



ASHRAF EL-METWALLY

Musculoskeletal Pain in Schoolchildren

Occurrence, prognosis and determinants



ACADEMIC DISSERTATION

To be presented, with the permission of
the Faculty of Medicine of the University of Tampere,
for public discussion in the Auditorium of
Tampere School of Public Health, Medisiinarinkatu 3,
Tampere, on August 14th, 2009, at 12 o'clock.

UNIVERSITY OF TAMPERE

ACADEMIC DISSERTATION
University of Tampere, School of Public Health
The Rheumatism Foundation Hospital, Heinola
Finland

Supervised by
Professor Anssi Auvinen
University of Tampere
Finland
Docent Marja Mikkelsen
University of Turku
Finland

Reviewed by
Professor Jaro Karppinen
University of Oulu
Finland
Docent Päivi Leino-Arjas
University of Tampere
Finland

Distribution
Bookshop TAJU
P.O. Box 617
33014 University of Tampere
Finland

Tel. +358 3 3551 6055
Fax +358 3 3551 7685
taju@uta.fi
www.uta.fi/taju
<http://granum.uta.fi>

Cover design by
Juha Siro

Acta Universitatis Tamperensis 1428
ISBN 978-951-44-7762-1 (print)
ISSN-L 1455-1616
ISSN 1455-1616

Acta Electronica Universitatis Tamperensis 858
ISBN 978-951-44-7763-8 (pdf)
ISSN 1456-954X
<http://acta.uta.fi>

Tampereen Yliopistopaino Oy – Juvenes Print
Tampere 2009

To my family

TABLE OF CONTENTS

	<u>Page</u>
LIST OF ORIGINAL PUBLICATIONS	7
ABBREVIATIONS	8
ABSTRACT	9
TIIVISTELMÄ	12
1. INTRODUCTION.....	15
2. REVIEW OF LITERATURE.....	17
2.1. Pathophysiology of pain.....	17
2.1.1. Peripheral pathways.....	17
2.1.2. Spinal pathways.....	18
2.1.3. Cereberal pathways.....	18
2.1.4. Pathophysiology of chronic widespread pain	19
2.2. Assessment of pain in schoolchildren	20
2.3. Disease-related musculoskeletal pain in schoolchildren	22
2.4. Occurrence of musculoskeletal pain in schoolchildren	24
2.4.1. Prevalence and incidence.....	24
2.4.2. Variation of occurrence estimates with age and sex.....	25
2.5. Burden of childhood musculoskeletal pain.....	32
2.5.1. Burden on the child.....	32
2.5.2. Burden on the family	33
2.5.3. Burden on healthcare services	33
2.6. Risk factors	34
2.6.1. “Any” musculoskeletal pain	34
2.6.2. Lower limb pain.....	35
2.6.3. Widespread pain	36
2.6.4. Back pain	37
2.6.4.1. Evidence from cross-sectional studies.....	37
2.6.4.2. Evidence from prospective studies	38
2.7. Natural course and predictive factors for chronicity	39
3. AIMS OF THE STUDY	41
4. MATERIALS AND METHODS	42
4.1. Study population.....	42
4.2. Research tools.....	44
4.2.1. Class-room administrated questionnaire.....	44
4.2.2. Hypermobility test	46
4.2.3. Shuttle run test	46
4.3. Case definitions of musculoskeletal pain	47
4.4. Statistical methods.....	47
4.4.1. Descriptive measures	47
4.4.2. Estimation of effect sizes and hypothesis testing	48
4.5. Ethics	51
5. RESULTS.....	52
5.1. Occurrence	52
5.1.1. Incidence of “Any” and site-specific musculoskeletal pain	52
5.1.2. Prevalence and physical limitations of lower limb pain	53
5.1.3. Prevalence and incidence of WSP	54
5.2. Risk factors	55

5.2.1. Risk factors of incident “Any” musculoskeletal pain	55
5.2.1.1. Risk factors of incident non-traumatic musculoskeletal pain	55
5.2.1.2. Risk factors of incident traumatic musculoskeletal pain	56
5.2.2. Risk factors of prevalent lower limb pain	57
5.2.3. Risk factors of incident widespread pain	60
5.3. Prognosis and predictive factors for chronicity	62
5.3.1. Prognosis of “Any” musculoskeletal pain	62
5.3.2. Prognosis of lower limb pain	65
5.3.3. Prognosis of widespread pain.....	67
6. DISCUSSION.....	69
6.1. Methodological considerations	69
6.1.1. <u>Participation and follow-up</u>	69
6.1.2. <u>Assessment of musculoskeletal pain</u>	71
6.1.3. <u>Assessment of potential predictors of musculoskeletal pain</u>	72
6.1.3.1. Hypermobility.....	72
6.1.3.2. Physical fitness	73
6.1.3.3. Other symptoms	74
6.1.3.4. Physical activity	75
6.1.3.5. Potential predictive factors not evaluated in this study	75
6.2. Main findings	76
6.2.1. <u>“Any” and site-specific musculoskeletal pain</u>	76
6.2.1.1. Incidence	76
6.2.1.2. Prognosis.....	77
6.2.1.3. Risk factors	78
6.2.1.4. Prognostic factors	79
6.2.2. <u>Lower limb pain</u>	81
6.2.2.1. Prevalence and consequences.....	81
6.2.2.2. Prognosis.....	81
6.2.2.3. Risk factors	82
6.2.2.4. Prognostic factors.....	84
6.2.3. <u>Widespread pain</u>	85
6.2.3.1. Occurrence	85
6.2.3.2. Prognosis.....	85
6.2.3.3. Risk factors	86
6.3. Un-answered questions and future plans	88
6.3.1. Heredity and family history	89
6.3.2. Smoking	90
6.3.3. Overweight/obesity	90
7. SUMMARY AND CONCLUSIONS	92
8. ACKNOWLEDGMENTS.....	94
9. REFERENCES	96
10. APPENDIX: BASELINE QUESTIONNAIRE	112
11. ORIGINAL PUBLICATIONS	115

LIST OF ORIGINAL PUBLICATIONS

1. **EI-Metwally A**, Salminen JJ, Auvinen A, Kautiainen H, and Mikkelsen M (2004). Prognosis of non-specific musculoskeletal pain in preadolescents: A prospective 4-year follow-up study till adolescence. *Pain* 110:550-559.
2. **EI-Metwally A**, Salminen JJ, Auvinen A, Kautiainen H, and Mikkelsen M (2005). Lower limb pain in a preadolescent population, prognosis and risk factors for chronicity: A prospective 1-and 4-year follow-up study. *Pediatrics* 116:673-681.
3. **EI-Metwally A**, Salminen JJ, Auvinen A, Kautiainen H, and Mikkelsen M (2006). Risk factors of traumatic and non-traumatic lower limb pain among preadolescents: a population-based study of Finnish Schoolchildren. *BMC Musculoskeletal Disorders* 7:3.
4. **EI-Metwally A**, Salminen JJ, Auvinen A, Macfarlane GJ, and Mikkelsen M (2007). Risk factors for development of non-specific musculoskeletal pain in preteens and early adolescents: a prospective 1- year follow-up study. *BMC Musculoskeletal Disorders* 8:46.
5. Mikkelsen M, **EI-Metwally A**, Kautiainen H, Auvinen A, Macfarlane GJ, and Salminen JJ (2008). Onset, prognosis and risk factors for widespread pain in schoolchildren. A prospective 4-year follow-up study. *Pain* 138:681-687

ABBREVIATIONS

ACR = American College of Rheumatology

BMI = Body Mass Index

CI = Confidence interval

CNS = Central Nervous System

FM = Fibromyalgia

IASP = International Association for the Study of Pain

LBP = Low back pain

NP = Neck pain

OR = Odds ratio

RR = Risk ratio

SD = Standard deviation

VAS = Visual analogue scale

VO₂ max = Maximal oxygen uptake

WHO = World Health Organisation

WSP = Widespread pain

ABSTRACT

The aim of this study was to increase understanding of the pattern and determinants of the onset and persistence of musculoskeletal pain (MSP) in early adolescence. To achieve this aim, a representative sample of 10–12 years old schoolchildren in the city of Lahti were assessed at three time points: Baseline (T0), 1-year follow-up (T1) and 4-year follow-up (T2). At T0, information was collected on MSP during the previous 3 months in the following locations: Neck, upper limb, chest, lower limb, upper back, lower back and buttock. Additional data were gathered regarding participants' experience of headache, abdominal pain, physical limitations attributed to pain, frequency of physical activity, day-time tiredness, sleeping problems and depressiveness. This information was collected in the class using a structured questionnaire that included a pain manikin and was pre-tested prior to the outset of the study. Children, at T0, were also examined for hypermobility using the Beighton method and for physical fitness using the shuttle run test. Data regarding MSP were assessed at both T1 (11–13 years) and T2 (14–16 years) using a questionnaire similar to that used at baseline.

Of the target population of 2118 children, 1756 (83%) completed the baseline questionnaire; 1637 (77%) were examined for hypermobility; and 1204 (57%) were evaluated for physical fitness. Of the children who completed the baseline questionnaire, 93% and 73% filled out the T1 and T2 questionnaires, respectively. The incidence proportion of MSP was 21% (95% CI 19–24) per year. The neck was the most commonly reported site with non-traumatic pain (pain not initiated by a direct trauma), while the lower limb was the most frequent site for traumatic pain (pain initiated by a direct trauma). Of the children who reported any MSP at T0, 54% (95% CI 49–59) had MSP at T1 and 64% (95% CI 59–68) had MSP at T2. The neck was the site with the most persistent/recurrent MSP, followed by the lower back and the lower limb. The latter had a persistence/recurrence proportion of 32% (95% CI 27–38) at T1 and 31% (95% CI 25–37) at T2. Children with traumatic lower limb pain reported significantly more physical limitations compared to children with non-traumatic lower limb pain ($P = 0.02$), but the former group had a significantly better prognosis at T1 (OR 0.61, 95% CI

0.32–0.98). The prevalence of widespread pain (contralateral pain in addition to axial skeletal pain; WSP) in the whole study population increased from 7% at T0 and 9% at T1 to 15% at T2. This condition seemed to have a fluctuating and a relatively favourable course, with only 10% (95% CI 4–14) of children with WSP at T0 consistently reporting these widespread symptoms at both T1 and T2.

With respect to risk factors of MSP in children, headache (OR 1.68, 95% CI 1.16–2.44) and day-time tiredness (OR 1.53, 1.03–2.26) at baseline predicted the onset of non-traumatic MSP at T1. The same two factors: headache (OR 1.88, 1.32–2.75), and day tiredness (OR 1.98, 1.29–2.87) predicted the onset of non-traumatic lower limb pain. The latter was also predicted by prior report of depressive mood (OR 1.74, 1.19–2.76). Self-reported vigorous exercise (OR 3.40, 1.39–8.31) and day-time tiredness (2.97, 1.4–6.26) were significant risk factors for traumatic MSP. The two factors (vigorous exercise [OR 2.04, 1.08–3.77]; and day tiredness [OR 2.81, 1.72–4.55]) were associated with traumatic lower limb pain, which was also correlated with a high level of physical fitness (OR 2.97, 1.67–5.78). Risk factors for WSP included female gender (OR 1.42, 1.13–1.89), depressive mood (OR 1.51, 1.12–2.23) and regional back pain (neck pain: OR 1.72, 1.13–2.42; upper back pain: OR 2.11, 1.14–4.13; lower back pain: OR 3.03, 1.62–5.71), suggesting that both psychological factors and somatic pain can predict future development of WSP in early adolescents. Hypermobility was a significant and independent predictive factor for a poorer four-year prognosis of both MSP (pain in any musculoskeletal location; RR 1.35, 1.08–1.68) and lower limb pain (OR 2.93, 1.13–7.70). The former was also predicted by headache (RR 1.28, 1.08–1.51), and reported pain in multiple sites (RR 1.18, 1.02–1.36), while the latter was also predicted by vigorous exercise (OR 2.43, 1.16–5.05).

In conclusion, musculoskeletal pains are common among Finnish schoolchildren. These symptoms do not appear to be constant, but rather have a fluctuating course. Practicing frequent exercise (5-7 times a week) predicts both the onset and prognosis of trauma-induced MSP, but is not associated with the onset nor the prognosis of non-traumatic type of MSP. Traumatic lower limb pain was also significantly associated with day-time

tiredness and high level of physical fitness. We have identified three symptoms that might be markers of children at risk for development of non-traumatic MSP: Headache, day-time tiredness and depressiveness. In addition, we have identified three factors which might be markers for chronicity of these symptoms: Self-reported headache, pain in multiple musculoskeletal areas and hypermobility.

Given the paucity of understanding about biological mechanisms and behavioural models that underlies pain in children, it is not clear whether these factors play an etiological role in the development/persistence of these symptoms or are just markers of other etiological factors not measured in our study. Nevertheless, these factors, except for hypermobility, are modifiable and can be assessed with ease, and hence can provide opportunities for both primary and secondary prevention strategies.

TIIVISTELMÄ

Tutkimuksen tavoitteena oli selvittää varhaisen nuoruusiän tuki- ja liikuntaelimestön (TULE) kipuoireiden syntyyn ja pysyvyyteen vaikuttavia tekijöitä. Tutkimusaineistona oli Lahdessa kerätty edustava väestöotos 10-12 vuotiaista koululaisista, joita seurattiin tutkimuksen alun jälkeen vuoden ja neljän vuoden kuluttua. Tutkimuksessa käytettiin esitestattua kyselylomaketta, jonka tutkittavat täyttivät luokassa tutkimuksen alussa, vuoden kuluttua (11-13 v.) ja neljän vuoden kuluttua (14-16 v.). TULE-kipuoireiden esiintyvyyttä kysyttiin edeltävän kolmen kuukauden ajalta kipualueittain (niska, rintakehä, yläraajat, yläselkä, alaselkä, pakarat). Kipualue pyydettiin merkitsemään lomakkeessa olevaan ihmisen kuvaan. Lomakkeessa oli kysymyksiä päänsärystä, vatsakivusta, kivusta johtuvasta toiminnanrajoituksesta, päiväväsyyksestä, univaikeuksista ja masentuneisuudesta. Lisäksi kysyttiin hengästymistä aiheuttavan liikunnan määrää. Tutkimuksen alussa tutkittavien nivelten yliliikkuvuus testattiin Beightonin menetelmän mukaan ja fyysistä kuntoa arvioitiin sukkelajuoksutestillä.

Aineistosta (n=2118) 1756 (83 %) täytti kyselylomakkeen alussa, 1637 (77 %) osallistui nivelten yliliikkuvuuden testaukseen, ja 1201 (57 %) osallistui sukkelajuoksutestiin. Vuoden kuluttua kyselylomakkeen täytti 93 % alussa mukana olleista ja 73 % täytti sen neljän vuoden kuluttua.

TULE-kipuja ilmaantui 21 %:lle (95 % luottamusväli (LV) 19-24) vuoden seurannassa. Niskakipu oli yleisin oire, jos tutkittava ei ilmoittanut kivun johtuvan vammasta. Alaraajakipu oli yleisin vammasta johtuva kipuoire. Niistä lapsista, jotka ilmoittivat TULE-kipua tutkimuksen alussa jossakin kohdassa, 54 % (95 % LV 49-59) raportoi kipua vuoden kuluttua ja 64 % (95 % LV 59-68) neljän vuoden kuluttua. Toistuvia tai pysyviä kipuoireita esiintyi eniten niskassa, sitten alaselässä ja alaraajoissa. Alaraajojen kipuoireiden pysyvyys vuoden kuluttua oli 32 % (95 % LV 27-38) ja 31 % (95% LV 25-37) neljän vuoden kuluttua. Vammoista johtuvaan alaraajakipuun liittyi merkitsevästi enemmän toiminnanrajoitusta kuin muihin alaraajakipuihin (P=0,02), mutta vammoista johtuvan alaraajakivun ennuste vuoden kuluttua oli parempi kuin muun alaraajakivun

ennuste (OR 0,61, 95 % LV 0,32-0,98). Laaja-alaisen kivun (kipua vartalon oikealla ja vasemmalla puolella sekä tukirangassa) esiintyvyys koko aineistossa oli alussa 7 %, vuoden kuluttua 9 % ja neljän vuoden kuluttua 15 %. Laaja-alaisen kivun esiintyminen samalla henkilöllä vaihteli ja sen ennuste oli kohtalaisen hyvä, koska vain 10 % (95 % LV 4-14) tutkittavista, joilla oli laaja-alaista kipua alussa, raportoi sitä myös vuoden ja neljän vuoden kuluttua.

Alussa esiintynyt päänsärky (OR 1,68, 95 % LV 1,16-2,44) ja päiväväsytys (OR 1,53, 95 % LV 1,03-2,26) ennustivat tuntemattomasta syystä johtuvan TULE-kivun esiintymistä vuoden kuluttua. Nämä samat tekijät ennustivat tuntemattomasta syystä johtuvan alaraajakivun esiintymistä (päänsärky OR 1,88, 95% LV 1,32-2,75 ja päiväväsytys 1,98, 95 % LV 1,9-2,7). Lisäksi masentuneisuus (OR 1,74, 95 % LV 1,19-2,76) ennusti alaraajakipua. Itse ilmoitettu runsas liikunnan määrä (OR 3,4, 95 % LV 1,39-8,31) ja päiväväsytys (OR 2,97, 95 % LV 1,41-6,26) ennustivat vammoista johtuvaa TULE- kipua. Nämä tekijät ennustivat myös vammoista johtuvaa alaraajakipua (liikunnan määrä OR 2,04, 95 % LV 1,08-3,77 ja päiväväsytys OR 2,81, 95 % LV 1,72-4,55). Hyvä fyysinen kunto ennusti vammoihin liittyvää alaraajakipua (OR 2,97, 95 % LV 1,7-5,78). Laaja-alaisen kivun ilmaantumisen riskitekijöitä olivat naissukupuoli (OR 1,42, 95 % LV 1,13-1,89), masentuneisuus (OR 1,51, 95 % LV 1,12-2,23), paikallinen niskakipu (OR 1,72, 95% LV 1,13-2,42), yläselän kipu (OR 2,11, 95% LV 1,14-4,13) sekä alaselkäkipu (OR 3,03, 95 % LV 1,62-5,71). Nämä viittaavat siihen, että sekä psyykkiset tekijät että somaattiset tekijät saattavat ennustaa laaja-alaisen kivun kehittymistä varhaisella nuoruusiällä. Nivelten yliliikkuvuus ennusti sekä TULE-kivun (RR 1,35, 95 % CI 1,08-1,68) että alaraajakivun (OR 2,93, 95 % LV 1,13-7,70) pysyvyyttä neljän vuoden kuluttua. Päänsärky (RR 1,28, 95 % LV 1,08-1,51) ja kipu usealla eri alueella (RR 1,18, 95 % LV 1,02-1,36) ennustivat myös TULE-kivun pysyvyyttä. Runsa liikunnan määrä ennusti alaraajakivun pysyvyyttä (OR 2,43, 95 % LV 1,16-5,05).

Johtopäätökset: TULE-kivut ovat tavallisia suomalaisilla koululaisilla. Ne eivät yleensä ole jatkuvia, vaan niiden esiintyminen vaihtelee. Liikunnan määrä 5-7 kertaa viikossa

ennusti vammoista johtuvaa TULE-kipua ja vaikutti sen ennusteeseen, mutta ei ollut yhteydessä muun TULE-kivun syntymiseen tai ennusteeseen. Vammaan liittyvää alaraajakipua ennustivat päiväväsytys sekä runsas liikunnan määrä. Tutkimuksen mukaan päänsärky, päiväväsytys ja masentuneisuus saattavat ennustaa muiden kuin vammoista johtuvien TULE-kipuoireiden kehittymistä. TULE-kipujen kroonistumista (pysyvyyttä) ennustavat päänsärky, kipu useassa eri paikassa ja nivelten yliliikkuvuus.

Koska lasten kivun biologisia ja käyttäytymiseen liittyviä mekanismeja tunnetaan puutteellisesti, ei ole selvää, ovatko yllämainitut tekijät kivun syntymisen tai pysyvyyden etiologisia tekijöitä vai ainoastaan osoituksia sellaisista tekijöistä, joita tässä tutkimuksessa ei mitattu. Joka tapauksessa yliliikkuvuutta lukuun ottamatta näihin tekijöihin voidaan vaikuttaa ja niitä voidaan helposti arvioida. Siten on mahdollista luoda strategioita sekä kipuoireiden ehkäisemiseksi että niiden ennusteen parantamiseksi.

1. INTRODUCTION

Musculoskeletal pain, which is pain originating within the musculoskeletal system, is commonly reported by schoolchildren (age 6-18). Estimates of occurrence vary widely according to the outcome definition and the age of children (Tables 2-5). In a large-scale survey among schoolchildren, musculoskeletal pain was found to be one of the most common health problems in young age groups (Peters and Murphy, 1993). With respect to the time trend in prevalence, recent research in Finland and the UK have found that musculoskeletal pain are becoming more and more common in adolescents (Hakala et al. 2002; Harkness et al. 2005). Although such pain might on occasion be indicative of a serious health problems (e.g. cancer, rheumatic diseases), most children complaining of these symptoms have no clinical evidence for underlying pathological conditions. This has led to the long-held belief that these symptoms are “functional” in origin and are attributed to the normal process of growth and development of children. However, this hypothesis was refuted, first by Naish and Apley (1951) on the grounds that pain occurs most frequently at an age when growth is far from being rapid, and then by other researchers (Salminen et al. 1984; Salminen et al. 1992_a; Kujala et al. 1997) based on studies using anthropometric indices. A possible association between musculoskeletal pain in childhood and development of musculoskeletal disorders in adults have been documented in a number of previous studies (Harreby et al. 1995; Leboeuf-Yde and Kyvik 1998; Salminen et al. 1999). Hence, a better understanding of determinants of these symptoms in children is important, not only for developing effective preventive strategies to the youth, but also for providing a better understanding of the origin of chronic pain in adults (Goodman and McGrath 1991).

A number of previous studies have focused on identifying factors that might predict occurrence of musculoskeletal pain in schoolchildren. These factors have included physical activity and fitness, after-school work, carrying a heavy backpack, smoking, psychological/behavioural factor, hypermobility and family history of musculoskeletal pain. Unfortunately, these studies have reported inconsistent findings and this has hampered development of evidence-based preventive guidelines. There is also a paucity of data on the natural course and factors predicting the long-term prognosis of

these symptoms. Given the high prevalence of these symptoms, it would be of benefit for health care providers to identify children who are at higher risk of developing persistent symptoms and ultimately who would benefit most from secondary preventive interventions.

This study is a continuation of prior research by Mikkelsen et al. (1998_a). The purpose of this work was to assess the occurrence, prognosis and determinants (risk factors and prognostic markers) of musculoskeletal pain in a representative sample of Finnish schoolchildren. Children were evaluated at three time points: At baseline (age 10-12), at one-year (Mikkelsen et al. 1998_b), and, in the current study, at four-year follow-up. While studying musculoskeletal pain in general, we focused particularly on lower limb pain and widespread pain. The former being the most commonly reported musculoskeletal pain site, while the latter having been very rarely studied in children.

2. REVIEW OF LITRETURE

2.1. Pathophysiology of pain

The common definition of pain is "an unpleasant sensory and emotional experience, associated with actual or potential tissue damage or described in terms of such damage" (International Association for the Study of Pain [IASP] Subcommittee on Taxonomy 1986). Acute pain in children (i.e. with recent onset and limited duration) has a biological value as it warns the child of actual or impending tissue damage and motivates him/her to escape or avoid further harm (Merskey and Bogduk 1994). Chronic pain, which is defined by IASP as pain that persists beyond normally expected healing, as quantified through medical experience (Merskey and Bogduk 1994), does not have any useful biological purpose and can cause substantial suffering to children. Hence, it is important to investigate determinants of chronic or recurrent pain in children in order to provide effective prevention and ensure appropriate treatment.

The anatomical requirements for pain are in place prior to birth (Anand and Hickey 1987), and it has also been clearly demonstrated that children experience pain from early life and are able to recall and describe it accurately (McGrath 1990; Savedra et al. 1988). Processes that can potentially or actually damage a body tissue are called "noxious stimuli". Nociception refers to the processing of pain signals induced by these stimuli by the central nervous system (CNS) through a group of pathways collectively called "nociceptive pathways". These pathways can be divided into 3 main pathways as following:

2.1.1. Peripheral pathways

The musculoskeletal system is abundantly supplied with both encapsulated receptors, which are found mainly in fibrous periarticular structures, and free nerve endings, which are widely distributed in fibrous capsules, adipose tissues, ligaments, menisci and periosteum (Fouquet 2003). Both encapsulated receptors and free nerve endings act as sensors that respond to tissue damage or potentially injurious stimuli, hence, they are called "nociceptors". The function of these receptors is not static but involves interaction

with the surrounding environment, leading to an enhancement or diminishment of their capacity to detect and respond to various stimuli (Lynn 1977; Cavanaugh et al. 2006). Sensory nerves or "afferents" arising from these nociceptors may be classified morphologically into two groups, myelinated A-delta fibers and unmyelinated C fibers. The latter form the vast majority of articular fibers (Langford and Schmidt 1983) and for the most part have exclusively nociceptive properties (Schaible and Grubb 1993).

2.1.2. Spinal pathways

Afferent neurons pass in the ventrolateral segment of the dorsal horn of the spinal cord and synapse with second-order neurons at the same level or one or two segments above or below (Fields 1987). Axons of the second-order neurons synapse onto the interneurons that synapse onto the other neurons in the spinal cord or onto the projection neurons that project to the thalamus and cortex through the contralateral spinothalamic and spinoreticular tracts. The principal neurotransmitters within the spinal cord are excitatory amino acids, including glutamine and aspartate. Substance P and other peptides are also released from central terminals of primary afferents and appear to play an important modulatory role in the spinal dorsal horn (Kidd 1999).

2.1.3. Cerebral pathways

Ascending neurons passing in the spinoreticular tract terminate in the brain stem, while those passing in the spinothalamic tract divide into lateral and medial branches as they approach the thalamus. Fibers in the lateral branch terminate in the lateral nuclei of the thalamus (the ventrobasal nucleus and the `posterior group` nuclei) in a somatotopically fashion. Nociceptive signals then pass relatively rapidly to the somatosensory cortex. This constitutes the `lateral pain system` that was initially considered to be concerned with the processing of acute pain. However, recent studies have found that the lateral system is dealing primarily with the sensory-descriptive aspects (Jones and Derbyshire 1996). Medial branches of the spinothalamic tract terminate in the medially situated intralaminar nuclei of the thalamus, which receives input from the brain stem reticular formation (Fields 1987) and form the `medial pain system`. Transmission within the medial pain system is slower than that in the lateral system and projects widely

within the ipsilateral cortex. Projections have also been noted to terminate in the anterior cingulate sections of the limbic cortex (involved in the integration of cognition, affect and response selection) as well as in the pre-frontal cortex. The medial pain system is concerned mainly with the motivational-affective components of the pain response (Kidd 1999). There are also connections with neurons involved in mediating autonomic, endocrine, mnemonic and hedonic components. At all anatomic levels modulatory mechanisms can limit or amplify pain experience (Sherry and Malleson 2002).

Pain sensations can potentially arise as a result of neural stimulations, injury or dysfunction at any point along the previously mentioned pathways. Pain processing does not simply relay on signals from the body to the brain, it is a dynamic, redundant multi-pathway process. (Milligan and Watkins 2009). However, not all pain experiences result from a noxious stimuli or an injury, nor do all noxious stimuli lead to the experience of pain through a neurological process (Lundeberg and Ekholm 2002). For that reason, it is crucial to keep in mind that a painful condition is a complex state that can be influenced by several psychological and physiological factors. The response to pain is also affected by the individual's age, cognitive level, and previous pain experiences (McGrath 1990).

2.1.4. Pathophysiology of chronic widespread pain

Studies on biological mechanisms of chronic widespread pain (WSP) in children are lacking. However, in recent years there have been some advances in understanding these mechanisms in adults (DeSantana et al. 2008; Nielsen and Henriksson 2007). Three main mechanisms has been proposed: Muscular dysfunction (Bengtsson and Henriksson 1989; Henriksson and Bengtsson 1991), deficit in pain-modulating systems (Kosek et al. 1996; Julien et al. 2005) and sensitisation of pain transmission neurons in the CNS - central sensitization (Staud et al. 1998; Price et al. 2002). Evidence for the latter mechanism is strongest and has been more extensively studied (Staud et al. 2001; Staud et al. 2005; Giovengo et al. 1999). Recent reviews have also suggested a

potential role of the peripheral nervous system in the pathophysiology of chronic pain (Vierck 2006; Staud and Rodriguez 2006). In addition, some authors have suggested a possible role of non-neuronal structures such as astrocytes and microglia (Milligan and Watkins 2009). In conclusion, the pathophysiological mechanisms underlying the development and maintenance of chronic pain are under investigation in adults and have not been studied at all in children. This underlines the important role of epidemiology. Epidemiological studies, if properly conducted, are able to identify high risk groups and modifiable conditions that can facilitate preventive actions, before these biological mechanisms become fully characterised.

2.2. Assessment of pain in schoolchildren

For measuring childhood pain, one must consider the complex and subjective nature of pain experience (Merskey and Bogduk 1994). Pediatric pain is multifaceted and includes physiologic responses (e.g. increased heart rate), behavioural responses (e.g. crying, description of pain or requests for help), and finally functional limitations, which are the observable responses to pain (e.g. decreased mobility, declining school attendance) (Franck et al. 2000). Another important aspect of pain experience for children involves emotional factors that control their anticipation of and response to pain. Child's developmental level is an important factor in his/her expression of pain. Younger children show more behavioral manifestations of acute distress and are less able to communicate pain experience (Von Baeyer and Spagrud 2007). This multi-dimensionality of pediatric pain and its close relationship with children's developmental levels renders assessment of pain difficult and might necessitate a thorough evaluation of pain involving (1) Physiologic measures including reflexes, sweat index and β -endorphin levels, (2) Behavioral observations, which may include body position, vocalizations (use of voice) and facial expression, (3) Direct assessment (child subjective report of pain) through interviews, questionnaires, pain thermometers, facial scale and visual analogue scale and (4) Projective psychological techniques, which may encourage a representation of pain experience through colors, shapes, stories, or drawing (McGrath 1990). Although such a comprehensive assessment is obviously not practical in epidemiological studies, elements from such evaluation may be appropriate

and feasible.

Physiologic measurements and direct observations of pediatric pain are difficult to conduct in epidemiological studies. Such measures, despite their lack of response bias and the apparent objectivity, can only evaluate current pain sensation and may not indicate the child's actual pain experience. Furthermore, neither physiological nor behavioural measures can discriminate well between the responses to pain and other forms of bodily stress. As a subjective experience, direct reports are probably the easiest way to assess musculoskeletal pain in children. This can be carried out by using questionnaires or interviews of children or their parents and teachers, depending on the age groups studied (McGrath 1990). A number of previous studies have found that parents are less likely to report subjective complaints in their children than the children themselves (Manne et al. 1992; Sundblad et al. 2006; Kröner-Herwig et al. 2009), while others have documented appropriateness of parental reports (Goodman and McGrath 1991). However, whenever the children are verbally capable of conveying their experiences, self-reports are usually preferred to surrogate reports (McGrath 1995). Several structured measurements have been developed to assess pain in children, including the Pain Experience Interview and the Varni-Thompson Pediatric Pain Questionnaire. The former instrument showed a high validity in screening acute, chronic and recurrent pain in children (McGrath et al. 2000), while the latter questionnaire, which includes a visual analogue scale (VAS) to measure pain intensity, showed high correlations between its pain ratings and measures of functional status in children with rheumatic diseases (Gragg et al. 1996).

Information about childhood musculoskeletal pain should be as detailed as possible, and should include data on the location, frequency, timing and severity of pain. VAS appears to be a valid measure of pain severity in children over 7 years (McGrath 1995). In a previous study, two visual analogue scales (Bieri Faces Pain Scale and Colored Analog Scale) were found to be valid in measuring injury-induced musculoskeletal pain in children (Bulloch and Tenenbein, 2002). Although frequency and severity are two separate pain characteristics, a recent study found a significant linear association

between the intensity and frequency of adolescent neck pain (Ståhl et al. 2004). This might indicate that in epidemiological studies the frequency of musculoskeletal pain in children can reflect the intensity of pain fairly well.

2.3. Disease-related musculoskeletal pain in schoolchildren

Musculoskeletal pain is the presenting symptom of a group of diseases affecting children and adolescents (Table 1). However, children and adolescents with these diseases represent only a minority of those with musculoskeletal complaints at the population level. The majority of schoolchildren with musculoskeletal pain tend to fall into the following two categories: (1) Trauma-related/overuse musculoskeletal pain and (2) non-specific musculoskeletal pain. The latter category can be further classified into growing pains, idiopathic regional pain, widespread pain, reflex sympathetic dystrophy, psychogenic pain and benign hypermobility syndrome. Such classification of non-specific musculoskeletal pain is not mutually exclusive or universally agreed upon. However, none of these conditions has specific clinical signs of any systemic disease associated with pain (and hence the terms un-explained or idiopathic musculoskeletal pain). Non-specific (or un-explained) musculoskeletal pain does not only constitute the majority of cases presenting to the primary care physician with these symptoms, they also represent sizeable subgroup of referrals to rheumatology clinics (Rosenberg 1990).

Table 1. Diseases associated with musculoskeletal pain in children

Inflammatory disorders

Juvenile idiopathic arthritis
Connective tissue diseases
Systemic Lupus Erythematosus
Juvenile dermatomyositis
Inflammatory bowel disease
Mixed connective tissue disease
Linear scleroderma
Progressive systemic sclerosis
Panniculitis
Chronic Recurrent Multifocal Osteomyelitis
Vasculitis
Kawasaki disease
Henoch-Schonlein purpura

Infection/post-infective

Viral/reactive arthritis
Rheumatic fever
Septic arthritis
Osteoarticular tuberculosis
Brucella/Lyme/fungal arthritis

Metabolic disorders

Gout
Mucopolidosis type III
Mucopolysaccharidoses
Fabry disease
Alkaptonuria
Lesch-Nyhan disease

Connective tissue/orthopaedic problems

Marfan syndrome
Ehlers-Danlos syndrome
Irritable hip
Perthes disease
Other osteochondritis
Slipped upper femoral epiphysis
Chondromalacia patella
Anterior patella syndrome

Neoplasia

Leukaemia
Neuroblastoma
Metastatic disease
Primary bone tumours: benign/malignant

Haematological problems

Sickle cell disease
Other haemoglobinopathies
Haemophilia

Other diseases

Sarcoidosis
Immune complex deposition
Cystic fibrosis
Serum sickness
Septicaemia
Immunodeficiency-related
Drug-induced

2.4. Occurrence of musculoskeletal pain in schoolchildren

2.4.1. Prevalence and incidence

Estimated occurrence reported in previous studies varies considerably. Prevalence figures have ranged from a 3-month period prevalence of 2% in 12-year olds to cumulative prevalence of 52% in 18-year olds for musculoskeletal pain (in any location) (Table 2); from a one-year period prevalence of 10% in children aged 7-16 years to a 50% cumulative prevalence at 11-15 years for LBP; from a 6-month period prevalence of 12% at 14-years old boys to 45% in 18-years old females for neck pain (Table 3); from a 1-year period prevalence of 12% in 8-year olds to a cumulative prevalence of 37% at 4-6 year olds for extremity pain (Table 4) and from a point prevalence of 6% in 9-15 year olds to a 15% 1-month period prevalence in 11-14 year olds for widespread pain (Table 5). Incidence estimates also vary significantly, from an annual incidence of 8% for WSP in 11-14 year olds (Table 5) to an incidence proportion of 74% at 6-20 years for LBP (Table 3). Differences in occurrence estimates across previous studies may be explained by the following:

- 1- Differences in case definitions of musculoskeletal pain (e.g. pain in any musculoskeletal area or pain in a specific area; pain in any frequency or pain with a minimum frequency of episodes).
- 2- Differences in types of measures of occurrence (e.g. point or period prevalence; 6-month or annual incidence).
- 3- Differences in age groups (e.g. preteens or late adolescents).
- 4- Differences in the methods used to assess musculoskeletal pain experience (e.g. child self-report or proxy reports from parents or care taker).

Obviously, these methodological differences between studies are likely to result in some variation in the estimates, with wider definitions of musculoskeletal pain yielding higher estimates of occurrence. However, regardless of the numerical occurrence estimates, current evidence shows: firstly, that childhood musculoskeletal pain is common (i.e. has a high prevalence), with estimates approaching those in adults and, secondly, that it has

high rate of occurrence (i.e. high incidence).

With respect to the time trend of musculoskeletal pain in children, there is some evidence that its prevalence is increasing over time. This finding has been documented in biennial nationwide postal surveys (1985–2001), and annual classroom surveys (1996–2001) in Finland (Hakala et al. 2002).

2.4.2. Variation of occurrence estimates with age and sex

Previous systematic reviews have demonstrated that the prevalence of musculoskeletal pain increases steadily with age (Balagué et al. 1999; McBeth and Jones 2007). A 4-year prospective study reported that the incidence of low back pain increased from 13% in subjects aged 12 years to 24% at the age of 15 years. Similarly, another study reported an increase in the incidence proportion of back pain from 23% among children aged 6–13 years to 33% among those aged 14–18 years (Mierau et al. 1989). Evidence concerning gender differences is not as conclusive; most studies reported significantly higher prevalence of musculoskeletal pain in girls (Perquin et al. 2000; Diepenmaat et al. 2006), while some studies found no gender differences (Olsen et al. 1992; Sundblad et al. 2007) and few studies showed male predominance (El-Metwally et al. 2008; Burton et al. 1996). Mikkelsen et al. (1997) reported significant sex-related differences in occurrence of chest and upper back pain, but not in other musculoskeletal sites. The same research group (Ståhl et al. 2004) reported a significant female predominance of neck pain at mid-adolescence (age 13-15) but not at early adolescence (age 10-12). These results suggest that gender differences in reporting musculoskeletal pain might be related to both the location of pain and the age of children

Table 2. Occurrence of “Any” musculoskeletal pain in schoolchildren

Authors	Sample	Age range	Definition of pain	Occurrence
Perquin, 2000	5423 from Holland	0-18 years	3-month period prevalence of pain in any location in the body, including head, abdomen, limb, ear, throat and back.	54%, of whom 62% suffered complaints for longer than 3 months
Roth-Isigkeit et al., 2004	715 from Germany	10–18 years	3-month period prevalence of pain in any location in the body, including head, abdomen, limb, ear, throat and back	85%, of whom 53% suffered complaints for longer than 3 months
Ehrmann-Feldman et al., 2002	502 from Canada	13-15 years	6-month cumulative incidence of Musculoskeletal pain in any location	27%
Bru et al., 1998	1071 from Norway	13 years	1-month period prevalence of muscle tension or musculoskeletal pain in the lower back, neck or shoulder	10%
Egger et al., 1999	4,500 from USA	9-13 years	3-month period prevalence of pain in any musculoskeletal area (with a frequency of at least 3 times per week)	1.7%
Qvindesland and Jonsson, 1999	267 from Iceland	12-year olds	Lifetime period prevalence of pain in any musculoskeletal area	52%

Table 3. Occurrence of back pain (low back pain [LBP] or neck pain) in school children

Authors	Sample	Age range	Definition of pain	Occurrence
Feldman et al., 2001	502, from Canada	13-15 years	One year incidence of LBP	17%
Gunzburg et al., 1999	392, from Belgium	9 years	Life-time prevalence of LBP	36%
Viry et al., 1999	123, from France	13-16 years	Point prevalence of LBP One year period prevalence of LBP	28% 83%
Troussier et al., 1999	972, from France	9-12 years 13-17 years	Point prevalence of LBP Point prevalence of LBP	14% 24%
Prendeville and Dockrell, 1998	200, from Ireland	13-17 years	Life time prevalence of LBP	42%
Taimela et al., 1997	1171, from Finland	7-16 years	One year period prevalence of LBP	10%
Burton et al., 1996	216, from England	11-15 years	Life time prevalence of LBP	50%
Troussier et al., 1994	1178, from France	6-20 years	Lifetime cumulative incidence of LBP	74%
Nissinen et al., 1994	859, from Finland	12-13 years	One year period prevalence of LBP	18%
Brattberg, 1994	471, from Sweden	8,11, and 13 years	Two year incidence of LBP	16% (8 yrs) 22% (11yrs) 22% (13 yrs)
Balagué et al., 1993	117, from Switzerland	10-16 years	Lifetime cumulative incidence of LBP One week period prevalence of LBP	33% 9%

Salminen et al., 1992 _a	1503, from France	14 years	Lifetime cumulative incidence of LBP One month period prevalence of LBP	30% 12%
Olsen et al., 1992	1242, from USA	11-17 years	Lifetime cumulative incidence of LBP One year period prevalence of LBP	30% 22%
Brattberg and Wickman, 1992	1245, from Sweden	8-17 years	Lifetime cumulative incidence of LBP	29%
Balagué et al., 1988	1715, from Switzerland	7-17 years	One week period prevalence of LBP	16%
Fairbank et al., 1984 _a	446, from England	11-17 years	Lifetime cumulative incidence of LBP	26%
Jones et al., 2003 _a	1046 from England	12-15 years	1-year incidence of LBP	Ranged from 13% at 12 years to 24% at 15 years
Hakala et al., 2002	189, 894 from Finland	12-18 years	6-month period prevalence of neck pain	24% to 45% in females and 12% to 19% in males
Ehrmann-Feldman et al., 2002 _b	502 from Canada	13-15 years	6-month cumulative incidence of neck and shoulder pain 1-year cumulative incidence of neck and shoulder pain	20% 28%

Sivvola et al., 2004	826 from Finland	15-18 years	Lifetime prevalence of neck and shoulder pain 7-year cumulative incidence of neck and shoulder pain	17% 59%
Murphy et al., 2007	679 from England	11-14 years	Pain for 1 day or more in the month preceding the questionnaire	Neck pain: 27%; Upper back pain: 18%; Lower back pain: 22%
Niemi et al., 1997	718 from Finland	16-18 years	12-month period prevalence of neck and shoulder pain (with a frequency of at least once a week)	21% in females and 10% in males

Table 4. Occurrence of limb pain in school children

Authors	Sample	Age range	Definition of pain	Occurrence
Abu-Arafeh and Russell, 1996	2165 from Scotland	5-15 years	1-year incidence of pains in arms or legs (growing pains)	3%
Oberklaid et al., 1997	183 from Australia	8 years	1-year period prevalence of pains in arms or legs (growing pains)	12%
Øster and Nielsen, 1972	2178 from Denmark	6-19 years	Annual incidence of pain in the extremities	16%
Evans et al., 2004	1445 from Australia	4-6 years	Life-time period prevalence of leg pain (growing pains)	37%
Shrier et al., 2001	502 from Canada	13-15 years	6-month cumulative incidence of lower limb pain	22%

Table 5. Occurrence of widespread pain (WSP) in school children

Authors	Sample	Age range	Definition of pain	Occurrence
Jones et al., 2003 _b	1440 from England	11-14 years	1-month period prevalence 1-year cumulative incidence	15% 8%
Mikkelsen et al., 2001	3578 from Finland	11 years	3-month period prevalence	10%
Buskila et al., 1993	338 from Israel	9-15 years	Point prevalence of fibromyalgia ^a	6%
Adamson et al., 2007	679 from England	11-14 years	1-month period prevalence	8.4%

^aChildren who fulfilled the American College of Rheumatology criteria of this disease, including the criteria of having chronic widespread pain.

2.5. Burden of childhood musculoskeletal pain

2.5.1. Burden on the child

Most previous studies that focused on investigating the burden of musculoskeletal pain on children were conducted on clinical samples. Children who are clinic-referred and warrant treatment are likely to represent the most extreme manifestation of the symptoms. Not surprisingly, results of these studies have shown a substantial impact of pain on the physical, psychological and emotional well-being of these children. They often miss school, have significant limitations in their everyday physical and social functioning, have sleep difficulties, and often suffer from depression and anxiety (Palermo 2000; Walters and Williamson 1999; Hunfeld et al. 2001; Konijnenberg et al. 2005; Konijnenberg et al. 2006; Eccleston et al. 2008).

Fortunately not all children with musculoskeletal pain have an equally severe burden, but still many can have considerable negative consequences. A study among 751 schoolchildren aged 4–18 years in Germany found that 68% of children with chronic pain had considerable restrictions in daily living due to pain, including school absences and social inactivity (Roth-Isigkeit 2005). In this study, 19% of children with back pain reported having been absent from school because of pain. This proportion was significantly lower than that of children with headache (51%) and abdominal pain (43%). However, in another study conducted in the Netherlands it was found that adolescents with musculoskeletal/limb pain report more physical limitations than their peers with other pains (Hunfeld et al. 2002_b).

With respect to lower limb pain, Fairbank et al. (1984_b) found that 18% of children aged 13–17 with knee pain had to stop playing sports during the past year because of their symptoms. In another study, 45% of schoolchildren aged 9–15 with lower limb pain reported moderate to severe physical limitation attributed to their pain (Vähäsarja 1995). Mikkelsen et al. found that pain interference with daily living was high among children with widespread pain, as almost half of them had had school absence because of pain. These children frequently report sleep problems, have high depressive scores and are

often described by their parents and teachers as having behavioural problems (Mikkelsen et al. 1997). Although the relation between pain and functional disability among adolescents with chronic pain has not been well explored, available research shows that the severity of pain and the adolescent perceptions of self-worth appear to play important roles (Claar et al. 1999; Guite et al. 2007).

2.5.2. Burden on the family

Musculoskeletal pain in schoolchildren can have a major impact on families. Almost all previous studies have been conducted on families of children treated for chronic pain. Compared to their healthy peers, children with chronic pain are more isolated and dependent on parents for support (Hunfeld et al. 2001; Palermo 2000). Parents are usually worried, distressed, frustrated and unable to alleviate their child's symptoms, and this in turn has a negative effect on the child's pain experience and emotional stability (Hunfeld et al. 2001; Hunfeld et al. 2002_a). Parents usually have to take paid or un-paid days off to care for their sick dependent. In a study among 52 families of adolescents with chronic pain, parents of adolescents missed, on average, 20% of the work days in a year to give care to their child. This clearly demonstrates the substantial negative consequences of adolescent chronic pain on both the family and parents' workplace (Beecham et al. 2001). Recently, a questionnaire was developed to assess changes in parenting functioning and behaviour attributed to adolescent pain. This UK-developed questionnaire was named as the Bath Adolescent Pain--Parental Impact Questionnaire (BAP-PIQ). Preliminary Psychometric evaluation of this inventory suggests it is a reliable and valid assessment tool (Jordan et al. 2007).

2.5.3. Burden on healthcare services

Few studies have investigated the use and the economic costs of healthcare services in the treatment of childhood and adolescent musculoskeletal pain. Van Eekelen et al. (2002) found no difference in the average yearly general practitioner's consultation rate between adolescents with and without non-malignant chronic pain (2.6 contacts per year for both groups). More recently, Sled et al. (2005) examined the medical records of a sample of adolescent patients with chronic pain attending specialised pain

management units or outpatients clinics. They estimated the yearly cost of illness of an adolescent with this condition to be approximately £8000 per year. Finally, Roth-Isigkeit et al. (2005) found that 51% of schoolchildren (aged 9-18 years) with chronic pain at any location (including headache and abdominal pain) sought professional help and/or reported the use of pain medications for their conditions. According to our knowledge no data are available on children's and parents' satisfaction on the quality of management of pediatric chronic musculoskeletal pain. However, in a recent survey of 260 pain clinicians and 80 general practitioners (GPs) in the UK, it was found that 77% of pain clinicians and 95% of GPs acknowledge a lack of adequate training for treating children with chronic pain (Bhatia et al, 2008).

2.6. Risk factors

While the majority of previous studies have focused on potential risk factors of back pain in childhood and adolescence, some studies have explored risk factors of other site-specific musculoskeletal pain, "Any" musculoskeletal pain (i.e. in any location), and widespread pain. The focus of the current study is on "Any" musculoskeletal pain, lower limb pain and widespread pain. However, an overview of the current state of knowledge with respect to risk factors of back pain would be important, for two reasons:

- 1- Back pain is the most extensively studied children's pain symptom and several prospective studies have been carried out to explore its risk factors.
- 2- Co-occurrence of musculoskeletal pain is well documented among children and adolescents (Mikkelsen et al. 1997; Salminen 1984) indicating that musculoskeletal symptoms probably share common risk factors.

2.6.1. "Any" musculoskeletal pain (pain in any musculoskeletal location)

Two cross-sectional studies have investigated potential risk factors of "Any" musculoskeletal pain in children and adolescents. Egger et al. (1999) examined the association between "Any" musculoskeletal pain and psychological problems in a population-based sample of 4,500 children (age 9-13) in North Carolina, USA. Psychological problems investigated included depression, anxiety disorders, conduct

disorder, oppositional defiant disorder, and attention-deficit hyperactivity disorder. A strict case definition was used in this study (Table 2) and hence a very low proportion of these children was classified as having “Any” musculoskeletal pain (1.7%). Co-occurrence of other somatic symptoms with musculoskeletal pain was very high as 41% of children with musculoskeletal pain reported headache and/or abdominal pain. Depression was associated with musculoskeletal pain in both girls (OR 12.9, 95% CI 4.5-37.0) and boys (OR 10.5, 95% CI 2.3-48.0), while anxiety disorders were associated with these symptoms only in girls (OR 3.4, 95% CI 1.5-8.0). Obviously, the wide confidence intervals are due to the small proportion of children who fulfilled the stringent criteria of “Any” musculoskeletal pain. In the second cross-sectional study, Qvindenland and Jonsson (1999) investigated the role of joint hypermobility on the risk of musculoskeletal pain (regardless of location) in a population-based sample of 267 Icelandic children aged 12 years. The proportion of children with hypermobility reporting musculoskeletal pain (55%) was similar to that in children with normal joint laxity (51%) suggesting that joint hypermobility may not be a risk factor for “Any” musculoskeletal pain in this age group.

Only one prospective study has been conducted to explore risk factors for incident “Any” musculoskeletal pain in children attending secondary school (Ehrmann-Feldman et al. 2002_a). The primary aim of this study was to determine whether after-school work is a risk factor for these symptoms. In addition, the effect of age, gender, height, BMI, smoking, growth spurt, psychological distress and sports activity was investigated. Information on these factors was collected from 502 Canadian schoolchildren (age 13-15) and musculoskeletal pain was re-evaluated at 6 (T1) and 12 months (T2) from baseline. Only two variables predicted the onset of pain at T1: After-school work (OR 2.21, 95% CI 1.04–4.70) and psychological distress (OR 1.68, 95% CI 1.19–2.39), while no factors predicted its development at T2.

2.6.2. Lower limb pain

Potential determinants of lower limb pain have been studied in children and adolescents, but the results have not been consistent. A positive relationship has been

reported between frequency of physical exercise and lower limb pain in some studies (Fairbank et al. 1984_b; Vähäsarja 1995), but no correlation was observed in a 1-year follow-up study (Shrier et al. 2001). Similarly, conflicting results have been reported for the predictive role of physical fitness (Knapik et al. 1993; Kujala et al. 1999) and psychosocial factors (Oberklaid et al. 1997; Bruusgaard et al. 2000). Evidence is also inconclusive with respect to the role of joint mobility and muscle flexibility in paediatric and adolescent lower limb pain/injuries, with some studies documenting a significant association (Orchard et al. 1997; Myer et al. 2008), while others show no association (Shrier et al. 2001). A recent study has found a significant age-adjusted association between weight and/or body mass index (BMI) and prevalent hip and knee pain in children and adolescents aged 3-18 years (Stovitz et al. 2008). Most previous studies have included both traumatic and non-traumatic lower limb pain in the case definition. This might be one of the reasons for conflicting results, as the proportion of subjects with traumatic pain within children with lower limb pain can vary considerably depending on the study settings and age group. A distinction of traumatic from non-traumatic pain was introduced into this study, aiming to provide a clearer insight in risk factors of lower limb pain.

2.6.3. Widespread pain

Only one prospective study has investigated risk factors for the development of widespread pain in schoolchildren. This one-year follow-up study was conducted on a sample of 1440 British schoolchildren aged 11-14 years. Children were asked, at both baseline and follow-up, whether they had experienced any pain, lasting at least one day, during the past month. Children who did not report WSP at baseline but indicated having the symptoms at follow-up were categorised as with new-onset WSP. The study found three independent predictors for onset of generalized pain: Adverse behavioural and emotional factors (RR 2.6, 95% CI 1.5-4.6), high level of sports activity (RR 2.0, 95% CI 1.1-3.9) and headache (RR 2.50, 95% CI 1.16-5.39), while age, sex, sedentary activities, sore throat, day tiredness and abdominal pain did not have a significant effect (Jones et al. 2003_a). Recently, a cross-sectional study among a sample of schoolchildren in England was conducted to investigate factors associated with WSP

(Adamson et al. 2007). This study was similar to the previously mentioned prospective study in the age of surveyed subjects (11-14), the potential predictors of WSP examined and the case definition of WSP used. The following factors showed significant associations with the outcome: Older age, female gender, bag weight to body weight, bag carrying method and headaches.

2.6.4. Back pain

Two review articles (Balagué et al. 1999; Jones and Macfarlane 2005) summarised the evidence with respect to risk factors for low back pain in children and adolescents. However, studies published recently were not included in the reviews. Results derived from cross-sectional and prospective studies are presented separately, with more weight given to longitudinal studies where a temporal relationship can be established between the exposure(s) and the outcome.

2.6.4.1 Evidence from cross-sectional studies

Most cross-sectional studies have reported no significant differences in weight between children with and without LBP (Grimmer and Williams 2000; Salminen et al. 1992_b; Watson et al. 2003). However, studies have provided conflicting evidence with respect to the role of height and rate of growth on occurrence of LBP (Fairbank et al. 1984_a; Salminen et al. 1992_b). One study has reported an association between spine mobility and severe LBP, but not with less severe back complaints (Harreby et al. 1999). A significant correlation between adolescent smoking and LBP was found in most studies that addressed this relationship (Balagué et al. 1988; Harreby et al. 1999).

Most studies documented an increased occurrence of LBP with high levels of physical activity and participation in competitive sports (Auvinen et al. 2008; Bejia et al. 2008; Balagué et al. 1988; Newcomer and Sinaki 1997), while some studies have found no correlation between the level of physical activity and LBP or low back strength (Salminen 1984; Sjolie 2000). Inconsistent results have been reported with respect to the role of sedentary activities (e.g. TV, video games), with some studies showing an association (Balagué et al. 1988) and others reporting no association (Gunzburg et al.

1999). Similarly, conflicting cross-sectional results have been reported with respect to association of LBP with weight of school bags (Gunzburg et al. 1999; Watson et al. 2003; Murphy et al. 2007; Viry et al. 1999; Grimmer and Williams, 2000; Whittfield et al. 2005) and parents' history of back pain (Balagué et al. 1995; Salminen 1984; Murphy et al. 2007; Bejia et al. 2008).

Results from almost all previous cross-sectional studies have found a strong association between childhood LBP and emotional problems or negative psychosocial experiences (Balagué et al. 1995; Watson et al. 2003; Murphy et al. 2007). However, the nature of cross-sectional data limits interpretation and makes it unclear whether these psychological problems/experiences precede or are consequences of pain.

There is some epidemiological and/or biomechanical evidence suggesting that childhood LBP might be associated with poor posture in class (Mandal 1994), some anthropometric factors, like sitting height and trunk asymmetry (Nissinen et al. 1994) and unsuitable school furniture (Murphy et al. 2007; Salminen et al. 1992_b; Parcels et al. 1999_b).

With respect to the role of heredity, a recently published cross-sectional study on a population-based sample of Finnish twins (age 11 years) found that genetic factors played, at most, a very minor role in occurrence of LBP in childhood; instead, symptoms seem to be related to a mixture of shared and unshared environmental factors (El-Metwally et al. 2008). These results are in accordance with an earlier twin study which found a weak genetic influence on LBP in twins aged 12–15 years (Hestbaek et al. 2004).

2.6.4.2. Evidence from prospective studies

Prospective cohort studies have found that incident LBP in children and adolescents cannot be predicted by baseline height (Kujala et al. 1997) or weight (Nissinen et al. 1994). Neither active or sedentary life styles are significant predictors of future development of LBP (Jones et al. 2003_a; Salminen et al. 1995), while a recent study

found that high-level physical activity in childhood protects against future low back pain at adolescence (Wedderkopp et al. 2008). However, in a Finnish study of 14-18-year-old adolescents, regular participation in organized sports increased the risk of hospitalization due to LBP (Mattila et al. 2008). A prospective study among early adolescents (age 11-14) in the UK found that the risk of LBP at the 1-year follow-up was not predicted by weight of school bags at baseline (both absolute and relative to child weight), but was significantly associated with baseline report of conduct and emotional problems (Jones et al. 2003_a). Two prospective studies found that smoking is a significant risk factor for future development of LBP among adolescents (Feldman et al. 2001; Mikkonen et al. 2008). Finally, one study found that low maximal lumbar mobility can predict the onset of LBP (Kujala et al. 1997).

2.7. Natural course and predictive factors for chronicity

There is a paucity of studies on the natural course of musculoskeletal pain in schoolchildren and on factors which predispose to persistence/recurrence of pain. The identification of such prognostic factors could provide important evidence for secondary prevention and counselling. Most previous studies were conducted on small, hospital- or clinic-based study populations. Clinic-based populations may not be representative of children and adolescents with musculoskeletal pain in the general population, who are not all referred to a hospital. However, few studies have used community-based samples. In a prospective 3- and 9-year follow-up study of 14-year-old children initially complaining of low back pain, 35% still reported recurrent LBP at 18 years of age and up to early adulthood. Early degeneration of lower lumbar discs was the most significant predictive factor for LBP persistence in this controlled study (Salminen et al. 1999). Another 1-and 2-year follow-up study was conducted on a cohort of 254 children (age birth to 18 years) with chronic pain (regardless of location). Of these children, 48% and 30% still experienced chronic pain at one-year and two-year follow-up, respectively, while 9% reported pain at both time points. The frequency and duration of pain, emotional stress, mother's health and location of pain (limb pain had a better prognosis compared to headache) predicted pain persistence. Emotional stress was the only independent predictor of pain status at follow-up (Perquin et al. 2003). Only one school-

based study evaluated the natural course of “fibromyalgia” in children (Buskila et al. 1995). This follow-up study re-evaluated 21 children (age 9 to 15 years) who had fibromyalgia at baseline and found that 27% of these children still fulfilled the disease criteria at the 30-month follow-up (Buskila et al. 1995). Finally, Mikkelsen et al. (1998_b), using the same study population as the present work, found that 52% of the schoolchildren with weekly musculoskeletal pain at baseline still reported musculoskeletal symptoms at the 1-year follow-up. Significant predictive factors for persistence included older age, day tiredness and physical limitations attributed to pain. Hypermobility and frequency of physical activity did not seem to alter the natural course of widespread pain in this study population, which was predominantly composed of children aged 10-12 years.

3. AIMS OF THE STUDY

The general aim of the study was to assess the occurrence, prognosis and determinants (risk factors and prognostic markers) of musculoskeletal pain in schoolchildren aged 10-12 years.

The specific aims of the study include:

- (1) To determine the occurrence of new-onset musculoskeletal pain in different regions of the body (article 1)
- (2) To estimate the prevalence of pain affecting different anatomical locations in the lower limb and investigate subjective physical limitations attributed to it (article 3).
- (3) To estimate the prevalence of widespread pain in schoolchildren as they grow from pre-teenage through early adolescence to mid adolescence, and determine the incidence proportion of this condition (article 5).
- (4) To identify risk factors of musculoskeletal pain (in any location), lower limb pain and widespread pain (article 1, 3 and 5).
- (5) To evaluate the short and long-term prognosis of musculoskeletal pain in different body regions (article 2, 4 and 5).
- (6) To determine predictive factors of persistence/recurrence (prognostic factors) of musculoskeletal pain (in any location) and specifically of lower limb pain (article 2 and 4).

4. MATERIALS AND METHODS

4.1. Study population

This study is based on 1- and 4-year follow-up of a cohort of primary school children in Lahti, Finland. Recruitment of subjects and collection of baseline data was conducted in March 1995. The 1- and 4-year follow-ups were conducted in March 1996 and March 1999, respectively (Figure 1). The source population for the baseline survey of this study consisted of all 3rd and 5th grade primary schoolchildren residing in the city of Lahti in Southern Finland in May 1995. Lahti had a population of 94,827 inhabitants in 1995 (the year of baseline data collection). The city had 21 primary schools in that year, all of which were invited to take part in the baseline survey. Two primary schools refused to participate, and all pupils from the third and fifth grades in the remaining 19 schools and present at school on the day of the survey participated in the study. Two special schools (the hospital school and the school for the hearing- and physically-disabled and the mentally handicapped) were not invited to participate because the physical fitness test was not suitable for their pupils. The Steiner school was also not invited. Based on acquired information, this school does not use physical fitness tests in primary school in general. The final sample consisted of 1756 children representing 82.9% of the children of these grades attending normal or special school in Lahti, and 96% of children attending the participating schools (Mikkelsen et al. 1997). Of these children, 423 were 3rd grade boys, 439 were 3rd grade girls, 444 were 5th grade boys and 450 were 5th grade girls. The mean ages of the 3rd and 5th grade students was 9.8 years (SD 0.3) and 11.8 (SD 0.4), respectively.

At the one-year follow-up, 1628 children participated in the study. This sample represented 76.9% of the children of the studied age groups, and 92.7% of the baseline study population. At the four-year follow-up, 1282 children participated in the study. This sample represented 60.5% of the children of the studied age groups, 73.0% of the baseline study population and 63.4% of the baseline population who also participated at the 1-year follow-up. Occurrence estimates of musculoskeletal pain at baseline evaluation are presented in Table 6 (Mikkelsen et al. 1997).

Figure 1. Flow chart of the study procedures

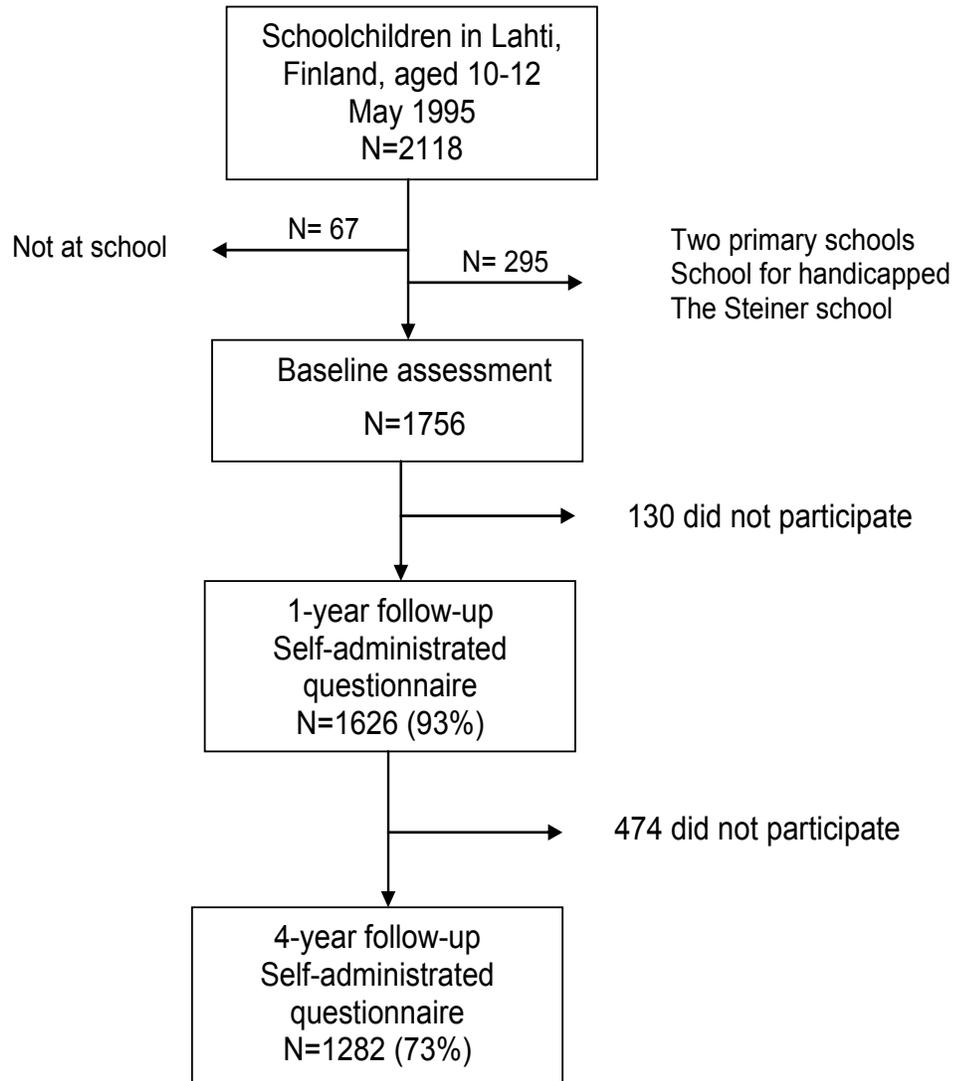


Table 6. Prevalence of musculoskeletal pain at baseline (N = 1756; Mikkelsson et al. 1997)

<i>Musculoskeletal pain</i>	<i>Prevalence, % (number of cases)</i>
General pain (any musculoskeletal location)	32.1 (564)
Neck pain	15.0 (264)
Upper limb	6.4 (113)
Chest	5.4 (94)
Upper back	6.2 (108)
Lower back	4.2 (74)
Lower limb	18.3 (321)
Buttock	2.2 (39)
Widespread pain	7.5 (132)

4.2. Research tools

4.2.1. Class-room administrated questionnaire

At baseline, pain was assessed using a structured questionnaire that was designed by Mikkelsson et al. (1996) to assess musculoskeletal pain (neck, upper limb, chest, upper back, lower back, lower limb and buttock) during the previous three months. Musculoskeletal pains were classified according to pain frequency (seldom or never, once a month, once a week, more than once a week, almost daily). The 5-level frequency classification was adopted from the questionnaire used in the Canadian nationwide survey on health and health-related behaviours in schoolchildren by the World Health Organisation (King et al. 1996). The body area concerned was indicated on a figure placed next to the question to help the child recognize the named area. Furthermore, the children were asked to mark the exact site of pain in the lower extremity (foot, ankle, leg, knee, thigh and hip) if they have indicated experiencing lower limb pain. If the child had pain due to a direct trauma (e.g. injured when exercising, fallen down, stumbled) in any musculoskeletal region, they were asked to indicate the

traumatized area on the pain drawing with a different colour (Mikkelsen et al. 1996; 1997). Other symptoms (headache, abdominal pain, depressive mood, day tiredness, difficulties in falling asleep, waking up during nights) were asked about with the same frequency categorization as for musculoskeletal pain. Presence of each symptom was defined as occurrence at least once a week. Disability due to pain was assessed by the following questions: A) *Do you have difficulties in falling asleep because of your pain or does your pain disturb your sleep?*; B) *Do you have difficulties while sitting during lessons?*; C) *Do you feel pain if you walk more than one kilometre?*; D) *Do you feel pain during physical exercise class?*; and E) *Does your pain interfere with your hobbies?*. A subjective disability index (1 point for presence of each, maximum 5) was calculated from answers to these questions. Absence from school during the preceding 3 months due to pain or aches was also asked. In addition, the children were asked about the frequency with which they undertook exercise, for at least half an hour, during the preceding 3 months (none, 1-2, 3-4, and 5-7 times a week; Appendix).

During the preparation phase, two versions of the pain questionnaire were tested in two different schools in Nastola, a neighbouring community of Lahti. Special attention was paid to the wording and phrases which children might find hard to understand. The teacher's comments were also considered. The final version of the questionnaire was completed twice by a sample of 22 pupils in the 3rd year and 17 pupils in the 5th year during a lesson at the beginning and at the end of the week. The test-retest reliability of the questionnaire for pain occurring at least once a week was excellent (kappa 0.9). The concurrent validity of the pain questionnaire was also examined by comparing it with similar questions asked in interviews of 31 third- and 25 fifth-grade children on the same day of the survey. The agreement between pain questionnaire and interview was 86% (95% CI 74 to 94%) and kappa was 0.67 (Mikkelsen et al. 1997).

The same pain questionnaire was used to evaluate the schoolchildren at 1-year and at 4-year follow-ups.

4.2.2. Hypermobility test

Hypermobility was tested using Beighton's method (Beighton et al. 1973). In this test, children were asked to perform the following movements: A) Passive dorsiflexion of the little fingers beyond 90°; B) Passive apposition of the thumbs to the flexor aspects of the forearm; C) Hyperextension of the elbows beyond 10°; D) Hyperextension of the knees beyond 10°; and E) Forward flexion of the trunk, with knees straight, so that the palms rest easily on the floor. A score from 0 to 9 was given to each student according to these movements (one point for each side of the body for tests A-D and one point for test E): A nurse, specially trained for performing the tests, examined the children during school lessons. No stretching was allowed before the test. Intra- and inter-observer reliabilities were evaluated earlier with kappa coefficients of 0.75 and 0.78, respectively (Mikkelsen et al. 1996). Out of 1756 children taking part in the initial survey, 1726 (98.3%) were tested for hypermobility. School absence on the examination date was the reason for not being tested. Of those who were examined for hypermobility, 65 (3.8%) did not fill in the pain questionnaire and were therefore excluded. The final sample included 1637 children, 835 girls and 802 boys, mean ages 10.8 (SD 1.0) years and 10.9 (SD 1.1) years, respectively. The sample represented 77.3% of all the schoolchildren in the studied age groups in Lahti and 93.2% of the baseline study sample. The Beighton score of six was used as the cut-off point for hypermobility. Children were also categorized into two groups (with and without regional knee hypermobility) in part of the analysis of article 3.

4.2.3. Shuttle run test

The 20-meter shuttle run test (Léger and Lambert 1982) is an indoor test of maximal performance. It provides a valid and reliable index of cardio-respiratory endurance or maximal oxygen uptake (VO₂ max) in adults and children (Liu et al. 1992; Léger and Gadoury 1989). The test was carried out for all the study subjects, excluding children with acute musculoskeletal injury, acute respiratory infection, or other diseases precluding maximal physical strain. The test was conducted outdoors for children at schools that did not have room for the 20-meter distance required for the test. The test

began at a slow running pace (8 km/hour) and ended when the subject could no longer sustain the pace. The participants ran a 20-metre track back and forth in accordance with a pace dictated by a sound signal from a tape recorder. The running speed was increased every minute by 0.5 km/hour. The subject was stopped if, on two consecutive laps, he/she failed to reach a line 3 meters from the end or felt tired and unable to continue. The stage at which the subject dropped out was the test result and VO_2 max could be estimated on the basis of the known speed at the last stage (Committee of Experts on Sports Research. 1988, p.24). Out of 1756 children, who participated in the baseline survey, 1655 (94.2%) underwent the test. Of them, 1204 (68.6%) took the test indoors (624 girls and 580 boys, mean age 10.8 [SD 1.1] years). On the basis of the distribution of the results (median: 51.1 ml/kg per min), children were categorized into three groups according to their VO_2 max measurements. This categorisation was used in articles 2 and 3, while a continuous variable was used in article 1.

4.3. Case definitions of musculoskeletal pain

Several case definitions of musculoskeletal pain have been used in this research work, depending on the aims of each article. A complete list of terms describing musculoskeletal pain in this study together with their case definitions are presented in Table 7.

4.4. Statistical methods

4.4.1. Descriptive measures

Data were summarized using frequency tables and were expressed as means and SDs, median frequencies or percentages. The most important descriptive values were expressed with 95% CIs. Prevalence of lower limb pains (traumatic and non-traumatic; in different locations) were estimated as ratios of children with the pain conditions of interest to total number of study participants at baseline. Incidence proportion of musculoskeletal pain was estimated as a ratio of children with musculoskeletal pain at the 1-year assessment to total number of schoolchildren who did not meet, at baseline, the same case definition of the musculoskeletal pain of interest. Persistence of

musculoskeletal pain was estimated as a ratio of children with musculoskeletal pain at the 1-year follow-up to total number of children who had, at baseline, the same musculoskeletal pain of interest. Recurrence of musculoskeletal pain was estimated as a ratio of children with musculoskeletal pain at the 4-year follow-up to total number of children who had, at baseline, the same musculoskeletal pain of interest. It must be noted that all through this report the term “pain persistence” is used to describe musculoskeletal pain that was reported at both baseline and 1-year follow-up, while the term “pain recurrence” is used to describe pain that was reported at both baseline and 4-year follow-up. However, the case definitions of the study outcomes, at both follow-ups, referred only to symptoms within three months prior to the surveys. This did not provide information covering the entire follow-up period. Therefore, analytically speaking, it is not possible to distinguish between recurrent (following remission during the first nine months of follow-up) and persistent symptoms.

Differences between traumatic and non-traumatic lower limb pain groups related to their reported subjective pain disability index and school absence were assessed using 2-independent-samples t-test and Fisher’s exact test, respectively. A list of case definitions of terms describing musculoskeletal pain in this study are presented in Table 7.

4.4.2. Estimation of effect sizes and hypothesis testing

Three types of regression analyses were used to estimate effect measures and to examine the association between musculoskeletal pain and potential risk and prognostic factors.

- a) General linear models (GLM) for a binomial outcome measure (presence or absence of musculoskeletal pain at 4-year follow-up) with log link function were used to identify predictive factors for recurrence of musculoskeletal pain in adolescence with risk ratio as effect measure (article 1).

Table 7. Case definitions of musculoskeletal pain conditions

Condition	Case definition
"Any" musculoskeletal pain	Pain present in any musculoskeletal location(s) at least once a week during the previous 3 months.
Site-specific musculoskeletal pain	Pain present in a specific musculoskeletal location (e.g. lower limb) at least once a week during the previous 3 months.
Regional musculoskeletal pain	Pain present in only one specific musculoskeletal location (e.g. only in the lower back) at least once a week during the previous 3 months.
Combined musculoskeletal pain	Pain present in more than one musculoskeletal location (e.g. neck and lower limb) at least once a week during the previous 3 months in all affected sites.
Widespread pain (WSP)	Musculoskeletal pain as classified in the American College of Rheumatology 1990 criteria for FM, which is "Pain involving at least two contralateral body quadrants and the axial skeleton for at least 3 months" (Wolfe et al. 1990). To fulfil the case definition of WSP, children should report musculoskeletal pain according to this classification with a frequency of at least once a week.
Non-traumatic musculoskeletal pain	Pain, not initiated by a direct traumatic event, present in any musculoskeletal location(s) at least once a week during the previous 3 months.
Traumatic musculoskeletal pain	Pain, initiated by a direct traumatic event, present in any musculoskeletal location (s) at least once a week during the previous 3 months.

- b) The Generalized Estimating Equation (GEE) model was used to assess potential risk factors for the onset of widespread pain during the four year follow-up outcome within those who had no WSP at baseline (with odds ratio as an effect measure). The GEE model is applicable to repeated assessments of a binary outcome (WSP, no WSP) in repeated assessments (1-year and 4-year follow-up). This model accommodates the lack of independence of outcome evaluation at both follow-ups. Semi-robust estimates were used to ensure valid standard errors even if the dependence of repeated measures is not exactly as modelled.
- c) Logistic regression analyses were used to identify factors associated with lower limb pain at baseline (article 2), predictive factors for persistence and of lower limb pain at 1-year follow-up and predictive factors for recurrence of lower pain at 4-year follow-up (regardless of pain status at 1-year follow-up; articles 2 and 3). Logistic regression analysis was also used to investigate risk factors for new-onset childhood musculoskeletal pain at the 1-year follow-up (article 4). Cases comprised children with any musculoskeletal pain at the 1-year follow-up, but free from all musculoskeletal at baseline. Children who remained free from pain were included as controls. Odds ratio was the effect measure derived from logistic regression analyses.

In order to investigate risk factors for the onset of general and widespread musculoskeletal (articles 4 and 5), regression models were first fitted with each independent (predictor) variable separately to estimate the unadjusted odds ratios (ORs) or risk ratios (RRs) for each potential determinant in relation to occurrence or persistence of musculoskeletal pain. Multivariate models were then constructed to determine the relative contributions of the factors previously identified as potential important predictors. Variables that reached a statistical threshold of $P \leq 0.20$ in the univariate models were entered in multivariate models.

A backward elimination method was used to investigate predictive factors for recurrence of “Any” musculoskeletal pain (article 1); examine factors associated with lower limb

pain at baseline (article 2); and factors predicting lower limb pain chronicity (article 3). In this stepwise method, all independent variables were initially included in the regression equation and elimination of variables, at each step, was based on likelihood ratio test at 10% level of significance.

Modification by sex was assessed by evaluating interactions between sex and other potential risk/prognostic factors. Interactions between variables were tested all through the analyses. In all statistical tests, a P value of less than 0.05 (two-tailed) was considered statistically significant. All statistical analyses were performed using SPSS (for Windows), version 10.0.

4.5. Ethics

Prior to conducting the three surveys (baseline, 1-year and 4-year follow-up) the parents were informed about the study by a letter. They were asked to call the researcher or inform the teacher if they would not allow their child to participate. Child also had the possibility of refusing. The study protocol was approved by the Ethics Committee of the Health Care Centre of the city of Lahti.

5. RESULTS

5.1. Occurrence

5.1.1. Incidence of “Any” and site-specific musculoskeletal pain

Children who reported no musculoskeletal pain at baseline (N =1192) were followed up for one year to estimate the incidence proportion (risk) of developing musculoskeletal pain. A total of 1113 children completed the pain questionnaire at the follow-up (completeness of follow-up 93%). Of these children, 239 (21.47%, 95% CI 18.5–23.7) reported new-onset musculoskeletal pain in at least one part of the body (“Any” musculoskeletal pain). Of them, 216 children (19.4%, 95% CI 18.5–23.4) reported non-traumatic musculoskeletal pain and 44 children (4.0%, 95% CI 3.1–4.6) had traumatic pain. Twenty-one children reported both types of pain episodes (9.7% of the non-traumatic pain group and 47.7% of the traumatic pain group). The neck was the most commonly reported site with non-traumatic musculoskeletal pain, while the lower limb was the most common site for traumatic pain. Of the 1113 pain-free preteens at baseline, 107 (9.6%, 95% CI 7.7–11.3) had non-traumatic neck pain and 32 (2.9%, 95% CI 2.2–3.4) had traumatic lower limb pain at the one-year follow-up (Table 8).

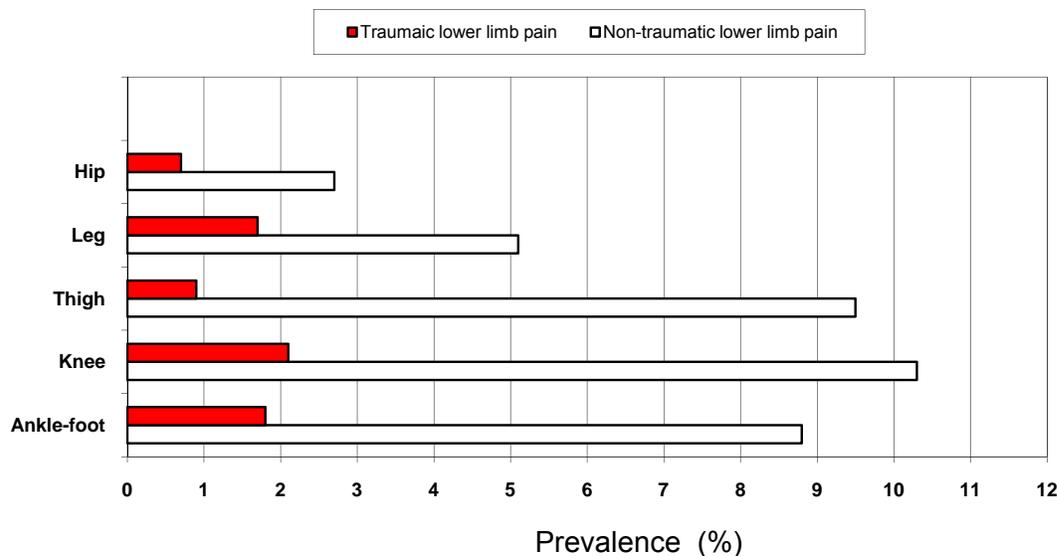
Table 8. Numbers and percentages of children with new-onset musculoskeletal pain at the 1-year follow-up (out of 1131 subjects who were pain-free at baseline)

Musculoskeletal region	Non-traumatic pain	Traumatic pain
Neck	107 (9.6%)	8 (0.7%)
Upper limb	34 (3.1%)	1 (0.1%)
Chest	31 (2.8%)	3 (0.3%)
Upper back	37 (3.3%)	1 (0.1%)
Lower back	26 (2.3%)	2 (0.2%)
Lower limb	83 (2.3%)	32 (2.9%)
Buttock	7 (0.6%)	1 (0.1%)

5.1.2. Prevalence and physical limitations of lower limb pain

Of the 1756 children who participated at baseline, 321 (18.3%) reported pain affecting their lower limb. Of them, 216 (12.3%) had non-traumatic pain and 105 (6.0%) traumatic pain. Out of those with non-traumatic lower limb pain, 95% (N = 205) reported that their pain was diffuse and not limited to one specific lower limb site. On the other hand, only 21% (N = 22) of the traumatic group reported that they had pain affecting more than one lower limb site. The knee was the most commonly affected site for both traumatic and non-traumatic lower limb pain. Non-traumatic pain involved frequently the thigh, while the ankle-foot was a common site for traumatic pain (Figure 2). Injuries were reported by 34% (N = 54) of children with regional lower limb pain, and by 32% (N = 52) of children with combined lower limb pain.

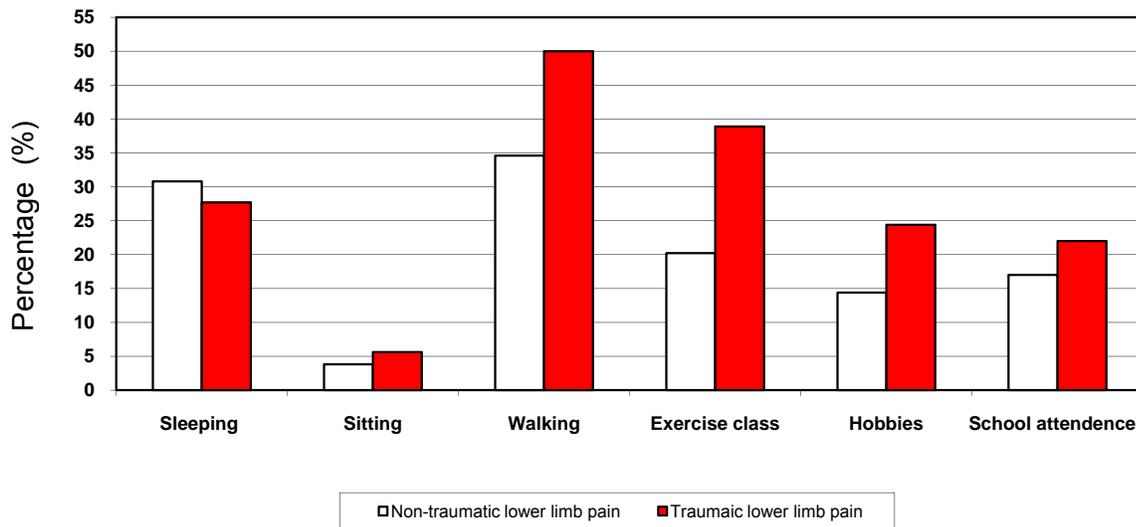
Figure 2. Prevalence of non-traumatic and traumatic pain in different anatomical regions in the lower limb



The extent of physical limitations due to lower limb pain was evaluated at baseline to determine the impact of these pain symptoms on schoolchildren. The analysis was limited to those who had lower limb as the only musculoskeletal pain area (regional lower limb group) to eliminate possible effect of other musculoskeletal pains. Out of 158 children with regional lower limb pain, 70% (N = 110) reported disability attributed to

their pain, 40% (N = 63) had pain disturbing walking > 1 km, 30% (N = 47) had pain disturbing their sleep. In addition, 27% (N = 42) reported that pain interfered with their physical exercise classes, 18% (N = 28) had problems with hobbies and 4% (N = 7) reported pain affecting their sitting comfort. School absence due to pain, for one or more days during the preceding 3 months, was reported by 19% (N = 30) of these children. Children with regional traumatic lower limb pain had a significantly higher subjective disability index than children with regional non-traumatic lower limb pain ($t = 2.36$, $P = 0.02$). Children with traumatic lower limb pain had more physical limitations related to daily activities, while those with non-traumatic pain had more sleeping problems (Figure 3). There was no significant difference in school absence between the children with traumatic and non-traumatic pain.

Figure 3. Percentages of children with lower limb pain reporting interference with their usual daily activities



5.1.3. Prevalence and incidence of WSP

The prevalence of WSP among children who participated in the baseline survey and both follow-ups (N = 1282) increased from 7% at baseline (93 children, 10-12 years) to 9% at the 1-year follow-up (110 children, 11-13 years) to 15% at the 4-year follow-up (195 children, 14-16 years).

Approximately 7% and 14% of children who had no WSP pain at baseline developed WSP at the 1-year and 4-year follow-ups, respectively (Table 9). The incidence of WSP was considerably higher among children who had “Any” musculoskeletal pain at baseline, as compared to the incidence among those who had no musculoskeletal pain.

Table 9. Incidence estimates of WSP at the 1-year and 4-year follow-ups

	<i>Cumulative incidence (No. of cases)</i>			
	At 1-year follow-up	At 4-year follow-up	At either follow-ups	At both follow-ups
In children with no musculoskeletal pain (N = 366)	1.4 (5)	8.2 (30)	9.3 (34)	0.3 (1)
In children with “Any” musculoskeletal pain (N = 823)	9.2 (76)	16.7 (137)	22.4 (184)	3.5 (29)
In both groups (N = 1089)	6.8 (81)	14.1 (167)	18.3 (218)	2.5 (30)

5.2. Risk factors

5.2.1. Risk factors of incident “Any” musculoskeletal pain

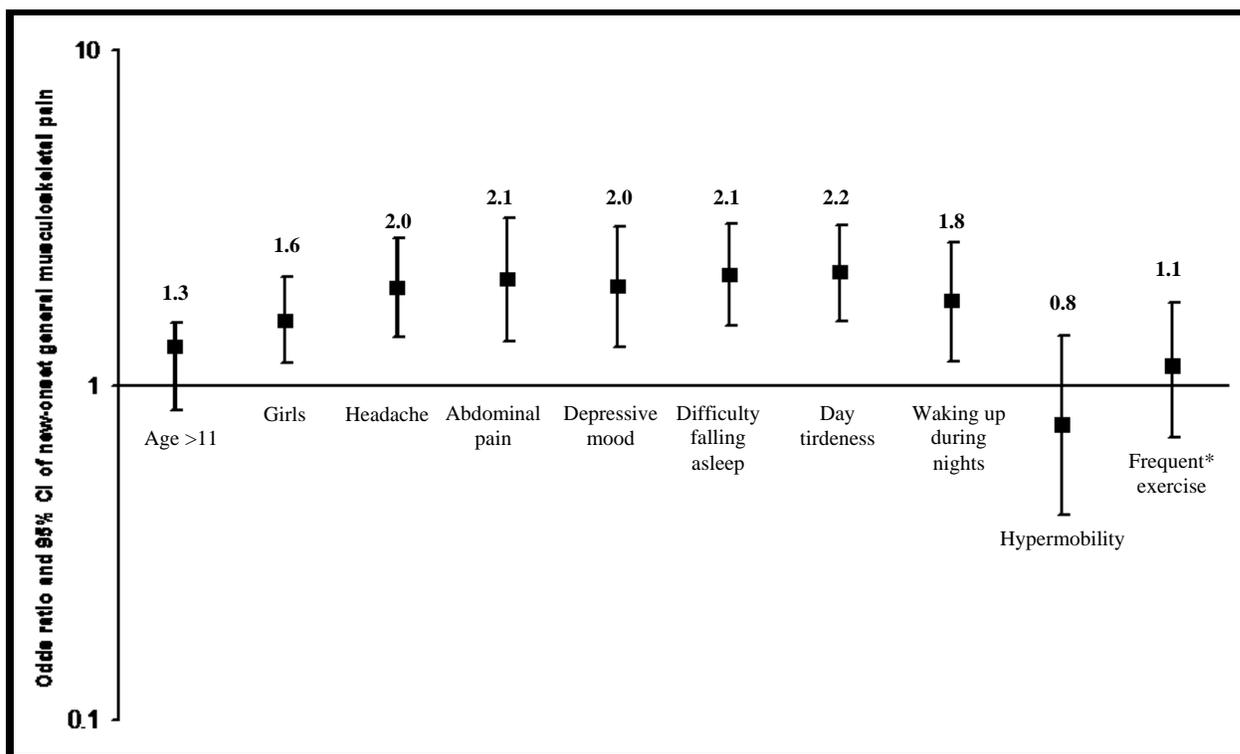
Children who reported no musculoskeletal pain at baseline (N =1192) were followed up for one year. Data from 1113 children who participated to the 1-year follow-up was analysed in order to identify risk factors of incident/new-onset musculoskeletal pain at the 1-year follow-up.

5.2.1.1. Risk factors of incident non-traumatic musculoskeletal pain

In the univariate analyses, significant associations were found between incident non-traumatic musculoskeletal pain and female gender and all self-reported symptoms (Figure 4). In the multivariate analysis, the predictive factors for development of non-traumatic pain were headache (OR = 1.68, [95% CI 1.16–2.44]) and day-time tiredness

(OR = 1.53, [95% CI 1.03–2.26]). Furthermore, borderline significance was found for female gender (OR = 1.39 [95% CI 0.99–1.94]) and difficulty in falling asleep (OR = 1.48 [95% CI 0.99–2.23]). Hypermobility did not predict development of non-traumatic musculoskeletal pain. Almost indistinguishable results were found when we reanalysed the data using a cut-off point of ≥ 4 in the Brighton score.

Figure 4. Risk factors of new-onset "Any" non-traumatic musculoskeletal pain



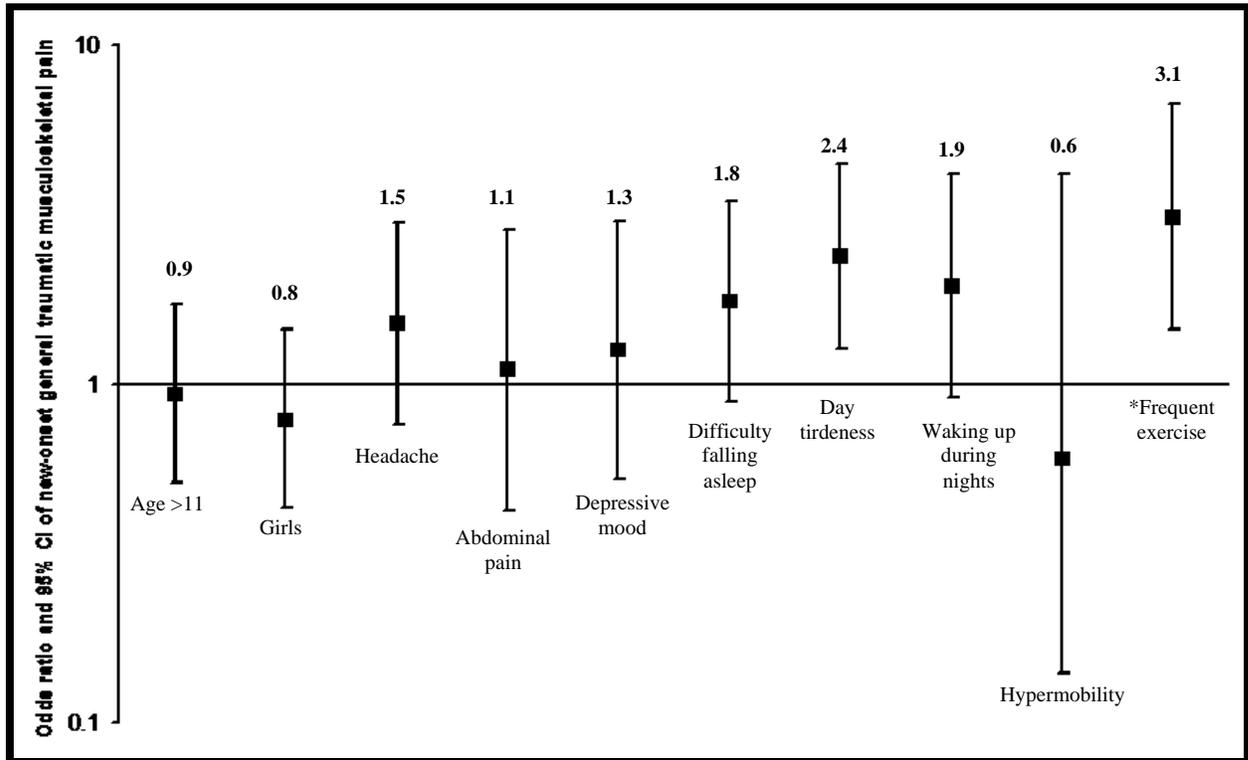
* Practiced exercise 5–7 times a week, reference category 0-2 times a week.

5.2.1.2. Risk factors of incident traumatic musculoskeletal pain

In the univariate analyses, significant associations were found between incident traumatic musculoskeletal pain and day tiredness and vigorous exercise (Figure 5). In the multivariate analysis, frequent exercise (OR = 3.40 [95% CI 1.39–8.31]) and day-time tiredness (OR = 2.97 [95% CI 1.41–6.26]) were found as independent predictors. Hypermobility was not associated with an increased risk of traumatic musculoskeletal

pain. Similar non-significant findings were obtained when data was re-analysed using a cut-off point of ≥ 4 in the Brighton score.

Figure 5. Risk factors of new-onset “Any” traumatic musculoskeletal pain



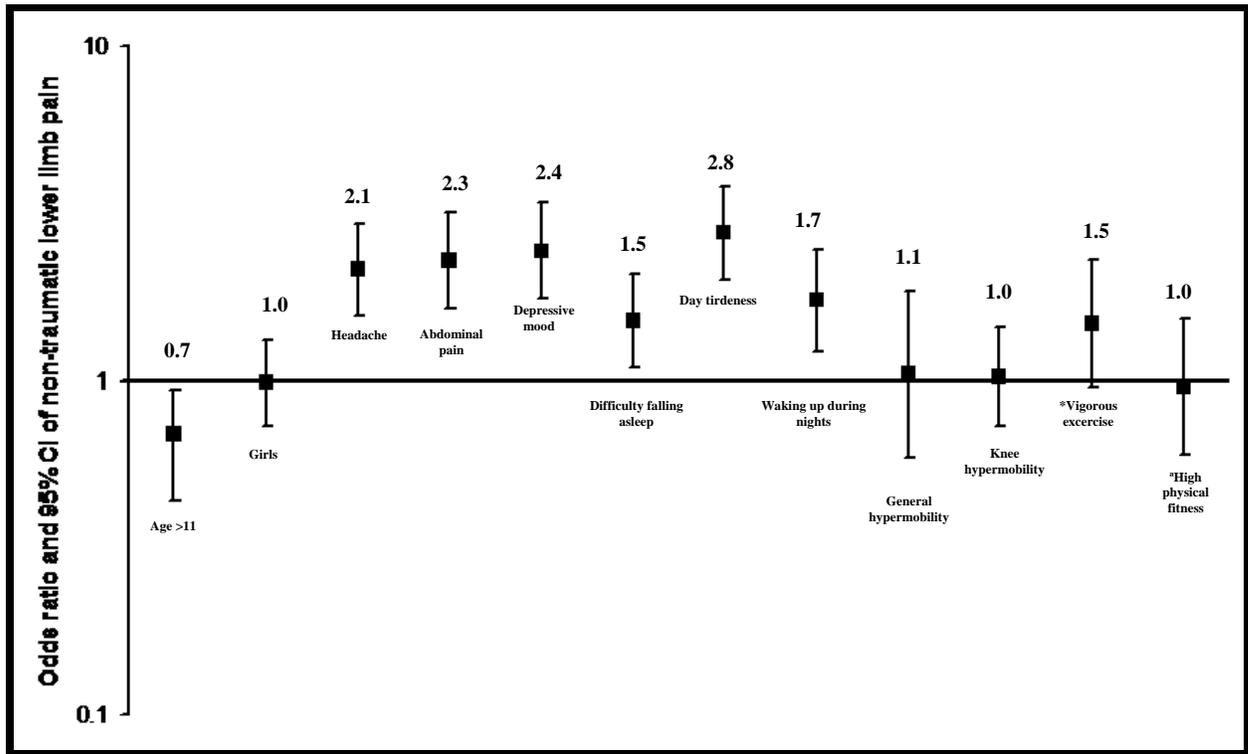
* Practiced exercise 5–7 times a week, reference category 0-2 times a week.

5.2.2. Risk factors of prevalent lower limb pain

Children who reported lower limb pain at baseline (N =321) were compared to those who did not report such pain in order to identify associated factors (probable risk markers) for its occurrence.

In the univariate analyses, all self-reported symptoms were positively associated with non-traumatic and traumatic lower limb pain (Figure 6 and 7).

Figure 6: Risk factors of non-traumatic lower limb pain (univariate analysis)



* Practiced exercise in a frequency of 5–7 times a week, reference category 0-2 times a week.

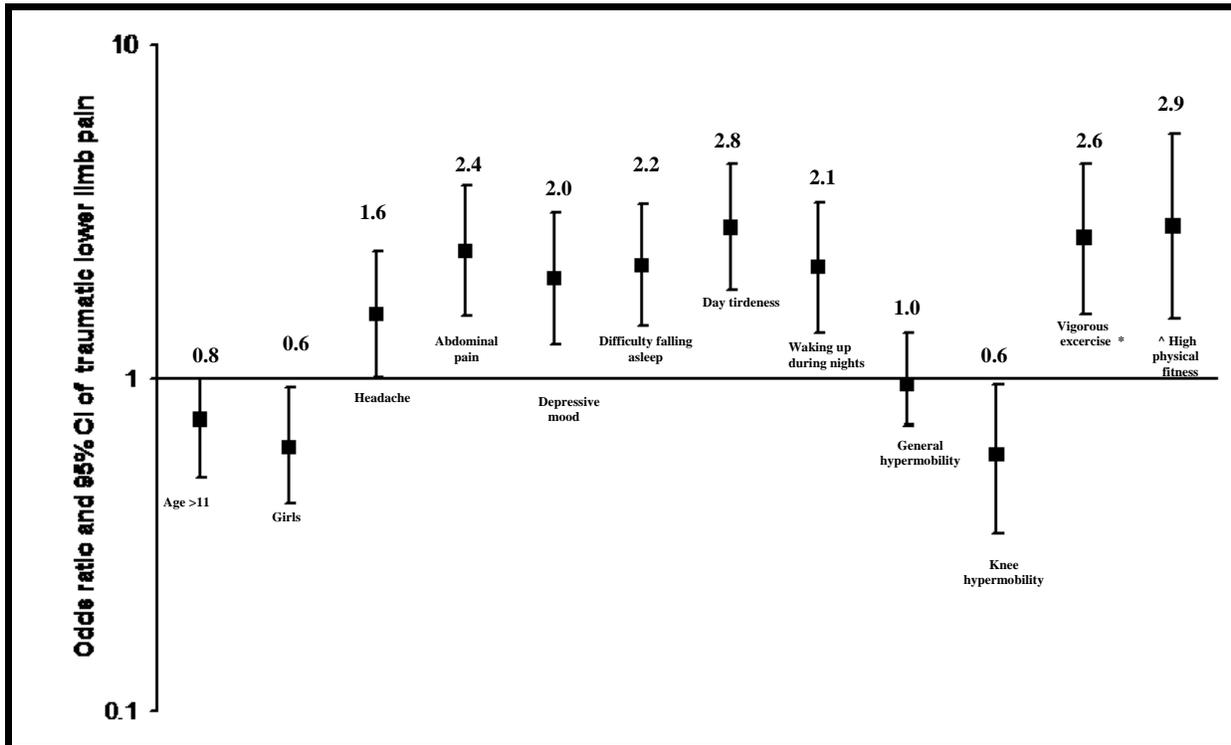
^a Above the 75th percentile, reference category below the 25th percentile

In the multivariate analysis, day tiredness was the only symptom associated with traumatic pain, while headache, depressive feelings and day tiredness were positively related to non-traumatic pain (Table 10).

No relationship was found between physical activity or physical fitness and occurrence of non-traumatic pain in the lower extremity (Figure 6). On the other hand, both frequent exercise and good physical fitness were significantly and independently associated with traumatic lower limb pain (Table 10). Furthermore, a significant synergistic interaction was found between these two factors ($p = 0.015$). The effect of high physical fitness on occurrence of traumatic lower limb pain increased with the amount of exercise. The association between high physical fitness and traumatic pain increased steadily from an OR of 2.13 (95% CI 1.12–4.42) in children who practiced infrequent exercise, to an OR

of 3.35 (95% CI 1.22–5.88) in children who practiced moderate exercise, and finally to an OR of 7.54 (95% CI 0.86–10.72) in children who practiced vigorous exercise.

Figure 7: Risk factors of traumatic lower limb pain (univariate analysis)



* Practiced exercise in a frequency of 5–7 times a week, reference category 0-2 times a week.

^Above the 75th percentile, reference category below the 25th percentile

Similar to the crude results, age was inversely associated with both traumatic and non-traumatic lower limb pain. Hypermobility was not associated with either traumatic or non-traumatic pain, and no significant interaction was found between physical exercise and hypermobility on occurrence of the two conditions. Children with regional knee hypermobility were less likely to have traumatic pain compared to children with normal joint laxity (OR = 0.59 [95% CI 1.22–5.88]). However, the latter association was only significant in the univariate but not in the multivariate analysis. A possible explanation for this un-adjusted association might be that children with regional knee hypermobility are not engaged in competitive sports as their peers.

Table 10. Factors associated with non-traumatic and traumatic lower limb pain (Multivariate model*)

<i>Variables</i>	<i>Non-traumatic pain</i>	<i>Traumatic pain</i>
	<i>OR (95% CI)</i>	<i>OR (95% CI)</i>
Aged > 11 years	0.67 (0.4-0.9)	
Headache	1.9 (1.3-2.8)	
Depressive feelings	1.7 (1.2-2.8)	
Day tiredness	2.0 (1.3-2.9)	2.8 (1.7-4.6)
Frequency of exercise		
0-2 times a week		Reference
3-4 times a week		0.9 (0.6-1.7)
5-7 times a week		2.0 (1.1-3.8)
^a VO ₂ max		
Average		Reference
Low		1.5 (0.9-2.2)
High		13.0 (1.7-25.8)

*Using backward stepwise procedure. Only the included variables are shown. Results based on data from 1199 schoolchildren who completed the pain questionnaire and were tested for both hypermobility and physical fitness.

^a Measured in ml/kg/min, categorized into 3 groups (below the 25th percentile (low), between the 25th and the 75th percentiles (average), and above the 75th percentile (high))

5.2.3. Risk factors of incident widespread pain

The independent predictors of WSP were age >11 years, female gender, depressive mood and pain in the neck, upper back and lower back (Table 11).

Table 11. Risk factors for development of WSP

<i>Baseline factors</i>	<i>Age and sex-adjusted analysis</i>	<i>Multivariate analysis[^]</i>
	<i>OR (95% CI)</i>	<i>OR (95% CI)</i>
Aged > 11 years ¹	1.4 (1.1-1.8)	1.3 (0.99-1.8)
Females ¹	1.5 (1.2-2.0)	1.4 (1.1-1.9)
Somatic pain symptoms [†]		
Headache	1.8 (1.4-2.4)	1.2 (0.8-1.6)
Abdominal pain	1.9 (1.4-2.6)	1.2 (0.8-1.7)
Neck pain	2.5 (1.7-3.5)	1.7 (1.1-2.4)
Upper back pain	4.1 (2.1-7.8)	2.1 (1.1-4.1)
Lower back pain	5.0 (2.7-9.1)	3.0 (1.6-5.7)
Upper limb pain	2.5 (1.3-4.7)	1.7 (0.9-3.4)
Lower limb pain	1.8 (1.3-2.6)	1.4 (0.97-2.1)
Chest pain	1.2 (0.6-2.3)	Not included in model
Other symptoms		
Depressive mood	2.4 (1.8-3.2)	1.5 (1.1-2.2)
Day tiredness	1.9 (1.4-2.5)	1.1 (0.8-1.6)
Difficulty falling asleep	1.8 (1.3-2.4)	1.2 (0.9-1.7)
Waking up during nights	1.7 (1.2-2.3)	1.1 (0.8-1.6)
Vigorous exercise ^α	1.1 (0.8-1.7)	Not included in model
Hypermobility [~]	1.0 (0.9-1.1)	Not included in model
Time (per year)	1.3 (1.2-1.4)	1.3 (1.2-1.4)

¹ Adjusted for only age or only sex, as appropriate.

^α Practiced exercise till breathlessness for at least 5 days in a week at baseline.

[~] Had a Beighton score of 6 or higher at baseline.

[†] Reported in a frequency of at least once a week at baseline.

[^]Figures adjusted for all factors that predicted WSP with a significance of $p < 0.2$ in the age and sex-adjusted analyses.

5.3. Prognosis and predictive factors for chronicity

5.3.1. Prognosis of “Any” musculoskeletal pain

Children who reported “Any” musculoskeletal pain at baseline (N=564) were followed up at one and four years to determine the prognosis. A total of 403 children completed the pain questionnaire at both follow-ups (completeness of follow-up 71%). Of them, 53.8% (95% CI 48.8–58.8) reported “Any” musculoskeletal pain at the 1-year follow-up, while 63.5% (95% CI 58.7–68.1) had general pain at 4 years. The majority of the children who had musculoskeletal pain at baseline and at the 1-year follow-up still reported musculoskeletal pain at the 4-year follow-up (74.7%; 95% CI 68.5–80.0). About half of the children who had musculoskeletal pain at baseline, but did not report it at the 1-year follow-up had these symptoms at the 4-year follow-up (50.5%; 95% CI 43.3–57.6). Those who reported “Any” musculoskeletal pain at both baseline and the 1-year follow-up (persistent preadolescent musculoskeletal pain) had approximately three times (OR 2.9 [95% CI 1.9–4.4]) higher risk of musculoskeletal pain recurrence at 4-year follow-up compared to those who reported “Any” musculoskeletal pain at baseline only. The most persistent/recurrent musculoskeletal pain site was the neck. Of the 187 children reporting site-specific neck pain at baseline, 48.1% (95% CI 40.7–55.5) had neck pain at the 1-year follow-up and 52.4% (95% CI 45.2–59.5) at the 4-year follow-up (Figure 8).

At both 1-and 4-year follow-ups, children with regional musculoskeletal pain at baseline (i.e. with a single affected musculoskeletal site) had better prognosis than those with combined musculoskeletal pain (i.e. with several affected musculoskeletal pain sites). Among those who had combined musculoskeletal pain at baseline and reported persistent/recurrent musculoskeletal pain, pain remained combined in the majority at both 1-year follow-up (66.7%) and 4-year follow-up (62.9%). On the other hand, of those who had regional musculoskeletal pain at baseline and reported persistent/recurrent musculoskeletal pain, combined pain was reported by 35% at 1-year follow-up and by 51% at 4-year follow-up (Figure 9).

Figure 8. Persistence/recurrence of site-specific musculoskeletal pain symptoms at the 1-year and 4-year follow-ups (N = 403).

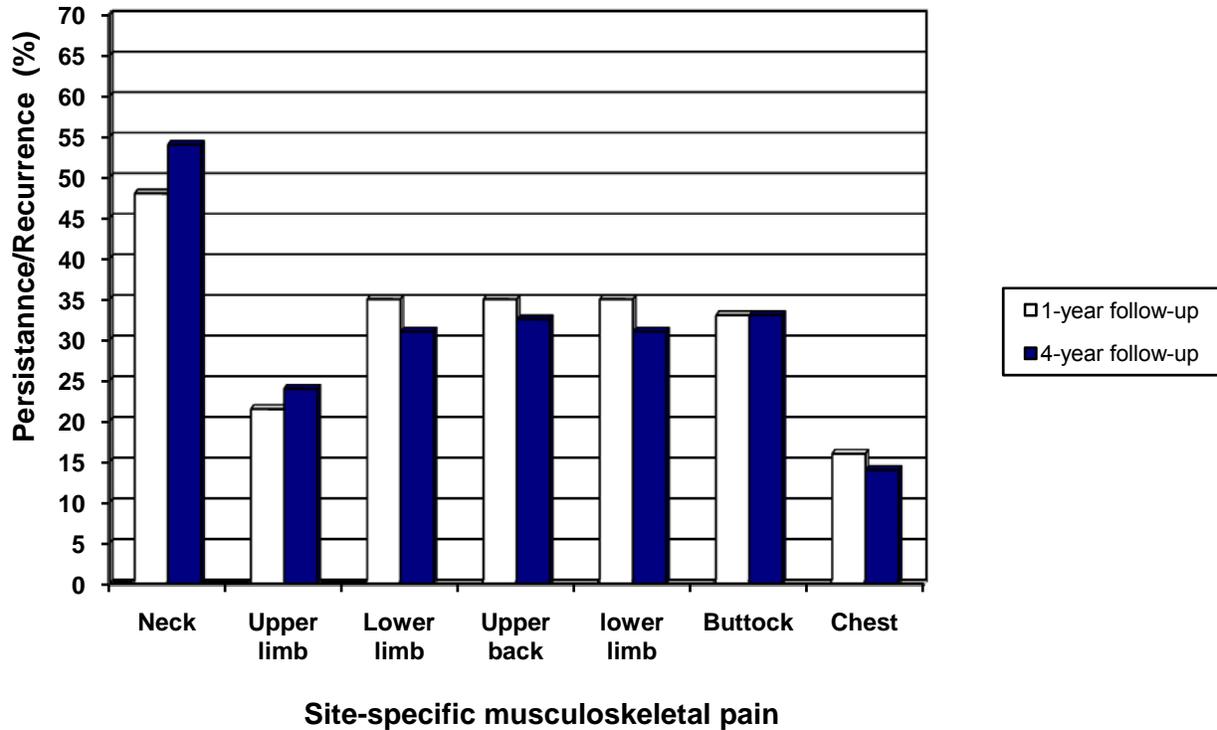
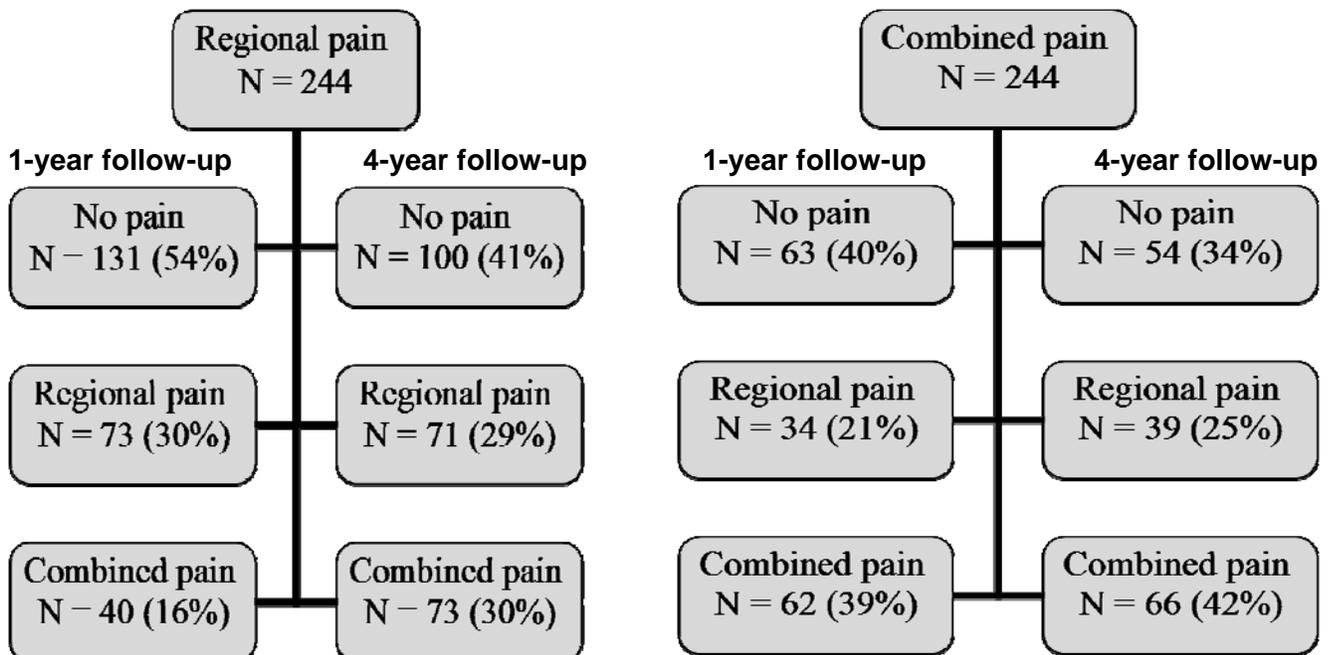


Figure 9. Prognosis of regional versus combined musculoskeletal pain at the 1- and 4-year follow-ups



Children who had “Any” musculoskeletal pain at baseline (N =564) were followed up for four years. Data from 403 children who participated to the 4-year follow-up were analysed in order to identify predictive factors for persistence/recurrence of these symptoms.

The following baseline factors were significantly associated with persistence/recurrence of pain in the univariate analysis: Female gender, age >11, headache, abdominal pain, depressive feelings, high disability index, having pain in more than one musculoskeletal location (combined musculoskeletal pain, and hypermobility (Figure 10). However, in the multivariate analysis, only age >11 (RR 1.28, 95% CI 1.10–1.49), headache (RR 1.28, 95% CI 1.08–1.51), hypermobility (RR 1.35, 95% CI 1.08– 1.68), and combined musculoskeletal pain (RR 1.18, 95% CI 1.02–1.36) were independently predictive of pain persistence/ recurrence.

Figure 10. Predictive factors for persistence/recurrence of “Any” non-traumatic musculoskeletal pain at the 4-year follow-up (long-term prognostic factors)



*Reported 3-5 physical limitations, reference category 0/1 physical limitation.

5.3.2. Prognosis of lower limb pain

Children who reported lower limb pain at baseline (N=321) were followed up for one and four years to determine its prognosis at the short- and long-term, respectively. A total of 295 children (92%) completed the pain questionnaire at the 1-year follow-up and a total of 228 children (71%) completed the pain questionnaire at the 4-year follow-up.

Persistence or recurrence of lower limb pain was reported by 32% and 31% at the 1-year and 4-year follow-up, respectively, and 14.5% had lower limb pain at both follow-up evaluations. Compared with preadolescents who did not report lower limb pain at baseline, those with lower limb pain had almost 3-fold risk for occurrence of lower extremity pain at both 1-year (risk ratio 2.76; 95% CI: 2.21–3.44) and 4-year follow-up (risk ratio 2.79; 95% CI: 1.16– 3.62).

In the univariate analyses, age, sex and baseline characteristics of pain and all self-reported symptoms did not affect the short- or long-term prognosis of lower limb pain (Table 12). Of the mechanical/physical factors, vigorous exercise and hypermobility were the only factors predicting short- term and long-term prognosis, respectively (Figure 11).

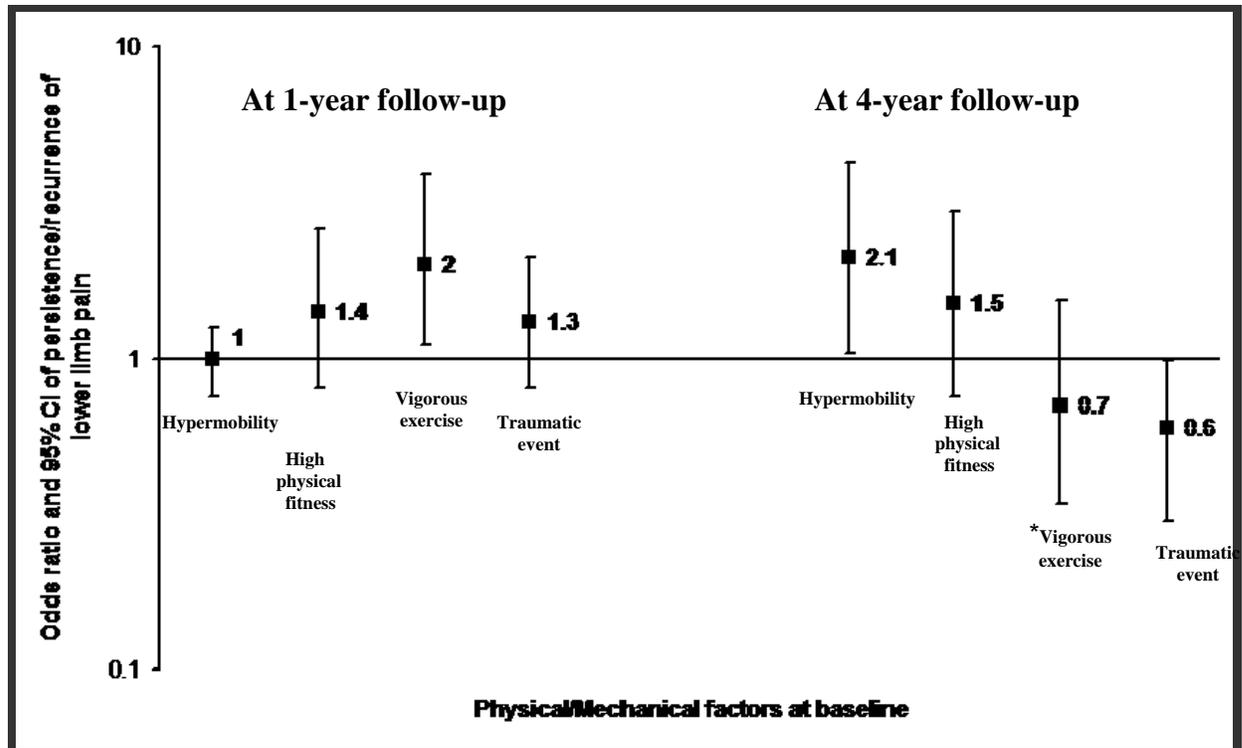
In the multivariate analysis, frequent exercise at baseline was the only factor predicting persistence of lower limb pain at the 1-year follow-up (OR 2.43; 95% CI 1.16–5.05). With respect to predictors of long-term prognosis, the odds of a child having persistent/recurrent lower limb pain is half as high in the traumatic group as the non-traumatic group (OR 0.48; 95% CI 0.19-0.92). In addition, hypermobility was associated with about 3-fold OR for pain recurrence compared with the non-hypermobile group (OR 2.9; 95% CI 1.13–7.70).

Table 12. Relationship between age, gender, self-reported symptoms and pain characteristics versus persistence and recurrence of lower limb pain (univariate analysis)

<i>Variables</i>	<i>Persistence of pain at 1-Year Follow-up</i>	<i>Recurrence of pain at 4-Year Follow-up</i>
Total N	295	228
Age		
9–11 y	Reference	Reference
11–14 y	1.14 (0.70–1.86)	0.88 (0.49–1.56)
Gender		
Male	Reference	Reference
Female	0.82 (0.50–1.34)	1.03 (0.58–1.83)
Self-reported symptoms		
Headache	1.14 (0.70–1.87)	1.66 (0.93–2.96)
Abdominal pain	1.42 (0.86–2.34)	1.29 (0.72–2.31)
Depressive feelings	1.26 (0.77–2.06)	1.09 (0.61–1.95)
Difficulties in falling asleep	1.12 (0.68–1.84)	0.66 (0.36–1.21)
Day tiredness	1.30 (0.63–1.69)	0.88 (0.49–1.56)
Waking up during nights	1.47 (0.87–2.49)	1.50 (0.81–2.81)
School absence as a result of pain		
Never absent	Reference	Reference
Absent	1.23 (0.72–2.09)	0.84 (0.44–1.60)
Disability symptoms		
≤2 symptoms	Reference	Reference
≥3 symptoms	1.59 (0.87–2.92)	0.85 (0.47–1.54)
Frequency of lower limb pain		
Once a week	Reference	Reference
More than once a week	1.34 (0.80–2.22)	0.82 (0.54–1.26)
Extent of lower limb pain~		
Regional pain	Reference	Reference
Combined pain	1.36 (0.85–2.25)	0.66 (0.37–1.18)

~Reported lower limb as the only musculoskeletal area with pain (regional) or reported lower limb pain together with pain in other musculoskeletal areas (combined).

Figure 11. Odds ratios of persistence/recurrence of lower limb pain at the 1- and 4-year follow-ups by physical/mechanical factors at baseline (univariate analysis)



* Practiced exercise in a frequency of 5–7 times a week, reference category 0-2 times a week.

5.3.3. Prognosis of widespread pain

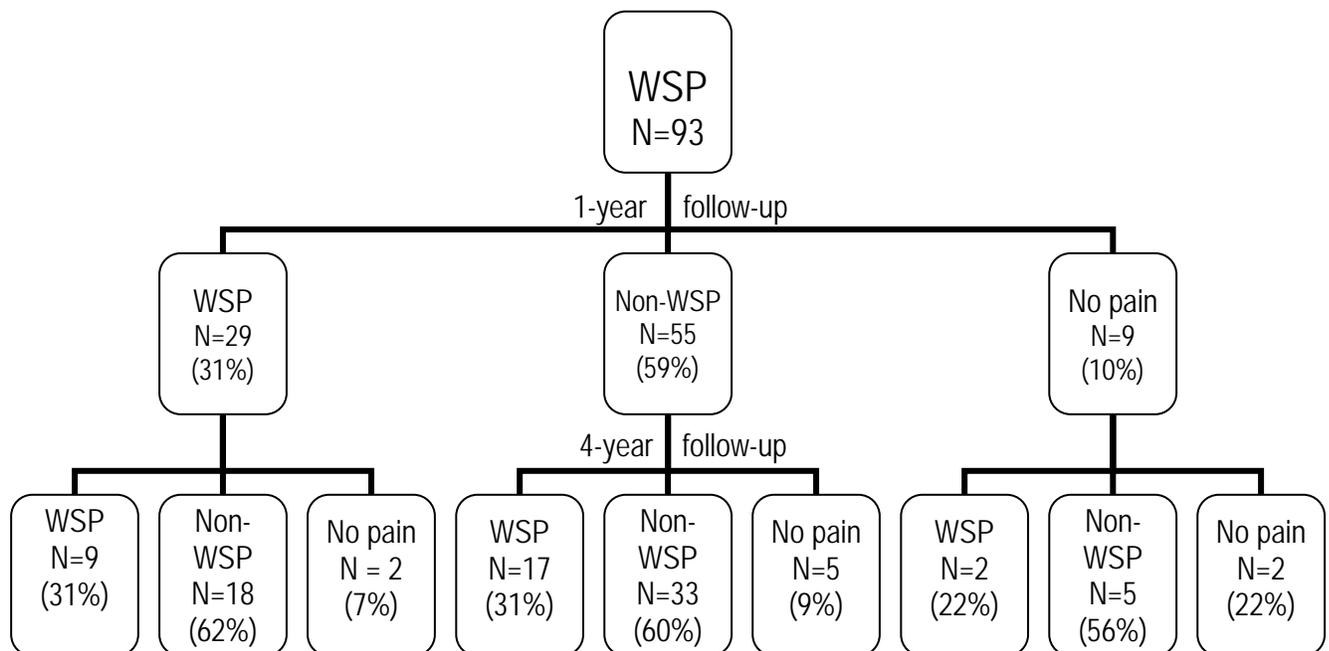
Of the 93 children who had WSP at baseline, 31% reported persistent/recurrent symptoms at the 1-year, and 30% reported these symptoms at the 4-year follow-up. Of the children affected at baseline, 52% reported WSP at either follow-up, and 10% at both follow-ups. Of the 81 children who developed new-onset WSP at the 1-year follow-up, 37% (30 children) reported persistent/recurrent symptoms at the 4-year follow-up

(Figure 12). Overall, only 0.7% (9 children out of 1282) reported WSP at all three time points.

Of the children who had regional pain at baseline (i.e. pains that do not meet criteria of WSP), 22% developed WSP at the 1-or 4-year follow-up, 9% had no pains at both follow-ups and 69% still reported regional pain at the 1 and 4-year follow-up (Figure 12).

Of the children who reported no musculoskeletal pain at baseline, 25.4% remained painless at both follow-ups (representing 7.3% of the whole 1282 baseline study population), 9.3% developed WSP at either the 1- or 4-year follow-up, while 65.3% reported regional pain(s) at both follow-ups. Overall, a total of 614 children (representing 47.5% of the whole baseline study population) reported pain in one or more musculoskeletal locations at all three time points of assessments (Figure 12).

Figure 12. Prognosis of widespread pain (WSP) at the 1-year and 4-year follow-ups.



6. DISCUSSION

6.1. Methodological considerations

6.1.1. *Participation and follow-up*

This is a 4-year follow-up study of a representative sample of Finnish schoolchildren residing in the city of Lahti. The study was set up in March 1995 with a city-wide survey of schoolchildren in the third and fifth grades in primary schools in this small city located in the southern part of Finland. The proportion of children attending grades 3 and 5 in these schools who actually participated in our survey was very high (83%). Children who participated in the baseline survey (Time 0; T0) were then followed-up after 1 year (Time 1; T1) and then after 4 years (Time 2; T2). The proportion of children at T0 who completed the follow-up questionnaires at T1 and T2 were 93% and 77%, respectively. The proportion of children at T0 who completed both T1 and T4 were 73%. We consider our participation and follow-up proportions to be comparable or larger than other previously published classroom follow-up surveys on musculoskeletal pain in children. For example, in a 1-year follow-up study of Canadian secondary school students, 85% of the children who were originally invited to participate actually took part in the baseline assessment. Of them, only 62% were re-assessed at the follow-up (Ehrmann-Feldman et al. 2002_a). Similarly, a 4-year follow-up study of secondary school children in England reported participation and follow-up rates of 94% and 58%, respectively (Jones et al. 2003_a).

Attrition (participation/lost to follow-up) bias is a potentially important problem in epidemiological studies, particularly in long-term follow-up (Kleinbaum et al. 1981). This type of selection bias might threaten the internal validity of the study if children had different probability of being included (or followed-up) according to their exposure and outcome of interest. Participation bias is not a major problem in our study for two reasons. Firstly, and as mentioned earlier, we had an excellent participation rate of 93% and secondly, the vast majority of children who did not participate in the baseline survey came from schools which declined to take part in the study (2 out of 21 schools). However, a systematic error might have affected our results if the relationships between

the exposures of interest (e.g. physical activity, age, hypermobility) and the outcome of interest (i.e. musculoskeletal pain) in the group who participated at follow-up were considerably different from that in the group who were lost at follow-up. In this study, both groups (i.e. children who were found and lost at follow-up) were similar with respect to almost all baseline characteristics. In addition, a multivariate logistic regression analysis was conducted and none of baseline variables significantly influenced children's drop-out rate. This kind of analysis can confirm that children who participated in the follow-up assessments had a similar distribution of baseline-measured potential determinants of musculoskeletal pain. However, it cannot confirm that the relationship between these factors and musculoskeletal pain in the group who participated in the follow-up assessment was comparable to that in the drop-outs. In fact, no statistical test can prove or negate this, simply because data on occurrence of musculoskeletal pain in drop-outs is missing. It is possible that some baseline children who were not found at follow-up have changed schools. However, it is also possible that some of the children were absent from school on the day of the follow-up assessment due to poor health (which might include poor musculoskeletal health). If this is the case, then we might have underestimated the occurrence of musculoskeletal pain (incidence and persistence) at follow-ups, and probably, have underestimated or overestimated the relationships of our baseline potential predictors and musculoskeletal pain.

Prospective cohort studies are considered the "gold standard" of observational epidemiological designs to investigate determinants of disease occurrence (Samet and Munoz 1998). This study design proceeds in a logical sequence (i.e. from exposure to outcome) and has the advantage of elucidating the temporal relationship between exposure and disease. However, it has also several limitations; some of which might not be applicable to other "less prestigious" observational designs (e.g. case-control studies). Lost-to follow-up bias is the most notable example of such unique limitations of prospective cohort studies (Greenland 1977).

6.1.2. Assessment of musculoskeletal pain

We have gathered information on pain experience using a structured questionnaire, which included a body map to help the child recognise the exact site of musculoskeletal pain experience. Previous research has demonstrated that self-report tools are appropriate for children aged 4 years and older and provide the most reliable and valid approach to measuring pain in children (McGrath et al. 1996). School-aged children are also able to be very specific in locating pain (Gaffney and Dunne 1986). Current evidence indicates that using a variety of tools in assessing childhood pain would provide a richer description of pain experience (McGrath 1990). However, in this study, we have only used one tool (pain questionnaire) to evaluate musculoskeletal pain. In addition, we did not evaluate pain intensity at baseline. It is possible that psychological factors or other aspects of the children's personality could have influenced their pain reports. However "psychogenic pain", which is neither well defined nor accurately measured (McGrath 1995), cannot be separated from somatic pain in population-based epidemiological studies.

We have also collected information regarding whether pain was initiated by trauma. This is important information which has always been missed in most previous studies. We have hypothesised that distinction of traumatic from non-traumatic pain would provide a clearer picture of determinants of musculoskeletal pain in schoolchildren. For that reason, we have presented estimates of occurrence and risk associated with exposures separately for traumatic and non-traumatic pain. Prior to the study, attempts were made to achieve good face and content validity of the pain questionnaire with a careful design procedure. Both the teachers' and children's comments were considered during the pre-testing phase. The questionnaire was found to be reliable within a short time period (Mikkelsen et al. 1996). In addition, comparison of the questionnaire with interviews showed good concurrent validity in identifying children with frequent pain symptoms (Mikkelsen et al. 1997). However, the 3-month recall time of pain among the children has not been tested against self-completed pain diaries. For that reason the contrast validity of our pain questionnaire (i.e. the capability of the questionnaire to identify children with musculoskeletal pain) has not been established prior to baseline survey. It

must be noted that we have solely relied on self-report of symptoms. Therefore, our study might have detected symptoms that were, on average, milder than those commonly seen in clinical settings. This might have led to overestimation of the prevalence and new-onset of WSP but, possibly, underestimation of both the persistence/recurrence estimates and the strength of risk associations.

In this study we have used the term “pain persistence” to describe musculoskeletal pain that is reported at both T0 (baseline) and T1 (1-year follow-up), while we used the term “pain recurrence” to describe musculoskeletal pain that is reported at both T0 and T2 (4-year follow-up). However, these might not be the correct terms for both. Occurrence of musculoskeletal pain in a frequency of at least once a week during the 3-month period preceding the T1 does not necessarily indicate that the child had musculoskeletal pain with the same frequency during the whole preceding year, which might be assumed by using the term persistence. On the other hand, occurrence of musculoskeletal pain at T2 might have been persistent musculoskeletal pain if the child had had pain during the whole 4-year follow-up period. Unfortunately, we did not have this information. Our questionnaire evaluated the occurrence of musculoskeletal pain only during the preceding 3 months at each assessment point. We have used this rather short time scale to avoid difficulties with recall of pain. Recall problems have been reported in several previous studies which have used a protracted recall time scale in collecting data about pediatric and adolescent pain (Goodman and McGrath 1991; Savedra et al. 1988; Ehrmann-Feldman et al. 2002_b).

6.1.3. Assessment of potential predictors of musculoskeletal pain

6.1.3.1 Hypermobility

We have used the Beighton method (Beighton et al. 1973) to test joint hypermobility at baseline. Being quick and easy to implement, this method is by far the most commonly used test for examining hypermobility in children in epidemiological surveys. It is a modified version of Carter and Wilkinson hypermobility test, which was developed in 1964 as a screening tool for the identification of adults with general joint hypermobility

(Carter and Wilkinson 1964). According to our knowledge, this method has not been formally validated for examining joint laxity in children in population-based studies. However, we have examined the precision of this method, prior to our baseline assessment, by testing its intra and inter-observer reliability, and found that this method is sufficiently reproducible, with Kappa of 0.84 and 0.80, respectively (Mikkelsen et al 1996).

Most of previous studies in adults have used a cut-off score of 4 to categorize study participants as with (a score of 4 or more) or without high joint laxity (Simmonds and Keer 2007). In addition, achieving a Beighton score of 4 has also been included in the validated criteria “Brighton Criteria” that is currently being used to identify patients with joint hypermobility syndrome (Grahame 2000). Children, in general, have a greater range of motion of their joints than adults (Bridges et al. 1992; Larsson et al. 1993; Russek 1999), so using a cut-off point of 4 would have classified almost one-third of the children as having hypermobility at baseline. For that reason it was decided to use a cut-off point of 6, and according to this classification, 7.8% (95% CI 6.6-9.2) of the children were categorised as hypermobile (Mikkelsen et al. 1996). Nevertheless, all through the statistical analysis of this study, a re-examination at a cut-off level of 4 has consistently led to similar risk/predictive estimates.

6.1.3.2. Physical fitness

In this study the level of physical fitness of children at baseline was examined using 20-meters Shuttle Run test (Léger and Lambert 1982). Prior studies, in both adults and children, have confirmed the validity and reliability of this approach to estimate the peak VO₂ and to assess the cardio-respiratory endurance (Léger and Lambert 1982; Léger et al. 1988; Anderson 1992). Shuttle Run test holds several advantages over other tests used to evaluate the level of physical fitness (e.g. the one-mile run test or the one-mile walk test). Firstly, the multi-stage progressive nature of this test closely imitates the graded, speed-incremented treadmill test used in laboratory settings. Secondly, being speed-controlled, variation in pacing between children does not influence the test results. Thirdly, unlike other tests, maximal effort is only required at the end of the test,

and this motivates children to participate, and lastly, this test is usually conducted in small groups and this adds a competitive element, which further motivates the children to reach their maximal capacity (Cairney et al. 2008). In this study, the same examiner tested all the children and tried to motivate and stimulate them in the same way. As its name implies, this test needs a room of at least 20 meter size to be properly conducted. Prior to our baseline assessment, we have anticipated that all schools taking part in the survey would have rooms of that size. However, this was not the case. Four out of the 19 schools that participated in our baseline survey did not have a room with that size. The bicycle ergometer test would have been a possible way to estimate the level of physical fitness of children registered in these schools. However, this method would have been too time-consuming, and therefore was not used. As mentioned earlier, only 69% of the children who participated in the baseline survey undertook shuttle run test (Mikkelsen 1998_a).

6.1.3.3. Other symptoms

We have used a self-completed questionnaire to collect information on headache, abdominal pain, depressive mood, day tiredness, difficulties in falling asleep, waking up during nights. It must be noted that, in some of our publications, we have used the term ‘psychosomatic symptoms’ to refer collectively to these symptoms, although it might be argued that some of these symptoms are not related to emotional/psychological problems in childhood. Based on previous research in children, these symptoms are chiefly considered to be expressions of psychological stress in children rather than manifestations of organic disorders. Depressive mood is certainly a psychological symptom. Childhood abdominal pain and headache are believed to be having a psychosomatic origin in the great majority of cases (Bury, 1987; Alfvén, 1986). However, it might be questionable whether difficulty in falling asleep, waking up during nights and day tiredness were manifestations of psychological stress or consequences of chronic pain. The term ‘psychosomatic symptoms’ has also been used by other researchers to refer to these symptoms (Tamminen et al. 1991; Aro et al. 1987).

6.1.3.4. Physical activity

We have used a self-completed questionnaire, rather than objective tools, to gather information on frequency of physical activity. Wedderkopp et al. have documented a weak correlation between self reported physical activity in children and accelerometer measurements (Wedderkopp et al. 2003). However, using accelerometer measurements would have also substantially increased the costs of the study.

6.1.3.5. Potential predictive factors, not evaluated in this study

We did not gather information about weight, anatomic/structural factors (except for hypermobility), socioeconomic factors, family history of pain, heritability and several life style factors (e.g. smoking). Some previous research have found that these factors might be related to either (or both) the onset and prognosis of musculoskeletal pain in children (Salminen et al. 1999; Aasland et al. 1997; Balagué 1999; Mikkonen et al. 2008; Salminen et al. 1992_b; Feldman et al. 2001; Rhee 2005). A confounding bias is possible if some (or all) of these un-measured factors have a causal connection to childhood musculoskeletal pain and, at the same time, are unequally distributed across categories of the exposures being investigated. However, it must be noted that evidence with respect to the role of these factors is not conclusive. Some prospective studies have found that weight and BMI at baseline does not predict the onset of musculoskeletal pain at follow-up (Nissinen et al. 1994; Feldman et al. 2001; Salminen et al. 1995; Ehrmann-Feldman et al. 2002_b). Similarly, recent twin studies suggest a weak genetic influence on LBP and WSP in childhood or early adolescence (El-Metwally et al. 2007; Hestbaek et al. 2004; Mikkelsen et al. 2001). There is also conflicting evidence concerning the association between socioeconomic status and musculoskeletal pain in adolescents (Jones et al. 2003_a; Rhee 2005). Evidence is stronger with respect to the role of family history of pain (Balagué et al. 1995; Salminen 1984; Brattberg 1994; Gunzburg 1999) and adolescent smoking (Feldman et al. 2001; Mikkonen et al. 2008). Future studies should collect data on family history of pain and smoking (particularly in mid-and late adolescents) in order to be able to control for their potential confounding effect.

6.2. Main findings

6.2.1. “Any” and site-specific musculoskeletal pain

6.2.1.1. Incidence

This study showed that the incidence of musculoskeletal pain is high among early adolescents, with 22% of schoolchildren, who were pain-free at baseline, reporting new-onset episodes of pain in at least one musculoskeletal site at the 1-year follow-up (19 % reporting new-onset non-traumatic pain and 4% reporting traumatic pain). The neck was the most commonly reported site with non-traumatic pain, while the lower limb was the most common site for traumatic pain. It is difficult to compare our occurrence estimates with those of previous longitudinal studies, for two main reasons. Firstly, most of previous studies have used a longer pain recall period (6 months or 1 year); while in this study we have collected information about pain experience during the previous 3 months. Secondly, the study populations of almost all previous studies were older than ours. This might partially explain the considerably higher incidence of regional musculoskeletal pains reported in previous studies compared to ours, given the strong positive association between age and musculoskeletal pain in children and adolescents (Burton et al. 1996; Balagué et al. 1988; Troussier et al. 1994). That becomes evident when we compare our site-specific incidence figures with those of Ehrmann-Feldman et al. (2002_a) cohort study of schoolchildren aged 13–15 years. In their prospective Canadian study, the 6-month incidence proportion of lower limb pain, upper limb pain, low back pain (all with a frequency of at least once a week) were estimated to be 22%, 20%, 13%, respectively. All these site-specific figures were 2–3 times higher than those found in our study population. Despite these differences, the overall incidence of all musculoskeletal pain in our preteen/early-adolescent study subjects (22%) was just slightly lower than that found in the Ehrmann-Feldman et al's study of middle-adolescent subjects (27.1%). This might indicate that co-occurrence of different localized musculoskeletal pains is more commonly reported by middle-adolescents than preteens and early-adolescents.

It must be noted that, unlike other site-specific musculoskeletal pains, the incidence

proportion of neck pain in our study population (9.4%) is comparable to that found in the previously mentioned Canadian study (10%) (Ehrmann-Feldman et al. 2002_b). This might indicate that neck pain, unlike other musculoskeletal pains, follows a steady pattern of incidence increase with age and that this trend starts as early as preadolescence. This pattern is different from low back pain, for example, where there is a steep increase of reporting in adolescence with the annual incidence almost doubling between the ages 12 and 15 years olds (Burton et al. 1996). A similar steep increase in incidence of neck pain seems to happen in early adulthood, and this becomes evident in a 7-year follow-up study of Finnish schoolchildren (age 15 to 18), where the prevalence of weekly neck and shoulder pain increased from 17% at baseline to 28% at follow-up (Siivola et al. 2004).

6.2.1.2. Prognosis

This study showed that musculoskeletal pains are not as transient and self-limiting as previously assumed. At the 1-year follow-up, 54% of the children reported pain persistence, while at the 4-year follow-up, 64% of them had musculoskeletal pain. The neck was the site with most persistent/recurrent musculoskeletal pain. Children who had regional musculoskeletal pain at baseline reported more combined than regional musculoskeletal pain in adolescence. This might indicate that musculoskeletal pain tends to be more generalized as the child grows up, a finding which further confirms our earlier interpretation when we compared the incidence estimates of general and site-specific pains in this early adolescent population with that reported in the Canadian (Ehrmann-Feldman et al. 2002_a) study of middle-adolescent subjects.

Our 4- year recurrence proportion of musculoskeletal pain of roughly 65% is in agreement with the recurrence proportion of 59% found in a clinic-based 9-year follow-up study (Flatø et al. 1997). The high recurrence proportion in our study should be interpreted with caution due to the wide case definition and the short recall time of musculoskeletal pain. However, musculoskeletal pain is an intermittent phenomena and the pattern of recurrence rather than continuity may be a more realistic description of an individual's experience of a chronic musculoskeletal problem (Deyo 1993). Another

possibility for our high recurrence figures would be that we evaluated musculoskeletal pain during winter when symptoms can be more frequent (Takala et al. 1992; Ehrmann Feldman et al. 2002_a).

The 30% recurrence proportion of low-back pain in our study is somewhat lower than that of a follow-up study of 14-year-old children with low back pain (LBP) at baseline (Salminen et al. 1995). In their sample, 29% of the boys and 60% of the girls had recurrent LBP at the 3-year follow-up, and 35% after 9 years from baseline (Salminen et al. 1999). In another population-based follow-up study, 27% of children with fibromyalgia at baseline still had similar symptoms at the 30-month follow-up (Buskila et al. 1995). As mentioned above, the comparison of the studies is difficult. However, all these studies indicate that there are subpopulations among children with a tendency to develop recurrent or chronic pain.

6.2.1.3. Risk factors

In this study, girls had approximately 40% higher risk for development of non-traumatic musculoskeletal pain compared to boys. Although this association was only of borderline significance in the multivariate analysis, it is unlikely that this association is only a chance finding, given the narrow confidence interval and evidence from the majority of previous studies (Balagué et al. 1992; Brattberg 1994; Balagué 1994, 1995; Viikari-Juntura 1991; Hakala et al. 2002).

Significant associations were found between non-traumatic pain and both headache and day-time tiredness. This is in accordance with earlier reports that documented the predictive role of headache on future low back pain in adolescents (Jones et al. 2003_a) and a significant association between day-time tiredness and persistence of musculoskeletal pain in children (Mikkelsen et al. 1998_b).

Two risk factors for trauma-induced musculoskeletal pain were identified: vigorous exercise and day-time tiredness. Both factors had an independent role in pain development. The role of vigorous exercise on occurrence of trauma-induced

musculoskeletal pain in adolescents is supported both by previous studies (Goldstein et al. 1991; Kujala et al. 1999) and by common sense (the more the child participates in sports, the more chance of being injured). The strong role of day-tiredness on development of traumatic musculoskeletal pain cannot be explained by the confounding effect of vigorous exercise, as day-time tiredness independently predicted the onset of traumatic pain in the multivariate analysis (i.e. after adjusting for the effect of exercise frequency). One possible explanation would be that children with day-time tiredness are exhausted, fatigued and unable to adjust their movement or posture to protect themselves from being injured in sports fields (and possibly in other settings) regardless of the frequency of exercise performed. This assumption is in accordance with a previous report identifying "overtiredness" as a one of the contributing factors to sports injuries (Micheli et al. 2000).

Occurrence of new-onset traumatic and non-traumatic musculoskeletal pain did not differ between children with and without hypermobility. This finding is in accordance with another Nordic study in preteens (Qvindesland and Jonsson 1999). However, most previous cross-sectional studies have reported a clear association between hypermobility and arthralgia in children (Beighton et al. 1973; Gedalia and Press 1991; Viswanathan et al. 2008; Yazgan et al. 2008). Therefore, more studies are still warranted to unveil the role of hypermobility in childhood musculoskeletal pain.

6.2.1.4. Prognostic factors

The following factors significantly and independently predicted recurrence of "Any" musculoskeletal pain at the 4-year follow-up: age, headache, hypermobility and multiple painful musculoskeletal areas. Results of this study are in accordance with previous cross-sectional studies, which have shown that prevalence of musculoskeletal pain in older children is higher than in younger subjects (Salminen, 1984; Balagué et al. 1988, 1994; Troussier et al. 1994; Burton et al. 1996) and that headache and musculoskeletal pain in children frequently co-exist (Sherry et al. 1991; Anttila et al. 2002). However, the cross-sectional design strongly limits the conclusions of these earlier studies. The contributing factors of musculoskeletal pain recurrence are to a great extent similar to

the previous results based on one-year follow-up of the same study subjects (Mikkelsen et al. 1998_b). However, in the current study, a significant association between hypermobility at preadolescence and musculoskeletal pain recurrence at adolescence was found. This is in contrast to Mikkelsen's et al earlier findings, where hypermobility was not associated with preadolescent musculoskeletal at baseline nor was it predictive of musculoskeletal pain persistence at 1-year follow-up (Mikkelsen et al. 1996; Mikkelsen et al. 1997; Mikkelsen et al. 1998_b). An association between hypermobility and different musculoskeletal symptoms has been previously reported in a number of cross-sectional studies on schoolchildren (Beighton et al. 1973; Gedalia et al. 1991, 1993; Viswanathan et al. 2008). However, we are not aware of any previous reports on the role of hypermobility in predicting recurrence of childhood musculoskeletal pain in adolescence.

Our study showed differences in the predictors of recurrent musculoskeletal pain between boys and girls. Age, depressive feelings, waking up during nights and hypermobility were predictive factors only in girls. Gender differences in the determinants of paediatric and adolescent chronic pain have been previously reported (Passchier and Orlebeke 1985; Merlijn et al. 2003). Psychosomatic symptoms more likely predicted musculoskeletal pain recurrence in girls compared to boys. This is in line with earlier studies where a relatively stronger association between psychosomatic-psychosocial factors and musculoskeletal pain was found in girls (Sherry et al. 1991; Merlijn et al. 2003). Joint hypermobility strongly predicted pain recurrence in girls but not in boys. Females show a greater joint mobility at all ages (Giannini and Brewer 1982), and hypermobility syndrome is more prevalent among females (Beighton et al. 1973; Jesse et al. 1980). However, confirming the prognostic relevance of hypermobility in children needs a larger sample size of hypermobile children complaining of musculoskeletal pain at baseline in order to have enough statistical power to evaluate the gender difference in musculoskeletal pain recurrence.

6.2.2. Lower limb pain

6.2.2.1. Prevalence and consequences

On the basis of our cross-sectional analysis at baseline, the knee was the most common site of pain in the lower limb, followed by the ankle and foot. This is in accordance with previous studies in children and adolescents (Smedbraten et al. 1998; Adirim and Cheng 2003). The knee was also the most common location of pain due to a direct trauma, as has been reported previously (Yates and Grana 1990). About half the children who had lower limb pain reported pain also in other musculoskeletal location. This figure is substantially higher than the 19% prevalence of musculoskeletal pain in those without lower limb pain. This finding is consistent with previous surveys, which have demonstrated frequent co-occurrence of different musculoskeletal complaints (Kujala et al. 1999; Salminen 1984). Lower limb pain – both traumatic and non-traumatic – was more common in the younger age group (less than 11 years old) than among the older children (from 11 to 13 years old). This contradicts a previous study, which showed a clear increase in prevalence of knee pain from 4% in the 9–10 -year-olds to 19% in the 14–15 -year-old schoolchildren (Vähäsarja 1995). However, this might be due to the comparatively different age distribution of our study population; which was composed of two age groups (9–10 and 11–12 years); and the wide case definition of lower limb pain used in our study (including pain in all lower limb areas). In this study, traumatic lower limb pain was more common among boys. Likewise, Smedbraten and co-workers found the knees to be the only site in which pain was more common among boys (Smedbraten et al. 1998).

Difficulty in walking long distances was the most common disability, reported by approximately 40% of children with lower limb pain. This is much higher than the 11% proportion reported in a previous study about knee pain in schoolchildren (Vähäsarja 1995). However, the minimum distance was not specified in the latter study.

6.2.2.2. Prognosis

Our study shows that approximately one third of preadolescents with lower limb pain at baseline had persistent pain at the 1-year follow-up, and almost the same proportion

reported pain recurrence at the 4-year follow-up. We also found that about 15% of these children reported lower limb pain at both follow-up assessments. These figures are similar to the persistence/ recurrence proportions for children with low back pain and upper back pain in the same study population. To our knowledge, this is the first follow-up study of children with lower limb pain from early until mid-adolescence. In their controlled interventional study, Baxter and Dulberg (1998) prospectively followed up children (ages 5 to 14 years) who had growing pains at baseline for a period of 18 months. The control group was simply reassured of a self-limiting outcome, showed a gradual decline in the average number of pain episodes during this follow-up period, reaching an average of 2 monthly episodes over the 18-month period. In another long-term follow-up study of female adolescents with idiopathic anterior knee pain at baseline, defined by the authors as knee pain without definitive diagnosis by history, examination, and plain radiographs, Nimon et al. (1998) found that 50% of these girls had persistent knee pain, with at least the same subjective magnitude as at baseline, during a mean follow-up of 3.8 years. Of these subjects, 27% still complained of knee pain after a mean follow-up period of 16 years. Comparing our results with both of these studies might not be appropriate due to the differences in case definitions of lower limb pain and ages of study subjects. However, all of these studies showed that the assumption of a self-limiting, favourable prognosis of lower limb pain in children and adolescents is not always true and this necessitates additional research to help understand the etiologic features of this condition in children.

6.2.2.3. Risk factors

On the basis of our cross-sectional analysis at baseline, practicing vigorous exercise was associated with lower limb pain. Prior studies have reported conflicting results about the role of physical exercise in lower limb pain in schoolchildren (Fairbank et al. 1984_b; Vähäsarja 1995; Shrier et al. 2001). We have hypothesized that psychosomatic symptoms are associated only with non-traumatic lower limb pain, and physical exercise is only related to traumatic lower limb pain, and this might be the reason for these conflicting results. As we expected, our stratified analysis showed that practicing vigorous exercise was associated with pain in the traumatic group but not in the non-

traumatic group. After adjusting for physical activity and all other baseline predictors in our multivariate analysis, day tiredness was the only significant psychosomatic factor in the traumatic group. Day tiredness might have been a consequence of pain experience rather than being psychological in origin. High levels of physical fitness were independently associated with the occurrence of traumatic lower limb pain and practicing vigorous exercise was a significant effect modifier for this relationship. These results seem to contradict previous findings by Knapik et al. (1993) who reported that musculoskeletal injuries in young soldiers were associated with lower aerobic fitness. However, several factors may prevent a valid comparison between our results and those of the latter study. Firstly, the age groups and the study settings in these studies were different. Secondly, Knapik et al. were studying the relationship between physical fitness and all kinds of musculoskeletal injuries, including overuse injuries. Overtraining injury is not caused by a direct trauma but is related to repetitive loading on musculoskeletal structures without sufficient recovery time. For that reason these type of injuries were excluded from our case-definition of traumatic lower limb pain.

Similar to our results for “Any” musculoskeletal pain, occurrence of traumatic and non-traumatic lower limb pain did not differ between children with and without general hypermobility. However, our analysis also shows that regional knee hypermobility has an inverse association with traumatic lower limb pain, and that this association was not explained by differences in the frequency of physical exercise between children with and without traumatic pain. Although, the latter finding should be interpreted with caution as it might be distorted by residual confounding attributable to physical activity or by un-addressed confounders, the overall results of this study with respect to hypermobility go well with the previous observations that hypermobility is not associated with increased athletic injuries (Krivickas and Feinberg 1996) and that stretching plays an important role in decreasing the rate of injury (Hartig and Henderson 1999). These studies, as well as ours, challenge the recommendation that children with hypermobility should avoid strenuous physical activities.

6.2.2.4. Prognostic factors

Practicing vigorous exercise was the only baseline factor that was predictive of persistence of lower limb pain at the 1-year follow-up. A positive association has been reported between frequency of physical exercise and lower limb pain in a number of previous studies (Vähäsarja 1995; Kujala et al. 1999; Fairbank et al. 1984_b). For that reason we would recommend that children with lower limb pain should refrain from strenuous exercise, as this might help the children achieve a quicker relief of pain. Our results have also shown that children with trauma-induced lower extremity pain had a significantly better long-term prognosis compared with children with non-traumatic lower limb pain. These findings, combined with our baseline results, demonstrate the favourable long-term outcome of the relatively more disabling traumatic type of lower limb pain. This further proves our a priori hypothesis that traumatic and non-traumatic lower limb pain should be regarded as different entities. Hypermobility was the only contributing factor of lower limb pain recurrence at the 4-year follow-up (at adolescence). This finding is similar to what we have observed when we used the wide case definition of musculoskeletal pain (“Any” musculoskeletal pain). Hence, for both “Any” musculoskeletal pain and lower limb pain, hypermobility was not a significant risk factor for occurrence nor for persistence of pain at the 1-year follow-up, whereas it was a significant predictor for pain recurrence at 4 years. One possible explanation for this finding is that there is a group within the hypermobile children who are more prone to experience musculoskeletal pain from childhood to adolescence, which can be seen by the differences in the recurrence proportions between hypermobile and non-hypermobile children with persistent preadolescent musculoskeletal pain. However, our finding with respect to recurrence of lower limb pain is based on only 18 hypermobile children who had lower limb pain at baseline and were found at both follow-ups and, therefore, requires confirmation in larger studies.

6.2.3. *Widespread pain*

6.2.3.1. Occurrence

In this study, the prevalence of WSP increased from 8% at baseline (10–12 years) to 9% at the 1-year follow-up (11–13 years) to 15% at the 4-year follow-up (14–16 years). Furthermore, in the follow-up of children free of WSP, we found that the incidence proportion of this condition was 7% at 1 year and 14% at 4 years. Our prevalence figures are in accordance to that observed among Finnish twins (9.9% in 11-year-old children) (Mikkelsen et al. 2001) and in British schoolchildren whose prevalence was 12.5% in children aged 11–12 years and 17% in those aged 13–14 years (Jones et al. 2003_b). The same research team reported a 1-year incidence proportion of 7.7% for WSP among British children, an estimate which is also very similar to that found in this study. Other epidemiological studies have reported a prevalence of WSP ranging from 7.3% to 15.3% (Gran 2003). Our results, in the light of all the previously mentioned studies, indicate that WSP is as common in children and adolescents as in adults, but it still remains unclear whether children with WSP will grow into adults with the same symptoms.

6.2.3.2. Prognosis

A previous 7-year follow-up study in adults found that the proportion of general population with complete recovery of WSP is very low, suggesting a chronic nature of WSP in adulthood (Papageorgiou et al. 2002). Based on our results, prognosis of WSP in children seems to be more favourable. Our results show that WSP in children tends to have a fluctuating course, with one third of children with WSP at baseline reporting persistence/recurrence of pain at either follow-up, and only 10% of the children who reported WSP at baseline reporting the same symptoms at both follow-ups. This course is similar to that of “Any” musculoskeletal pain and lower limb pain in this study population. This indicates that the fluctuating nature of pain is not a unique feature of WSP, but rather a common feature of almost all musculoskeletal complaints in schoolchildren.

Results of this research show that only one out of every four schoolchildren with no musculoskeletal pain at baseline remained pain-free at both follow-ups. In addition, only 7.3% of the whole study population reported no musculoskeletal pain (in any location) at all three assessment times, compared to 47.9% reporting pain in at least one musculoskeletal location at all assessments. These results clearly show that musculoskeletal pain is a common, but a fluctuating, experience in early adolescent life, and that identification of its risk factors is crucial in order to point out preventive measures.

6.2.3.3. Risk factors

The onset of WSP was predicted by age, female gender, depressiveness and all regional back pains. To our knowledge this is the second population-based study conducted to investigate risk factors of onset of WSP in schoolchildren. The first study, which was conducted by Jones et al. (2003_b) on a representative sample of British schoolchildren, found three independent predictors for the onset of WSP: psychosocial difficulties, high level of sports activity and headaches, while age and sex did not have a significant effect. In our study, headache predicted the onset of WSP only in the univariate analysis, but not after adjustment for other factors. Although both studies were similar with respect to the predictive role of depressiveness, there were several inconsistent findings, particularly regarding the role of age, sex and physical exercise. However, there are several possible explanations for this. First, the follow-up period in our study was 4 years compared to only 1 year in the British study. Secondly, the assessment of potential risk factors as well as their categorisation for statistical analyses in the British study was different from ours. For example in the current study the frequency of physical exercise was measured as the average weekly number of practicing exercise (until feeling out of breath) during the previous 3 months. In the British study, frequency of physical activity was evaluated as the time spent (in minutes) practicing sports during the previous week. Thirdly, and maybe most importantly, the case definition of WSP used in our study was based on the criteria of chronic widespread pain set by the American College of Rheumatology (i.e. history of pain for at least 3 months), while in the British study, pain needed to be present for only 1 day in

the past month. Therefore, widespread but minor and short-term pain would have fulfilled the case definition of WSP in that study. In an accompanying editorial (Schanberg 2003), it was suggested that the significant predictive role of sports participation found in this study might mainly be due to the nature of the case definition used to gauge the outcome.

Our results are in accordance with the majority of research on risk factors of WSP in adults. Almost all studies among adults have identified female gender as the most important risk factor for WSP and fibromyalgia (Gran 2003). There is also a body of evidence demonstrating that psychological factors play a crucial role in the aetiology of these syndromes (Clauw and Crofford 2003; Macfarlane 1999), which has lead some authors to speculate that the bi-directional association between mental and somatic symptoms is a reflection of a common underlying liability or disorder (Leino and Magni 1993). In addition, our finding that regional musculoskeletal pain in the neck and back is a strong predictor of the onset of WSP in children is well supported by epidemiological studies in adults (McBeth et al. 2001; Papageorgiou et al. 2002). In one study among adults, 141 subjects were evaluated for musculoskeletal pain at baseline and followed up for a median of 27 months to determine changes of musculoskeletal pain classifications. Of the subjects with regional pain musculoskeletal pain at baseline, 19% reported WSP and 65% still reported regional pain at follow-up. In addition, none of the subjects with WSP at follow-up were pain-free at baseline (McBeth et al. 2001).

There are two possible explanations for the predictive effect of regional back pain on the onset of WSP: First, regional pain may be a part of the pathway in the development of WSP, particularly axial skeleton pains, which is a key element in the criteria for WSP. Second, regional pain in the back tends to expand and become more widespread due to secondary hyperalgesia, resulting in changes in the excitability threshold of dorsal horn neurons, a phenomenon known as central sensitization (Staud and Smitherman 2002). Such changes lead to the generation of referred pain and hyperalgesia across multiple spinal segments (Coderre et al. 1993).

6.3. Un-answered questions and future plans

This 4-year follow-up study of 1756 Finnish schoolchildren (age 10-12) aimed to increase understanding of the pattern and determinants of musculoskeletal pain in early adolescence. Such information will provide foundations for the development of effective preventive interventions. This study mainly focused on identifying factors that can predict the onset of these symptoms (i.e. risk factors) and factors that can predict their persistence/recurrence (i.e. prognostic factors). Identifying risk factors is important because we would expect that the incidence of these symptoms would decrease if such factors were modified (i.e. reduced or eliminated), and this is the goal of primary prevention. For common conditions, such as musculoskeletal pain, the identification of factors that can predict the persistence/recurrence of symptoms, following onset, is of at least equivalent importance. Such information is crucial for classifying children presenting with musculoskeletal pain into strata according to the more likely long-term outcome of their symptoms, and limiting the implementation of secondary preventive strategies (i.e. treatment), depending on the availability of resources, to children who fall in the “more likely poor outcome” strata.

This 4-year follow-up study, which is a continuation of previous research conducted by Mikkelsson and co-workers (Mikkelsson 1998_a), have investigated the epidemiology of musculoskeletal pain in a representative sample Finnish schoolchildren, with special reference to lower limb and widespread pain. Strengths of the study are its population-based design; fairly long prospective follow-up; children’s self-report of pain, as previously recommended in pediatric pain research (Goodman and McGrath 1991); and the use of a valid pain questionnaire which classifies musculoskeletal pain according to frequency and location, aided by a manikin. A unique feature of this study is that estimates of occurrence and risk associations were presented separately for non-traumatic and traumatic pain (a distinction which was not investigated in prior research).

This study, however, did not evaluate all potential risk factors of musculoskeletal pain in schoolchildren. Summarizing the evidence with respect to the predictive role of genetic

influence, overweight/obesity and smoking (some potential risk factors that has not been assessed in this research) is important for understanding the broader epidemiological context of these symptoms. This can provide the basis for planning future research.

6.3.1. Heredity and family history

The role of familial factors in the aetiology of musculoskeletal pain in children has been examined in a number of studies. Familial aggregation of lumbar disc herniation (Gunzburg et al. 1990; Matsui et al. 1992; Varlotta et al. 1991), spondylolysis (Afshani and Kuhn 1996) and non-specific low back pain (Balagué et al. 1995; Salminen 1984; Brattberg 1994; Gunzburg 1999) has been described. These results have formed the basis for subsequent research on the genetic influence of non-specific low back pain in children and adolescents by using classical twin studies. Hestbaek et al. (2004) reported a weak genetic influence on the cumulative prevalence of LBP in 12-15-year-old Danish twins. Similar results were obtained by El-Metwally et al. (2008) among 11-year old Finnish twins. Results of these twin studies might imply that the observed familial aggregation of non-specific LBP is related to shared exposure to environmental factors or to the family role as "models" for expression of pain. Genetic studies on adults have suggested a strong genetic predisposition to intervertebral disc degeneration, vertebral end-plate Modic changes, sciatica and LBP (Hestbaek et al. 2004; Varlotta et al. 1991; Sambrook et al. 1999; Battie' et al. 1995; Karppinen et al. 2008). The current limited evidence suggests a weaker genetic influence on LBP in childhood and early adolescence.

With respect to the role of heredity on WSP in schoolchildren, a Finnish study among 1789 (11-year-old) twins showed that genetic factors seem to play at most a minor role in the development of these symptoms at this age (Mikkelsen et al. 2001). This is contrary to the results of other twin studies among adults that show a strong genetic background in fibromyalgia symptoms (Markkula et al. 2008) and chronic WSP (Kato et al. 2006).

Studies on the potential role of heritability on other childhood musculoskeletal pain symptoms are lacking. Such studies are needed to confirm whether this weak genetic predisposition applies to all musculoskeletal pain conditions.

6.3.2. Smoking

Several studies have investigated the potential predictive role of smoking on musculoskeletal pain in adolescents. In a cross-sectional study of 13- to 16-year-old Danish school children, smoking was significantly associated with severe LBP (Harreby et al. 1999). A cohort of 14-year-old school children in Canada was followed up for 1 year to investigate the role of smoking on the onset of musculoskeletal pain symptoms. Subjects who smoked did not have an increased risk of neck and upper limb pain (Ehrmann-Feldman et al. 2002_b), but had a two-fold higher risk of reporting LBP when compared to non-smokers (OR = 2.46, 95% CI 1.0-6.1) (Feldman et al. 2001). In this study population, smoking habits were also associated with the development of “Any” musculoskeletal pain (pain in any musculoskeletal location), although this association did not reach statistical significance (OR = 1.64, 95% CI 0.94-2.72) (Ehrmann-Feldman et al. 2002_a). More recently, a larger 2-year follow-up study in Finland was conducted on adolescents (aged 16 years at baseline) to investigate the potential role of smoking on predicting the onset and prognosis of LBP. In girls, daily smoking of over 9 cigarettes at baseline was significantly associated with both the onset and persistence of LBP (OR = 2.5, 95% CI 1.4 -4.5). The study also documented a dose-response relationship between the accumulated number of pack-years smoked by girls and development/persistence of LBP. A similar significant association was not found among boys (Mikkonen et al. 2008). In conclusion, previous research provides moderate evidence that smoking in adolescence is associated with the onset and prognosis of LBP, particularly among girls. Further large-scale studies are needed to obtain conclusive evidence.

6.3.3. Overweight/obesity

Overweight/obesity has been associated with greater prevalence of musculoskeletal disorders in adults, particularly with lower limb pain syndromes (Kortt and Baldry 2002;

Tsuritani et al. 2002). Comparative data are scarce in children and adolescents. Most (Grimmer et al. 2000; Salminen et al. 1992_b; Watson et al. 2003), but not all (Fairbank et al. 1984_a) studies have reported that overweight/obesity is not associated with LBP in cross-sectional studies. In prospective designs, most studies have found that weight at baseline does not predict the onset of LBP at follow-up (Nissinen et al. 1994; Feldman et al 2001; Salminen et al 1995). Similarly, BMI was neither associated with "Any" musculoskeletal (Ehrmann-Feldman et al. 2002_a) nor with neck and shoulder pain (Ehrmann-Feldman et al. 2002_b). On the other hand, other studies have found that "Any" musculoskeletal pain was more common in children with higher BMI z-scores across the weight spectrum (Bell et al. 2007), and that being overweight and obesity are risk factors for childhood injury (Bazelmans et al. 2004), upper extremity fractures (Goulding et al. 2005) and some lower limb pain diseases such as Blount's disease (Dietz et al. 1982) and slipped capital femoral epiphysiolysis (Loder et al. 1993). In addition, a recent study reported that obese children have a higher risk of long-term morbidity after ankle sprains compared to children of normal BMI (Timm et al. 2005). Another cross-sectional study on obese children (age 5-18) found that extra body weight was significantly associated with pain in the knee and hip joints (Stovitz et al. 2008).

In conclusion, there is some evidence that being overweight/obese is associated with musculoskeletal injuries and some lower limb diseases. However, evidence with respect to its relationship with non-specific musculoskeletal pain is inconclusive. Further large-scale prospective studies are needed to clarify its predictive role in the development of general and site-specific pain symptoms in children and adolescents.

7. SUMMARY AND CONCLUSION

Descriptive results of this study show that approximately one of every five Finnish schoolchildren (age 10-12) report new-onset musculoskeletal pain (in any location) over a period of one year. The vast majority of these children develop pain, which is not initiated by a direct trauma to the site of pain. Musculoskeletal pain in this age group is not a self-limiting condition, as approximately half to two third of these children will still have these symptoms after one and/or 4 years from their initial report of pain. With respect to the location of pain, the neck is the most commonly reported musculoskeletal site with non-traumatic pain, while the lower limb is the most common site for traumatic pain. The knee is the most common site of pain in the lower limb followed by the ankle-foot and thigh. Approximately one of every 3 children will report persistence/recurrence of lower limb pain after 1 and/or 4 years of their initial report of pain. Traumatic lower limb pain appears to be more disabling than non-traumatic lower limb pain, but the former also appears to have a significantly better prognosis. WSP is also not uncommon in schoolchildren, with occurrence estimates approaching those in adults and ranging from 7% in 10-12 olds to 15% in 14-16 olds. However, unlike its course in adults, WSP in children tends to have a fluctuating and a relatively more favourable course, with only 10% of such children consistently reporting these widespread symptoms after 1 and 4 years of their initial assessment.

With respect to risk factors of musculoskeletal pain in children, this study shows that both headache and day-time tiredness can significantly and independently predict the onset of non-traumatic musculoskeletal pain, including non-traumatic lower limb pain. The latter can also be predicted by prior report of depressiveness. Self-report of day-time tiredness and of practicing vigorous exercise (5-7 times a week) are significant risk factors for traumatic musculoskeletal pain, including traumatic lower limb pain. The latter is also correlated to a high level high level of physical fitness. Risk factors for WSP, identified in this study, include female gender, depressiveness and regional back pain, suggesting that both psychological factors and somatic pain symptoms, which

might be manifestations of the same underlying mechanism, can predict future development of WSP in early adolescents.

With respect to predictive factors for the chronicity of musculoskeletal pain, our study shows that hypermobility, which is not associated with the onset and 1-year prognosis of musculoskeletal pain, is a significant and independent predictive factor for the 4-year prognosis of both non-specific musculoskeletal pain and lower limb pain. The former is also predicted by headache and reporting pain in multiple sites, while the latter is also predicted by vigorous exercise.

In conclusion, this research work - whose results were published in a series of 5 articles, strengthens the previous findings that musculoskeletal pain is commonly reported by Finnish preadolescents and adolescents. These symptoms do not appear to be constant, but rather have a very fluctuating course. Although most children with musculoskeletal pain frequently report some sort of physical limitations attributed to their pain, only a minority of these children miss school days. Children's self report of practicing vigorous exercise (5-7 times a week) predicts both the onset and prognosis of trauma-induced musculoskeletal pain, but neither the onset nor the prognosis of the more commonly encountered non-traumatic type of musculoskeletal pain. Traumatic lower limb pain was also significantly associated with self-report of day-time tiredness and high level of physical fitness. We have identified 3 self-reported symptoms that might be markers of children at risk for development of non-traumatic musculoskeletal pain: headache, day-time tiredness and depressiveness. We have also identified 3 factors which might be markers for chronicity of these symptoms: self-report of headache, self-report of pain in multiple musculoskeletal areas and hypermobility (not through exercise). Given, the paucity of understanding about biological mechanisms and behavioural models that underlies pain in children, it is not clear whether these factors play an aetiological role in the development/persistence of these symptoms or are just markers of other aetiological factors not measured in our study. However, these factors, except for hypermobility, may be modifiable and can be assessed with ease, and hence can provide a basis for both primary and secondary prevention strategies.

8. ACKNOWLEDGMENTS

This study was carried out at Tampere School of Public Health and the Rheumatism Foundation Hospital in Heinola, Finland. I am very grateful to the University of Tampere and The Ministry of Education in Finland for the support given through The Doctoral Programme of Public Health (DPPH).

There are a number of people to whom I remain indebted for their hard work, patience counsel and inspiration. I would first like to acknowledge and express my sincere gratitude to my principal supervisor Dr Marja Mikkelsson (MD., PhD.); thank you for believing in me and being of great support during these years. I always felt strong and encouraged after every meeting with you about the studies, and when writing this thesis.

I sincerely thank my supervisor Professor Anssi Auvinen (MD., PhD.); thank you for your insightful lectures in epidemiology and providing your professional advice and your expertise. Working with you has been very important for me and for my development as a researcher.

I am deeply thankful to Professor Jouko Salminen (MD., PhD.); thank you for contributing with your time, reading manuscripts and with your encouraging interest and significant input. Without your support, the accomplishment of this research work would have not been possible. I would also like to acknowledge Hannu Kautiainen; thank you for your statistical expertise and advice during the study.

I owe my warm thanks to Professors Markku Hakala, Markku Kauppi and other members of The Rheumatism Foundation Hospital for their hospitality and financial support during the study. I am also very much thankful to current and former staff and PhD students of Tampere School of Public Health, particularly to Catarina Ståhle-

Nieminen, Rahman Shiri and Mia Artama for their encouragement, humour, and support. I also owe my warm thanks to Dr. Lasse Mikkelsen and all members of the Mikkelsen's family, who made me part of their family during my studies in Finland.

I would like to sincerely thank Professor Gary Macfarlane from the University of Aberdeen (UK) For his stimulating discussions and helpful suggestions. Thank you, Professor Gary, for your valuable contribution to this study. I would also like to thank Dr. Art Schneider from the Higher Colleges of Technology (UAE) for revising the English language of the thesis and Dr. Gareth Jones from the University of Aberdeen (UK) For his expert epidemiological advices.

I would like to thank my family. Thank you, Hadal (my beloved wife); you have been an endless well of support and patience through the years of my studies. Thank you Fares (my son) and Mariam (my daughter), both of you gave me the strength and the necessary push to finish this work. My deepest thanks to my brother (Ahmed) and sisters (Mona and Hoda) for guiding and supporting me throughout this project. Lastly, and most of all, I would like to express my sincere gratitude to my parents: *My mother*, the queen of my heart and the purest essence of my beloved land Egypt, and *my father*, the first and ever inspiring teacher who didn't live to see it finished but always said I could do it. You and my mother did not only give me life, but taught me how to live life with dignity, integrity and compassion.

This research work was supported by grants from PATU and EVO Development Projects, The Spine Society of Europe, the Signe and Ane Gyllenberg Foundation, the Medical Research Funds of the Rheumatism Foundation and Tampere University hospitals. I would like to thank all these research funding agencies for their generous contributions.

9. REFERENCES

- Aasland A, Flatø B and Vandvik IH (1997): Psychosocial factors in children with idiopathic musculoskeletal pain: a prospective, longitudinal study. *Acta Paediatr* 86: 740–746.
- Abu-Arafeh I and Russell G (1996): Recurrent limb pain in school children. *Arch Dis Child* 74: 336–339.
- Adamson G, Murphy S, Shevlin M, Buckle P and Stubbs D (2007): Profiling schoolchildren in pain and associated demographic and behavioural factors: a latent class approach. *Pain* 129: 295–303.
- Adirim TA and Cheng TL (2003): Overview of injuries in the young athlete. *Sports Med* 33: 75–81.
- Alfven G (1986): Psychological tension headaches among children, a survey. *Läkartidningen* 45: 3827–3828 (in Swedish).
- Anand KJ and Hickey PR (1987): Pain and its effects in the human neonate and fetus. *N Engl J Med* 317: 1321–1329.
- Anderson GS (1992): The 1600-m run and multistage 20-m shuttle run as predictive tests of aerobic working capacity in children. *Ped Ex Sci* 4: 312–318.
- Anttila P, Metsähonkala L, Aromaa M, Sourander A, Salminen J, Helenius H, Alanen P and Sillanpää M (2002): Determinants of tension-type headache in children. *Cephalalgia* 22: 401–408.
- Aro H, Paronen O and Aro S (1987): Psychosomatic symptoms among 14–16 year old Finnish adolescents. *Soc Psychiatry* 22: 171–176.
- Auvinen J, Tammelin T, Taimela S, Zitting P and Karppinen J (2008): Associations of physical activity and inactivity with low back pain in adolescents. *Scand J Med Sci Sports* 18: 188–194.
- Balagué F, Damidot P, Nordin M, Parnianpour M and Waldburger M (1993): Cross-sectional study of the isokinetic muscle trunk strength among school children. *Spine* 18: 1199–1205.
- Balagué F, Dutoit G and Waldburger M (1988): Low back pain in schoolchildren: An epidemiological study. *Scand J Rehabil Med* 20: 175–179.
- Balagué F, Nordin M., Skovron ML, Dutoit G, Yee A and Waldburger M (1994): Nonspecific low-back pain among schoolchildren: A field survey with analysis of some associated factors. *J Spinal Disord* 7: 74–79.

Balagué F, Skovron ML, Nordin M, Dutoit G and Waldburger M (1995): Low back pain in school children: a study of familial and psychological factors. *Spine* 20: 1265–1270.

Balagué F, Troussier B and Salminen JJ (1999): Non-specific low back pain in children and adolescents: risk factors. *Eur Spine J* 8: 429–438.

Battie´ MC, Videman T, Gibbons L, Fisher LD, Manninen H and Gill K (1995): Determinants of lumbar disc degeneration: a study relating lifetime exposures and MRI findings in identical twins. *Spine* 20: 2601–2612.

Baxter MP and Dulberg C (1988): “Growing pains” in childhood—a proposal for treatment. *J Pediatr Orthop* 8: 402–406.

Bazelmans C, Coppieters Y, Godin I, Parent F, Berghmans L, Dramaix M and Leveque A (2004): Is obesity associated with injuries among young people? *Eur J Epidemiol* 19: 1037–1042.

Beecham J and Knapp M (2001): Costing psychiatric interventions. In: Thornicroft G, editor. *Measuring mental health needs*. 2nd edition London: Gaskell; pp. 200–224.

Beighton P, Solomon L and Soskolne CL (1973): Articular mobility in an African population. *Ann Rheum Dis* 32: 413–418.

Bejia I, Abid N, Ben Salem K, Letaief M, Younes M, Touzi M and Bergaoui N (2005): Low back pain in a cohort of 622 Tunisian schoolchildren and adolescents: an epidemiological study. *Eur Spine J* 14: 331–336.

Bell LM, Byrne S, Thompson A, Ratnam N, Blair E, Bulsara M, Jones TW and Davis EA (2007): Increasing body mass index z-score is continuously associated with Complications of Overweight in Children, Even in the Healthy Weight Range. *J clin Endocrinol Metab* 92: 517–522.

Bengtsson A and Henriksson KG (1989): The muscle in fibromyalgia - a review of Swedish studies. *J Rheumatol Suppl* 19: 144–149.

Bhatia A, Brennan L, Abrahams M and Gilder F (2008): Chronic pain in children in the UK: A survey of pain clinicians and general practitioners. *Paediatr Anaesth* 18: 957–66.

Brattberg G (1994): The incidence of back pain and headache among Swedish school children. *Qual Life Res* 3 (suppl 1): 27–31.

Brattberg G and Wickman, V (1993): [A longitudinal study of schoolchildren. Rehabilitate early in backache/headache]. *Lakartidningen* 90: 1452-54, 1459–60.

Brewer EJ and Giannini EH (1982): Standard methodology for Segment I, II, and III Pediatric Rheumatology Collaborative Study Group studies II: Analysis and presentation of data. *J*

Rheumatol 9: 114–122.

Bridges A (1992): Joint hypermobility in adults referred to rheumatology clinics. *Ann Rheum Dis* 51: 793–796.

Bru E, Boyesen M, Munthe E and Roland E (1998): Perceived social support at school and emotional and musculoskeletal complaints among Norwegian eighth grade students. *Scand J Educ Res* 42: 339–356.

Bruusgaard D, Smedbraten BK and Natvig B (2000): Bodily pain, sleep problems and mental distress in schoolchildren. *Acta Paediatr* 89: 597–600.

Bulloch B and Tenenbein M (2002): Validation of 2 Pain Scales for Use in the Pediatric Emergency Department. *Pediatrics* 110: e33 – 33.

Burton AK, Clarke RD, McClune TD and Tillotson KM (1996): The natural history of low back pain in adolescents. *Spine* 21: 2323–2328.

Bury RG (1987): A study of 111 children with recurrent abdominal pains. *Aust Paediatr J* 23: 117–119.

Buskila D, Neumann L, Hershman E, Gedalia A, Press J and Sukenik S (1995): Fibromyalgia syndrome in children-an outcome study. *J Rheumatol* 22: 525–528.

Buskila D, Press J, Gedalia A, Klein M, Neumann L, Boehm R and Sukenik S (1993): Assessment of non-articular tenderness and prevalence of fibromyalgia in children. *J Rheumatol* 20: 368–370.

Cairney J, Hay JA, Faught BE, Ger I and Mathers B (2008): Generalized self-efficacy and performance on the 20-metre shuttle run in children. *Human Biology* 20: 132–138.

Carter C and Wilkinson J (1964): Persistent joint laxity and congenital dislocation of the hip. *J Bone Joint Surg* 46B: 40–45.

Cavanaugh JM, Lu Y, Chen C and Kallakuri S (2006): Pain Generation in Lumbar and Cervical Facet Joints. *J Bone Joint Surg Am* 88-A(Supp 2): 63–67.

Clauw DJ and Crofford LJ (2003): Chronic widespread pain and fibromyalgia: what we know, and what we need to know. *Best Pract Clin Rheumatol* 17: 685–701.

Claar RL, Walker LS and Smith CA (1999): Functional disability in adolescents and young adults with symptoms of irritable bowel syndrome: The role of academic, social, and athletic competence. *J Pediatr Psychol* 24: 271–280.

Coderre TJ, Katz J, Vaccarino AL, and Melzack R (1993): Contribution of central neuroplasticity to pathological pain: review of clinical and experimental evidence. *Pain* 52:

259–285.

Crook J, Weir R and Tunks E (1989): An epidemiological follow-up survey of persistent pain sufferers in a group family practice and specialty pain clinic. *Pain* 36: 49–61.

DeSantana JM and Sluka KA (2008): Central mechanisms in the maintenance of chronic widespread noninflammatory muscle pain. *Curr Pain Headache Rep* 12: 338–343.

Deyo RA (1993): Practice variations, treatment fads, rising disability. Do we need a new clinical research paradigm? *Spine* 18: 2153–2162.

Diepenmaat AC, van der Wal MF, de Vet HC and Hirasig RA (2006): Neck/shoulder, low back, and arm pain in relation to computer use, physical activity, stress, and depression among Dutch adolescents. *Pediatrics* 117: 412–416.

Dietz WH, Gross WL and Kirkpatrick JA (1982): Blount Disease (Tibia Vara): Another Skeletal Disorder Associated with Childhood Obesity. *J Pediatr* 101: 161–164.

Eccleston C, Wastell S, Crombez G and Jordan A (2008): Adolescent social development and chronic pain. *Eur J Pain* 12: 765–774.

Egger HL, Costello EJ, Erkanli A and Angold A (1999): Somatic complaints and psychopathology in children and adolescents: stomach aches, musculoskeletal pains, and headaches. *J Am. Acad. Child. Adolesc. Psychiatry* 38: 852–860.

Ehrmann-Feldman D, Shrier I, Rossignol M and Abenham L (2002_a): Work is a risk factor for adolescent musculoskeletal pain. *J Occup Environ Med* 44: 956–961.

Ehrmann-Feldman D, Shrier I, Rossignol M and Abenham L (2002_b): Risk factors for the development of neck and upper limb pain in adolescents. *Spine* 27: 523–528.

El-Metwally A, Mikkelsen M, Ståhl M, Macfarlane GJ, Jones GT, Pulkkinen L, Rose RJ and Kaprio J (2008): Genetic and environmental Influences on non-specific low back pain in children: A twin study. *Eur Spine J* 17: 502–508.

Evans AM and Scutter SD (2004): Prevalence of "growing pains" in young children. *J. Pediatr* 145: 255–258.

Fairbank JC, Pynsent PB, Van Poortvliet JA and Phillips H (1984_a): Influence of anthropometric factors and joint laxity in the incidence of adolescent back pain. *Spine* 9: 461–463.

Fairbank JC, Pynsent, PB, Van Poortvliet JA and Phillips H (1984_b): Mechanical factors in the incidence of knee pain in adolescents and young adults. *J Bone Joint Surg Br* 66: 685–693.

Feldman DE, Shrier I, Rossignol M and Abenham L (2001): Risk factors for the development

of low back pain in adolescence. *Am J Epidemiol* 154: 30–36.

Fields HL (1987). *Pain*. New York: McGraw-Hill.

Flatø B, Aasland A, Vandvik IH and Forre O (1997): Outcome and predictive factors in children with chronic idiopathic musculoskeletal pain. *Clin Exp Rheumatol* 15: 569–577.

Fordyce WE (1976): *Behavioural methods for chronic pain and illness*. St. Louis, MO: Mosby.

Fouquet B (2003): Clinical examination as a tool for identifying the origin of regional musculoskeletal pain. *Best Pract Res Clin Rheumatol* 17: 1–15.

Franck LS, Greenberg CS and Stevens B (2000): Pain assessment in infants and children. *Pediatr Clin North Am* 47: 487–512.

Gaffney A and Dunne EA (1986): Developmental aspects of children's definitions of pain. *Pain* 26: 105–117.

Gedalia A and Press J (1991): Articular symptoms in hypermobile schoolchildren: A prospective study. *J Pediatr* 119: 944–946.

Gedalia A, Press J, Klein M and Buskila D (1993): Joint hypermobility and fibromyalgia in schoolchildren. *Ann Rheum Dis* 52: 494–496.

Giovenco SL, Russell IJ and Larson AA (1999): Increased concentrations of nerve growth factor in cerebrospinal fluid of patients with fibromyalgia. *J Rheumatol* 26: 1564–1569.

Goldstein JD, Berger PE, Windler GE and Jackson DW (1991): Spine injuries in gymnasts and swimmers. An epidemiologic investigation. *Am J Sports Med* 19: 463–468.

Goodman JE, McGrath PJ (1991): The epidemiology of pain in children and adolescents: A review. *Pain* 46: 247–264.

Goulding A, Grant AM and Williams SM (2005): Bone and body composition of children and adolescents with repeated forearm fractures. *J Bone Miner Res* 20: 2090–2096.

Gragg RA, Rapoff MA, Danovsky MB, Lindsley CB, Varni JW, Waldron SA and Bernstein BH (1996): Assessing chronic musculoskeletal pain associated with rheumatic disease: Further validation of the Pediatric Pain Questionnaire. *J Pediatr Psychol* 21: 237–250.

Grahame R (2000): The revised (Brighton 1998) criteria for the diagnosis of benign joint hypermobility syndrome (BJHS). *J Rheumatol* 27: 1777–1779.

Gran, JT (2003): The epidemiology of chronic generalized musculoskeletal pain. *Best Pract Res Clin Rheumatol* 17: 547–561.

- Greenland S (1977): Response and follow-up bias in cohort studies. *Am J Epidemiol* 106: 184–187.
- Grimmer K and Williams M (2000): Gender-age environmental associates of adolescent low back pain. *Appl Ergon* 31: 343–360.
- Guite JW, Logan DE, Sherry DD and Rose JB (2007): Adolescent self-perception: associations with chronic musculoskeletal pain and functional disability. *J Pain* 8: 379–386.
- Gunzburg R, Balagué F, Nordin M, Szpalski M, Duyck, D, Bull D and Mélot C (1999): LBP in a population of school children. *Eur. Spine J* 8: 439–443.
- Hakala P, Rimpela A, Salminen JJ, Virtanen SM and Rimpela M (2002): Back, neck, and shoulder pain in Finnish adolescents: national cross sectional surveys. *Br Med J* 325: 743–746.
- Harkness EF, Macfarlane GJ, Silman AJ and McBeth J (2005): Is musculoskeletal pain more common now than 40 years ago? Two population-based cross-sectional studies. *Rheumatology (Oxford)* 44: 890–895.
- Harreby M, Neergaard K, Hesselsoe G and Kjer J (1995): Are radiologic changes in the thoracic and lumbar spine of adolescents risk factors for low back pain in adults? A 25-year prospective cohort study of 640 schoolchildren. *Spine* 20: 2298–2302.
- Harreby M, Nygaard B, Jessen T, Larsen E, Storr-Paulsen A, Lindahl A, Fisker I and Laegaard E (1999): Risk factors for low back pain in a cohort of 1389 Danish school children: an epidemiologic study. *Eur Spine J* 8: 444–450.
- Hartig DE and Henderson JM (1999): Increasing hamstring flexibility decreases lower extremity overuse injuries in military basic trainees. *Am J Sports Med* 27: 173–176.
- Henriksson KG and Bengtsson A (1991): Fibromyalgia - a clinical entity ? *Can J Physiol-Pharmacol* 69: 672–677.
- Hestbaek L, Iachine IA, Leboeuf-Yde C, Kyvik KO and Manniche C (2004): Heredity of Low Back Pain in a Young Population: A Classical Twin Study. *Twin Research* 7: 16–26.
- Hunfeld JA, Perquin CW, Batina W, Hazebroek-Kampschreur AA, Suijlekom-Smit LW, Koes BW, van der Wouden JC and Passchier, J (2002_b): Stability of pain parameters and pain related quality of life in adolescents with persistent pain: Three year follow-up, *Clin J Pain* 18: 99–106.
- Hunfeld JA, Perquin CW, Hazebroek-Kampschreur AA, Passchier J, van Suijlekom-Smit LW and van der Wouden JC (2002_a): Physically unexplained chronic pain and its impact on children and their families: the mother's perception. *Psychol Psychother* 75: 251–260.

Hunfeld JAM, Perquin CW, Duivenvoorden HJ, Hazebroek-Kampschreur AAJM, Passchier J, van Suijlekom-Smit LWA and van der Wouden JC (2001): Chronic pain and its impact on quality of life in adolescents and their families. *J Pediatr Psychol* 26: 145–153.

International Association for the Study of Pain Subcommittee on Taxonomy. (1986): Classification of chronic pain syndromes and definitions of pain terms. *Pain* 3 (Suppl. 3): S1–S226.

Jesse EF, Owen DS and Sagar KB (1980): The benign hypermobile joint syndrome. *Arthritis Rheum* 23: 1053–1056.

Jones AKP and Derbyshire SWG (1996): Cerebral mechanisms operating in the presence and absence of inflammatory pain. *Ann Rheum Dis* 5: 411–420.

Jones GT and Macfarlane GJ (2005): Epidemiology of low back pain in children and adolescents. *Arch Dis Child* 90: 312–316.

Jones GT, Silman AJ and Macfarlane GJ (2003_b): Predicting the onset of widespread body pain among children. *Arthritis Rheum* 48: 2615–2621.

Jones GT, Watson KD, Silman AJ, Symmons DP and Macfarlane GJ (2003_a): Predictors of low back pain in British schoolchildren. a population-based prospective cohort study. *Pediatrics* 111: 822–828.

Jordan A, Eccleston C and Osborn M (2007): Being a parent of an adolescent with chronic pain: An Interpretative Phenomenological Analysis. *Eur J Pain* 11 : 49–56.

Julien N, Goffaux P, Arsenault P and Marchand S (2005): Widespread pain in fibromyalgia is related to a deficit of endogenous pain inhibition. *Pain* 114: 295–302.

Karppinen J, Daavittila I, Solovieva S, Kuisma M, Taimela S, Natri A, Haapea M, Korpelainen R, Niinimäki J, Tervonen O, Ala-Kokko L and Männikkö M (2008). Genetic factors are associated with modic changes in endplates of lumbar vertebral bodies. *Spine* 33: 1236–1241.

Kato K, Sullivan PF, Evengard B and Pedersen NL (2006): Importance of genetic influences on chronic widespread pain. *Arthritis Rheum* 54: 1682–1686.

Kidd BL (1999): What are the mechanisms of regional musculoskeletal pain? *Baillieres Best Pract Res Clin Rheumatol* 13: 217–230.

Kleinbaum DG, Morgenstern H and Kupper LL (1981): Selection bias in epidemiologic studies. *Am J Epidemiol* 11: 452–463.

Knapik J, Ang P, Reynolds K and Jones B (1993): Physical fitness, age, and injury incidence

in infantry soldiers. *J Occup Med* 35: 598–603.

Konijnenberg AY, de Graeff-Meeder ER, van der Hoeven J, Kimpfen JL, Buitelaar JK and Uiterwaal C (2006): Psychiatric morbidity in children with medically unexplained chronic pain: diagnosis from the pediatrician's perspective. *Pediatrics* 117: 889–897.

Konijnenberg AY, Uiterwaal CS, Kimpfen JL, van der Hoeven J and Buitelaar JK (2005): Children with unexplained chronic pain: substantial impairment in everyday life. *Arch Dis Child* 90: 680–686.

Krivickas LS and Feinberg JH (1996): Lower extremity injuries in college athletes: relation between ligamentous laxity and lower extremity muscle tightness. *Arch Phys Med Rehabil* 77: 1139–1143.

Kortt M and Baldry J (2002): The association between musculoskeletal disorders and obesity. *Aust Health Rev* 25: 207–214.

Kosek E, Ekholm J and Hansson P (1996): Modulation of pressure pain thresholds during and following isometric contraction in patients with fibromyalgia and in healthy controls. *Pain* 64: 415–423.

Kröner-Herwig B, Morris L, Heinrich M, Gassmann J and Vath N (2009): Agreement of parents and children on characteristics of pediatric headache, other pains, somatic symptoms, and depressive symptoms in an epidemiologic study. *Clin J Pain* 25: 58–64.

Kujala UM, Salminen JJ, Taimela S, Oksanen A and Jaakkola L (1992): Subject characteristics and low back pain in young athletes and nonathletes. *Med Sci Sports Exerc* 24: 627–632.

Kujala UM, Taimela S and Viljanen T (1999): Leisure physical activity and various pain symptoms among adolescents. *Br J Sports Med* 33: 325–328.

Kujala UM, Taimela S, Oksanen A and Salminen JJ (1997): Lumbar mobility and low back pain during adolescence. A longitudinal three-year follow-up study in athletes and controls. *Am J Sports Med* 25: 363–368.

Langford LA and Schmidt RF (1983): Afferent and efferent axons in the medial and posterior articular nerves of the cat. *Anat Rec* 206: 71–78.

Larsson LG, Baum J, Mudholker GS and Kollia GD (1993): Hypermobility: prevalence and features in a Swedish population, *Br J Rheumatol* 32: 116–119.

Leboeuf-Yde C and Kyvik KO (1998): At what age does low back pain become a common problem? A study of 29,424 individuals aged 12–41 years. *Spine*, 23: 228–234.

Leino P and Magni G (1993): Depressive and distress symptoms as predictors of low back

pain, neck-shoulder pain, and other musculoskeletal morbidity: a 10-year follow-up of metal industry employees. *Pain* 53: 89–94.

Léger L and Gadoury C (1989): Validity of the 20 m shuttle run test with 1 min stages to predict VO₂max in adults. *Can J Sport Sci* 14: 21–26.

Leger LA and Lambert J (1982): "A maximal multistage 20m shuttle run test to predict VO₂ max". *Eur J Appl Physiol* 49: 1–5.

Liu NYS, Plowman SA and Looney MA (1996): The reliability and validity of the 20-meter shuttle test in American students 12 to 15 years old. *Res Q Exerc Sport* 63: 360–365.

Loder RT, Aronson DD and Greenfield ML (1993): The epidemiology of bilateral slipped capital femoral epiphysis. A study of children in Michigan. *J Bone Joint Surg Am* 75: 1141–1147.

Tsuritani I, Honda R, Noborisaka Y, Ishida M, Ishizaki M and Yamada Y (2002). Impact of obesity on musculoskeletal pain and difficulty of daily movements in Japanese middle-aged women. *Maturitas*, 42: 23–30.

Lundeberg T and Ekholm J (2002): Pain from periphery to brain. *Disabil Rehabil* 24: 402–406.

Lynn B (1977): Cutaneous hyperalgesia. *Br med Bull* 33: 103–108.

Macfarlane GJ (1999): Generalized pain, fibromyalgia and regional pain: an epidemiological view. *Best Pract Res Clin Rheumatol* 13: 403–414.

Mandal AC (1994): The prevention of back pain in school children. In: R. Lueder and K. Noro, Editors, *Hard Facts About Soft Machines: The Ergonomics of Seating*, Taylor and Francis, London, pp. 269–277.

Manne S, Jacobsen P and Redd W (1992): Assessment of acute pediatric pain: do child self-report, parent ratings, and nurse ratings measure the same phenomenon? *Pain* 48: 45–52.

Markkula R, Järvinen P, Leino-Arjas P, Koskenvuo M, Kalso E and Kaprio J (2008): Clustering of symptoms associated with fibromyalgia in a Finnish Twin Cohort. *Eur J Pain* Oct 18 (in press).

Mattila V, Saarni L, Parkkari J, Koivusilta L and Rimpelä A. (2008): Predictors of low back pain hospitalization - A prospective follow-up of 57,408 adolescents. *Pain* 139: 209–217.

McBeth J, Macfarlane GJ, Benjamin S and Silman AJ (2001): Features of somatisation predict the onset of chronic widespread pain: results from a large population-based study. *Arthritis Rheum* 44: 940–946.

- McGrath PA (1990): *Pain in Children: Nature, Assessment and Treatment* New York, NY, Guilford.
- McGrath PA (1995): Aspects of pain in children and adolescents. *J Child Psychol Psychiatry* 36: 717–731.
- McGrath PA, Seifert CE, Speechley KN, Booth JC, Stitt L and Gibson MC (1996): A new analogue scale for assessing children's pain: an initial validation study. *Pain* 64: 435–443.
- McGrath PA, Speechley KN, Seifert CE, Biehn JT, Cairney AE and Gorodzinsky FP (2000): A survey of children's acute, recurrent, and chronic pain: validation of the pain experience interview. *Pain* 87: 59–73.
- Merlijn VP, Hunfeld JA, van der Wouden JC, Hazebroek-Kampschreur AA, Koes BW and Passchier J (2003): Psychosocial factors associated with chronic pain in adolescents. *Pain* 101: 33–43.
- Merskey H and Bogduk N (1994): *Classification of chronic pain: Description of chronic pain syndromes and definitions of pain terms*. Seattle, WA: IASP.
- Micheli LJ, Glassman R and Klein M (2000): The prevention of sports injuries in children. *Clin Sports Med* 4: 821–823.
- Mierau D, Cassidy JD and Yong-Hing K (1989): Low-back pain and straight leg raising in children and adolescents. *Spine* 14: 526–528.
- Mikkelsson M. Musculoskeletal pain and fibromyalgia in Preadolescents (1998_a): Prospective 1-year follow-up study. Turun yliopisto. Sarja D Osa 320.
- Mikkelsson M, Kaprio J, Salminen JJ, Pulkkinen L and Rose RJ (2001): Wide spread pain among 11-year old Finnish twin pairs. *Arthritis Rheum* 44: 481–485.
- Mikkelsson M, Salminen JJ and Kautiainen H (1997): Non-specific musculoskeletal pain in preadolescents. Prevalence and 1-year persistence. *Pain* 73: 29–35.
- Mikkelsson M, Salminen JJ, Sourander A and Kautiainen H (1998_b): Contributing factors to the persistence of musculoskeletal pain in preadolescents: A prospective 1-year follow-up study. *Pain* 77: 67–72.
- Mikkelsson M, Salminen JJ and Kautiainen H (1996): Joint hypermobility is not a contributing factor to musculoskeletal pain in pre-adolescents. *J Rheumatol* 23: 1963–1967.
- Mikkelsson M, Sourander A, Piha J and Salminen JJ (1997): Psychiatric 489 symptoms in pre-adolescents with musculoskeletal pain and 490 fibromyalgia. *Pediatrics* 100: 220–227.
- Mikkonen P, Leino-Arjas P, Remes J, Zitting P, Taimela S and Karppinen J (2008): Is

smoking a risk factor for low back pain in adolescents? A prospective cohort study. *Spine* 33: 527–32.

Milligan E and Watkins L (2009): Pathological and protective roles of glia in chronic pain. *Nat Rev Neurosci* 10: 23–36.

Murphy S, Buckle P and Stubbs D (2007): A cross-sectional study of self-reported back and neck pain among English schoolchildren and associated physical and psychological risk factors. *Appl Ergon* 38: 797–804.

Myer GD, Ford KR, Paterno MV, Nick TG and Hewett TE (2008): The effects of generalized joint laxity on risk of anterior cruciate ligament injury in young female athletes. *Am J Sports Med* 36: 1073–1080.

Naish JM and Apley J (1951): “Growing pains”: a clinical study of non-arthritic limb pains in children. *Arch Dis Child* 26: 134–140.

Newcomer K and Sinaki M (1994): Occurrence of low-back pain in children and its relationships to back strength and level of physical activity. *Arch Phys Med Rehabil* 75: 1048–1049.

Nielsen LA and Henriksson KG (2007): Pathophysiological mechanisms in chronic musculoskeletal pain (fibromyalgia): The role of central and peripheral sensitization and pain disinhibition. *Best Pract Res Clin Rheumatol* 21: 465–480.

Niemi SM, Levoska S, Rekola KE and Keinänen-Kiukaanniemi SM (1997): Neck and shoulder symptoms of high school students and associated psychosocial factors. *J Adolesc Health* 20: 238–242.

Nimon G, Murray D, Sandow M and Goodfellow J (1998): Natural history of anterior knee pain. a 14- to 20-year follow-up of nonoperative management. *J Pediatr Orthop* 18: 118–122.

Nissinen M, Heliövaara M, Seitsamo J, Alaranta H and Poussa M (1994): Anthropometric measurements and the incidence of low back pain in a cohort of pubertal children. *Spine* 19: 1367–1370.

Oberklaid F, Amos D, Liu C, Jarman F, Sanson A and Prior M (1997): "Growing pains": clinical and behavioral correlates in a community sample. *J Dev Behav Pediatr* 18: 102–106.

Olsen TL, Anderson RL and Dearwater SR (1992): The epidemiology of low back pain in an adolescent population. *Am J Public Health* 82: 606–608.

Orchard J, Marsden J, Lord S and Garlick D (1997): Preseason hamstring muscle weakness associated with hamstring muscle injury in Australian footballers. *Am J Sports Med* 25: 81–85.

- Palermo TM (2000): Impact of recurrent and chronic pain on child and family daily functioning. a critical review of the literature. *J Dev Behav Pediatr* 26: 145–153.
- Øster J and Nielsen A (1972): Growing pains: A clinical investigation of a school population. *Acta Paediatr Scand* 61: 329–334.
- Papageorgiou AC, Silman AJ and Macfarlane GJ (2002): Chronic wide-spread pain in the population: a seven year follow up study. *Ann Rheum Dis* 61: 1071–1074.
- Parcells RN, Stommel M and Hubbard RP (1999): Mismatch of classroom furniture and student body dimensions: Empirical findings and health implications, *J Adolesc Health*, 24: 265–273.
- Passchier J and Orlebeke JF (1985): Headaches and stress in schoolchildren: An epidemiological study. *Cephalalgia*, 5: 167–176.
- Perquin CW, Hazebroek-Kampschreur AAJM, Hunfeld JAM, Bohen AM, van Suijlekom-Smit LWA, Passchier J and van der Wouden JC (2000): Pain in children and adolescents: A common experience. *Pain* 87: 51–58.
- Perquin CW, Hunfeld JAM, Hazebroek-Kampschreur AAJM, van Suijlekom-Smit LWA, Passchier J, Koes BW and van der Wouden JC (2003): The natural course of chronic benign pain in childhood and adolescence: A two-year population-based follow-up study. *Eur J Pain* 7: 551–559.
- Peters L and Murphy A (1993): Adolescent Health Survey, Province of British Columbia. Burnaby, The McCreary Centre Society.
- Prendeville K and Dockrell S (1998): A pilot study to investigate the incidence of low back pain in school children. *Physiotherapy Ireland* 19: 3–7.
- Price DD, Staud R, Robinson ME, Mauderli AP, Cannon R and Vierck CJ (2002): Enhanced temporal summation of second pain and its central modulation in fibromyalgia patients. *Pain* 99: 49– 59.
- Qvindedland A and Jonsson H (1999): Articular hypermobility in Icelandic 12-year-olds. *Rheumatology* 38: 1014–1016.
- Rocha ES and Pedreira AC (2001): Common orthopedic problems in adolescents. *J Pediatr (Rio J)* 77(Suppl 2): S225-33. (in Portuguese).
- Rosenberg AM (1990): Analysis of a pediatric rheumatology clinic population. *J Rheumatol* 17: 827–830.
- Roth-Isigkeit A, Thyen U, Raspe HH, Stöven H, and Schmucker P (2004): Reports of pain among German children and adolescents: an epidemiological study. *Acta Paediatr* 93: 258–

263.

Roth-Isigkeit A, Thyen U, Stoven H, Schwarzenberger J and Schmucker P (2005): Pain among children and adolescents: Restrictions in daily living and triggering factors. *Pediatrics* 115: 152–162.

Rhee H (2005): Racial/ethnic differences in adolescents' physical symptoms. *J Pediatr Nurs* 20: 153–162.

Russek L (1999): Hypermobility syndrome, *Phys Ther* 79: 591–597.

Salminen J, Maki P, Oksanen A and Pentti J (1992_b): Spinal mobility and trunk muscle strength in 15-year-old school children with and without low-back pain. *Spine* 17: 405–411.

Salminen JJ (1984): The adolescent back; A field survey of 370 Finnish school children. *Acta Paediatr Scand* 315 [Suppl]: 1–122.

Salminen JJ, Erkintalo M, Laine M and Pentti J (1995): Low back pain in the young. A prospective three-year follow-up study of subjects with and without low back pain. *Spine* 20: 2101–2108.

Salminen JJ, Erkintalo MO, Pentti J, Oksanen A and Kormano MJ (1999): Recurrent low back pain and early disc degeneration in the young. *Spine* 13: 1316–1321.

Salminen JJ, Pentti J and Terho P (1992_a): Low back pain and disability in 14-year-old schoolchildren. *Acta Paediatr* 81: 1035–1039.

Sambrook PN, MacGregor AJ and Spector TD (1999): Genetic influences on cervical and lumbar disc degeneration: a magnetic resonance imaging study in twins. *Arthritis Rheum* 42: 366–372.

Samet JM and Munoz A (1998): Evolution of the cohort study. *Epidemiol Rev* 20: 1–14.

Savedra MC, Tesler MD, Ward JD and Wegner C (1988): How adolescents describe pain. *J Adolesc Health Care* 9: 315–320.

Schaible HG and Grubb BD (1993): Afferent and spinal mechanisms of joint pain. *Pain* 55: 5–54.

Schanberg LE (2003): Widespread pain in children: when is it pathologic? *Arthritis Rheum* 48: 2402–2405.

Sherry DD and Malleson PN (2002): The idiopathic musculoskeletal pain syndromes in childhood *Rheum Dis Clin North Am* 28: 669–685.

Sherry DD, McGuire T, Mellins E, Salmonson K, Wallace CA and Nepom B (1991):

Psychosomatic musculoskeletal pain in childhood: clinical and psychological analyses of 100 children. *Pediatrics* 88: 1093–1099.

Shrier I, Ehrmann-Feldman D, Rossignol M and Abenhaim, L (2001): Risk factors for development of lower limb pain in adolescents. *J Rheumatol* 28: 604–609.

Siivola SM, Levoska S, Latvala K, Hoskio E, Vanharanta H and Keinänen-Kiukaanniemi S (2004): Predictive factors for neck and shoulder pain: a longitudinal study in young adults. *Spine* 29: 1662–1669.

Simmonds JV and Keer RJ (2007): Hypermobility and the hypermobility syndrome. *Man Ther* 12: 298–309.

Sjolie AN (2000): Access to pedestrian roads, daily activities, and physical performance of adolescents. *Spine* 25: 1965–1972.

Sleed M, Eccleston C, Beecham J, Knapp M and Jordan A (2005): The economic impact of chronic pain in adolescence: methodological considerations and a preliminary costs-of-illness study. *Pain* 119: 183–190.

Smedbraten BK, Natvig B, Rutle O and Bruusgaard D (1998): Self-reported bodily pain in schoolchildren. *Scand J Rheumatol* 27: 273–276.

Staud R and Rodriguez ME (2006): Mechanisms of disease: pain in fibromyalgia syndrome. *Nat Clin Pract Rheumatol* 2: 90–98.

Staud R and Smitherman ML (2002): Peripheral and central sensitization in FM: pathogenic role. *Curr Pain Headache Rep* 6: 259–266.

Staud R, Vierck CJ, Mauderli A, et al. (1998): Abnormal temporal summation of second pain (wind-up) in patients with the fibromyalgia syndrome. *Arthritis Rheum* 41: S353.

Staud R, Vierck CJ, Cannon RL, Mauderli AP and Price DD (2001): Abnormal sensitization and temporal summation of second pain (wind-up) in patients with fibromyalgia syndrome. *Pain* 91: 165–175.

Staud R, Vierck CJ, Robinson ME and Price DD (2005): Effects of the Nmethyl-D-aspartate receptor antagonist dextromethorphan on temporal summation of pain are similar in fibromyalgia patients and normal control subjects. *J Pain* 6: 323–332.

Stovitz SD, Pardee PE, Vazquez G, Duval S and Schwimmer JB (2008): Musculoskeletal pain in obese children and adolescents. *Acta Pædiatrica* 97: 489–493.

Ståhl M, Mikkelsen M., Kautiainen H, Häkkinen A, Ylinen J and Salminen JJ (2004): Neck pain in adolescence. A 4-year follow-up of pain-free preadolescents. *Pain* 110: 427–431.

- Sundblad GM, Saartok T and Engstrom LM (2007): Prevalence and co-occurrence of self-rated pain and perceived health in school-children: Age and gender differences. *Eur J Pain* 11, 171–180.
- Sundblad GM, Saartok T and Engström LM (2006): Child-parent agreement on reports of disease, injury and pain. *BMC Public Health* 6: 276.
- Taimela S, Kujala UM, Salminen JJ and Viljanen T (1997): The prevalence of low back pain among children and adolescents. A nationwide, cohort-based questionnaire survey in Finland. *Spine* 22: 1132–1136.
- Takala EP, Viikari-Juntura E, Moneta GB, Saarenmaa K and Kaivanto K (1992): Seasonal variation in neck and shoulder symptoms. *Scand J Work Environ Health* 18: 257–261.
- Tamminen TM, Bredenberg P, Escartin T, Kaukonen P, Puura K, Rutanen M, Suominen I, Leijala H and Salmelin R (1991): Psychosomatic symptoms in preadolescent children. *Psychother Psychosom* 56: 70–77.
- Timm NL, Grupp-Phelan J and Ho ML (2005): Chronic ankle morbidity in obese children following an acute ankle injury. *Arch Pediatr Adolesc Med* 159: 33–36.
- Troussier B, Davoine P, de Gaudemaris R, Fauconnier J and Phelip X (1994): Back pain in school children. A study among 1178 pupils. *Scand J Rehabil Med* 26: 143–146.
- Troussier B, Tesniere C, Fauconnier J, Grison J, Juvin R and Phelip X (1999) : Comparative study of two different kinds of school furniture among children, *Ergonomics* 42: 516–526.
- Van Eekelen FC, Perquin CW, Hunfeld JA., Hazebroek-Kampschreur AA, van Suijlekom-Smit LW, Koes BW, Passchier J and van der Wouden JC (2002): Comparison between children and adolescents with and without chronic benign pain: Consultation rate and pain characteristics. *Br J Gen Pract* 52: 211–213.
- Varlotta GP, Brown MD, Kelsey JL and Golden AL (1991): Familial predisposition for herniation of a lumbar disc in patients who are less than twenty-one years old. *J Bone Joint Surg Am* 73:124–128.
- Vierck CJ Jr (2006): Mechanisms underlying development of spatially distributed chronic pain (fibromyalgia). *Pain* 124: 242–263.
- Viikari-Juntura E, Vuori J, Silverstein A, Kalimo R, Kuosma E and Videman T (1991): A life-long prospective study on the role of psychosocial factors in neck-shoulder and low-back pain. *Spine* 16:1056–1061.
- Viry P, Creveuil C and Marcelli C (1999): Non-specific back pain in children: a search for associated factors in 14-year-old schoolchildren, *Rev. Rhum* 66: 381–388.

- Viry P, Creveuil C and Marcelli C (1994): Non-specific low back pain among school children: A field survey with analysis of some associated factors. *J Spinal Disord* 7: 374–379.
- Viswanathan V and Khubchandani RP (2008): Joint hypermobility and growing pains in school children. *Clin Exp Rheumatol* 26: 962–966.
- Von Baeyer CL and Spagrud LJ (2007): Systematic review of observational (behavioral) measures of pain for children and adolescents aged 3 to 18 years. *Pain* 127: 140–150.
- Vähäsarja V (1995): Prevalence of chronic knee pain in children and adolescents in northern Finland. *Acta Paediatr* 84: 803–805.
- Walters AS and Williamson GM (1999): The role of activity restriction in the association between pain and depression. A study of pediatric patients with chronic pain. *Children's Health Care* 28: 33–50.
- Watson KD, Papageorgiou AC, Jones GT, Taylor S, Symmons DPM, Silman AJ and Macfarlane GJ (2003): Low back pain in schoolchildren: The role of mechanical and psychosocial factors. *Arch Dis Child* 88: 12–17.
- Wedderkopp N, Kjaer P, Hestbaek L, Korsholm L and Leboeuf-Yde C (2009): High-level physical activity in childhood seems to protect against low back pain in early adolescence. *Spine J* 9: 134–141.
- Wedderkopp N, Leboeuf-Yde C, Andersen LB, Froberg K and Hansen HS (2003): Back pain in children: No association with objectively measured level of physical activity. *Spine* 28: 2019–2024.
- Whittfield J, Legg SJ and Hedderley DI (2005): Schoolbag weight and musculoskeletal symptoms in New Zealand secondary schools. *Appl Ergonomics* 36: 193–198.
- Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, et al (1990): The American college of rheumatology 1990 criteria for the classification of fibromyalgia. Report of the multicenter criteria committee. *Arthritis Rheum* 33: 160–172.
- Yates CK and Grana WA (1990): Patellofemoral pain in children. *Clin Orthop* 255: 36–43.
- Yazgan P, Geyikli I, Zeyrek D, Baktiroglu L and Kurcer MA (2008): Is joint hypermobility important in prepubertal children? *Rheumatol Int* 28: 445–451.

10. APPENDIX: BASELINE QUESTIONNAIRE

KOULULAISTEN KIPU
Kyselylomake

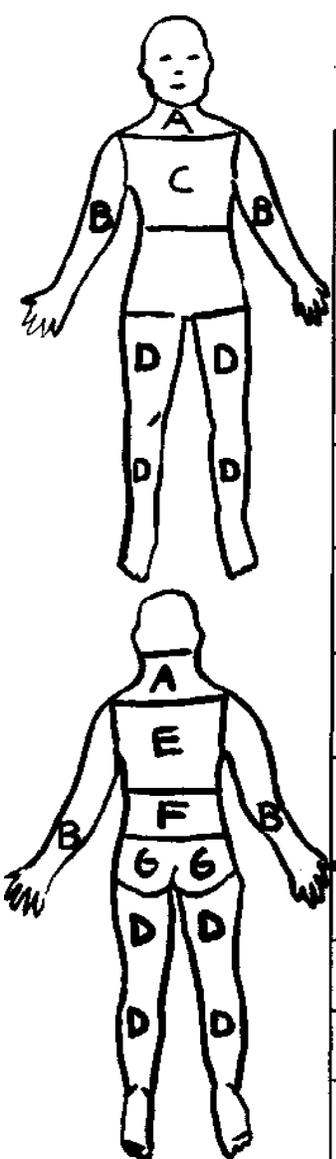
Päivämäärä:
Koulu
Luokka

Nimi:

Syntymäaika:

MERKITSE X SOPIVAN VAIHTOEHDON KOHDALLE (vain yksi vaihtoehto jokaisen oikeen kohdalle)!

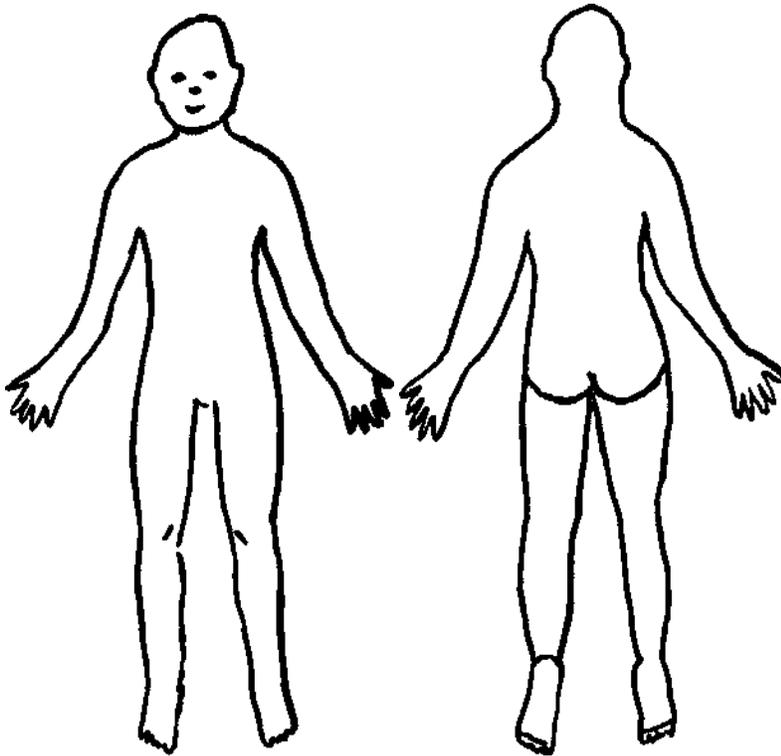
1. Mieti viime joulun jälkeistä aikaa tähän päivään asti. Kuinka usein sinulla on ollut seuraavia oireita viime joulun jälkeen (vartalon osat määritelty viereisissä kuvissa)?



	Lähes päivittäin	Useammin kuin kerran viikossa	Noin kerran viikossa	Noin kerran kuukaudessa	Harvemmin tai ei koskaan
Niska-hartiakipua tai särkyä (A)					
Yläraajojen kipua tai särkyä (B)					
Rintakehän kipua tai särkyä (C)					
Alaraajojen kipua tai särkyä (D)					
Yläselän kipua tai särkyä (E)					
Alaselän kipua tai särkyä (F)					
Pakaroiden kipua tai särkyä (G)					
Päänsärkyä					
Vatsakipu					
Masentuneisuutta					

Vaikeuksia päästä uneen					
Väsymyksen tunnetta päivisin					
Heräilemistä öisin					

2. KIPUPIIRROS. Väritä alla oleviin kuviin punaisella ne alueet, joissa sinulla on ollut kipua tai särkyä vähintään kerran kuukaudessa viime joulun jälkeen. Jos sinulla ei ole ollut kipuja, jätä kuva värittämättä kokonaan.



3. Oletko loukannut jonkin yllä väritetyn kipualueen (esim. kaatunut, kompastunut, loukannut urheilussa jne.)? Vastaa merkitsemällä X sopivan vaihtoehdon kohdalle.

D Ei

D Kyllä. Jos vastasit kyllä, ympäröi kuvasta kipualue sinisellä

4. Merkitse X, jos väite on ollut totta sinun kohdallasi joulun jälkeen.

D Kivut ja säröt haittaavat nukahtamistani.

D Kipu tai särky häiritsee rauhallista yöuntani.

D Kipu haittaa istumistani koulutunnilla.

D Kipu haittaa, jos kävelen yli kilometrin.

CU Kivun takia minulla on vaikeuksia liikuntatunnilla.

D Kipuja särky haittaavat vapaa-ajan harrastuksiani.

D Minulla ei ole ollut kipuja.

5. Oletko ollut kipujen tai särkyjen takia poissa koulusta? Vastaa merkitsemällä X sopivan vaihtoehdon kohdalle.

D Ei

P Kyllä. Montako päivää tänä lukukautena?

6. Merkitse X, jos väite on ollut totta sinun kohdallasi joulun jälkeen.

D Rasitus pahentaa kipuoireitani (esimerkiksi juoksu, luistelu, hiito jne).

D Minulla on turvotuksen tunnetta käsissä tai jaloissa.

D Nukun huonosti.

D Tunnen itseni päivisinkin väsyneeksi.

D Olen jännittänyt ja hermostunut.

D Huonot säät pahentavat kipujani.

D Käsissäni ja jaloissani on puutumisen tunnetta.

D Hermostuminen pahentaa kipuoireitani.

D Minulla on mahavaivoja (ilmavaivoja, ummetusta, ripulia).

G Päätäni särkee.

7. Merkitse X sopivan vaihtoehdon kohdalle!

Olen harrastanut hengästymiseen johtavaa liikuntaa / urheilua joulun jälkeen vähintään puoli tuntia kerrallaan

D 1 -2 kertaa viikossa.

D 3-4 kertaa viikossa.

D 5-7 kertaa viikossa.

D En harrasta liikuntaa tai urheilua lainkaan.

8. Onko sinulla jokin pitkäaikainen sairaus, jonka vuoksi käyt säännöllisesti lääkärin luona tai käytät sairautesi jotain lääkettä?

D Ei.

D Kyllä. Mikä sairaus? _____

KIITOS VASTAUKSISTASI!

11. ORIGINAL PUBLICATIONS