 55).

Previous injury

Generally, previous injury is proposed to be a risk factor for subsequent injury, with re-injury rates ranges from 6% to 50% (18, 19, 56, 57), as these injury rates often reflect a variety of sports and participation levels and injury types, most often not presented by specific body parts (18). In a single study of 12-year old competitive gymnasts, re-injury rates were higher when isolating the same body part, body size, type of injury, nature of onset and history of injury the previous year, although specific rates were not presented for knee re-injuries (58). In the aforementioned study, knee re-injury rates were remarkably higher for overuse injuries (83%) as for traumatic injuries (17%) (58). In children, there seems to be a lack of knowledge of knee re-injuries, which should be reported for at least specific body parts and injury type.

Controversy exists for intrinsic risk factors, which may be depending on age and sports type, and there seems to be a lack of information of these risk factors in a general population of children.

Generalised Joint Hypermobility

Another suggested intrinsic risk factor for knee injuries in children is flexibility, such as joint hypermobility. GJH is a variation of normal joint mobility, defined as an increase in mean joint range of motion (59). The prevalence of GJH in the general children population has been reported to vary from 7-29%; the large variation is likely due to heterogeneity of the studied population regarding age, sex and/or a variation in test procedures, interpretation of results and criteria used (60-62). GJH is most often classified by the Beighton Tests (BT) for hypermobility, a 0-9 scoring system (63). Possible methodological shortcomings of BT can arise, as the tests do not include detailed descriptions of performance or interpretation, leaving uncertainty of the validity and the inter-tester reproducibility. There is no international consensus of a cut point for classification of GJH in children and adolescents, varying in cut points between 4-7 out of 9 (64).

Applying the BT as a clinical measure of hypermobility requires initially evaluations of inter-tester reproducibility, at a relevant cut point for classification of GJH in children. Also, the prevalence of different methods of performing the BT must be calculated in order to justify comparisons between studies.

A positive association between GJH and knee injuries was reported in a recent systematic review of both children and adults including meta-analyses, where sport participants (9-39 years) with GJH at BT≥4/9 had five times higher risk of knee injuries, especially during contact sport activities in high school, college and all levels of sport (65). In studies of adults only, ACL injuries were more frequent in patients with GJH at BT≥6/9 and knee hypermobility in the contralateral, uninjured knee in a case-control study of ACL reconstruction (66). Similar, female soccer players (14-39 years) with GJH at BT≥4/9 had more than 5 times higher odds for injuries, primarily knee injuries in a prospective cohort study registering injuries resulting in time-loss from practice and/or matches (67). In contrast, no such associations were found between knee injuries and GJH or knee joint laxity, measured as increased anterior-posterior tibio-femoral translation, in female, adult soccer players at BT≥4/9 in a prospective cohort study using weekly text messages for time-loss injuries and exposure in training and matches (68).

In studies of children and adolescents with GJH or knee hypermobility, an overall increased risk of knee or lower extremity injuries was found in sports-specific populations with BT≥5/9 or knee hypermobility (Figure 2). In a cross-sectional study of junior netball players (6-16 years) at all levels, the odds of sustaining an injury, primarily in the ankles and knees, were three times higher for the GJH group at BT≥5/9 (69). In a prospective case-control study of female soccer and basketball players (14-19 years) at high school and collegiate level, the odds of ACL injuries were five times greater for participants with only knee hypermobility in the BT (70). Similarly, in a prospective study, female elite soccer players (16-26 years) with BT≥5/10 (Söderman I, Figure 2) or knee hyperextension (Söderman II, Figure 2) measured by sagittal laxity, Lachmann´s test and valgus/varus laxity, had three respective two and a half times higher odds for sustaining a lower extremity injury (71). Contrary, no association was found between GJH at BT≥4/9 and lower extremity injuries in a prospective cohort study of soccer players (13-19 years) (72).

In the aforementioned sports-specific studies reporting only GJH, it is not clear if the presented BT score represents one or more positive knee hyperextension tests (67, 69, 71, 72). GJH classified at a relative high cut point, comprising knee hypermobility, and/or knee joint laxity itself, may increase the risk of knee injuries in sports with jumping, landing and pivoting (Figure 2), which are situations requiring a high level of knee joint stabilisation.

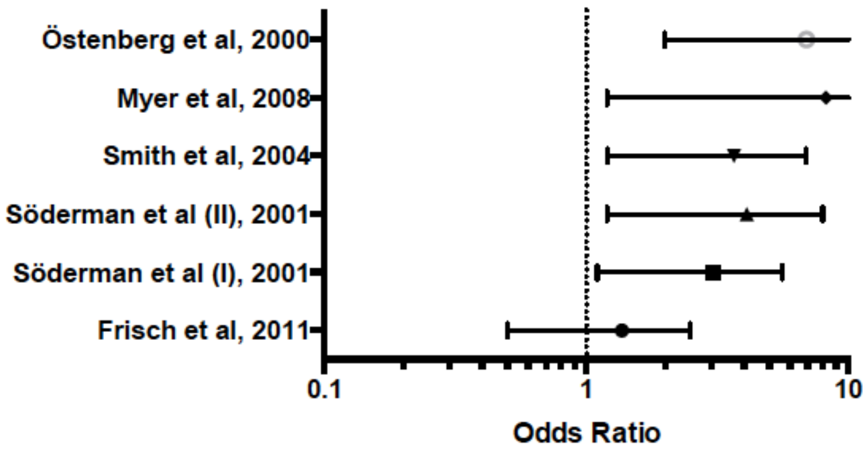

Figure 2. Odds ratios presented with CI for knee or lower extremity injuries in children and adolescents with Generalised Joint Hypermobility or knee hypermobility.

As studies reporting a positive association of GJH and knee injuries are sports-specific, it is unknown, whether there is an increased risk of knee injuries in a general population of children and adolescents with GJH, stressing the need to identify knowledge gaps in this population, potentially being at risk for knee injuries.

Risk factors for knee injuries in children– a biomechanical model

At step two in the injury sequence prevention model by Meeuwisse (40), risk factors or mechanisms of knee injuries can be studied and evaluated. At this step, the epidemiological model for sport injuries may well be supplemented with a basic biomechanical model, taking tissue properties as well as load characteristics into account (73). Injury results from a transfer of energy to the tissue, and the mechanical properties of human tissue, such as stiffness, strength, elasticity and critical stress affect the individuals respond to physical loads (73). Properties differ for each tissue and are dependent on the nature and type of load, its rate, the frequency of load repetition, the magnitude of energy transfer, and intrinsic factors such as genetics, age, sex, and physical condition. In the biomechanical model, the relation between load and load tolerance determines whether the inciting event in the epidemiological model results in an injury or not.

Load and load tolerance can be influenced in different ways by the main elements of the epidemiological model with intrinsic and extrinsic risk factors, and an incident event. Although all of the three elements influence load, load tolerance is mainly determined by intrinsic risk factors, e.g. the biomechanical and material properties and size of ligaments (37).

Load tolerance may be altered in individuals with GJH, as this condition implies decreased stiffness of the connective tissue, including skin, joint capsules and ligaments (74). From a functional perspective, possible compensation strategies for reduced passive knee joint stability could be increased muscle activation, rate of force development and/or maximum strength to increase the active stability of the knee joint (75-77). The focus of this thesis is limited to knee joint neuromuscular control, including muscle activity level, time of onset and co-contraction.

Only few studies of muscle activity in individuals with GJH have been performed (78-80). One study of children (10-year old) with GJH and at least one hypermobile knee found neuromuscular coordination and control strategies to differ from controls (78). This was seen during a submaximal isometric knee flexion task, where hamstring muscle activity was reduced. During the same task, knee muscle co-activation ratio was increased, which was suggested to be a compensatory strategy for the lower hamstrings activity (78). Furthermore, decreased maximum isokinetic knee extension and flexion strength were seen in 10-year old girls and women with GJH and also, decreased knee strength balance (Hamstring/Quadriceps ratio) was seen in adults with GJH (81). However, these results were all obtained during sitting in an isokinetic dynamometer or in tasks requiring static knee stability. In a static balance tasks, adults with GJH and hypermobile knee joints performed equally as well as controls, but had increased knee muscle co-contraction (82).

It is difficult to predict to what extent laboratory joint loading set-ups in fact are comparable to real-time injury situations, with respect to the dynamic and complex interaction of multiple risk factors and inciting events, presented by existing epidemiological and biomechanical models. Therefore, in order to understand some of the underlying intrinsic mechanisms of knee stability in GJH, and hence target preventive interventions, knee joint neuromuscular control must also be investigated during dynamic loading conditions like a hop test, simulating components of high load sports or play situations.

Implications of GJH and knee hypermobility on neuromuscular function of the knee joint during dynamic performance tests are not well studied, but may contribute to our understanding of intrinsic risk factors that may influence functional knee joint stability.

To our knowledge, there are no studies focusing at incidence, intrinsic and extrinsic risk factors for knee injuries and knee joint neuromuscular control during dynamic loading in children with GJH and simultaneous knee hypermobility, within the general child population.

Aim and objectives of the thesis

General aim

To achieve more knowledge of intrinsic and extrinsic risk factors for knee injuries in a cohort of school children aged 8-15 years, with special emphasis on children with GJH.

Objectives

1. To determine the inter-tester reproducibility and inter-method agreement of BT for hypermobility (Paper I)
2. To report the distribution and incidence of traumatic and overuse knee injuries and identify potential risk factors for these injuries, focusing at the intrinsic factors of sex, age, height, BMI, GJH, previous knee injuries, and the extrinsic factors of amount of organised sport participation and sports type (Paper II)
3. To evaluate the extent of knee injuries in children with GJH and knee hypermobility and to examine the risk of knee injuries specifically for the GJH group when compared with controls (Paper III)
4. To identify potential differences in knee joint neuromuscular control, defined as muscle activity, time of onset and co-contraction, in children with GJH and knee hypermobility compared with controls before and after landing from a hop test (Paper IV)

Methods

Setting

The studies in this thesis are all based on data from The Childhood Health, Activity and Motor Performance School Study Denmark (the CHAMPS-Study DK). The CHAMPS-Study DK is a longitudinal cohort study launched in 2008, following children from 10 public schools in the Municipality of Svendborg, Denmark (83). The overall aim of the CHAMPS-Study DK is to evaluate the effect of increased physical education on childhood health in general, extensively described elsewhere (83). Data for the thesis involves the period spring 2011 to July 2014 from all schools.

Ethics

The Regional Scientific Ethics Committee for Southern Denmark approved the experimental protocol (ID S-20080047 HJD/csf) and the study was reported to the Danish Data Protection Agency. Written and oral information about participation in the study was provided to the parents or guardians of each child according to the Declaration of Helsinki (84). Written informed consent for participation was received from the parents, and all participation was voluntary with the option to withdraw from the project at any time.

Prior to every clinical examination for knee injuries, an additional verbal agreement was obtained from each child and his/her respective parents.

Study population

In August 2011, totally 1888 children from the second to the eighth grade, 8-15 years, from 10 public schools, were invited to participate in the longitudinal registration of musculoskeletal injuries, sports participation and sports type.

The CHAMPS-Study DK is an open cohort, with the on-going possibility for children to leave or enter the study.

Paper I

Participants in this methodological study were 103 healthy children from two different grades: first grade (7-8 years) and fourth grade (10-12 years). Exclusion criteria were pain in the involved joints on the day of testing and movement restrictions, such as mild cerebral palsy, which would affect the results of the tests.

Paper II

In this longitudinal study, 1326 children participated at baseline August 2011 in the on-going registration of musculoskeletal injuries, sports participation and sports type by cell-phone surveys. The children were followed for 128 weeks to July 2014, excluding summer and Christmas holiday periods.

Inclusion criteria were children participating in the on-going survey, answering at least 80% of the survey of musculoskeletal pain and participation in one or more test rounds in spring 2011, spring 2012, and spring 2013. Exclusion criteria for the current study were children with a diagnosis of chronic musculoskeletal or neurological condition, or pain in the regions being examined in the BT at the day of testing. The prevalence of children with BT≥5/9 was 10%.

Paper III

In this longitudinal study, during 63 weeks from March 2012 to June 2013, 1326 children participated in the registration of musculoskeletal injuries, sports participation and sports type, from which 999 children were tested at both test rounds included in the period.

Inclusion criteria were children participating in the on-going survey, answering at least 80% of the survey of musculoskeletal pain and participation in both test rounds in spring 2012 and spring 2013. Exclusion criteria for the current study were children with a diagnosis of chronic musculoskeletal or neurological condition, or pain in the regions being examined in the BT for hypermobility on the day of testing. The prevalence of children with BT≥5/9 was 9-11%.

Paper IV

For the electromyography (EMG) study exclusively, children with GJH and controls were selected from the cohort and contacted individually via their parents to participate in this case-control study. The status of GJH or control was determined from the BT results from test round 2013, testing the entire cohort along with other tests, one month prior to the current study. In total, 56 children were recruited, 26 with GJH and 30 controls, matched by age and sex at a group level.

Inclusion criteria for children with GJH were a BT score of ≥5/9 and at least one hypermobile knee (positive standing knee hyperextension as in the BT, and further confirmed by using a goniometer during supine lying) (85, 86). Inclusion criteria for controls were a BT score of no higher than 1/9 and no hypermobile knee. Exclusion criteria for both groups were current pain in the back or lower extremities affecting the ability to jump, previous or current knee trauma, BMI >25 and hereditary diseases like Ehlers-Danlos Syndrome, Marfan Syndrome and Osteogenesis Imperfecta.

The measurements applied in the studies are extensively described in the following, with an overview of the measurements as related to papers I-IV provided in Table 1.

Paper	**I**	**II**	**III**	**IV**
Knee injuries		x	x	
Sports participation		x	x	x
Sports type		x		
Beighton Tests	x	x	x	x
Single Leg Hop for Distance				x
Electromyography				x

Table 1. Measurements applied in papers I-IV.

Longitudinal measurements

In the following, the on-going data collection of musculoskeletal pain and knee injuries, sports participation and sports type undertaken in the period August 2011 - July 2014 is described.

SMS surveys

A prospective, longitudinal data collection of musculoskeletal pain, sports participation and sports type was undertaken using Short Message Service (SMS) survey (87). SMS survey is a Software-as-a-Service platform that makes it possible to gather information from respondents via text messaging (87). Cell phones are commonly used in the current study population and their parents, making it possible to receive, read and answer text messages in an expeditious way. Questions received on a cell phone are more often read and answered, than those received by ordinary letters or e-mail, thereby providing a high response rate (88, 89).

Every week, the children and their parents received an SMS with questions regarding musculoskeletal pain, sports participation and sports type. Parents were used as a ´filter´ or informants on behalf of their child, as self-reported data from children may be inaccurate (90, 91). If parents forgot to answer, reminders were sent twice with an interval of 48 hours. If parents did not answer or answered in invalid ways, they were contacted by telephone by research assistants to clarify facts. SMS answers were stored directly in a database. Collection of data was suspended during six weeks of summer holiday and one week of Christmas holidays during the study period.

Knee injuries

Registration of knee injuries was performed in two steps:

1) Every Sunday, the children and their parents received an SMS, asking ´Has your child had any pain during the past week´? The possible answer options were one of four numbers, corresponding to pain or complaints located in 1) the back, 2) the arms, 3) the legs or 4) no pain. Information of children, who answered 1), 2) and/or 3) were extracted from the database, and every Monday, the parents were contacted via telephone by physiotherapists and chiropractors from the CHAMPS-Study DK to determine the need for a clinical examination. On-going pain or complaint previously registered and diagnosed in the study was reported with the related number and a * mark by the parents, to avoid the same pain or injury being registered more than once.

2) The need for clinical examination was based on the character and the extent of the child´s musculoskeletal pain or complaint, as described by the parents. The children with a need for clinical examination were examined at their respective schools every week or fortnight by physiotherapists or chiropractors blinded to the status of GJH during the test rounds. The traumatic and overuse injuries were classified according to the ICD-10 by WHO (92). If needed, the child was referred for further para-clinical examination, such as X-ray, ultrasound or magnetic resonance imaging scan. To get a complete data collection of injuries, information of children being diagnosed elsewhere (e.g. hospital emergency departments) during the study period was collected concurrently. Only data

of knee injuries were used for the studies of this thesis.

SMS survey as a method for injury registration has been shown to be satisfactory for capturing both severe and less severe, traumatic, and overuse musculoskeletal injuries (24).

Organised sports activity

The weekly amount of organised sport, reported by the parents to each child as the number of times spent in organised sport, was also registered by the SMS survey every Sunday. The question was: ´How many times did your child participate in organised leisure time sport within the last week?´ with the possibility of answering the relevant number between 0 (none) and 8, with 8 corresponding to more than 7 times. The weekly amount was expressed in times, which is not equivalent to hours for all sports types. Therefore, the term ´sport participations´ is used throughout the text.

Type of sport

If the answer to the amount of organised sport was a number between 1-8, it was followed by the question: ´Which type of sport?´ with 10 options for answering: 1: Soccer, 2: Handball, 3: Basketball, 4: Volleyball, 5: Rhythmic gymnastics, 6: Tumbling gymnastics, 7: Swimming, 8: Horseback riding, 9: Dancing and 10: Other sports.

Cross-sectional measurements

The methods applied for the data collection of status of GJH and anthropometrics was undertaken at three time points at the test rounds of spring 2011, spring 2012 and spring 2013, and is described in the following. The EMG study was carried out in spring 2013, and the methods applied for this study being the Single Leg Hop for Distance test (SLHD), Maximum Voluntary Contraction (MVC), muscle activity, time of onset and co-contraction is outlined below.

Beighton Tests

The children were clinically examined in the three test rounds with BT and criteria for GJH (63), with the version applied for the CHAMPS-Study DK described in details in Appendix 1 and 2. BT consist of five manoeuvres: 1) passive dorsiflexion of the little fingers beyond 90˚, 2) passive apposition of the thumbs to the flexor aspects of the forearm, 3) hyperextension of the elbows beyond 10˚, 4) hyperextension of the knees beyond 10˚ and 5) forward flexion of the trunk with the knees straight, resting the palms easily on the floor (63).

One point was allocated for each of the tests being positive as described, bilaterally for manoeuvres 1-4, with a total score ranging from 0-9. Cut-point ≥5/9 was chosen for the analyses. The children were categorised as GJH or controls according to the described cut-point. The child and the parents were not informed about the status of GJH.

The children were tested with BT in the mornings and did not attend any physical education classes, nor perform warm-up exercises or stretching before the BT. The children were tested with BT in a random order by a team of 25 physiotherapy students on each test round. Two experienced physiotherapists (Tina Junge and Lisbeth Runge Larsen) trained the testers in a standardised protocol for the BT, describing the test procedures in detail.

BT are often used for classification of GJH for adults as well as for child populations, but many scientific articles lack systematic descriptions and analyses for intra- and inter-tester reproducibility (59). Strict protocols for standardization of potential test variations, e.g. starting position of the body with the extremities bent or stretched, placement or positioning of the hand of the tester, pressure applied and precise benchmarks for positive scores are important for obtaining an excellent reproducibility, making comparison across studies possible (93).

Inter-tester reproducibility and inter-method agreement of the Beighton Tests

Therefore, in paper I, an inter-tester reproducibility study was performed for tests and scoring criteria of two different test batteries for the BT (hereafter referred to as Method A and Method B) in a standardised protocol format. Secondly, the inter-method agreement of the prevalence of GJH for Methods A and B was determined, using the criterion of BT ≥5 for GJH.

The two methods of BT were both in accordance with the original text of Beighton et al. (63). The original study from Beighton et al. has an unclear description of the test performance, with no description of the procedures for each test. This is among others the reason, why diversion exists regarding these procedures for BT, and very few of these test batteries have been tested for reproducibility. The BT in the reproducibility study were performed in two different procedures for each test varying slightly in starting positions and benchmarks, reflecting diversions of daily clinical practice (Appendix 1). Besides variation in starting positions and benchmarks, the test batteries also differed in whether the tests were performed actively or passively, how they were influenced by gravity and whether the surrounding soft tissue was in a stretched or relaxed position (Appendix 2). Two of the authors of the current reproducibility study (Tina Junge and Eva Jespersen) made detailed descriptions regarding starting positions and benchmarks for the two different BT batteries (Appendix 2).

The BT started with a visual demonstration by the tester of the single test along with an oral instruction on how to perform the test before the children performed the test themselves. In the two methods, the children were asked to bring the joint to the most extreme position according to Methods A or B, tested consecutively by four different testers with approximately half an hour between testing sessions. All tests were performed in a random order with respect to right and left sides and to the test sequence.

The same four testers evaluated the two different test batteries on the same children; two testers (Tester 1 and Tester 2) for Method A and two testers (Tester 3 and Tester 4) for Method B. The testers were physiotherapy students on the last year bachelor program, well trained in the performance and the interpretation of the BT. The number of participants in the three phases was 10, 70 and 39 respectively.

Inter-tester reproducibility for the Beighton Tests for hypermobility

For the inter-tester reproducibility study, a standardised protocol for clinical reproducibility studies was followed, including a three-phase study with a training phase, an overall agreement phase and a test phase (93) for each of the two different test batteries, Method A and Method B.

Phase 1: The training phase was performed in an open study in order to discuss and standardise every detail of performing and interpreting the BT among testers, thus improving their ability to follow strict test procedures, whether these were on adults or on children. In this phase, the testers were not blinded to GJH status or test results. The training phase was carried out in 10 adult cases.

Phase 2: Using a blinded study, the main aim of the overall agreement phase was to obtain an overall percentage agreement of at least 80% for finding ≥5 positive tests out of 9 as the criterion for GJH. In this phase, testers were blinded with respect to both GJH status and the other testers' results. Two observers were responsible for the randomisation of the test order, the selection of Method A or B and instructing the children not to comment on their status and the test outcome.

Phase 3: In the test phase, the aim was to determine the kappa value (agreement adjusted by chance), using a blinded study, while ensuring an approximate 50% prevalence in order to optimise the kappa statistics validity (94, 95) (Figure 3). Knowledge about the children with GJH score ≥5 found in Phase 2 from both methods A and B was used to select children in advance for the test phase (Phase 3), so as to recruit as many children with GJH as possible. As a result, 19 children with GJH and 20 controls from Method A and Method B were sent to the allocated testers. The test phase consisted of 39 children, who were tested with both Methods A and B, and by all four testers. Mean age was 9.6 years, 54% were boys.

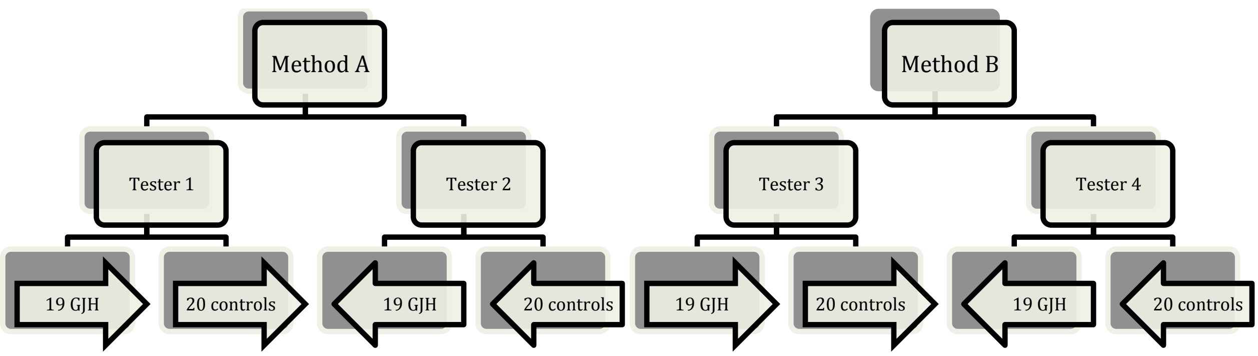

Figure 3. Phase 3; test phase with prevalence 50% method in the inter-tester reproducibility study

Inter-method agreement of the Beighton Tests for hypermobility

For the inter-method agreement study of the prevalence of GJH, the a priori choice of comparing data from Tester 1 with Tester 3, and Tester 2 with Tester 4, was arbitrarily used. The prevalence of GJH for both Methods A and B was compared with the criterion of ≥5/9 as a cut-off level.

The inter-method agreement study involved data from 103 consecutively recruited children, who had been tested in both Method A and Method B during the inter-tester reproducibility study. Six children were not a part of the inter-method analyses, as they were only tested with one method due to lack of time. All together, 62 children (60%) represented 7-8 year olds and 41 children (40%) 10-12 year olds.
Results from the inter-tester reproducibility study and the inter-method agreement study are presented in the Results section.

Single Leg Hop for Distance test

The SLHD test applied in the EMG study was modified slightly from the original version describing the arms to be held behind the back (96). The child was asked to jump on the test leg as far as possible allowing arm swing assistance and to land standing steadily on the test leg for at least 2-3 s. The child had one trial to familiarise and then three SLHD tests, and further additional jumps, until no further progress in jump length was observed. Between each test the child had a 30 s rest. The longest jump, measured in cm from the toe in the starting position to the backside of the heel in the landing position, was used for the EMG analyses. Inter-session reproducibility for SLHD in children aged 11 and 14 years had ICC values of 0.93 respectively 0.84 (unpublished data, the CHAMPS-Study DK), also previously shown in adults (97).

Maximum Voluntary Contraction

For the EMG study, MVC for knee flexion and extension was performed during sitting with a straight back without support, the hips at 90° flexion, the knees at 60° flexion and both arms placed across the chest (98). The moment arm for knee flexion and extension was measured as the distance between the centre of rotation of the knee joint and a line projected perpendicular to the direction of force applied just proximal to the lateral malleolus.

For measuring ankle plantar flexion MVC, the children were supine on an examination bench with an extended knee and the ankle placed in 10° dorsal flexion, free of the bench. To minimize trunk and hip movement during the test, a tester stabilized the hip. A strap connected to the force transducer was positioned around the forefoot. The moment arm for ankle plantar flexion was measured as the distance from the medial malleolus (an indication of the centre of ankle joint rotation) perpendicular to the line of force application at the middle of the foot strap. Three maximum attempts were performed for measuring MVC with 1 min´s rest in between. The testers verbally encouraged the child in a standardised way during each MVC.

MVC was measured with a strain-gauge force transducer (Nobel Load Cells KIS-2 2kN, England) expressed in Nm and normalized to body mass (Nm/kg) for knee extension, knee flexion and ankle plantar flexion. Further, isometric strength ratios of maximum knee flexion and knee extension (KF/KE) as well as the ratio of maximum plantar flexion and knee extension (PF/KE) were calculated, since the PF also have a knee flexor function.

Electromyography

Bipolar surface EMG signals from the knee flexor and knee extensor muscles (Gastrocnemius medialis: GM; Gastrocnemius lateralis: GL; Semitendinosus: ST; Biceps femoris: BF; Quadriceps–vastus medialis: VM; Quadriceps–vastus lateralis: VL) were measured during MVC and during the SLHD test.

Prior to testing, skin preparation procedures included hair removal, light abrasion and disinfection. Electrode placement and orientation was positioned according to the SENIAM recommendations (99). The Ag/AgCl EMG electrode (Blue sensor N, Ambu Denmark) had a pre-gelled diameter of 10 mm and an inter-electrode distance of 2 cm. An accelerometer was positioned over the trochanter major for definition of the landing. All electrodes and cables were subsequently attached to the leg with elastic bands to keep them properly fixed to the skin. To control for cross talk between the ST and the BF muscles, the recommended electrode position from SENIAM was used and a short inter electrode distance chosen to be as selective as possible on each muscle. A visual inspection was performed of the simultaneous signal from the two muscles to make sure that the two adjacent muscles showed distinct activation in different standard tasks indicating a minimum of cross talk.

The EMG signal and acceleration were sampled via a telemetry EMG system (Telemyo DTS and Telemyo mini receiver, Noraxon U.S.A. Inc.) through integration with a computer equipped with data collection software (MyoResearch xp master, Noraxon U.S.A. Inc). The EMG signal was A/D converted and sampled at 1500 Hz using the Telemyo DTS system with low-pass cut-off filtering at 500 Hz and a 1st order high-pass at 10 Hz. EMG signals were amplified with a total gain of 500 Hz. Accelerometer data were sampled at 1500 Hz with a low-pass cut off at 500 Hz. The sensitivity was +/-0.67 V/g.

Landing during SLHD was defined as the time point where the acceleration exceeded 5*g* (Figure 4). Maximal Voluntary Electrical activity (MVE) for each muscle was defined as the highest EMG activity measured as the root mean square (RMS) amplitude in a 100 ms moving window across the whole MVC. EMG activity was calculated 100 ms before and 50 ms after landing of SLHD as RMS amplitude, and for each muscle normalized to MVE of the relevant test and presented as %MVE.

Time of onset

Time of onset for muscle activity in ms was defined for each muscle, relative to landing time, determined by the accelerometer. An increase in muscle activity was defined as the signal exceeding a set trigger level of 2.5% of maximum EMG during each jump in a 20 ms window, identified by an algorithm. Afterwards, this time of onset was evaluated by visual inspection, previously considered a valid evaluation of EMG activation characteristics (100).

Co-contraction index

A muscle co-contraction index (CCI), defined as the simultaneous activation of two muscles (101), was calculated cumulative for the

Quadriceps (Q) and Hamstring (H) groups (H/Q). Also, the single medial or lateral knee muscles of the latter muscle groups as well as the Gastrocnemius muscle group was combined in indices of two: Quadriceps and Hamstring, Q-H (VL-BF and VM-ST), Quadriceps and Gastrocnemius, Q-G (VL-GL and VM-GM), and the Hamstring and Gastrocnemius muscles, H-G (ST-GM and BF-GL). Co-contraction was determined using the following equation: MVEmin/MVEmax * (MVEmin + MVEmax) (101). MVEmin was the level of activity in the less active muscle and MVEmax was the level of activity in the more active muscle before landing. This index was multiplied by the total activity of the two muscles, providing an estimate of the relative simultaneous activation of the suggested agonist and antagonist, as well as the magnitude of the co-contraction (82).

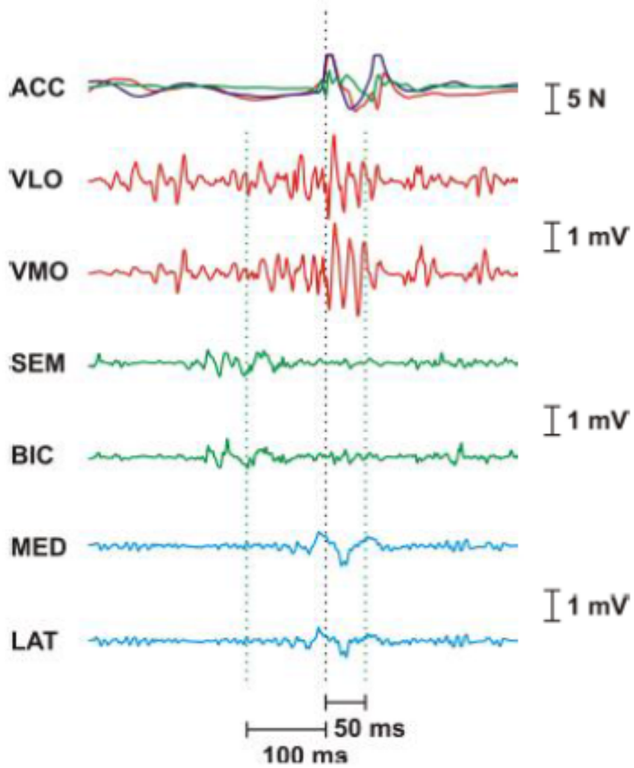

Figure 4. Example of EMG recordings in mV of the six investigated muscles: Quadriceps vastus lateralis: VLO; Quadriceps – vastus medialis: VMO; Semitendinosus: SEM; Biceps femoris: BIC; Gastrocnemius medialis: MED; Gastrocnemius lateralis: LAT. Top line is the accelerometer data indicating impact of landing with the vertical line. The time frames indicate 100 ms before landing and 50 ms after landing.

Statistics

Paper I	Outcome	BT score GJH ≥5/9
	Quantification of inter-tester reproducibility	Kappa statistics
	Quantification of inter-method comparison	McNemar´s test
	Interpretation of inter-tester reproducibility	Kappa>0.61: Substantial
Paper II	Primary exposure	Sex, age, height, BMI, GJH ≥5/9, previous knee injury, sport participation and sports type
	Primary outcome	Traumatic knee injuries Overuse knee injuries
	Descriptive statistics	Means (Range)
	Longitudinal analyses	Multi-nomial logistic regression
	Potential confounders	Grade level, school type
Paper III	Primary exposure	GJH ≥5/9 GJH ≥5/9 and knee hypermobility GJH≥5/9 ±1 point GJH≥5/9 ±1 point and knee hypermobility
	Primary outcome	Traumatic knee injuries Overuse knee injuries
	Descriptive statistics	Means (SD)
	Longitudinal analyses	Logistic regression and Poisson regression model
	Potential confounders	Sex, age, growth, sport participation, grade level and school type
Paper IV	Primary exposure	GJH ≥5/9 and knee hypermobility
	Primary outcome	MVC and MVC ratios, relative EMG activity level, CCI and time of onset
	Descriptive statistics	Means (CI)
	Cross-sectional analyses	Multi-level linear regression
	Potential confounders	Sex, grade, height, weight and sports participations

Table 2. Overview of primary outcomes and exposures, statistical methods and adjustment of potential confounders in the four papers.

Paper I

For the inter-tester reproducibility study, Cohen's kappa statistics were used for each of the single tests and for the criterion for classification of GJH. Kappa values for reproducibility studies of tests for GJH are often not high despite standardised test protocols, as the magnitude of kappa is affected by the prevalence of the condition in the population (102). A practical method for independency of prevalence is to influence this in advance by ´the prevalence 0.50-method´ (93). For inter-tester reproducibility studies, both blinded testers will find an equal number of participants with positive and negative tests, whom will be tested by the other tester, and this way trying to get as close as possible to a prevalence of 0.50 (93).

Kappa values were classified as <0.0 = poor, 0.0-0.20 = slight, 0.21-0.40 = fair, 0.41-0.60 = moderate, 0.61-0.80 = substantial, and 0.81-1.00 = almost perfect (103).

For the study of inter-method comparison, McNemar's test was used to test for significant differences between the two testers within each method and the prevalence obtained by methods A and B.

Paper II

A multi-nomial logistic regression model extended to the longitudinal setting (104), was used to evaluate the nominal outcome variables, being one of the four competing states: 1) no injury, 2) a traumatic knee injury, 3) an overuse knee injury or 4) a lower extremity injury other than a knee injury. The explanatory variables were intrinsic risk factors from demographics of the test rounds; sex, age, height, BMI and GJH as well as information of previous knee injuries up till two years prior to the index injury. Extrinsic factors were weekly information of the amount of sport participation and sports type, while classes were random effects. The results are presented as Odds Ratios (OR). In the bi-variate analyses, sports type was stratified into the amount of sport participations.

Assumptions of the multinomial logistic regression model were verified, as the data are case specific; that is, each independent variable has a single value for each case. Also, the dependent variable cannot be perfectly predicted from the independent variables for any case.

Paper III

An un-paired t-test was used to compare mean age, height, weight, BMI, school type and sports participation between groups.

A logistic regression model (for analysis of group 1a and 1b) and Poisson regression model (for analysis of group 2a and 2b) with robust standard errors were used to test the associations between GJH and knee injuries, taking into account clustering on school class levels.

The following groups were defined for the analyses:

1)

a) Children with a constant status of GJH, meaning that the child had a BT score of ≥5/9 on both tests rounds (n=36).

b) A further stratification of this group (1a) into a subgroup having simultaneous knee hypermobility of at least one knee during at least one of the test rounds (n= 26).

Due to an observed fluctuation of the status of GJH between test rounds (for example, a child could be classified control on the first test round with a BT score of 4, while on the second test round the BT score could be 5, classifying the child as GJH), further subgroup analyses were performed. As a measurement error of 12% (overall agreement 88%) was seen in paper I and in a previous study for the BT score (105), scores from the children classified with GJH were allowed to fluctuate one point in the BT score (from 4 in 2012 to 5 in 2013 and vice versa). Therefore, post hoc analyses on the following groups were calculated for:

2)
   a) Children with a constant status of GJH, as described in 1a, but including children fluctuating one point in BT between test rounds (n=119)
   b) This group (2a) was further stratified into a subgroup having simultaneous knee hypermobility of at least one knee during at least one of the test rounds (n= 56).

Included in all analyses were potential confounders of sex, age, school type, sports participation and growth, with growth expressed as a delta value for the increase in height between the two test rounds. Post estimation included checking underlying assumptions for the chosen model.

Paper IV

Based on power calculations from previous EMG laboratory studies of children with GJH (78), a subsample of 19 children in each group was calculated to be necessary to detect a statistically difference of 10% in MVC knee flexion, with a power of 0.80 and a significance level of 0.05.

An un-paired t-test was used to compare mean age, height, weight, sports participation and jump length between groups. In this paper only, mean sport participation during four weeks was used for analyses.

A multi-level linear regression model was used to evaluate group differences for MVC and MVC ratios, relative EMG activity level, CCI and time of onset for the six knee muscles presented (one at a time). In all models, status of GJH, sex, grade, height, weight and sports participation were introduced as potential confounders. Post estimation included checking underlying assumptions for the chosen model.

All statistical analyses were performed using Stata (version 13.0: Statacorp, College Station, Texas, USA). *P*-values ≤ 0.05 were considered significant, and borderline significance were presented when $0.5 < p < 1.0$.

Results

Throughout the study period, a weekly response rate of 97% for the SMS survey was registered.

In the following, the basic descriptive statistics presenting the anthropometrics of the participants in paper II, III and IV are presented (Table 3). Overall, no differences were observed in anthropometric characteristics (age, height, weight and BMI) or sport participation in children with GJH and controls in paper III and IV.

Table 3. Baseline characteristics of the study participants included in paper I, II, III and IV. Ia: Inter-tester reproducibility study, Ib: Inter-method agreement study. Values are mean ± SD. Age is presented with range.

Paper	Participants n	Sex (% boys)	Age (yrs)	Height (cm)	Weight (kg)	BMI (kg/m^2)	Sports participation (weekly mean)
Ia							
GJH	19	54	9.6 (7-11)	-	-	-	-
Controls	20	54	9.6 (7-11)	-	-	-	-
Ib	103	52	8.7 (7-12)	-	-	-	-
II	1327	47	10.9 (8-14)	147.1 (10.7)	38.8 (9.6)	17.5 (2.5)	1.7 (1.7)
III							
GJH	108	37	11.0 (8-14)	150.4 (10.3)	40.7 (9.7)	17.7 (2.4)	1.8 (1.2)
Controls	1135	50	11.2 (8-14)	152.1 (10.8)	42.4 (10.4)	18.1 (2.6)	1.7 (1.2)
IV							
GJH	25	12	11.5 (10-15)	154.3 (10.4)	43.7 (10.3)	18.1 (2.5)	2.3 (1.9)
Controls	29	10	11.6 (10-14)	153.8 (9.4)	41.7 (6.6)	17.5 (1.7)	2.6 (1.9)

Paper I

The inter-tester reproducibility of the test items of Methods A and B was moderate to substantial (κ 0.49-0.94 (mean 0.70) for Method A, 0.30-0.84 (mean 0.59) for Method B), using a standardised study protocol. The described methods for performing the BT was found to be reproducible for children aged 7-8 and 10-12 years, using a cut-off level of ≥5/9 for classification of GJH. No significant difference in prevalence was found when using the two current test batteries, why both BT methods presented are considered suitable for comparative studies of children, when using a GJH criterion of ≥5/9.

Paper II

Epidemiology of knee injuries

Totally, 2127 lower extremity injuries including knee injuries were diagnosed in the present study. From these, 952 were knee injuries; hereby 15% (146) traumatic knee injuries and 85% (806) overuse knee injuries. There was a peak incidence of overuse injuries in 11 and 12 years old.

Traumatic knee injuries consisted mainly of sprains and contusions; while for overuse knee injures it were primarily traction apophysitis (Mb. Sinding-Larsen-Johansson, Mb. Osgood-Schlatter) (Figure 5).

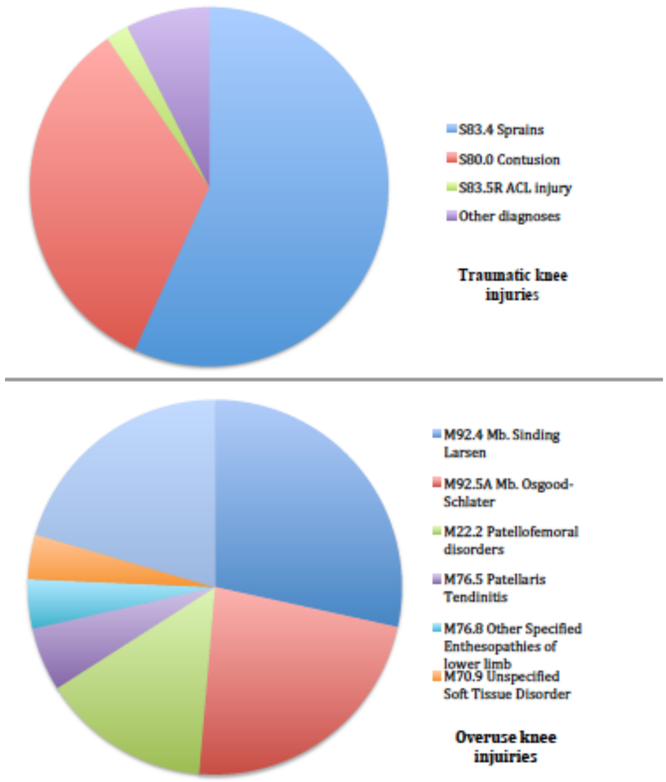

Figure 5. Distribution of traumatic and overuse knee injuries by ICD-10 diagnoses.

The injury incidence per 1000 sport participations for traumatic and overuse knee injuries was 0.8 and 5.4, respectively. On average, the children had 1.7 times sport participations per week (range 0–8) in organised sport. For both sexes, the highest incidence of traumatic injuries was seen in tumbling gymnastics and handball, while for overuse injuries it was handball and rhythmic gymnastics.

Risk factors for traumatic knee injuries

In the multi-variate analyses, the only significant extrinsic risk factor for traumatic knee injuries was children participating in tumbling gymnastics (OR 2.14, CI 1.01-4.57) (Table 4). There were no increased odds for the intrinsic risk factors, except for a borderline significant result for children with GJH having an OR of 1.69 (CI 0.92-3.09) for sustaining a traumatic knee injury (Table 4).

In the bi-variate analyses, with the specific sports type stratified into amount of sport participation, higher odds were found for traumatic knee injuries for children participating in the most popular sports four times per week; soccer (OR 2.40, CI 1.27-4.52) and handball (OR 2.33, CI 1.05-5.16) and for children participating in tumbling gymnastics twice or more per week (OR 3.16, CI 1.68-5.96). For children playing handball only once a week, odds were more than three times higher (OR 3.61, CI 1.71-7.65) for sustaining a traumatic knee injury.

Risk factors for overuse knee injuries

In the multi-variate analyses, intrinsic risk factors for overuse injuries were sex, with girls having odds of 1.38 (CI 1.10-1.74) compared to boys. Also, having a previous knee injury increased the odds to 1.78 (CI 1.37-2.33). Results regarding BMI was borderline significant (Table 4).

For the extrinsic risk factors, significantly higher odds of sustaining an overuse knee injury was found for children participating in specific sports like soccer, handball, basketball, rhythmic and tumbling gymnastics compared to children not participating in sports (Table 4).

In the bi-variate analyses, children participating more than two times per week in specific sports as soccer, handball, dance, tumbling and rhythmic gymnastics had increased odds for overuse knee injuries. However, the odds of reporting an overuse knee injury were higher for children participating in soccer and handball at all levels.

Table 4. Adjusted Odds Ratios (OR) estimates by injury type for the included intrinsic risk factors of sex, age, height, BMI, GJH, previous knee injury, and the extrinsic risk factors of sport participation and type, taking into account competing risks.

	Traumatic knee injuries OR (95% CI)	***p*-value**	**Overuse knee injures OR (95% CI)**	***p*-value**
Intrinsic factors				
Sex	1.03 (0.64-1.66)	0.882	**1.38 (1.10-1.74)**	**0.005**
Age	1.04 (0.81-1.35)	0.719	1.01 (0.92-1.10)	0.821
Height	1.01 (0.97-1.04)	0.566	0.99 (0.98-1.01)	0.619
BMI	1.03 (0.93-1.14)	0.490	1.03 (0.99-1.08)	0.073
GJH	1.69 (0.92-3.09)	0.089	1.12 (0.79-1.59)	0.517
Previous knee injury	1.38 (0.86-2.22)	0.179	**1.78 (1.37-2.33)**	**0.001**
Extrinsic factors				
Sport participation	1.02 (0.87-1.21)	0.746	0.96 (0.89-1.04)	0.368
Sports type				
Soccer	1.14 (0.54-2.40)	0.723	**1.64 (1.12-2.39)**	**0.010**
Handball	1.32 (0.56-3.11)	0.523	**1.95 (1.31-2.92)**	**0.001**
Basketball	0.96 (0.19-4.83)	0.965	**2.07 (1.10-3.90)**	**0.023**
Volleyball	2.01 (0.41-9.79)	0.379	0.69 (0.25-1.87)	0.472
Rhythmic gymnastics	0.64 (0.09-4.38)	0.657	**1.98 (1.04-3.76)**	**0.035**
Tumbling gymnastics	**2.14 (1.01-4.57)**	**0.047**	**1.74 (1.02-2.94)**	**0.039**
Swimming	0.72 (0.08-6.13)	0.770	1.03 (0.60-1.75)	0.907
Horse riding	-	-	0.90 (0.47-1.72)	0.769
Dancing	1.27 (0.34-4.79)	0.716	1.08 (0.56-2.07)	0.810

BMI: Body Mass Index, GJH: Generalised Joint Hypermobility

Paper III

Epidemiology of knee injuries in children with Generalised Joint Hypermobility

During 63 weeks, totally 15 knee injuries were recorded in children with a constant status of GJH. The traumatic knee injuries in the GJH group corresponded to 5% of all traumatic knee injuries in the cohort. The ratio of traumatic to overuse knee injury was 1:3, while in the group with GJH and simultaneous knee hypermobility, the ratio was 1:2 for traumatic to overuse knee injury.

In paper II, with a study period of 143 weeks, traumatic knee injuries for children with GJH corresponded to 14% of all traumatic knee injuries. These knee injuries were reported from children participating in soccer (n=8), swimming (n=3), tumbling gymnastics (n=2) and handball (n=1) and no sport (n=6).

The most frequent knee injuries seen in the GJH group were similar to controls as described in paper II.

Generalised Joint Hypermobility as a risk factor for knee injuries in children

No associations were found between GJH and the total amount or type of knee injuries, whether traumatic or overuse knee injuries, nor when stratifying GJH with knee hypermobility or taking into account fluctuation of BT with one point.

Paper IV

There was no difference between groups in performance of the SLHD test. Furthermore, no between-group differences were seen for isometric muscle strength in ankle plantar flexion, knee extension or knee flexion. Similarly, no group differences were found for isometric strength ratios of KF/KE or PF/KE.

Before landing, children with GJH activated ST significantly less than controls, corresponding to 33% lower activity. GM was activated significantly more before landing for children with GJH than controls, corresponding to 32% higher activity. After landing, children with GJH activated ST significantly less than controls, corresponding to 36% lower activity (Table 5).

For time of onset prior to landing, there was a borderline significance for children with GJH to activate ST 31% earlier and a borderline significance for activating VM 13% later than controls. There was no group difference in time of onset after landing (Table 5).

A significantly higher CCI for children with GJH than for controls was observed before landing for the lateral knee muscle group of Quadriceps-Gastrocnemius (VL-GL), corresponding to a 39% higher CCI. There was no group difference in any other CCI: cumulative Hamstring/Quadriceps (H/Q,), Quadriceps-Hamstring (VL-BF, VM-ST), Quadriceps-Gastrocnemius (VM-GM), Hamstring-Gastrocnemius (ST-GM, BF-GL) (Table 5).

Table 5: Electromyography measurements of six knee muscles for children with Generalised Joint Hypermobility (GJH) and controls**.** Values are mean with 95% confidence intervals. Significant p-values, $p<0.05$, are in bold. (GJH, n= 25 and controls, n=29). Vastus Medialis (VM), Vastus Lateralis (VL), Gastrocnemius Medialis (GM), Gastrocnemius Lateralis (GL), Biceps Femoris (BF), Semitendinosus (ST).

	Group		
	GJH	**Controls**	***p*-value**
Pre activation (%MVE)[a]			
VM	28.6 (22.2-34.9)	26.7 (20.7-32.8)	0.68
VL	25.83 (19.8-31.7)	28.57 (22.9-34.1)	0.50
GM	32.52 (26.5-38.5)	22.17 (16.5-27.8)	**0.01**
GL	25.56 (19.2-31.8)	28.67 (22.7-34.6)	0.47
BF	26.64 (20.1-33.2)	26.55 (20.4-32.6)	0.98
ST	21.64 (15.4-27.8)	32.29 (26.3-38.2)	**0.01**
Post activation (%MVE)[b]			
VM	27.03 (20.7-33.3)	24.04 (18.1-29.9)	0.49
VL	27.69 (21.4-33.9)	23.55 (17.6-29.4)	0.16
GM	26.09 (19.6-32.4)	25.18 (19.1-31.3)	0.84
GL	27.61 (21.3-33.8)	24.01 (18.1-30.0)	0.41
BF	24.75 (18.5-30.9)	26.34 (20.3-32.3)	0.71
ST	18.71 (13.1-24.2)	29.31 (23.8-34.7)	**0.01**
Time of onset relative to landing (ms)			
VM	-.13 (-.14; -.11)	-.15 (-.16; -.13)	0.06
VL	-.11 (-.13; -.10)	-.13 (-.14; -.11)	0.20
GM	-.12 (-.13; -.11)	-.12 (-.13; -.11)	0.24
GL	-.12 (-.13; -.11)	-. 12 (-.13; -.11)	0.38
BF	-.15 (-.16; -.15)	-.15 (-.16; -.14)	0.70
ST	-.16 (-.17; -.14)	-.11 (-.15; -.13)	0.06

[a] 100 ms before landing

[b] 50 ms after landing

Discussion

Main findings

This thesis is based on the results of four studies (papers I-IV), studying the extent of knee injuries and risk factors for these injuries in school children, with special emphasis on children with GJH.

Growth-related overuse knee injuries were the most frequent injury type with an increased risk for girls, previous knee injury and for children participating in the most popular sports in Denmark. Surprisingly, only tumbling gymnastics was a risk factor for traumatic knee injuries. Participation in sports above two times/week increased the risk of both types of injury. (Paper II).

BT for hypermobility had a moderate to substantial inter-tester reproducibility, and was applied as a method for classification of GJH and knee hypermobility (Paper I).

Remarkably, a fluctuation of the individual child´s status of GJH was observed between test rounds. No difference in injury type or risk for knee injuries was found in children with GJH compared to children not classified as GJH, nor if the variability of GJH was taking into account (Paper III).

Nevertheless, children with GJH had a different knee joint neuromuscular strategy than controls before and after landing from the SLHD test, although no difference in jump length was found between groups. Generally, ST was activated less in children with GJH than in controls, both before and after landing from the SLHD test. At the same time, an increased activation of GM and a larger CCI of the lateral knee muscle group (VL-GL) was seen for the GJH group before landing, while no increased GM activity was seen after landing. Reduced pre and post-activation of the ST may present a risk factor for future traumatic knee injuries in participants with GJH and knee hypermobility (Paper IV).

Epidemiology of knee injuries in children

Totally, 952 knee injuries were diagnosed through 143 weeks; hereby 15% (146) traumatic knee injuries and 85% (806) overuse knee injuries. Traumatic knee injuries consisted mainly of sprains and contusions, while the most frequent overuse knee injuries were traction apophysitis (Mb. Sinding-Larsen-Johansson, Mb. Osgood-Schlatter).

Incidence rates for overuse knee injuries were 5.4/1000 sport participations, ranging highest in children participating in handball and lowest in children horseback riding, which must be considered characteristic, taking into account the high loads and the repetitive contractions of the quadriceps muscle in handball, implying traction of the apophysis. Comparison of incidence rates to other studies is complicated by the small number of available studies on epidemiology of overuse knee injuries in children, with divergences in age and reporting methods. With the current cohort representing 6-12 year olds, a comparable overuse incidence rate for the lower extremities of 3.7/1000 athletic exposures was found, although the latter definition comprised both physical education exposures and participation in organised sport, being slightly different from the definition of sport participation used in the current thesis (88). In a sports clinic setting, 54% of injuries registered were lower extremity overuse injuries, mainly apophyseal injuries (106), similar to this thesis. Few studies are reporting overuse injuries in children, none specific for the knee, why this thesis contributes with new knowledge to this area of sports medicine.

As expected, the growth-related overuse knee injury diagnoses comprised more than half of the overuse injuries in this cohort of maturing children. Until recently, there has been a lack of epidemiological studies of overuse injures, including growth-related injuries, and their representation in the full picture of injuries in children. In the current thesis, overuse knee injuries were reported more than fivefold to traumatic injury, confirming the phenomenon of traumatic injuries being only the ´tip of the iceberg´ in children and adolescents (28, 36, 88, 107). A growing concern has been raised to this issue, as an increasing number of children are reported to have musculoskeletal injuries related to sport and physical activity (12, 108-110).

Reasons for the high number of overuse injuries in the current thesis may be due to the frequent and fine-meshed survey for injury reporting and hence registration of overuse knee injuries. The injury was registered, as it caused pain or complaints for the single child, but the actual consequences caused by the injury is not known. Still, this large cohort study provides a broad insight into the extent of overuse knee injuries in school-aged children, representative for the background population.

Growth-related overuse knee injuries are self-limiting by nature, and the implying pain and complaints can most often be reduced by a reduction in participation in sports and physical activity (111). Concerns regarding apophyseal injuries are, that the tolerance limits of the apophysis may be exceeded by the mechanical stress or by the repetitive physical loading required in sports such as soccer, gymnastics and running (25), in worst case leading to an avulsion injury (111), of which none was found in the current cohort.

The traumatic knee injury diagnoses, being mainly sprains and contusions, is similar to other school-based studies (19, 24), reports from hospital emergency departments or sports clinics (20, 21, 50), or across paediatric sports (18). Only a small number of severe traumatic knee injuries - in regards to public health costs – was registered through the study period, e.g. three ACL injuries. In reports from the Danish Knee Ligament Reconstruction Register, the peak incidence of ACL injuries is seen in girls at 15-19 years and boys 20-24 years (112), similar to international reporting of the main population at risk being 15-39 years (113, 114). Consequently, an increasing number of this diagnosis is expected, as the current cohort matures, undergoing anatomical, hormonal and neuromuscular changes, spending more time in specialised sports with increasing demands (113).

The incidence rate for traumatic knee injuries of 0.8/1000 sport participations is comparable to similar school-based studies (7, 46). Rates were highest in high-load and high-speed sports as tumbling gymnastics and handball and lowest in low-impact sports as rhythmic gymnastics and swimming, consistent with findings of others (22, 115). Incidence rates vary considerably in adolescent sport-specific studies, ranging from 2.38 to 142.86 traumatic injuries/1000 participation hours (22) and may be greatly influenced by the study design, population, culture, definition of injury and unit for time-at-risk preferred (7, 46), why comparison of results of this thesis to others may be difficult. The CHAMPS-Study DK is representative for Danish school children participating in the most popular and easiest accessible sports in Denmark being soccer, handball, gymnastics and swimming (83).

Risk factors for traumatic knee injuries in children

In this thesis, diverse intrinsic and extrinsic risk factors for knee injuries in children were studied in a prospective cohort design, including multiple assessments and observations throughout the study period, in an attempt to account for a potential risk factor change over time within a dynamic system (38, 72). Knee injuries have multi-factorial intrinsic and extrinsic origins interacting with an inciting event for traumatic injuries to occur or for overuse injuries to accumulate, but just as important in injury prevention is the division into modifiable and non-modifiable factors, both central when recognizing and accounting for characteristics in participants at risk.

Remarkably, no significant intrinsic risk factors for traumatic knee injuries were found in the present cohort of school children. This is opposing to other studies finding intrinsic risk factors as sex, age, growth and previous injury to increase the risk for lower extremity injuries (22), but registered in sport-specific populations. Identifying intrinsic risk factors in a dynamic, changing system as human beings may comprise challenges, especially in a cohort of maturing children becoming taller, heavier, developing and fine-tuning motor and technical skills, also in sport, during a relative short time span. These challenges may explain the inconsistent findings of this thesis and other studies and may question the validity of identifying intrinsic risk factors in maturing children in general. Also, the risk of type 1 error must be taken into account when testing multiple variables.

Sex was not a risk factor for traumatic knee injuries, similar to other school children cohort studies (7, 88, 116) but in contrast to other studies including an older age group, primarily diagnose specific or sports-specific studies (19, 22). Age was not recognised as a risk factor in this thesis either, similar to another school-based study (116), but in contrast to sports-specific studies, with adolescents above 13 years having a higher risk of lower extremity injuries than younger children (22, 41). The current school child cohort had a mean age of 11 years, plausibly explaining some of the differences to other studies of older age groups, as adolescents above 13 have started or reached puberty with the implying physical and physiological changes, affecting the injury risk (22).

No effect of height or BMI was found for the risk of traumatic knee injuries, in contrast to others finding a positive association (53, 117). It seems as conflicting evidence exists regarding anthropometric measurements and the risk of lower extremity injury (22) plausibly explained by the different injury types and physical demands for the specific sport.

Also, no association to previous knee injury for a subsequent (multiple or recurrent) traumatic knee injury was found, contrary to others (18, 22, 116, 118). Discrepancies may be due to differences in injury definition and methodological differences, including statistical considerations. Both previous traumatic and overuse knee injuries were included in the analyses for a subsequent traumatic knee injury, although aetiology and mechanisms of these injury types differ (17).

Remarkably, the only significant extrinsic risk factor for traumatic knee injuries was children participating in tumbling gymnastics, a term covering tumbling, power tumbling and TeamGym. Gymnastics is among the top three most popular sports in Denmark (45), with TeamGym being a relative new, but growing competition team sport, originated in Scandinavia, including three disciplines as floor exercise routine, tumbling on Trampette (mini trampoline) and on a fiber track. Team Gym and power tumbling demand intrinsic factors of force, power and motor control skills to make the body move fast and powerful in three planes on and off the ground, landing with high speed and high impact on different surfaces (119). These intrinsic and extrinsic demands may be critical for a maturing child if the skill level of the individual participant is not taken into consideration, potentially leading to an inciting event. Knee injuries are recognised as one of the most frequent injuries in paediatric gymnastics including tumbling (119-121), with special emphasis on the landing phase, as this phase seems critical to traumatic injuries (119). Items characterising tumbling gymnastics include amount and frequency of training and competition, trainers recognizing and distinguishing participants skill-level, education of trainers, rules, regulations and equipment as tumbling and landing surfaces, all being modifiable factors.

Surprisingly, children participating in popular sports as soccer and handball did not have a higher risk for traumatic knee injury, despite the multiple tackling, jumping, landing and pivoting situations as well as player-to-player contact situations. A higher proportion of boys participated in these sports, but as the current cohort represented a mean age of 11, the majority of boys were pre pubertal. Pre-pubertal boys are not presenting the same physical and physiological changes of maturation as older boys, being faster, stronger, heavier and generate more force on contact, which may lead to higher injury risk (18, 22, 47).

In the multi-variate analyses, increased amount of sport participation did not comprise a risk factor for traumatic knee injuries in general, but in the bi-variate analyses; higher odds were found for children participating in soccer and handball four times per week. In other large school-child surveys, the risk of injury was found to increase with more exposure time (122, 123), in contrast to a large school study of 9-12 year olds with self-reported sport participation level, reporting a decline in overall injury risk with increasing exposure (46). The effect of increased sport participation on traumatic knee injuries in school-aged children is to be considered inconclusive due to inconsistencies in study design, population and methodological differences, and is most likely depending on the age studied, and the definitions of sports type and sport participation applied.

For children participating in tumbling gymnastics twice or more per week, the odds of having a traumatic knee injury were remarkably three times higher than for children not participating in sports. This increase could plausibly be explained by more time spent during the sport meaning more exposure to injuries, or by children participating more times a week having a high competitive level, with more intensive training, tumbling skills and demands.

Summative, no significant intrinsic risk factors for traumatic injuries were found. The only extrinsic risk factors for traumatic injuries were children participating in tumbling gymnastics, as well as sport participation more than two times a week for popular sports.

Risk factors for overuse knee injuries in children

Girls were more at risk for overuse knee injuries than boys, in line with age matched studies (7, 46, 116, 124), but in contrast to a study of school children below 12 years of age (88). In the current thesis, most girls (primarily 11-13 years) had reached puberty with the implying physical and physiological changes, thereby being more exposed to growth-related overuse knee injuries (106). Although sex is a non-modifiable factor, knowledge of this risk factor may be accounted for in training programmes, modifying other factors influencing girls at risk for overuse injuries, e.g. decreasing the amount and frequency of training and minimizing stressful exercises for the quadriceps muscle.

An association with a large effect of previous knee injury for a subsequent (multiple or recurrent) overuse knee injury was found, as reported previously (18, 22, 116, 118). In this thesis, both previous traumatic and overuse knee injuries were included as one variable for analyses, hypothetically being expressions of inborn frailty with respect to the intrinsic factors for the single child, limited tissue healing, exposure to similar extrinsic factors or combinations thereof (118). Still, association does not prove causality (39), and results may be confounded by the maturing cohort, as the most frequent injury diagnose, apophyseal injuries, are known to be strongly associated with growth (111). Evaluating the complex issues associated with classifying and analysing injuries as recurrent, re-injury, exacerbations or new overuse lies outside the scope of this thesis (28, 118).

Higher odds for overuse knee injuries, primarily growth-related injuries, was seen for children participating in soccer, handball, basketball, tumbling gymnastics, and for sport participation more than two times a week for children participating in soccer, handball and both tumbling and rhythmic gymnastics. Increased sports participation may have some negative drawbacks for growth-related knee injuries, still, the relative low severity and the self-limiting nature of most of these injuries (125) must be taken into consideration, balanced by the many positive effects of sport and physical activity for children (126-128). Nevertheless, the amount and frequency of training can be modified and must be appropriate for the maturing child, recognizing that although repetition is important, it may induce harm such as injuries or burnout (31).

Summative, risk factors for overuse knee injuries were being a girl, previous knee injury and children participating in the most popular sports and sports participation more than two times a week.

Generalised Joint Hypermobility as a risk factor for knee injuries in children

The relative amount of traumatic knee injuries for children with GJH corresponded to 14% of all traumatic knee injuries in paper II, in contrast to paper III with 5% of all traumatic knee injuries in the GJH group. Paper II included a longer study period, following the oldest children in the cohort one year longer than paper III, until the age of 15 years (9th grade). The increase in the relative amount of traumatic knee injuries in GJH in paper II could plausibly be explained by a longer data collection period, and by older and more mature children being more exposed to traumatic knee injuries, as seen in other populations (22).

No significant association between GJH and knee injuries was found. In paper II, GJH was only borderline significant as risk factor for traumatic injuries, evaluated during 123 weeks in a large cohort. In paper III, during 63 weeks, children with a constant status of GJH with or without knee hypermobility in both test rounds were not at higher risk for traumatic or overuse knee injuries. Although the estimates did point in the same direction for GJH with/without knee hypermobility, indicating higher odds for traumatic injuries, results were not significant. The odds ratios found in paper II for GJH with knee hypermobility and traumatic knee injuries (OR 1.7, CI 0.9-3.1) are presented in Figure 6 as Junge et al, 2015 (II), as well as the odds ratios for GJH and traumatic knee injuries (OR 2.2, CI 0.6-8.2) found in paper III, presented in Figure 6 as Junge et al, 2015 (III). When taking into account the variability of BT by one point between test rounds, the odds ratios were still non-significant. For traumatic knee injuries for GJH OR was 1.45 (0.40-1.44) and for the group with GJH and knee hypermobility OR was 2.18 (0.63-7.52) (Paper III), not presented in Figure 6.

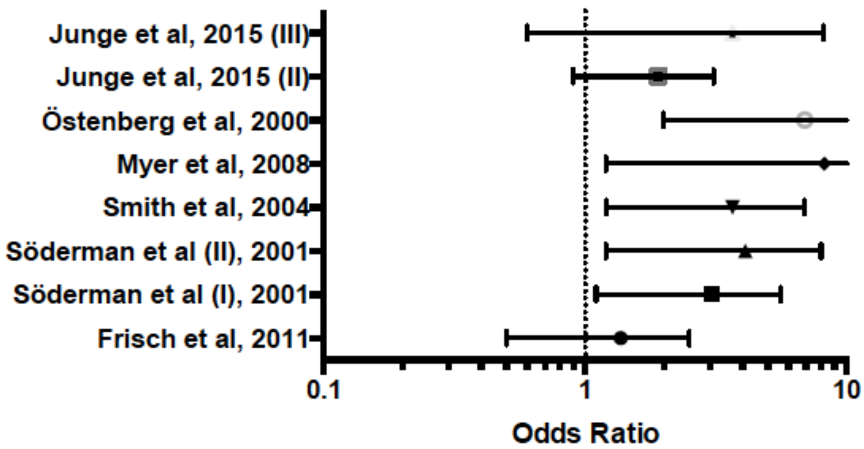

Figure 6. Odds ratios presented with CI for knee or lower extremity injuries in children and adolescents with Generalised Joint Hypermobility or knee hypermobility, including studies from the present thesis.

Odds ratios in Figure 6 are presenting sports-specific studies mainly including older adolescents, differing from the studies of this thesis, although a similar, but non-significant pattern was observed towards higher odds for knee injuries in children and adolescents with GJH. Sports-specific studies and studies of older adolescents, especially with female participants, may differ from the present study by typically revealing both a higher number of traumatic knee injuries, as participants are more exposed to high-risk injury situations like landing, pivoting and side-cutting (67, 70, 71, 89), still depending on the population studied, the study design and the data collection methods.

In the current cohort, no difference in injury risk was found in children in GJH compared to children not having GJH. An inborn frailty may be present in the current cohort of children with GJH, potentially triggered, as the children gets older and become more exposed to injuries when specializing in sports, as found in other sports-specific studies of participants with GJH or knee hypermobility (67, 69-71).

Knee joint neuromuscular control in children with Generalised Joint Hypermobility

A supplement to the epidemiological model of injury risk is the biomechanical model, making it possible to study mechanisms of plausible knee injury situations; in this thesis by assessing load characteristics and knee joint neuromuscular control measured by EMG in children with GJH during landing in a single-legged hop.

Generally, ST was activated less in a subgroup of children with GJH, being mainly girls, than in controls, both before and after landing from the SLHD test in the sagittal plane. Altered knee joint neuromuscular activation was seen for the GJH group, although this group had an efficient compensatory strategy in the SLHD test, with performance outcome being similar to controls. Decreased hamstring activity compared to quadriceps activation is in several studies suggested to predispose to ACL injuries (113), and especially ST in its function as a proprioceptive muscle seems important to knee joint stability and medial knee joint compression (129). During side cutting in the horizontal plane, female elite soccer and handball players (19-29 years, GJH or knee laxity not examined) displaying reduced EMG pre-activity of the ST were at increased risk of future non-contact ACL rupture (129). Lower ST pre-activation may imply lower ST contraction force during impact or on initial part of the ground contact (130), thereby increasing the load on the ACL and the risk of injury. Non-contact ACL injury situations range from 17 to 50 ms after initial ground contact (131), leaving no time for reflective or voluntary adjusting muscular activation to prevent injury, indicating the importance of adequate pre-activation programming (75).

For individuals with GJH and/or knee laxity, altered knee joint neuromuscular control may affect the load characteristics of the knee joint negatively during landing, which could be a plausibly underlying mechanism for traumatic knee injuries for this group, as seen in several sport-specific studies (67, 70, 71, 85, 86, 132-134). No studies have evaluated knee joint neuromuscular control in children with GJH during a dynamic performance test, but the altered knee joint neuromuscular strategy found in this thesis has similarities to other studies of children with GJH, demonstrating increased knee joint co-activation and reduced hamstring muscle activity in static balance tests or submaximal isometric contractions (78-80).

GM may potentially be a part of a compensatory strategy for the reduced passive joint stability in GJH, as seen in female basketball players (18-21 years) with knee joint laxity, demonstrating increased muscle pre-activity in GM and BF following a lower extremity perturbation (135). Still, the function of the Gastrocnemii on the knee joint in weight-bearing, high-load functional tasks, such as landing from a single leg jump, is inconclusive. In vitro studies indicate the Gastrocnemii muscles to act as antagonist to the ACL, as Gastrocnemii force causes Posterior Femoral Translation (PFT) relative to the tibia and hence strain the ACL (136, 137). Conversely, in vivo studies suggests increased Gastrocnemius forces to compensate for decreased hamstrings forces during the weight-acceptance phase of single leg jump landing (138), indicating a compensatory or agonist function to the ACL, similar to findings and hypothesis of the current study. However, the effect of the Gastrocnemii on the PFT is questioned, as a low moment of force of the Gastrocnemii was found at peak ground reaction force during single leg jump landing in male adults (139, 140). With large Gastrocnemius forces present, the knee joint reaction force will increase, which potentially could increase anteriorly directed tibia forces and consequently ACL loading (139).

The effect of the lower ST and higher GM activity for the GJH group in relation to knee injuries needs to be evaluated in future studies of older adolescents in sports specific studies, as this age group, especially exposed to injury risk situations as landing and side-cutting seems to have a potential underlying mechanism for traumatic knee injuries.

Along with the lower ST pre-activation and the higher GM pre-activation, the higher lateral CCI pre activity could hypothetically be a biomechanical strategy to distribute compression forces of the joint equally, in order to control sagittal and horizontal movements and to provide the limb with dynamic stability (75, 141, 142).

Although no increased risk for knee injuries was found for GJH in the current cohort, participants with GJH and/or knee hypermobility may be at risk for future traumatic knee injuries due to decreased passive knee stability and an altered knee joint neuromuscular activation during landing, plausibly mediated by other intrinsic risk factors as maturation, extrinsic risk factors as well as inciting events.

Methodological considerations

Participants

Though no association between GJH and knee injuries was found in the current cohort, there are some issues to be considered and interpreted with results. In paper II, the status of GJH from baseline was fixed in time one year ahead for injury risk and the actual status of GJH was associated to the occurring knee injury within that year, and likewise for the follow-up measurements. Analysing GJH as a static condition related to knee injuries is common in retrospective or prospective cohort studies of children and adolescents (70-72, 143), and in cross-sectional studies using the actual status of GJH, but often with retrospective questionnaires (69). Remarkably, a fluctuation of the single child's status of GJH was observed in a large proportion of children with GJH between test rounds, with either increasing or decreasing BT score. Therefore, the study population for analyses in paper III were only children classified with a status of constant GJH at both test rounds, totally 36 of 999 children. Hence, the corresponding number of knee injuries for the GJH group was low, especially for traumatic injuries, why the risk of type 2 error must be considered. Supplemental analyses of knee injuries for children with fluctuating BT were accomplished, also presenting no differences between groups.

Fluctuation in status of GJH in a child cohort has never been reported and discussed before. Other longitudinal, school-based cohort studies have not specifically reported the tracking of status of GJH for each child in the cohort, but in one study, only 1% (n=18) of the children who had both lower limb pain at baseline and were classified with GJH at cut-point ≥6/9 at baseline, had a constant status of GJH at follow-ups (61). Possible bias must be considered, when analysing status of GJH in retrospective or prospective cohort studies, including the current results of paper II, if a fluctuation of the actual status of GJH in maturing children, as found in paper III, is confirmed in other studies of GJH in relation to knee injuries.

The fluctuation in status of GJH for the single child could be affected by factors as growth and particularly growth spurt. During rapid growth phases, lengthening of bones occurs before muscles and tendons can stretch correspondingly (111), which may imply changes in joint mobility status. In the current study, the vast majority of the children was affected by growth, with boys aged 13 having the largest increase in height between test rounds (mean 8 cm, maximum 15 cm). For girls, the 11 year-olds had the largest increase of height (mean 7 cm, maximum 13 cm). Correspondingly, the prevalence of GJH for boys aged 13 was distinctly lower than for boys aged 12 at both test rounds, meaning that during growth, boys seems to have a decrease of mobility, similar to other studies (63, 144), but in contrast to one study (145). The reverse was seen in girls aged 11 at both test times, with prevalence of GJH increasing at the age of 12, similar to another study with increasing prevalence of GJH at a mean age of 12.7 years (145).

The increasing prevalence of GJH seen in girls could be explained by higher levels of relaxin due to maturation, why girls at the age of 9-14 years as in the current study may conquer or maintain a status of GJH. Relaxin may, modulated with oestrogen, have some involvement of joint mobility, as it is reported to affect the collagen synthesis, plausibly altering the properties of cartilage and tendons (146-148). Tendon stiffness is assumed to be reduced through activation of collagenase in some tendons (148), and similarly, relaxin may alter ligament mechanics (146). An increase in relaxin concentration was found to correlate with joint laxity in some studies (147, 149), but not in other studies (150, 151). Still, the mediating effect of GJH, knee joint laxity and relaxin levels in relation to knee injuries, e.g. ACL injuries, is not established (113).

A higher prevalence of girls with GJH than boys with GJH were seen in all studies, representing the general gender difference of prevalence of GJH, but possibly hampering generalizability. Interpretation of the association of GJH and knee injuries as well as the altered knee joint neuromuscular control may therefore be addressed girls.

Using a moderate to substantial reproducible method for the BT, and analysing both with and without taking fluctuations of GJH into consideration in the cohort, has provided new knowledge about potential fluctuations of GJH over time for the individual child.

Cross-sectional measurements

Beighton Tests

Fluctuation in the status of GJH may also be affected by the inter-tester reproducibility of BT. The BT was found to be moderate reproducible (κ 0.64) for this child population and comparable to the BT when performed a slightly different way, with no difference in the prevalence of GJH at cut-point ≥5/9 between methods. The reproducibility of the total BT score is especially affected by tests not having clearly described and therefore not easily identified starting positions and clear endpoints. This can be the case with the knee and elbow tests, as a judgment of knee or elbow hyperextension being ≥10 degrees by eye seems quite challenging, as described previously (105, 152). For the BT method applied to the current thesis, a substantial reproducibility was found for the knees (κ 0.62).

Besides high reproducibility, a clinical test must demonstrate good validity. The concurrent validity of BT for knee hypermobility is unknown due to a lack of ´golden standard´, but clinical measures of knee hypermobility and more objectively measures of knee joint laxity seem to correlate in both adolescents and adults (144, 153). Knee hyperextension as examined with the BT is measured during a state of active laxity, with gravity and muscle activity affecting joint motion, whereas knee joint laxity often is measured as passive knee joint anterior/posterior translation under a known applied load (154). In adults, GJH with simultaneous knee joint laxity was observed more frequently in ACL-injured persons (66), and correspondingly, GJH and knee joint laxity increased the risk of adult ACL injuries by 2.8 and 2.6 times, respectively (153). In line with this, the children with GJH in the current study were stratified into groups with/without knee hypermobility, with a higher traumatic to overuse knee injury ratio for those with knee hypermobility in addition to GJH, but still, no significant association between knee injury and GJH with/without knee hypermobility was found. GJH was classified by a relatively high cut-point of at least 5/9 BT points, but a requirement of also having to have simultaneous knee hypermobility may have a stronger association to knee injuries than GJH only, as indicated in other studies (66, 70, 71, 153). This hypothesis requires confirmation in future studies, but may explain why no association was found between knee injuries and GJH at lower cut-points not focusing on knee hypermobility in other studies (68, 155).

For the BT applied in the current thesis, the overall agreement of the total BT score was 88%, indicating a measurement error of 12%, which is acceptable for clinical agreement. However, the positive predictive value (PPV) of BT in adults is suggested to be as low as 21 to 36%, with a prevalence of 2-4% and sensitivity and specificity of the BT criteria of 93% (59). A low PPV questions the accuracy of the test in defining a condition. This means that classifying GJH positively may be a dilemma when examining the general population (59). Therefore, low prevalence of GJH at cut point ≥5/9 must be taken into consideration, as PPV is directly proportional to the prevalence of the condition (156). The present prevalence of GJH varied from 9-13% during the study period, affecting the PPV, which is unknown in a child population. A low PPV may bias the results of this thesis, questioning the classification of GJH.

Age and anthropometrics

In the analyses, the single child's age and anthropometric data of height and BMI from the baseline tests was assigned one year forward and associated to the relating traumatic or overuse knee injury within that year, with the same procedure for the follow-up test rounds. Although common, using chronologic age as a one-year fixed exposure variable does not account for the substantial variation in biologic age during maturation, potentially influencing the injury profile during childhood and adolescence (51).
Also, intrinsic factors as growth and particularly, growth spurt may be preferred when evaluating the maturing child's risk for knee injuries. Frequent measurements of height and weight every three months may therefore be implemented in future studies to capture the growth spurt phase and weight changes over time specifically (157, 158).

Electromyography

Supplying epidemiological measures for injury risk factors with a biomechanical study involving EMG measures of knee joint neuromuscular control can reveal more knowledge of movement strategies in children with and without GJH, thereby revealing potential underlying injury mechanisms.

The EMG analysis has some drawbacks to consider when interpreting results, as the amplitude may vary between electrode sites, individuals and also day-to-day measures of the same muscle site (159). EMG signals can be influenced by several external factors altering its shape and characteristic, as tissue characteristics, physiological cross talk, changes in the geometry between muscle belly and electrode site, external noise electrode and amplifiers (159). Nevertheless, the present method of normalizing EMG amplitude during landing to the MVC of a reference contraction may overcome these uncertainties, providing an estimation of the neuromuscular effort during the task completed (159).

In this thesis, a Co-Contraction Index (CCI) was applied, instead of a classical co-activation ratio as described by Winther et al. (160). However, the premise for the latter method, is a clear biomechanically based definition on which muscles act as antagonist and agonist in a certain time range of a standardised task. It is calculated as (antagonist EMG_{RMS} x agonist EMG_{RMS}^{-1}) x 100 (%), using for the antagonist EMG a mean of the 2 antagonist muscles, and for the agonist EMG a mean of the two agonist muscles. Preferences were made for the CCI, calculated as the ratio of co-contracting muscle activation multiplied by the instantaneous summed muscle activity (CCI=EMG activity %MVEmin/%MVEmax)* (%MVEmin +

%MVEmax)).

This decision was taken since the premise for the co-activation ratio i.e. that the agonist and antagonist can be clearly defined over time, is not fulfilled in a functional task as the SLHD test. In contrast, CCI can be used even though it is not possible to clearly define agonist and antagonist function in the SLHD test (101). It may be a further strength of the method that it includes a multiplication of a factor giving more weight to periods with large activity compared to periods with a smaller activity. This is the explanation for multiplying with the sum of min and max, as this provides a weighted ratio. Furthermore, it was feasible to use the present calculation of CCI, since it gives the opportunity to compare the results with previous studies of similar populations and using the same method of calculating CCI (79, 80).

Only surface EMG was measured, which limits the available muscles to those lying superficially. Since both mono-articular as well as bi-articular muscles are working in close cooperation to move and stabilise the knee joint, this limitation presents a challenge for interpretation. However, in the functional task studied there was no possibility to fix the ankle/hip joint of the bi-articular muscles to isolate the effect to be mono-articular. The present muscle groups included for the CCI calculation are similar to other studies of knee muscle co-activation (138, 140, 161). Since the primary aim was to study possible differences between GJH and controls in total knee joint loading, and since the analyses were performed in a uniform way for both GJH and controls, there is no reason to suspect a bias in the results for GJH.

Longitudinal measurements

SMS survey

Knee injuries

In the current thesis, a relatively large sample size was followed in a longitudinal, prospective cohort study design, providing the possibility for frequent measurements in a group of maturing children with a changing injury risk profile.

SMS survey as a method for injury registration has proven to minimize recall bias, providing a solid basis for collecting information of weekly pain or complaints (88, 89). The frequent data collection plausibly made it easier for children and their parents to recall and report more accurate information of pain or injuries. Bias of SMS surveys as method is eventually an over reporting of pain by some families and under reporting of pain by other families, but with an average response rate of 97% every week, data are assumed to be representative of a normal children population. So far, weekly SMS survey has proven to be valid, reliable, feasible, and user-friendly, with high compliance rates, capturing more overuse injuries than standard injury surveillance methods (88, 89, 162). The SMS survey of pain was further verified by the clinical examinations, limiting bias.

The knee injuries were categorised as traumatic or overuse, using an internationally accepted definition of injury classification (17). Such injury classification definition allows for registration of knee injuries not resulting in absence from school or sports, or injuries not requiring medical treatment, which is assumed not to lead to an underestimation of the actual number of overuse injuries. Although injury types and severity of injuries, expressed by ICD-10 diagnoses were presented, data of time loss, clinical outcome and economic cost could have been informative.

Sports participation

Frequent SMS survey may also provide a solid and precise source of information of the weekly number of sports participations, which may change from week to week depending on season, holidays, illness or injuries. Using this method with a high answering rate, children and parents revealed a mean sport participation of 1.7 times per week for this cohort of children participating in numerous sports, in contrast to children's self reported sport participation being 3-4 times a week in 41% of all respondents (response rate 50%), likely influenced by selection bias.

The child and/or parents counted the number of times the child participated in organised sport during a week, but without providing information of the actual hours and/or minutes spent in sports. Often, hourly exposure is preferred for incidence rates, but may also be reported per 1000 athletes exposure, which may be equivalent to sport participations used in this thesis (18). The interpretation and comparison of findings across studies may be restricted, when different units of time-at-risk often are used to calculate incidence rates (18, 23).

Sports type

Reporting weekly participation in specific sports types by SMS survey is advantageous when assessing a child cohort, where it is common that children e.g. are switching between sport and leisure time activities, dropping in and out of sports, participating in handball during winter times and soccer during summer times with overlapping periods (45). The choices of sports types to report was based on the most popular sports in Denmark for children, as described by The Sports Confederation of Denmark (163). Analysing knee injury risk associated to organised sport is providing a picture of the children participating in the specific sports, yet, there is a risk of missing important information of injury risk for children participating in unorganised sport and leisure time activity as e.g. running or fitness, which are becoming increasingly popular activities among children and adolescents (45).

Conclusions

Following a large cohort of school children aged 8-15 years prospectively with frequent measurements has provided new and important knowledge of the extent of knee injuries and intrinsic and extrinsic risk factors for these injuries, with special emphasis on children with GJH and knee hypermobility.

Paper I

The variant of BT for hypermobility applied in this thesis had a moderate to substantial inter-tester reproducibility, and was therefore used for reporting the intrinsic risk factor of GJH and knee hypermobility. No difference in the prevalence of GJH was found in the inter-method comparison study of this variant and a slightly different variant of the BT, why the current method was used in this child population.

Paper II

In the prospective study during 143 weeks, growth-related overuse knee injuries was the main injury type. Incidences for traumatic and overuse knee injuries were 0.8/1000 respectively 5.4/1000 sport participations. For traumatic knee injuries, tumbling gymnastics was an extrinsic risk factor. Intrinsic risk factors for overuse knee injuries were being a girl, previous knee injury and extrinsic factors were children participating in soccer, handball, basketball, rhythmic and tumbling gymnastic. Further extrinsic risk factors for both types of injury were participation in sports above two times/week.

Paper III

Similar frequent knee injury types, being sprains, contusions and apophysitis, was found in GJH and controls. Despite the moderate-substantial inter-tester reproducibility of BT, a large variation between the individuals child´s status of GJH was observed between test rounds. Hence, the number of children with a constant status GJH was low, with no significant increased risk for knee injuries for this group during a period of 63 weeks.

Paper IV

Children with GJH had a different knee neuromuscular strategy than controls before and after landing from the SLHD test, although no difference in jump length was found between groups. Generally, ST was activated less in children with GJH than in controls, both before and after landing from the SLHD test. At the same time, an increased activation of GM and a larger CCI of the lateral knee muscle group (VL-GL) was seen for the GJH group before landing, while no increased GM activity was seen after landing. Reduced pre and post-activation of the ST may present a risk factor for future traumatic knee injuries as in GJH with knee hypermobility.

Clinical implications and perspectives

The results of this thesis indicate that growth-related overuse knee injuries affects a major part of children and adolescents. Although these knee injuries are a self-limiting condition, the short and long term consequences of growth-related overuse knee injuries are not well documented. Considerations of pain level, training programmes, skill levels, frequency of training and the amount of sport participation are suggested for as well the parents, trainers, sports clubs and society. A reduction in activity or sports participation will often reduce the pain by minimizing the traction of the apophyses, with the injured child's sensation of pain must as the main guide during sport and physical activity (111). Still, the many advantages of sport and physical activity as well as the short and long-term consequences of growth-related overuse knee injuries in children must be included in considerations of advices for this condition. Future research should target healing time for knee apophysitis, and determine if this condition is a recurrent problem that could predict future knee problems.

Only tumbling gymnastics was a risk factor for traumatic knee injuries, and with an increasing popularity for this sport in children and adolescents (119), specific attention should be paid to this sport in future injury prevention studies, as the ´number needed to harm´, or the number of children participating in the sport needed to cause 1 injury per 1000 hours of sport participation is only 8, thus making tumbling the most risky sport in childhood, according to this study. Future studies should be performed on power tumbling and Teamgym to establish a pattern of risk for these sports.

GJH was in the present cohort not significantly associated to traumatic or overuse knee injuries, being only borderline to traumatic injuries. On basis of the present results, the clinical relevance of GJH for knee injuries in a general population of children aged 8-15 years is questionable, as when regarding GJH, the number of children with GJH needed to cause 1 injury for every 1000 hours of sport participations was 35. However, knee hypermobility must be assessed in future studies, as only 10 children per 1000 hours of sport participations were needed to cause 1 injury.

It seems as GJH may fluctuate over a relatively short time span, why final classification of GJH may not be clinically stable in the single subject or child until post puberty.

On basis of the present results, no specific advice, recommendations or cautions can be specified in regards to school children with GJH, similar to that reported in another study (164), but further studies are needed in regards to knee hypermobility and specific sports. For older adolescents with GJH participating in specific sports, recommendations may differ from the present results and needs to be studied further.

Due to decreased ST pre- and post-activity during the dynamic performance test SLHD, children or adolescents with GJH and knee hypermobility may present a group with future increased risk for traumatic knee injuries, depending on the interplay with extrinsic risk factors and inciting events. The implications of the findings on resultant functional joint stability for maturing children and adolescents with GJH and knee hypermobility support the need for future research regarding GJH and, especially taking into account our other findings, knee hypermobility as an intrinsic risk factor for knee injuries, following the cohort prospectively. If the current results can be confirmed in other studies, knee injury prevention may include specific ST training for participants with GJH, for those being exposed in high-risk sports as soccer, handball, basketball and tumbling gymnastics.

Clinicians identifying participants at risk for knee injuries often use sports specific tests as the SLHD test as a measure of single-leg performance, but as in the current thesis, these results can be biased, as no difference in performance between groups was seen due to a plausible compensatory strategy in GJH. Complementing clinical tests with neuromuscular screenings of these potential injury risk situations in sports specific studies could help us identify modifiable risk factors and hence target specific muscles and neuromuscular strategies in injury prevention interventions.

Summary

The current thesis aimed at achieving more knowledge of knee injuries and intrinsic and extrinsic risk factors for these injuries in a cohort of school children aged 8-15 years, with special emphasis on children with GJH.

This thesis was based upon four studies, with data obtained from The Childhood Health, Activity and Motor Performance School Study – Denmark. The number of participants in the studies varied from 39 to 1327 children, depending on the study design and purposes.

1. Study I evaluated the inter-tester reproducibility and inter-method agreement of BT for hypermobility
2. Study II reported the distribution and incidence of traumatic and overuse knee injuries and potential risk factors for these injuries, focusing at the intrinsic factors of sex, age, height, BMI, GJH, previous knee injuries, and the extrinsic factors of amount of organised sport participation and sports type
3. Study III assessed the extent of knee injuries in children with GJH and knee hypermobility and the risk of knee injuries for the GJH group
4. Study IV investigated potential differences in knee joint neuromuscular control in children with GJH compared with controls before and after landing in the Single Leg Hop for distance test

In study I, the variant of BT for hypermobility applied in this thesis had a moderate-substantial inter-tester reproducibility. No difference was found for the prevalence of GJH in the inter-method comparison study of this variant and a slightly different variant of the BT.

The main findings of study II were that growth-related overuse knee injuries was the main injury type. For traumatic knee injuries, tumbling gymnastics was an extrinsic risk factor and GJH was a borderline significant intrinsic risk factors. Intrinsic risk factors for overuse knee injuries were being a girl, previous knee injury and extrinsic factors were children participating in soccer, handball, basketball, rhythmic and tumbling gymnastic. Further extrinsic risk factors for both types of injury were participation in sports above two times/week.

In study III, similar frequent knee injury types were found in GJH and controls. No significant increased risk was found for knee injuries for the GJH group, but a large variation between the individuals child´s status of GJH was observed and included in the analyses between test rounds.

In the last study IV, children with GJH had a different knee neuromuscular strategy than controls before and after landing from the SLHD test, although no difference in jump length was found between groups. Generally, ST was activated less in children with GJH than in controls, both before and after landing from the SLHD test. At the same time, an increased activation of GM and a larger CCI of the lateral knee muscle group (VL-GL) was seen for the GJH group before landing, while no increased GM activity was seen after landing. Reduced pre and post-activation of the ST may present a risk factor for future

traumatic knee injuries in participants with GJH and knee hypermobility.

Dansk resumé

Formålet med denne afhandling var at opnå mere viden om knæskader og interne og eksterne risikofaktorer for disse i en kohorte af 8-15 årige skolebørn, med specielt fokus på børn med GJH.

Afhandlingen er baseret på fire studier baseret på data fra The Childhood Health, Activity and Motor Performance School Study – Denmark. Antallet af deltagere i de forskellige studier varierede fra 39 til 1327 børn, afhængig af studiedesign og formål.

1. Studie I vurderede inter-tester reproducerbarhed og inter-metode overensstemmelse af Beighton Tests (BT) for hypermobilitet.
2. Studie II rapporterede fordelingen og incidencen af traumatiske og overbelastningsknæskader og potentielle risikofaktorer for disse skader, med fokus på indre risikofaktorer som køn, alder, højde, BMI, tidligere knæskader og GJH, samt ydre risikofaktorer som børn, der deltog i bestemte sportsgrene og sportsdeltagelse.
3. Studie III evaluerede udbredelsen af og risikoen for knæskader hos børn med GJH og knæhypermobilitet.
4. Studie IV undersøgte potentielle forskelle i den neuromuskulære kontrol af knæet hos børn med GJH og knæhypermobilitet sammenlignet med en kontrolgruppe, før og efter landing i et et-bens længde hop (SLHD).

I første studie havde variationen af BT, som blev anvendt i denne afhandling, moderat-væsentlig inter-tester reproducerbarhed. Der var ingen forskel i prævalensen af GJH i studiet af inter-metode overensstemmelse mellem den anvendte version af BT og en alternativ version med mindre variationer.

Fundene i det andet studie var, at vækst-relaterede overbelastningsknæskader var den primære skadestype. Børn, der deltog i springgymnastik havde forøget risiko for traumatiske knæskader og GJH var grænsende til signifikant som intern risikofaktor. De interne risikofaktorer for overbelastningsknæskader var det at være en pige, tidligere knæskader og eksterne risikofaktorer var børn, der deltog i fodbold, håndbold, basketball, rytmisk og springgymnastik. Yderligere eksterne risikofaktorer for begge skadestyper var sportsdeltagelse mere end to gange om ugen.

I det tredje studie var det samme knæskadetyper man så hos børn med en konstant status af GJH og kontrolgruppen. Der var ingen signifikant forøget risiko for knæskader for gruppen med GJH, men en stor variation i GJH status blev observeret mellem testrunderne og medtaget i analyserne.

I det sidste studie havde børn med GJH en ændret neuromuskulær kontrol af knæet før og efter landing i SLHD testen, selvom der ikke var forskel på hoplængden mellem grupperne. Generelt var ST aktiveret mindre hos børn med GJH i forhold til kontrolgruppen, både før og efter landing i SLHD testen. Samtidig var der en forøget aktivering af GM og et højere CCI af den laterale knæmuskelgruppe (VL-GL) for gruppen med GJH før landing, mens der ikke

var en forøget GM aktivitet efter landing. Lavere ST pre-og post-aktivitet kan udgøre en mulig risikofaktor for fremtidige traumatiske knæskader hos deltagere med GJH og knæhypermobilitet.

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