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PAIN SYMPTOMS AND SLEEP PROBLEMS AMONG SCHOOL-AGED CHILDREN

Long-term prevalence changes, and pain symptoms as predictors of later mental health

by

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For all the children, and in particular Volter and Essi

"A wrong functioning of the psyche can do much to injure the body, just as conversely a bodily illness can affect the psyche; for psyche and body are not separate entities but one and the same life." (C.G. Jung 1953)

Terhi Luntamo

Pain symptoms and sleep problems among school-aged children. Long-term prevalence changes, and pain symptoms as predictors of later mental health

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ABSTRACT

Children's pain symptoms and sleep problems are among the most common health complaints. They distract children from activities, decrease the quality of life, contribute to a significant economic burden, and have shown continuity into adulthood. The main aims of this thesis were to investigate long-term changes in the prevalence of pain symptoms and sleep problems among Finnish school-aged children, and the later mental health of those who in childhood experience pain. Prevalence, co-occurrence, and associated psychosocial factors of pain symptoms and sleep problems were also assessed.

In study I, prevalence changes in eight-year-old children's pain symptoms and sleep problems were investigated in three cross-sectional population-based samples (years 1989: n=1038, 1999: n=1035, and 2005: n=1030). In study II, cross-sectional associations between pain symptoms, sleep problems, and psychosocial factors were assessed among 13-18-year-old adolescents (n=2476). In studies III and IV, associations between pain symptoms at age eight (n=6017), and register-based data on antidepressant use and severe suicidality by age 24, were examined in a nationwide birth cohort.

Pain symptoms and sleep problems were common and often co-occurred. A considerable number of children's pain symptoms remained unrecognized by the parents. The prevalence of pain symptoms, sleep problems, and multiple concurrent symptoms approximately doubled from 1989 to 2005. Psychiatric difficulties or demographic factors did not explain the increase. Psychosocial factors that were associated with pain, sleep problems, and a higher number of symptoms, were female sex, psychological difficulties, emotional symptoms, smoking, victimization, and feeling not cared about by teachers. In longitudinal analyses, the child's own report of headache, and to a smaller degree the parental report of the child's abdominal pain predicted later antidepressant use. Parental report of the child's abdominal pain predicted severe suicidality among males.

If one of the symptoms is present, health care professionals should inquire about other symptoms as well. Questions should be directed to the children, not only to their parents. Inquiring about psychiatric difficulties, substance use, victimization, and relations with teachers should be included as a part of the assessment. Further studies are needed to clarify the reasons that underlie the increased prevalence rates, and the factors that may increase or decrease the risk for later mental health problems among pain-suffering children.

Keywords: adolescent, child, cross-sectional studies, mental health, pain, prevalence, prospective studies, psychosocial aspects, sleep disorders, suicide

Terhi Luntamo

Koululaisten kipuoireet ja uniongelmat. Esiintyvyyden pitkän aikavälin muutokset ja kipuoireiden yhteys myöhempiin psyykkisiin vaikeuksiin

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TIIVISTELMÄ

Kipuoireet ja uniongelmat ovat lapsilla yleisiä vaivoja. Ne haittaavat arkea, huonontavat elämänlaatua, aiheuttavat huomattavia kustannuksia ja jatkuvat usein aikuisikään saakka. Tämän väitöskirjatutkimuksen päätavoitteina oli tutkia suomalaisten koululaisten kipuoireiden ja uniongelmien pitkän aikavälin esiintyvyyden muutoksia ja kipuoireiden yhteyttä myöhempään psyykkiseen vointiin. Lisäksi tutkittiin kipujen ja uniongelmien esiintyvyyttä, päällekkäisyyttä ja oireisiin liittyviä psykososiaalisia tekijöitä.

I osatyössä tutkittiin 8-vuotiaiden lasten kipuoireiden ja uniongelmien esiintyvyyttä vuosina 1989 (n=1038), 1999 (n=1035) ja 2005 (n=1030) normaaliväestöstä kerätyissä poikkileikkausaineistoissa. II osatyössä kartoitettiin 13-18-vuotiaiden nuorten (n=2476) kipuoireiden, uniongelmien ja psykososiaalisten tekijöiden keskinäisiä yhteyksiä. Osatöissä III ja IV tutkittiin kansallisessa syntymäkohortissa (n=6017) 8-vuotiaiden lasten kipuoireiden yhteyttä masennuslääkekäyttöön ja vakavaan itsetuhoisuuteen 24 ikävuoteen mennessä. Tiedot lääkkeiden käytöstä ja itsetuhoisuudesta kerättiin rekistereistä.

Kipuoireet ja uniongelmat olivat yleisiä ja esiintyivät usein samanaikaisesti. Merkittävä osa lasten raportoimista kipuoireista jäi vanhemmilta huomaamatta. Kipuoireiden, uniongelmien ja useiden samanaikaisten oireiden esiintyvyys kaksinkertaistui vuodesta 1989 vuoteen 2005. Psyykkiset vaikeudet tai demografiset tekijät eivät selittäneet esiintyvyyden kasvua. Psykososiaalisista tekijöistä naissukupuoli, psykologiset ja erityisesti emotionaaliset vaikeudet, tupakointi, kiusatuksi tuleminen ja kokemus opettajien välinpitämättömyydestä olivat yhteydessä kipuoireisiin, uniongelmiin ja useiden samanaikaisten oireiden esiintymiseen. Pitkittäisessä tutkimusasetelmassa lapsen oma ilmoitus päänsärystä ja vähäisemmässä määrin vanhemman ilmoitus lapsen vatsakivusta ennustivat myöhempää masennuslääkkeiden käyttöä. Vanhemman ilmoitus lapsen vatsakivusta ennusti vakavaa itsetuhoista käyttäytymistä pojilla.

Lapsen kärsiessä yhdestä oireesta terveydenhuollon työntekijöiden tulisi tiedustella myös muiden oireiden mahdollisuutta. Lisäksi tulisi kartoittaa mahdolliset psyykkiset vaikeudet, päihteidenkäyttö, kiusatuksi tuleminen ja ajatukset suhteista opettajiin. Kysymykset tulisi osoittaa myös lapselle itselleen, ei vain vanhemmille. Jatkossa tutkimuksissa tulisi selvittää syitä oireiden lisääntymiseen sekä niitä tekijöitä, jotka lisäävät tai vähentävät oireilevien lasten riskiä myöhempiin psyykkisiin vaikeuksiin.

Avainsanat: esiintyvyys, itsetuhoisuus, kipu, lapsi, mielenterveys, nuori, pitkittäistutkimus, poikkileikkaustutkimus, psykososiaaliset tekijät, univaikeudet

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ABBREVIATIONS

AP	abdominal pain
BP	back pain
CDI	Child Depression Inventory Scale
CI	confidence interval
COR	cumulative odds ratio
DF	difficulties falling asleep
HA	headache
HR	hazard ratio
LP	limb pain
MP	musculoskeletal pain
NS	non-significant
OR	odds ratio
OP	other pains
PS	pain symptoms
SD	standard deviation
SDQ	Strengths and Difficulties Questionnaire
SP	sleep problems
resp	response rate
RR	risk ratio
T	tiredness
κ	kappa coefficient

LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the following original publications:

I **Luntamo T**, Sourander A, Santalahti P, Aromaa M, Helenius H. Prevalence changes of pain, sleep problems and fatigue among 8-year-old children: years 1989, 1999, and 2005. J Pediatr Psychol. 2012 Apr;37(3):307-18. DOI:10.1093/jpepsy/jsr091

II **Luntamo T**, Sourander A, Rihko M, Aromaa M, Helenius H, Koskelainen M, McGrath PJ. Psychosocial determinants of headache, abdominal pain, and sleep problems in a community sample of Finnish adolescents. Eur Child Adolesc Psychiatry. 2012 Jun;21(6):301-13. DOI: 10.1007/s00787-012-0261-1

III **Luntamo T**, Sourander A, Sillanmäki L, Gyllenberg D, Aromaa M, Kumpulainen K, Moilanen I, Almqvist F, Tamminen T, Piha J. Pain at age eight as a predictor of antidepressant medication use by age 24: findings from the Finnish nationwide 1981 birth cohort study. J Affect Disord. 2012 Apr;138(1-2):153-9. DOI:10.1016/j.jad.2012.01.003

IV **Luntamo T**, Sourander A, Sillanmäki L, Gyllenberg D, Aromaa M, Tamminen T, Kumpulainen K, Moilanen I, Piha J. Do Headache and Abdominal Pain in Childhood Predict Suicides and Severe Suicide Attempts? Finnish Nationwide 1981 Birth Cohort Study. Child Psychiatry Hum Dev. In press. DOI: 10.1007/s10578-013-0382-x

The publications are referred to in the text by their roman numerals. They are reproduced at the end of the thesis with the permission of the copyright holders.

1 INTRODUCTION

Somatic symptoms or somatization, in particular various complaints of recurrent pain, are common among pediatric populations (Garralda 2008, Campo and Fritsch 1994). Somatization has been defined as the occurrence of physical complaints for which appropriate medical evaluation reveals no explanatory physical pathology or pathophysiologic mechanism or, when physical pathology is present, the physical complaints resulting in impairment are grossly in excess of what would be expected from the known physical findings (Kellner 1991). Psychosomatic medicine can be defined as a comprehensive, interdisciplinary framework for assessment of psychosocial factors affecting individual vulnerability, course and outcome of any type of disease (Fava and Sonino 2010). It refers to mind and body interactions in patients who are ill rather than being a reductionistic theory of psychogenic causation of disease (Gitlin et al., 2004).

Although it is widely accepted today that psychological factors play a role in somatic phenomena, and somatic problems affect psychological well-being, this has not always been the case. According to the Cartesian mind-body dualism introduced in the 17th century, diseases were considered dichotomously as being either organic or psychologically based. From the 19th century, an increasing interest in the associations between physiological and psychological phenomena started to emerge, and the concept, psychosomatic, was first introduced in 1818 by Heinroth when discussing causes of insomnia (Gitlin et al., 2004). The first psychosomatic theories were predominantly based on psychoanalytic approaches. Certain illnesses, such as hypertension or peptic ulcer, were considered as distinct psychosomatic diseases (Fava and Sonino 2010). The specificity theory in the mid-20th century even proposed that specific psychological conflicts contribute to the development of specific medical disorders. As empirical data did not support this view, more general models concerning the relations between psychological and somatic phenomena had to be considered. The concept of psychogenic pain has been removed from the Diagnostic and Statistical Manual of Mental Disorders, and pain specialists nowadays argue that neither empirical evidence nor clinical utility support the discrimination of discrete “organic” and “psychogenic” causes of pain (Gagliese and Katz 2000).

Engel (1977) considered that the biomedical reductionism, which neglected the impact of non-biological circumstances on biological processes, distorted perspectives and interfered with patient care. He proposed a biopsychosocial model, suggesting that illness is the product of interacting biological, psychological, and social factors. He suggested that a number of interacting factors, from the biochemical to the social, contribute to health and illness, and that a change in one affects change in the others. Present day psychosomatic medicine is predicated largely on the study of such interrelations, and the

biopsychosocial perspective has also been considered as most relevant in approaching pediatric somatization (Campo and Fritsch 1994). Pediatric psychosomatic medicine has been defined as concerning the relation between physiological and psychological factors in the causation or maintenance of disease states among children and adolescents (Ibeziako and Bujoreanu 2011).

Different kinds of somatic symptoms among pediatric populations represent a considerable public health problem, with various pain symptoms and sleep-related problems being among the most prevalent complaints (Petersen et al., 2003, van Litsenburg et al., 2010). These symptoms are common reasons for seeking health care, and are associated with decreased quality of life for children and their families (Kotagal 2003, Petersen et al., 2009). They have been linked with distractions from activities (e.g. meeting friends and pursuing hobbies) (Haraldstad et al., 2011, Roth-Isigkeit et al., 2005), impaired cognitive functions (Paavonen et al., 2010, Smedbråten et al., 1998), and increased school absenteeism (Haraldstad et al., 2011, Paavonen et al., 2002, Roth-Isigkeit et al., 2005), and even hospital admissions (Williams et al., 1999). Sleep problems have also been associated with an increased amount of unintentional injuries (Owens et al., 2005) and type II diabetes (Knutson and Van Cauter 2008). In addition, pain symptoms and sleep problems have been estimated to contribute to a significant economic burden (Pesa and Lage 2004, Stoller 1994), and it seems that a large number of children who have pain symptoms continue to suffer from the same or some other kinds of symptoms in adulthood (Apley and Hale 1973, Brna et al., 2005, Magni et al., 1987).

The number of studies on somatic symptoms among pediatric populations is remarkably lower than among adult populations. However, in Finland, there is a long tradition of studying children's and adolescents' different kinds of health complaints. Psychosomatic symptoms have been studied as symptom constellations (Aro et al., 1987, Aro et al., 1989, Kinnunen et al., 2010, Sourander et al., 2006, Stakes 2012), and as individual symptoms. In particular, there are a number of distinguished studies on headache, based on the pioneering work by Sillanpää (Anttila et al., 1999 and 2006, Aromaa et al., 1998, 1999, and 2000, Sillanpää 1976, Sillanpää and Anttila 1996). In addition, there have been many Finnish studies on musculoskeletal pains (Mikkelsson et al., 1997 and 1998, Ståhl et al., 2008), as well as sleep problems, and their associations with psychiatric difficulties (Paavonen et al., 2000, 2002, and 2003, Stakes 2012).

Pain symptoms and sleep problems often co-occur (Aromaa et al., 2000, Brun Sundblad et al., 2007, Bruusgaard et al., 2000, Groholt et al., 2003, Kröner-Herwig et al., 2008, Perquin et al., 2000, Petersen et al., 2006, Roth-Isigkeit et al., 2005), which may be due, for example, to common background factors. Similar physiological and lifestyle factors have been linked with both pain symptoms (Bakoula et al., 2006, Hershey et al., 2009, Malaty et al., 2007, Wilkinson et al., 1994) and sleep problems (Calhoun

et al., 2011, Lazaratou et al., 2012, Mindell et al., 2009). In addition, pain symptoms (Aromaa et al., 1998, Berntsson et al., 2001, Boey and Yap, 1999, Brown 2004, Galli et al., 2007, Sarioglu, et al., 2003, van Tilburg et al., 2010, Watson et al., 2003) and sleep problems (Berntsson et al., 2001, Harvey 2002, Smaldone et al., 2009, Smedje et al., 2001) have been found to be associated with psychiatric difficulties, negative life events, and dysfunctional cognitive mechanisms. However, despite many similar features that are shared by pain symptoms and sleep problems, most studies have focused on only one symptom, and there is a lack of studies examining the distinctions among the psychosocial determinants of pain and other kinds of health complaints (Beck 2008).

The above-mentioned associations between pain symptoms and psychopathology have been shown both in pediatric (Galli et al., 2007, Gordon et al., 2004, Liakopoulou-Kairis et al., 2002), and in adult populations (Breslau et al., 1991, Knaster et al., 2011, Lee et al., 2009). However, as gradually growing evidence from prospective population-based studies begin to show that both emotional and behavioral problems in childhood predict similar and other types of psychiatric difficulties in adulthood (Cannon et al., 2002, Clark et al., 2007, Odgers et al., 2008, Sourander et al., 2009), the current knowledge on the associations between pain symptoms in childhood and psychiatric difficulties in adulthood is largely lacking. Some studies have shown associations between pain in childhood and mental health in adulthood (Brattberg 2004, Fearon and Hotopf 2001, Hotopf et al., 1998), but a number of methodological limitations (such as lack of assessment of baseline psychiatric difficulties, and reliance on parental reports of the child's pain) restrict the conclusions that can be drawn. However, further knowledge of the associations between children's pain symptoms and later mental health would give valuable data both on long-term implications of childhood pain, and on risk factors for mental health problems in adulthood. Such information is important, for example, in the planning of health care services, and in preventive and treatment strategies, especially, as mental health problems in adulthood are among the most common reasons for early retirement (Kela 2012).

This thesis concerns pain symptoms and sleep problems among eight-year-old children and 13-18-year-old adolescents. Questionnaires are used to study headache, abdominal pain, other pains, sleep problems, and tiredness in population-based samples, and special emphasis is given to the child's own report of the symptoms. The study investigates possible changes in the prevalence of eight-year-old children's various pain symptoms and sleep problems during the past few decades. It focuses on the later mental health of those who in childhood experience pain symptoms. In addition, cross-sectional associations of pain symptoms and sleep problems with psychosocial, in particular psychiatric, factors are studied at age eight and in mid-adolescence. As two out of the four distinct studies concentrate only on pain symptoms, they are given greater emphasis in the theoretical parts of the thesis than sleep problems.

2 REVIEW OF THE LITERATURE

2.1 Prevalence of pain symptoms and sleep problems

2.1.1 Prevalence of pain symptoms

Table 1 presents a summary of the frequencies of pain symptoms found in different studies. It includes large-scale studies that were performed in non-clinical populations in Western countries, and investigated both adolescents and younger children. Only studies that investigated at least two different pain symptoms, were selected for the table. Among school-aged children, headache is the most commonly reported pain symptom, followed by abdominal pain and musculoskeletal pains, such as back pain. According to the studies presented in Table 1, the prevalence rates of recurrent headache, abdominal pain, and back pain, have been reported to vary from 10% to 48%, from 3% to 39%, and from 1% to 25%, respectively (Berntsson et al., 2001, Egger et al., 1998, Egger et al., 1999, Petersen et al., 2003, Stanford et al., 2008).

Among school-aged children, older children and girls are considered to suffer from pain symptoms more often than younger children and boys (Bruusgaard et al., 2000, Kinnunen et al., 2010, Perquin et al., 2000, Petersen et al., 200). Some studies have also revealed peaks in the prevalence of pain symptoms. One possible peak has been reported in early adolescence (Perquin et al., 2000). Another peak has been observed at the age of seven, indicating that starting school may be a stressful experience, and thus form a risk for increasing symptom levels (Anttila et al., 1999, Petersen et al., 2003). However, when considering various pain symptoms individually, also differences in age distributions have been shown. As headache and back pain clearly increase with age (Fearon and Hotopf 2001, van Gessel et al., 2011, Groholt et al., 2003, Kröner-Herwig et al., 2008, Ostberg et al., 2006, Petersen et al., 2003), the changes in the prevalence of abdominal pain are not as clear. While some studies show an increase with age, in particular among girls (Brun Sundblad et al., 2007, Petersen et al., 2003), others show a decline with age (Groholt et al., 2003, Ostberg et al., 2006). Nevertheless, abdominal pain is more common than headache during the early school years, whereas older children report headache as the most common pain symptom (Kinnunen et al., 2010, Petersen et al., 2003). Regarding sex, the prevalence of pain symptoms is mostly reported equally among younger age groups, with the female predominance only starting to emerge during or slightly before adolescence (Fearon and Hotopf, 2001, van Gessel et al., 2011, Petersen et al., 2003). The female predominance seems to be even clearer when studying children or adolescents who have chronic, frequent, or multiple pain symptoms (Kröner-Herwig et al., 2008, Perquin et al., 2000, Petersen et al., 2003). However, again, when

considering various pain symptoms individually, differences in sex distribution have been shown. Most studies have reported that headache and abdominal pain are more prevalent among girls (Brun Sundblad et al., 2007, Groholt et al., 2003, Kröner-Herwig et al., 2008, Ostberg et al., 2006, Stanford et al., 2008), but the studies on musculoskeletal pains have shown more conflicting findings (Egger et al., 1999, Groholt et al., 2003, Perquin et al., 2000, Petersen et al., 2003, Stanford et al., 2008).

In conclusion, as can be seen from Table 1, prevalence rates of pain symptoms vary widely among the studies. The variations are due, for example, to differences in study populations (country, age group, clinical versus general population) and methodology (interviews versus questionnaires, self- versus proxy reports, classification of the symptoms). For example, differences in the definition of the symptom, such as required frequency, duration, and severity, cause variation between prevalence rates found in different studies. In addition, as it has been shown that the agreement between self- and parental reports of the symptoms is poor (Garber et al., 1998, Haralstad et al., 2011, Santalahti et al., 2005, Sweeting and West 1998), the results also largely depend on the reporter. The issue of the agreement between self- and parental reports is presented in more detail later in the thesis (section 2.1.3).

2.1.2 Prevalence of sleep problems

The International Classification of Diseases (10th version) includes diagnostic categories of organic and non-organic sleep disorders. Non-organic sleep disorders include dyssomnias and parasomnias. Dyssomnias refer to problems in the quality or quantity of sleep, somnolence or falling asleep during the day, or circadian rhythm disturbances. Parasomnias refer to episodes during sleep, such as sleep walking, night terrors, and nightmares. Sleep-related breathing disorders, narcolepsy and cataplexy are included in the category of organic sleep disorders, while other sleep-related problems, such as periodical movement disorders and enuresis, are covered in yet other diagnostic categories.

Table 2 presents the frequencies of sleep problems in different studies. For the table, large-scale studies among non-clinical populations in Western countries, including both adolescents and younger children, were selected. Studies among general pediatric populations have found a high prevalence of recurrent sleep-related problems. For example, in a study among 10-18-year-old children, 36% suffered from weekly difficulties falling asleep (Ostberg et al., 2006). In another study, 31% of 6-13-year-old children reported at least weekly tiredness (Petersen et al., 2003). In a study in which different kinds of sleep problems were investigated among 2-14-year-old children, the following prevalences were found: 10% for daytime sleepiness, 9% for sleep duration, 9% for bedtime resistance, 7% for parasomnias, 7% for sleep anxiety, 6% for sleep onset

Table 1. Prevalence of pain symptoms

Publication, country, and study year	Participants, sex distribution, and response rate	Measures and reporter	Prevalence of pain	Sex differences	Age differences
Brun Sundblad et al., 2007; Sweden in 2002	An independent random selection of schools enrolling grades 3,6, and 9, i.e. ages 9,12, and 15 (n=1975); 51.2% males; resp:97%	Prevalence of pains (not caused by an injury or known medical disorder or disease) within last 10-14 weeks; self-report	Overall pain: 50% Weekly HA: 8% boys, 17% girls Weekly AP: 5% boys, 10% girls Weekly MP: 10% boys, 7% girls Multiple pains: 37%	Weekly pain: no difference HA: girls > boys AP: girls > boys at ages 12+15	Weekly pain: older > younger among girls HA: older > younger among girls AP: older > younger among girls and younger > older among boys
Bruusgaard et al., 2000; Norway in 1993	All pupils attending 4th, 7th, and 9th grade in the community, i.e. 10.5, 13.5, and 15.5-year-olds (n=677); 49.4% males; resp:86%	Prevalence of "usually" having pain; self-report	Usually having pain: 64% boys, 82% girls Mean number of pain localizations: 2.1 boys, 2.5 girls	Knee pain: boys > girls All other localizations: girls > boys	older > younger
van Gessel et al., 2011; Germany in 2003-2007	Random sample of households with 9-14-year-olds from the community register evaluated 4 times annually, until the ages of 12-17 years (n=3948); 49.7% males; resp (answered every time): 51%	6-month prevalence of recurrent pain symptoms; self-report	HA: 36-43% AP: 28-32% BP: 21-31% Multiple pains: 24-33%	HA: girls > boys at ages 11-17 AP: girls > boys at ages 10-17 BP: girls > boys at ages 11-17 Multiple pains: girls > boys at ages 10-17	HA: older > younger among girls AP: among girls: older > younger at ages 9-15, younger > older at ages 15-17 BP: older > younger Multiple pains: older > younger among girls
Stanford et al., 2008; Canada in 1994-2004	National cohort of 10-11-year-olds evaluated 5 times every 2 years, until age 18-19 (n=2488); 50.2-51.6% males	6-month prevalence of pains; self-report	Weekly HA: 26-32% Weekly AP: 14-22% Weekly BP: 18-26% Weekly HA + weekly AP: 7-15% Weekly HA + weekly BP: 10-14% Weekly AP + weekly BP: 6-12% All three symptoms weekly: 4-9%	girls > boys	
Östberg et al., 2006; Sweden in 2000-2003	National sample of adults ->10-18-year-olds living in these households (n=6573); 49.7% males; resp:82%	6-month prevalence of HA and AP; self-report	Weekly HA: 28% Weekly AP: 19%	girls > boys	HA: older > younger AP: younger > older

Publication, country, and study year	Participants, sex distribution, and response rate	Measures and reporter	Prevalence of pain	Sex differences	Age differences
Petersen et al., 2003 and Petersen et al., 2006; Sweden in 2001	A cluster sample, according to the size of schools, of randomly selected 6-13-year-olds (n=1155); 50.4% males; resp:97%	6-month prevalence of HA, AP, and BP; self-report (among 6-10-year-olds assisted by the parents)	Pain symptoms: 64% monthly, 35% weekly, 6% daily HA: monthly: 48%, weekly: 23% AP: monthly: 39%, weekly: 19% BP: monthly: 18%; weekly: 7% Multiple pains: 50% of children with pain had ≥1 other pain symptom, 9% had all 3 symptoms; 67% of children with weekly pain had multiple pain symptoms, most common combination was HA+AP	Monthly pain: no difference Weekly pain: girls > boys HA: girls > boys AP: girls > boys in monthly pain BP: no difference Single pains: no difference Multiple pains: girls > boys	Pain in general: older > younger HA: older > younger AP: older > younger in monthly pain BP: older > younger Multiple pains: older > younger 6-8-year-olds: AP most common 8-13-year-olds: HA most common
Berntsson et al., 2001; Denmark, Finland, Iceland, Norway, and Sweden in 1996	Random samples from the population registers of each country of 7-12 year-olds (n=3760); corresponding to the male/female ratio in each population; resp:65-79%	Prevalence of pain symptoms at least every other week; reported by parents with the child	HA: Denmark:14%, Finland:16%, Iceland:12%, Norway:12%, Sweden:11% AP: Denmark:13%, Finland:10%, Iceland:14%, Norway:10%, Sweden:8% BP: Denmark:4%, Finland:2%, Iceland:3%, Norway:2%, Sweden:1%		
Perquin et al., 2000; The Netherlands in 1996	A register-based random sample of 0-3-year-olds (n=1300), and a representative selection of 27 primary and 14 secondary schools: 4-18-olds (n=5336); 48.9% males; resp:82%	3-month prevalence of pains; among 0-7 year-olds parent-report, among 8-18-year-olds self-report	Overall pain: 54% Non-chronic (<3kk) pain: 24% Chronic (>3kk) pain: 25% HA: 23% AP: 22% LP: 22% Multiple pains: about 50%	Pain in general: girls > boys Non-chronic pain: no difference Chronic pain: girls > boys at ages 4-18 (in particular at ages 12-18) HA: no difference AP: girls > boys LP: boys > girls Multiple pains: girls > boys	Pain in general: older > younger 0-8-year-olds: AP most common 8-18-year-olds: HA most common
Roth-Isigkeit et al., 2005; Germany	Children of one elementary school and two secondary schools, aged 6-18 years (n=1003); 47.4% males; resp:80.3%	3-month prevalence of pain symptoms; parent-report for 6-9-year-olds; self-report for 10-18-year-olds	Overall pain: 83% Weekly pain: 35% HA: 61% AP: 43% LP: 34% BP: 30%		

Publication, country, and study year	Participants, sex distribution, and response rate	Measures and reporter	Prevalence of pain	Sex differences	Age differences
Grøholt et al., 2003; Denmark, Finland, Iceland, Norway, and Sweden in 1996	Random samples from the population registers of each country of 7-17-year-olds (same target population as in Berntsson et al., n=6230); corresponding to the male/female ratio in each population; resp:65-69%	Prevalence of pain symptoms at least every other week; reported by parents alone (50%), or together with the child (50%)	HA: 13% boys, 17% girls AP: 6% boys, 11% girls BP: 4% boys, 6% girls HA+AP: 3% HA+BP: 2% AP+BP: 1%	HA: girls > boys AP: girls > boys BP: girls > boys	HA: older > younger AP: younger > older BP: older > younger
Egger et al., 1999 and Egger et al., 1998; United States in 1992-1996	Samples of 9-, 11-, and 13-year-old children evaluated 4 times annually, until the ages of 12, 14, and 16 years (n=4500); resp:80-94%	HA and AP: at least weekly and lasting at least 1 hour during the last 3 months, MP: at least 3 times a week during the last 3 months; parent-report	HA: 10% AP: 3% MP: 2%	HA: no difference AP: girls > boys MP: no difference	HA: older > younger AP: no difference MP: no difference

Note: For the table, large-scale studies among non-clinical populations in Western countries, including both adolescents and younger children, were selected. Only studies that investigated at least two different pain symptoms, were included. Studies are presented in the following order: studies based on self-reports, studies based on self-reports assisted by parents, studies based partly on self- and partly on parental reports, and studies based on parental report only. AP=abdominal pain, BP=back pain, HA=headache, LP=limb pain, MP=musculoskeletal pain, resp=response rate.

Table 2. Prevalence of sleep problems

Publication, country, and study year	Participants, sex distribution, and response rate	Measures and reporter	Prevalence of sleep problems	Sex differences	Age differences
Russo et al., 2007; Italy	Four randomly selected schools, 8-14-year-olds (n=1114); 50.8% males; resp= 96.3%	DF during past two weeks and T; self-report	DF during past two weeks: Delay over 15 min: 41% Delay over 30 min: 20%	DF: no difference T: no difference	DF: younger > older T: no difference
Brun Sundblad et al., 2007; Sweden in 2002	An independent random selection of schools enrolling grades 3,6, and 9, i.e. ages 9,12, and 15 (n=1975); 51.2% males; resp:97%	Prevalence of SP and T within last 10-14 weeks; self-report	Weekly SP: 12% of both sexes Weekly T: 16% of both sexes	SP: girls > boys at age 15 only T: girls > boys at ages 12+15	SP: younger > older among boys T: older > younger
Bruusgaard et al., 2000; Norway in 1993	All pupils attending 4th, 7th, and 9th grade in the community, i.e. 10.5, 13.5, and 15.5-year-olds (n=677); 49.4% males; resp:86%	Prevalence of having problems with falling asleep or disturbed sleep; self-report	Problems with falling asleep or disturbed sleep: Now and then: 32% boys, 46% girls Often: 9.9% boys, 11.5% girls		
Östberg et al., 2006; Sweden in 2000-2003	National sample of adults ->10-18-year-olds living in these households (n=6573); 49.7% males; resp:82%	6-month prevalence of DF; self-report	Weekly DF: 36%	no difference	younger > older
Paavonen et al., 2003; Finland in 1989 and 1993	A random sample of school districts, 8-9-year-olds, evaluated again 4 years later (n=1320); 51.3% males; resp:98%	6-12-month prevalence of SP by parent-reports; two-week prevalence of SP by self-report	SP at age 8-9 or 12-13: 50% SP at ages 8-9 and 12-13: 12%	no difference	Parent-reported SP: younger > older Self-reported SP: no difference
Petersen et al., 2003; Sweden in 2001	A cluster sample, according to the size of schools, of randomly selected 6-13-year-olds (n=1155); 50.4% males; resp:97%	6-month prevalence of T in the morning; self-report (among 6-10-year-olds assisted by the parents)	Occasional or frequent T : 75% Weekly T: 31% Daily T: 16%	no difference	older > younger

Publication, country, and study year	Participants, sex distribution, and response rate	Measures and reporter	Prevalence of sleep problems	Sex differences	Age differences
Berntsson et al., 2001; Denmark, Finland, Iceland, Norway, and Sweden in 1996	Random samples from the population registers of each country of 7-12 year-olds (n=3760); corresponding to the male/female ratio in each population; resp:65-79%	Prevalence of sleeplessness at least every other week; reported by parents with the child	Sleeplessness at least every other week: Denmark: 1% Finland: 3% Iceland: 2% Norway: 2% Sweden: 2%		
van Litsenburg et.al, 2010; The Netherlands in 2006-2007	14 randomly chosen daycare centers and elementary schools in urban and suburban areas, 2-14-year-olds (n=2453); 52% males; resp:63%	SP during the last week; among 2-6-year-olds parent-report, among 7-14-year-olds self-report (youngest assisted by an adult)	Parent-reported SP during the last week: 25%; 10% related to F, 9% to bed-time resistance, 6% for sleep onset delay, and 3% for night awakenings	Parent-reported SP: girls > boys Self-reported SP: no difference	Parent-reported SP: In general: no difference Sleep onset delay and T: older > younger Bedtime resistance and night awakenings: younger > older Self-reported SP: younger > older

Note: For the table, large-scale studies among non-clinical populations in Western counties, including both adolescents and younger children, were selected. Studies are presented in the following order: studies based on self-reports, studies based on both self- and parental reports, studies based on self-reports assisted by parents, and studies based partly on self- and partly on parental reports. DF=difficulties falling asleep, T=tiredness, resp=response rate, SP=sleep problems

delay, 3% for night wakening, 1% for sleep-disordered breathing, and 25% for any of the above-mentioned sleep problem (van Litsenburg et al., 2010). Regarding age, the prevalence of sleep problems in general, as reported by school-aged children themselves, appears to decrease as children get older (Brun Sundblad et al., 2007, van Litsenburg et al., 2010, Ostberg et al., 2006, Russo et al., 2007). However, it is charasterictic of sleep problems, that the changes with age are different for various types of sleep disorders. For example, bedtime resistance is typical among younger children, and sleep onset delay and tiredness most often occur among older children and adolescents (van Litsenburg et al., 2010). Regarding sex differences, among younger school-aged children, the prevalence of sleep-related problems appears to be similar among both sexes, but in adolescence, girls report higher prevalence than boys (Brun Sundblad et al., 2007, Petersen et al., 2003, Russo et al., 2007, van Litsenburg et al., 2010).

In conclusion, it can be stated that the prevalence of sleep-related problems also varies widely among the studies. In addition to the differences, for example, in study populations, time frames, frequency classifications, and the use of self- versus parental reports, differences in the symptom definitions further complicate the comparison of the studies. While in several studies sleep problems have been asked about with one general question (Brun Sundblad et al., 2007, Paavonen et al., 2003), others have inquired about a number of differentiating problems, such as bed-time resistance, sleep-onset delay, night awakenings, and tiredness (van Litsenburg et al., 2010).

2.1.3 Agreement between reporters of pain symptoms and sleep problems

In the field of pediatrics, parental reports of different kinds of symptoms have traditionally been most commonly asked for, as parents often make the final decisions on when to contact health care, and also due to uncertainty about the cognitive or verbal capacity of children to report their own symptoms. However, recently, more emphasis has been directed to the importance of the child's own report.

A number of studies have shown poor concordance between the child's own and proxy reports of pain symptoms and sleep problems. While some studies have found that parents report fewer pain symptoms and sleep problems for their children than children themselves (Sweeting and West 1998), others have shown contradictory findings (Garber et al., 1998, Haralstad et al., 2011, Paavonen et al. 2000). Finnish studies have found that a remarkable portion of the most recurrent pain symptoms and sleep problems among eight-year-old children remain unnoticed by the parents (Paavonen et al., 2000, Santalahti et al., 2005). As pain is a subjective experience, it seems logical that its assessment should be based on the individual's own report. Correspondingly, objective measurements of sleep have been found to correlate better with self-reports than with parental reports of sleep problems (Owens 2009), and child-reported problems

have also been shown to associate with and predict psychiatric difficulties more strongly than parent-reported sleep problems (Paavonen et al., 2003).

There are a number of factors that may underlie the differing reports of children and their parents, and complex interactions between these factors are supposed to determine the degree of correspondence (Kröner-Herwig et al., 2009). While some studies have observed that the agreement between self- and parental reports gets worse as children get older (Paavonen et al., 2003), others have not found differences between age groups (Garber et al., 1998, Kröner-Herwig et al., 2009). It is also possible that the direction of the disagreement changes with age. In one study (Haraldstad et al., 2011), parents of 8-18-year-old boys and 8-15-year-old girls reported more pain symptoms for their children than the children themselves, whereas parents of 16-18-year-old girls reported fewer symptoms than the adolescents themselves. Similar results have also been reported for sleep problems (Paavonen et al., 2003). Regarding sex, most studies have not found differences in child-parent agreement (Garber et al., 1998, Kröner-Herwig et al., 2009). Additional factors that have been suggested to underlie variations in reported prevalence rates between children and their parents, include differences in recall, differences in definitions of normality, health and illness, as well as communicational barriers between the two generations (Sundblad et al., 2006, Sweeting and West 1998). In addition, the child's as well as the parents' health has been associated with the reporting of the symptoms. For example, it has been shown (Garber et al., 1998) that the agreement between child- and parental reports of pain was better in the group of healthy children than in the groups of children who suffered from pain or emotional disorders. In addition, maternal distress was associated with an increased discordance in the direction of mothers reporting more symptoms for their children than the children themselves.

Due to the low levels of agreement between different reporters, the use of multiple informants is recommended, as neither the child's nor the parents' report can be considered as "right" or "wrong". Rather, both informants see the problem from different point of views and thus complement each other. (Garber et al., 1998) Still, when using multiple informants, the question of how to combine the information, emerges, as each possibility leads to differing results. One of the possibilities is to study child- and parental reports of the symptoms separately. Other possibilities are to define as symptomatic individuals either only children with both self-and parent-reported symptoms (resulting in a lower prevalence), or with either self- or parent-reported symptoms (resulting in a higher prevalence).

2.1.4 Long-term prevalence changes of pain symptoms and sleep problems

Among adolescents, there are both international (World Health Organization 2011) and national population-based studies on long-term prevalence changes of pain symptoms

and sleep problems, with data collected at several time points. Table 3 presents Finnish studies among non-clinical adolescent populations. For example, in the Finnish School Health Survey, the prevalence of pain symptoms and tiredness among pupils from 8th and 9th grade (age range 14-17) has been assessed every two years between the years 1996/1997 and 2010/2011 (Stakes 2012). Weekly headache has increased from 24% in 1996/1997 to 31% in 2010/2011, and almost daily tiredness from 7% to 15%. Furthermore, as is shown in more detail in the table, the prevalence of back, shoulder, and neck pain has increased among Finnish adolescents from 1985 to 2001 (Hakala et al., 2002). However, as adolescence is characterized by changes in hormonal factors, lifestyle, and demands as regards to social role expectations, which may play a part in the emergence of the symptoms (Gordon et al., 2004, Haraldstad et al., 2011, Johnson et al., 2006b, Paananen et al., 2010), these results cannot be applied to younger age groups.

There are only a few population-based studies on long-term prevalence changes of pain symptoms and sleep problems among younger children (see Table 3). Two studies have assessed changes between two time points. A Finnish study showed an increase in the prevalence of headache and abdominal pain among eight-year-old children between the years 1989 and 1999 (Santalahti et al., 2005). Another study, including all five Nordic countries, reported an increase in the prevalence of psychosomatic symptoms (including pains and sleep problems, but also other somatic symptoms) among 7-12-year-old children from 1984 to 1996 (Berntsson and Köhler 2001). However, the difference between two time points could also reflect a long-term fluctuation in the symptom frequencies, as it is customary for these symptoms to fluctuate over time. The only study including more than two data collections is a Finnish study on headache, which showed that the risk of frequent headaches among seven-year-old children had more than doubled in 2002 compared to 1974 (Anttila et al., 2006). There are no similar studies about other pain symptoms or sleep-related problems. It does seem that the prevalence of, for example, tiredness has increased, as it was not considered a common problem in the 1970s among preadolescents, but in 2001, over 40 % of the children in the same age group felt tired at least once a week (Anders et al., 1978; Petersen et al., 2003). However, as prevalence estimates vary widely even between studies that have been conducted the same year (Brun Sundblad et al., 2007, Ostberg et al., 2006), it is possible that the supposable increase is primarily due to methodological differences. Thus, it is important that information about changes in the prevalence is gathered repeatedly using directly comparable study procedures and measures. In addition, the use of general population samples is important, as studies among clinical populations are affected by a number of other factors than the exact prevalence of the symptoms, such as availability of health care services and differences in diagnostic practises. However, if a constant increase in prevalence rates is found, it would be meaningful from both the individual's and the community's point of view, as pain symptoms and sleep problems have been shown to

be associated with a number of disadvantages for the child, the family, and the society (Haraldstad et al., 2011, Kotagal 2003, Paavonen et al., 2010, Pesa and Lage 2004, Petersen et al., 2009, Smedbråten et al., 1998). In addition, such findings would call for identifying the risk factors for the symptoms, in order to be able to develop preventive and treatment strategies.

2.2 Co-occurrence of pain symptoms and sleep problems

2.2.1 Co-occurrence of different pain symptoms

Different kinds of pain symptoms often co-occur, and having one pain symptom increases the odds for suffering from other pain symptoms as well (Groholt et al., 2003). Different studies report that about one third to three fourths of children with one pain symptom also suffer from at least one other pain symptom (Brun Sundblad et al., 2007, Haraldstad et al., 2011, Perquin et al., 2000, Petersen et al., 2006). A community-based study among 10-15-year-old children and adolescents showed that the mean number of affected pain regions (e.g. headache, abdominal pain, or back pain) was 2.1 for boys, and 2.5 for girls (Bruusgaard et al., 2000). The most commonly co-occurring pain symptoms are headache and abdominal pain (Groholt et al., 2003, Haraldstad et al., 2011, Stanford et al., 2008).

Multiple pain symptoms seem to have characteristics similar to those of pain symptoms in general, as older children and girls more often report several symptoms than younger children and boys (van Gessel et al., 2011, Perquin et al., 2000, Petersen et al., 2006). With higher pain frequency, the odds for suffering from multiple pains increases, as half of the children suffering from monthly pain, and two thirds of the children suffering from weekly pain, reported multiple pains (Petersen et al., 2006). The high prevalence of co-occurring symptoms is important, as the number of pain symptoms has been associated with increasing mental distress (Bruusgaard et al., 2000). Longitudinal studies have also shown that having one pain symptom predicts later suffering from another pain symptom (El-metwally et al., 2007), as well as from multiple pain symptoms (Larsson and Sund, 2007). The possible mechanisms underlying the associations between various pain symptoms, such as common background factors, will be considered in the discussion of the results (section 6.3).

Table 3. Long-term prevalence changes of childhood pain symptoms and sleep problems

Publication	Study population	Methods	Results
Anttila et al., 2006 and Sillanpää and Anttila 1996; Finland	Data collected in 1974 (n=2169, resp: 90.3%), in 1992 (n=1533, resp: 95.5%) and in 2002 (n=1316, resp: 81%) among children starting school (age 7), in the city of Turku	Questionnaires (parent-report) inquiring about the prevalence of HA	Increased prevalence of HA: from 4.7% to 11.7% for at least monthly HA; from 1.3% to 2.5% for weekly HA Increased 6-month incidence of migraine (RR 2.5) and at least monthly HA (RR 2.1)
Berntsson and Köhler 2001; Finland, Denmark, Iceland, Norway, and Sweden	Data collected in 1984 and 1996 among 2-17-year-old children in Finland, Denmark, Iceland, Norway, and Sweden (n = about 3000 in each country at each sampling, resp: 67% / 70%)	Questionnaires (parent-report, together with the child if possible) inquiring about the prevalence of stomach complaints, HA, sleeplessness, dizziness, backaches or loss of appetite every or every other week	Increased prevalence of psychosomatic symptoms in all countries except for Iceland; At least one symptom: in 1984: 17%, in 1996: 24%; At least one symptom among 7-12-year-olds: in 1984: 17%, in 1996: 25%; At least one symptom in Finland: in 1984: 13%, in 1996: 25%
Hakala et al., 2002; Finland	Data collected between 1985 and 2001 every or every other year among 12-, 14-, 16-, and 18-year-old adolescents (two different populations: n = 61 677 / 127 217, resp: 70-88%)	Questionnaires (self-report) inquiring about the 6-month prevalence of at least weekly back, shoulder and neck pain	Increased prevalence of neck-shoulder pain (ORs 1.4-1.7), and lower back pain (ORs 1.2-1.5) among both sexes
Santalahti et al., 2005; Finland	Data collected in 1989 (n=1038, resp: 94-95%), and in 1999 (n=1035, resp: 86-99%) among 8-year-old children in South-West Finland	Questionnaires (self- and parent-report) inquiring about the prevalence of HA and AP	Parent-report: Increased 12-month prevalence of HA among both sexes (CORs 1.4-1.9); Child-report: Increased prevalence of AP among both sexes (CORs 1.9-2.3), and of HA among girls (COR 1.9) during past two weeks
Finnish school health survey; Finland	Data collected every two years between 1996/1997 and 2010/2011 among 14-16-year-old adolescents	Questionnaires (self-report) inquiring about the 6-month prevalence of HA, pain in the back or neck, and T	Increased prevalence of pains and T: from 24% to 31% for weekly HA; from 21% to 30% for weekly back- or neck pain; from 7% to 15% for almost daily T

Note: Studies among children before adolescence, and Finnish studies among adolescents, in non-clinical populations are included. AP=abdominal pain, T=tiredness, HA=headache, OR=odds ratio, resp=response rate, RR=risk ratio.

2.2.2 Co-occurrence of pain symptoms and sleep problems

Pain symptoms have been found to be associated with sleep problems. In a population-based sample, of the children with sleep problems, 40%, 28%, and 17% suffered from headache, abdominal pain, and back pain, respectively. The corresponding numbers among children without sleep problems were 14%, 8%, and 4%. (Groholt et al., 2003) The other way around, of the children suffering from pain, over a half reported that pain caused sleep problems (Roth-Isigkeit et al., 2005). The studies were based partly on parental, and partly on self-reported symptoms, but the results were not reported separately for different reporters. Sleep problems have been associated with various pain symptoms (i.e. headache, abdominal pain, and back pain) to a similar degree as pain

symptoms have been associated with each other, apart from the stronger association between headache and abdominal pain (Groholt et al., 2003). There also seems to be a dose-response relationship, as a higher number of pain symptoms has been associated with an increasing frequency of sleep problems (Bruusgaard et al., 2000). Longitudinal studies have also shown associations between pain and sleep-related problems, as tiredness prognosticated abdominal pain in a four-year prospective study (El-Metwally et al., 2007), and sleep problems at age three predicted headache at school entry (Aromaa et al., 1998). The high prevalence of co-occurring symptoms is important, as sleep problems among pain-suffering individuals have been associated with poorer health-related quality of life, more functional limitations, and increased amount of emotional problems (Palermo and Kiska 2005).

2.3 Psychosocial stress associated with pain symptoms and sleep problems

2.3.1 Stress and negative life events associated with pain symptoms and sleep problems

Stress is defined as a threat to the homeostasis of an organism by real or perceived threats, and can be posed by either inside or outside events. The behavioral and physical changes due to stress are normally adaptive and time-limited, and serve to increase the survival of the individual. However, too intense activation of the stress system may lead to physical or psychological problems. (Charmandari et al., 2003)

Several ordinary life situations or stresses, whether physiological, environmental, or psychosocial in nature, have been associated with the occurrence and maintenance of pain symptoms (Roth-Isigkeit et al., 2005) and sleep problems (Calhoun et al., 2011, Mindell et al., 2009, Smaldone et al., 2009). For example, in a study investigating children's conceptions about possible reasons for their pain, factors such as weather, nutrition, physical activities, use of technology, school, family conditions, lack of sleep, disputes, and unpleasant emotional experiences, were cited as possible triggers (Roth-Isigkeit et al., 2005). Regarding sleep, different problems or disorders have been considered to have different etiological factors. For example, parasomnias are often seen as a part of normal childhood development, even if sleep deprivation, stressful experiences and psychiatric difficulties are also considered as possible aggravating factors (Bloomfield and Shatkin 2009). For insomnia, on the other hand, medical and psychiatric conditions, maladaptive cognitions and experience of stress, poor sleep habits and life-style issues, are often considered to be predisposing or perpetuating factors (Owens and Mindell 2011). A number of studies have shown that both different pain symptoms (Boey and Yap 1999, Kröner-Herwig et al., 2008, Sarioglu et al., 2003, van Tilburg et al., 2010, Walker

et al., 2001) and sleep problems (Noll et al., 2006, Paavonen et al., 2002, Smaldone et al., 2009) are associated with negative life events and psychosocial distress. Associations have been found with both daily hassles, such as problems at home or with peers, and major traumatic experiences, such as sexual or physical abuse. The association between stress and pain has also been supported by an experimental study among children who suffered from recurrent pain (Dufton et al., 2008). In that study, children who were instructed to complete a stress-producing task before a pain-coping task, showed a lower pain tolerance than children who completed the pain-coping task first. Some studies, however, have not found associations between stressful life events and the occurrence of pain symptoms. Rather, it has been proposed, that children reporting these complaints do not experience more stressful life events (Scholl and Allen 2007, Walker et al., 2007), but instead they experience them as more stressful (Powers et al., 2006, Walker et al., 2007), do not use effective coping strategies (Brown 2004, Conrad et al., 2007, Keefe et al., 2000, Powers et al., 2006, Walker et al., 2007), or react to them with stronger physiological changes than other children (Aromaa et al., 2000, Dorn et al., 2003).

2.3.2 Psychiatric difficulties associated with pain symptoms and sleep problems

The majority of both clinical and population-based studies have shown that pain symptoms and sleep problems are associated with psychiatric difficulties and disorders, and co-occurring psychological difficulties have been considered as a marker for a poorer prognosis for children who suffer from pain symptoms or sleep problems (Connelly and Bickel 2011, Guidetti et al., 1998, Mulvaney et al., 2006, Patten et al., 2000, Powers et al., 2006, Ståhl et al., 2008).

Children with pain symptoms or sleep problems have elevated rates of psychiatric difficulties when compared to controls (Campo et al., 2004, Gordon et al., 2004, Johnson et al., 2006b, Liakopoulou-Kairis et al., 2002, Paavonen et al., 2002, Paavonen et al., 2003). The strength of the associations vary widely among the studies. For example, in a clinical population of 8-13-year-old children with recurrent abdominal pain or headache, 82% and 84%, respectively, had a psychiatric diagnosis (most commonly anxiety and depressive disorders), as compared to 15% of the controls (Liakopoulou-Kairis et al., 2002). In a population-based study among 12-13-year-old adolescents, in turn, of the children reporting frequent headaches, 21% were considered to suffer from depression, and 19% from anxiety or emotional disorder, while the respective figures for children with infrequent or no headaches were 4% and 7% (Gordon et al., 2004). Regarding sleep problems, in a population-based sample of 13-16-year-old adolescents, 53% of the individuals suffering from insomnia also had a psychiatric disorder (Johnson et al., 2006b). Correspondingly, children who suffer from psychiatric difficulties, report more pain symptoms and sleep problems than control children (Johnson et al., 2006a, Pine et al., 2006). This would also seem to be highly expected, as pain symptoms and sleep

problems are included as a part of the diagnostic requirements for some of the emotional disorders.

Internal symptoms, such as depression and anxiety, have been studied more, and have been shown to be more strongly associated with pain symptoms and sleep problems than externalizing symptoms, such as hyperactivity and conduct problems (Aromaa et al., 1998, Campo et al., 2004, Fearon and Hotopf, 2001, Galli et al., 2007, Gordon et al. 2004, Guidetti et al., 1998, Johnson et al., 2006b, Kröner-Herwig et al., 2008, Liakopoulou-Kairis et al., 2002, Paavonen et al., 2002, Paavonen et al., 2003, Pine et al., 1996, Smedje et al., 2001, Watson et al., 2003). The above-mentioned associations are considered bi-directional, even though contradictory findings have also been reported. For example, among adolescents, depression predicted the onset of headache, but headache did not predict depression or depressive symptoms (Pine et al. 1996). However, in another study, headache predicted depressive symptoms and low self-esteem, while depressive symptoms and low self-esteem were found to predict headache among girls, but not among boys (Rhee 2000). Correspondingly, contradictory findings have also been reported for sleep problems. For example, in one study, sleep problems in early childhood predicted emotional, behavioral, and attention problems in adolescence, whereas psychiatric problems, apart from attention problems, did not predict sleep problems (Gregory and O'Connor 2002). On the other hand, in another study, depressive symptoms did predict later sleep problems (Patten et al., 2000).

2.3.3 Familial factors associated with pain symptoms and sleep problems

Studies assessing the impact of demographic factors, i.e. family structure and socioeconomic status, have yielded inconclusive results. Whereas some have found that children in single-parent families more often suffer from pain symptoms and sleep problems (Kröner-Herwig et al., 2008, van Litsenburg et al., 2010), others have not confirmed these findings (Aromaa et al., 1998, Bakoula et al., 2006, Johnson et al., 2006b, Ostberg et al., 2006). One study showed that divorce within the previous year, but not earlier, was associated with pain symptoms (Larsson and Sund 2007). Correspondingly, while some studies have found lower socioeconomic status to be associated with higher levels of symptoms (Berntsson et al., 2001), others have not confirmed these findings (Aromaa et al., 1998, Bakoula et al., 2006, Kröner-Herwig et al., 2008, Ostberg et al., 2006). On the other hand, high academic expectations towards the child may also increase the prevalence of the symptoms (Gordon et al., 2004). Economic hardship, however, has more consistently been associated with increased symptom levels (Berntsson et al., 2001, Kröner-Herwig et al., 2008, Ostberg et al., 2006).

The majority of studies investigating familial interactive patterns have found connections with pain symptoms and sleep problems. Factors such as poor communication, conflicts

between family members, dysfunctional parenting patterns, insecure attachment style, and, on the other hand, parental solicitousness or over-involvement, have been associated with the symptoms (Kröner-Herwig et al., 2008, Liakopoulou-Kairis et al., 2002, Smaldone et al., 2007, Tremblay and Sullivan 2010, Vaughn et al., 2011). Conversely, a positive family climate has been found to be a protective factor (Kröner-Herwig et al., 2008). It has also been suggested that if the pain symptom is constantly acknowledged and the child gets to avoid unpleasant tasks or situations, this can lead to increasing pain behavior and functional impairment (Kerns and Otis 2003, Walker and Zeman 1992), in particular among those who also have a tendency towards anxiety, and difficulties in managing social or academic situations (Peterson and Palermo 2004, Walker et al., 2002).

Parents' both somatic and psychiatric health problems have been associated with children's pain symptoms and sleep problems (Apley and Hale 1973, Aromaa et al., 1998 and 1999, Campo et al., 2001, Fearon and Hotopf, 2001, Hotopf et al., 1998, Kröner-Herwig et al., 2008, Liakopoulou-Kairis et al., 2002, Marmorstein et al., 2009, Oster, 1972, Paavonen et al., 2000, Ramchandani et al., 2006, Robinson et al., 1990, Smaldone et al., 2007, Walker and Greene 1989, Zuckerman et al., 1987). As underlying mechanisms for these associations, for example, genetic factors, shared environmental factors, and the possibility of the child modeling the parent's illness-related behavior have been suggested (Turk et al., 1987). In addition, as familial problems may lead to the occurrence or maintenance of the child's symptoms, the child's symptoms may also affect the family by changing the communicational patterns, and causing emotional distress (Schulte et al., 2010).

2.3.4 Friend- and school-related factors associated with pain symptoms and sleep problems

Pain symptoms and sleep problems have been associated with difficulties at school and with friends. Factors such as lack of peace and quiet in the classroom, negative feelings about school, school stress, fear of failure, and being unfairly treated by or lacking support from teachers have been connected with the symptoms (Ghandour et al., 2004, Gordon et al. 2004, Hjern et al., 2008, Kröner-Herwig et al., 2008, Natvig et al., 1999, Wålinder et al., 2007). In addition, pain symptoms and sleep problems have been associated with lacking friends, as well as with being bullied (Gini and Pozzoli, 2009, Paavonen et al., 2002, Robinson et al., 1990, Smedje et al., 2001, Williams et al., 1996) and, to a lesser extent, bullying others (Fekkes et al., 2004, Gini and Pozzoli, 2009, Natvig et al., 2001, Paavonen et al., 2002), even though controversial results also exist (Gordon et al. 2004). Conversely, pain symptoms and sleep problems can negatively affect school attendance and performance, as well as peer relations (Haraldstad et al., 2011, Paavonen et al., 2002, Powers et al., 2006, Randazzo et al., 1998, Roth-Isigkeit et al., 2005, Smedbråten et al., 1998).

2.3.5 Life-style factors associated with pain symptoms and sleep problems

A number of life-style factors have been associated with the occurrence of pain symptoms and sleep problems. Examples of these are the use of technology (Bakoula et al., 2006, Hoftun et al., 2012, Kröner-Herwig et al., 2008, Mindell et al., 2009) and nutritional habits, such as the use of soft drinks high in caffeine (Gromov and Gromov 2009, Hering-Hanit and Gadoth 2003). In addition, risk-taking behavior, such as substance use (Kröner-Herwig et al., 2008, Levy et al., 1986, Patten et al., 2000, Waldie et al., 2008), has been associated with pain symptoms and sleep problems, and the association seems to be bi-directional (Gromov and Gromov 2009, Hoftun et al., 2012, Wong et al., 2004). Long-term associations have also been reported. For example, pain in childhood has been shown to increase the risk of smoking in adulthood (Waldie et al., 2008).

2.3.6 Pain symptoms in childhood predicting psychiatric difficulties in adulthood

It is now well known that pain symptoms are associated with a number of psychosocial problems, including psychiatric difficulties, in the short term, but current knowledge about long-term psychosocial consequences of pediatric pain is limited, as most longitudinal studies have had short-term follow-up periods, have used only adolescents or adults as study populations, or have been retrospective and thus exposed to recall bias (Breslau et al., 2003, Campo et al., 2001, Kinnunen et al., 2010, Pine et al., 1996, Ramchandani et al., 2007). However, long-term prospective studies are important as they give further information about the relationship and possible mechanisms between pain and psychiatric difficulties, about the consequences of childhood pain, and about risk factors for adulthood mental health problems. This kind of information is important, for example, in the planning of preventive and treatment strategies.

A summary of longitudinal studies that investigated pain symptoms in childhood, including at least some subjects before adolescence, and psychiatric difficulties in adulthood, is presented in Table 4. Apley and Hale (1973) were the first to show that children with abdominal pain reported high levels of anxiety in adulthood. Two other clinical studies that assessed the associations between abdominal pain in childhood or adolescence, and later psychiatric problems, also included a control group (Campo et al., 2001, Walker et al., 1998). While the first one did not find an association between pain and later depressive symptoms (Walker et al., 1998), the other showed that pain predicted anxiety disorders, and additionally, a trend suggesting an association with mood disorders and psychiatric disorders in general was also found (Campo et al., 2001). However, possible psychiatric difficulties or disorders at baseline were not assessed in these studies. One clinical study on headache (Guidetti et al., 1998), and another clinical study on pains in general (Knook et al., 2012), which also took baseline psychiatric difficulties into account, showed that a fourth of the individuals who in childhood suffered from pain, later had anxiety or co-morbid anxiety and depression (Guidetti et

al., 1998), or a psychiatric disorder (Knook et al., 2012). However, these studies did not include a control group. Furthermore, as there is selection in the subjects who seek medical help, the associations that have been found in clinical studies may be due to this bias, and cannot be generalized to larger populations.

Population-based studies have mostly included either adolescents, or both adolescents and younger children, and the results have not been reported separately for these different age groups (see Table 4). A British study (Hotopf et al., 1998) showed that the parental report of the child's abdominal pain on three different occasions (ages 7, 11, and 15) predicted psychiatric disorders at age 36. However, possible psychiatric difficulties or disorders at baseline were not included in the analyses. Two studies assessed the association between headache and later psychiatric difficulties. A British study (Fearon and Hotopf 2001) showed that parental report of the child's headache (at ages 7 and 11) predicted psychiatric difficulties at age 33, even after adjusting for teacher-reported childhood depressive symptoms, childhood separation experiences, parents' chronic illnesses, and mental health problems in the family. An American study (Pine et al., 1996) showed that self-reported headache among adolescents (mean age 16) did not predict a new onset of depression or depressive symptoms as assessed 6-7 years later. And finally, a Swedish study (Brattberg 2004) found that self-reported headache and abdominal pain among 10-, 13-, and 16- year-old children and adolescents predicted emotional problems after an 11-year follow-up.

In conclusion, it seems that pain symptoms in childhood predict later psychiatric disorders, and in particular anxiety. However, several limitations of previous studies restrict the conclusions that can be drawn. The majority of the studies have either not included a control group or have not considered possible psychiatric difficulties at baseline. Furthermore, the studies among younger children have only included parental reports of the child's pain. And finally, all of the studies used a one-time follow-up assessment only, which was based on the subject's own report. Due to the possibility of recall bias, this can be seen as an additional limitation (Angst 1992).

2.4 Associations between pain symptoms and suicidality

At worst, psychiatric difficulties may lead to suicidal behavior (Apter et al., 1993, Brent et al., 1999, Marttunen et al., 1991, Qin 2011, Renaud et al., 2009). Suicide is the second most common cause of death worldwide among adolescents and young adults (Patton et al., 2009), and Finland is among the countries with the highest suicide rates (Hawton et al., 2012).

Even though suicides are often preceded by mental health disorders, such as depression (Apter et al., 1993, Brent et al., 1999, Marttunen et al., 1991, Qin 2011,

Renaud et al., 2009), a remarkable proportion of suicide victims are not getting any kind of psychiatric treatment (Renaud et al., 2009) and do not give any warnings before the suicide attempt (Miranda et al., 2008). For example, according to a study among children and adolescents, 90% of suicide victims had suffered from mental health disorders, but only 44% had received a diagnosis, and only 13% had had a treatment contact within the month prior to the suicide (Renaud et al., 2009). It is important to further investigate the risk factors, in order to be able to better recognize the at-risk individuals.

A number of studies among adults have associated pain symptoms with suicide attempts (Breslau et al., 1991, Fishbain et al., 1991, Ilgen et al., 2008, Keefe et al., 2000), and these associations have remained even after controlling for psychiatric conditions (Breslau et al., 1991, Magni et al., 1998) and somatic diseases (Breslau et al., 1991, Knaster et al., 2011, Lee et al., 2009), thus suggesting that not only psychiatric, but also pain symptoms should be taken into account when assessing the risk of suicide. However, there are hardly any studies on the subject among children and adolescents. Some cross-sectional studies have shown an association between pain symptoms and suicidal ideation (Aromaa et al., 2000, van Tilburg et al., 2011, Wang et al., 2007) or acts (Laukkanen et al., 2009), but apparently only one study has used a prospective design. In a population-based sample of adolescents (n=9970), headache, abdominal pain and muscle/joint ache (at least weekly during the previous year), depressive symptoms (during the previous week), and suicidal ideation / attempts (during the previous year) were asked about at baseline and after one year. Headache (OR(95%CI): 1.2(1.01-1.5)) and abdominal pain (OR(95%CI): 1.4(1.1-1.7)) predicted suicidal ideation after the one-year follow-up among adolescents who had not reported suicidal ideation at baseline. Abdominal pain (OR(95%CI): 1.6(1.2-2.1)) and muscle/joint ache (OR(95%CI): 1.5(1.1-2.1.)) predicted suicide attempts among adolescents who had not reported attempts at baseline. However, when depression at baseline was taken into account, only the association between headache and suicidal ideation (OR(95%CI): 1.2(1.01-1.5)) remained significant. (van Tilburg et al., 2011) Whether pain symptoms among a pediatric population similarly predict suicidal ideation, acts, and severe suicidality, is not known, as no studies have been conducted concerning pain in childhood and later severe suicidality or suicide mortality. Previous studies have, however, shown that childhood psychopathology is differently associated with self-reported suicidal ideation or behavior versus suicides or severe suicide attempts, as, for example, self-reported emotional problems in mid-childhood correlated with suicidal thoughts and behaviour, but not with severe suicidality (Sourander et al., 2001, Sourander et al, 2009). Further limitations of the existing research are that most studies have investigated suicidal attempts on the basis of self-reports (e.g. van Tilburg et al., 2011, Wang et al., 2007), and only few, even when taking the studies among adults into account, have included suicide mortality (Fishbain et al., 1991).

Table 4. Associations between pain symptoms in childhood and psychiatric difficulties in adulthood

Publication and country	Assessment at baseline	Assessment at follow-up	Results	Methodological considerations
		Clinical studies		
Apley and Hale, 1973; UK	About 120 recurrent AP patients (≥ 3 episodes of medically unexplained AP during ≥ 3 months and affecting the activities)	60 patients (about 50% males) followed for 8-20 years (age 16-28, resp: about 50%)	38% reported anxiety, and <10% depression at the end of the follow-up	Including both adolescents and younger children, no information on how psychiatric difficulties were assessed, no control group or psychiatric assessment at baseline, one-time follow-up assessment only
Walker et al., 1998; US	76 (33% males) 6-18-year-old recurrent AP patients (pain for at least 3 months and no identifiable medical explanation), and 49 control subjects (53% males) treated for minor illness or injury	Contact after 5 years (resp /patients: 84%, resp /controls: 94%): questionnaire about depression	AP did not predict depressive symptoms (anxiety not investigated)	Including both adolescents and younger children, one-time follow-up assessment only
Campo et al., 2001; US	49 children aged 6-17 years evaluated for recurrent AP (≥ 3 episodes of medically unexplained AP during last 3 months and affecting the activities) in 1980's	Contact in young adulthood (mean age 23.7, 25% males, resp:57%), compared with 28 individually matched former childhood participants in a study of tonsillectomy and adenoidectomy: psychiatric interview	AP predicted: 1. current treatment with psychoactive medication, 2. lifetime (46% versus 18%) and current (21% versus 0%) anxiety disorders, and 3. anxiety symptoms. No significant associations (albeit trend) with affective disorders (57% versus 29%) and psychiatric disorders in general (82% versus 54%)	Including both adolescents and younger children, no psychiatric assessment at baseline, one-time follow-up assessment only
Guidetti et al., 1998; Italy	100 (40% males) 4-18-year-old patients with primary HA: physical examination and psychiatric assessment (interview and psychometric tests) in 1988	In 1996 (age 12-26, resp: 77%): psychiatric assessment (interview)	25% of subjects with HA had a new onset of anxiety or co-morbid anxiety and depression (but not "pure" depression) during the follow-up	Including both adolescents and younger children, no control group, one-time follow-up assessment only
Knook et al., 2012; The Netherlands	134 (28% males) 8-18-year-old (mean age 12) children referred to a hospital due to unexplained pain in 2000-02: physical and psychiatric (semistructured interview) assessment	In 2006-2007 (mean age 18, resp: 68%): psychiatric interview	24% of subjects with pain had a new onset of psychiatric disorder during the follow-up (no data on separate disorders)	Including both adolescents and younger children, no control group, one-time follow-up assessment only
		Population-based studies		
Hotopf et al., 1998; UK	Individuals of the birth cohort of 1946 assessed of the ages of 7, 11, and 15: physical examination including recurrent AP (pain on all occasions, organic reasons excluded)	In 1982 (age 36, resp: 44%): psychiatric disorders (a semistructured interview)	AP predicted psychiatric disorders (OR 2.7) (no data on separate disorders)	Assessment of pain based on parental report only, no inclusion of base-line psychiatric difficulties in the analyses, one-time follow-up assessment only

Publication and country	Assessment at baseline	Assessment at follow-up	Results	Methodological considerations
Fearon and Hotopf 2001; UK	Individuals of the birth cohort of 1958 assessed at the ages of 7 and 11: parental report of "frequent HA"	In 1991 (age 33, resp: 69%): psychological symptoms (15 item subscale of a malaise inventory)	HA predicted psychiatric morbidity (18% versus 13% among children with versus without HA, OR 1.4), even after adjusting for teacher-reported depressive symptoms at age 7, childhood separation experiences, parents' chronic illnesses, and mental health problems in the family (OR 1.2) (no data on separate disorders)	Assessment of pain based on parental report only, one-time follow-up assessment only
Pine et al., 1996; US	776 (51% males) 11-20-year-olds (mean age 16) assessed in 1985-6: psychiatric interview (depression) and life-time history of activity-limitating HA	In 1992 (resp: 92%): psychiatric interview (depression)	HA did not predict new onset of depression or depressive symptoms at age 17-26 (mean age 22) (anxiety not investigated)	Including both adolescents and younger children, one-time follow-up assessment only
Brattberg 2004; Sweden	597 pupils aged 10,13, and 16 assessed in 1991: questionnaire (self-report) about aches and pains	In 2002 (resp:74%): questionnaire about anxiety/depression	Having HA and AP "commonly" predicted anxiety/depression (OR:s 2.2-2.9) in young adulthood	Including both adolescents and younger children, no psychiatric assessment at baseline, one-time follow-up assessment only

Note: Studies are presented in the following order: clinical studies (1. on AP, 2. on HA, and 3. on pain symptoms in general) and population-based studies (1. on AP, 2. on HA, and 3. on pain symptoms in general). AP=abdominal pain, HA=headache, OR=odds ratio, resp=response rate.

3 AIMS OF THE STUDY

The aims of this thesis were to investigate

1. changes in the prevalence of eight-year-old children's self-reported headache, abdominal pain, other pains, sleep problems, and tiredness between the years 1989, 1999 and 2005 (study I)

2. whether possible changes in the prevalence are related to socio-demographic factors or the child's psychiatric difficulties (study I)

3. associations between pain symptoms, sleep problems, and several psychosocial factors among 13-18-year-old adolescents (study II)

4. self- and parent-reported pain symptoms at age eight as possible predictors of antidepressant use by age 24 (study III)

5. whether self- or parent-reported pain symptoms at age eight are associated with suicides and severe suicide attempts by age 24 (study IV)

4 MATERIAL AND METHODS

4.1 Three cross-sectional samples of eight-year-old children (study I)

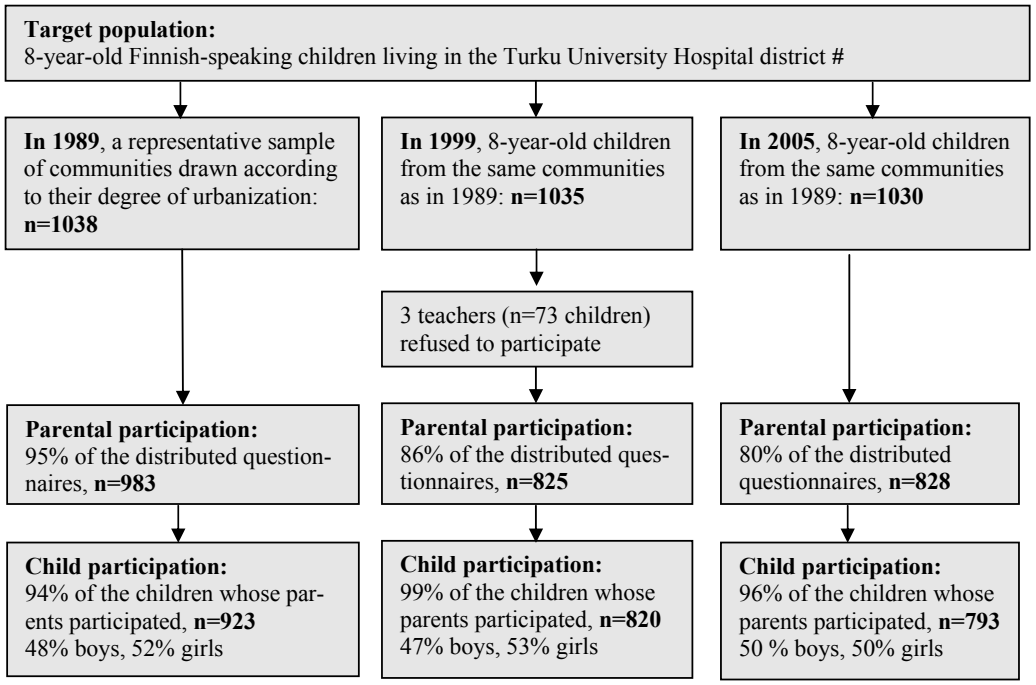
4.1.1 Participants and procedure

Study I considers three cross-sectional population-based samples of eight-year-old children, collected in 1989, 1999, and 2005.

The 1989 sample is a subsample of the "Finnish 1981 Nationwide Birth Cohort Study" (Almqvist et al., 1999), which was originally planned to investigate the prevalence of psychiatric and psychosomatic symptoms among eight-year-old children. In this nationwide birth cohort, a representative sample of all Finnish-speaking children was drawn in 1989 from the communities according to their degree of urbanization (urban, suburban and rural). From the small communities, all children were included in the sample, and from the large cities, a representative subsample from all the school districts was drawn. The sample included altogether 6017 children from all five University Hospital districts (Helsinki, Kuopio, Oulu, Tampere, and Turku) of Finland. The response rate was high (96.6%). The sample was controlled for demographic and socio-economic factors in the general population and was found to have good generalizability. The subsample of Turku University Hospital District, representing 13 % of the age cohort in the area (n=1038), was used in study I. The completed parental questionnaire was taken as consent for the child's participation in the study.

In 1999 (n=1035) and 2005 (n=1030), all eight-year-old children from the same communities as in 1989 belonged to the sample. The distribution of sex and family composition in the 1999 and 2005 samples corresponded to the figures of the national statistics in Finland for this age group (Kartovaara et al., 2007). Parents' written consent for their child's participation in the study was required in both study years. A summary of the participants and response rates is presented in Figure 1.

Study procedures were implemented through the schools. They started in November, and were identical every study year. The researchers delivered the material to the teachers, who sent the questionnaires and information sheets via the children to their parents. The parents returned the questionnaires to the teachers in sealed envelopes, or mailed them directly to the researchers. The children filled in their questionnaires in the classroom. Children returned the questionnaires in sealed envelopes to the teachers, who sent all the questionnaires to the researchers.



Note: # Severely disabled children, e.g. children who had severe mental retardation and did not attend school, were excluded from the study.

Figure 1. Summary of the participants and response rates in study I

4.1.2 Measures

The frequencies of different types of ***pain symptoms, sleep problems and tiredness*** were inquired about from the children, who were asked to choose the alternative that best described their situation during the previous two weeks: 1. I have headache seldom / often / almost every day, 2. I have abdominal pain seldom / often / almost every day, 3. I have other pains seldom / often / almost every day, 4. I sleep fairly well / I have difficulties sleeping often / I have difficulties sleeping every night, and 5. I am tired occasionally / often / continuously. An additional variable, the number of frequent symptoms (including answer alternatives 2. and 3.), was created: having 1. one symptom, 2. two symptoms, 3. three symptoms, or 4. four-five symptoms. The questions concerning sleep problems were derived from the Child Depression Inventory Scale (CDI) (Kovacs, 1992). The questions concerning pain symptoms were designed especially for the study.

The Child Depression Inventory Scale charts depressive symptoms during the previous two weeks (Kovacs, 1992), but is better used to measure emotional distress or disturbance than simply depression because of insufficient discrimination from, e.g. anxiety disorders (Brent and Weersing, 2008, Saylor et al., 1984). It includes 27 items rated 0 (indicating an absence of symptom), 1 (indicating mild symptom), or 2 (indicating definite symptom), and thus the total score varies between 0 and 54. In the present study,

the question concerning suicide was omitted from the questionnaire for ethical reasons, as it was assumed that it might have confused children of the age group involved, especially in the absence of an opportunity to discuss the issue with an adult. The ***Rutter Parent and Teacher Questionnaires*** were used to measure overall psychiatric difficulties. The items are rated as 0 (does not apply), 1 (applies somewhat), or 2 (certainly applies). The parental questionnaire consists of 31 items (total score 0-62), and the teacher's questionnaire of 26 items (total score 0-52). The Rutter Questionnaires are widely used and valid screening methods for assessing a child's general psychopathology during the previous twelve months (Kresanov et al., 1998, Rutter 1967, Rutter et al., 1970). They include three subscales: neuroticism (5 items on parent and 4 items on teacher questionnaire), antisocial (5 items on parent and 6 items on teacher questionnaire), and hyperkinetic (3 items on both questionnaires). These subscales are later in the text referred to as emotional difficulties, hyperkinetic problems, and conduct problems, respectively. The items in the subscales include symptoms such as worrying, withdrawal, depression, and anxiousness; restlessness, inattention and irritability; disobedience, lying, stealing and aggressive behavior, respectively. In addition to the subscales, the total scores of the Questionnaires include some additional items, such as speech problems, aches and pains, and in the Parent Questionnaire only, eating difficulties and sleep problems. To avoid over-evaluation of the associations with pain symptoms and sleep problems, some items were omitted from the total scores before statistical analysis (CDI: aches and pains, tiredness, and sleep problems; total score 0-46, Rutter Parent Questionnaire: headache, abdominal pain and sleep problems; total score 0-56, Rutter Teacher Questionnaire: aches and pains; total score 0-50). In statistical analyses, all scales were used as continuous variables.

In addition to pain symptoms, sleep problems, and psychiatric difficulties, some ***demographic factors*** were inquired about in the parental questionnaire: 1. family composition (living with two biological parents versus other type of family composition), and 2. the mother's educational level (upper secondary level education versus lower).

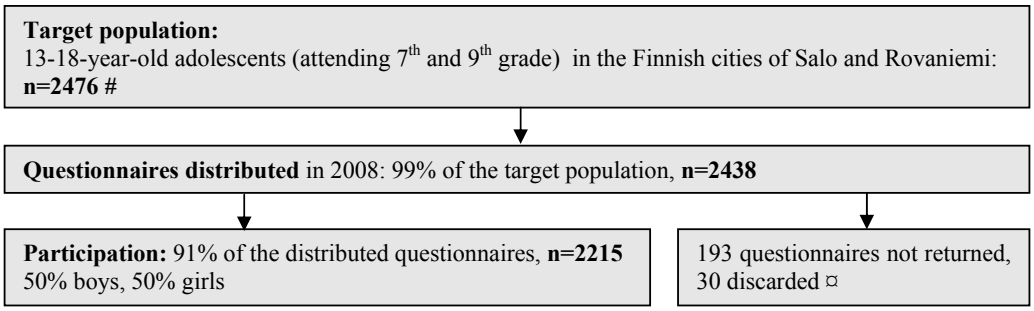
4.2 Cross-sectional study among 13-18-year-old adolescents (study II)

4.2.1 Participants and procedure

The study population included middle adolescents attending 7th (13 – 14 years) and 9th (15 – 18 years) grade from both the northern (Rovaniemi) and the southern (Salo) parts of Finland (n=2476). The city of Salo consisted of 25 825 inhabitants, and the city of Rovaniemi of 58 964 inhabitants. They are middle-sized Finnish cities, which, according to the official classification, included both urban and suburban areas. However, since the density of population in Finland is low, and the cities consist of large geographical areas including several diverse communities, rural communities are commonly represented as part of the cities that are officially classified as urban. The

mean age of the participants was 14.4 (SD 1.1) years. Altogether 51.6 % were 7th-graders (mean age 13.4 (SD 0.6) years), and 48.4 % were 9th-graders (mean age 15.4 (SD 0.5) years). The characteristics of the participants concerning sex distribution, family composition and ethnic background were practically identical when compared with the statistics of the same age group in the whole country. A summary of the participants and response rates is presented in Figure 2.

The study procedures were implemented through the schools in March-April 2008. The teachers distributed the questionnaires to the adolescents, who filled them in anonymously during a school lesson, and returned them to the teachers in sealed envelopes. The teachers put the questionnaires into a larger envelope, sealed it in front of the pupils, and sent it to the researchers.



Note: # 38 children (1.5%) attending classes for the handicapped or mentally retarded were excluded from the study. ¤ Not completed to an acceptable degree.

Figure 2. A summary of the participants and response rates in study II

4.2.2 Measures

Middle adolescents were asked about ***pain symptoms and sleep problems*** during the previous six months: 1. headaches that distracted from activities, 2. recurring abdominal pain, and 3. problems with falling asleep or sleeping. Answer categories were: 1. less frequently than monthly, 2. at least monthly, and 3. at least weekly. An additional variable, the number of monthly symptoms (including answer alternatives 2. and 3.), was also created: having 1. no symptoms, 2. one symptom, 3. two symptoms, and 4. three symptoms.

The self-report version of the ***Strengths and Difficulties Questionnaire*** (SDQ) was used in the present study to assess psychiatric symptoms during the previous six months (Goodman 1997). The emotional symptom subscale, later in the text referred to as emotional difficulties, includes items about unhappiness, nervousness, worrying, and aches and pains. The hyperactivity-inattention subscale, later in the text referred to as hyperkinetic problems, includes items about restlessness, attentional problems and impulsivity. The conduct problem subscale includes items about disobedience, dishonesty,

lack of self-control, and fighting. The peer problem subscale includes items about having friends and being victimized. The prosocial behavior subscale includes items about being nice, helpful, and caring towards other people. Each subscale includes five items. Twenty items (difficulties) are scored 0 = not true, 1 = somewhat true, or 2 = certainly true, and five positively worded items (strengths) in the opposite direction (0 = certainly true etc.). The prosociality scale is not included in the total score of 0-40. The self-report version of the SDQ has been shown to discriminate community and clinical samples satisfactorily (Goodman 1999), and the reliability and validity of the Finnish version have been found adequate (Koskelainen 2008). In the present study, to avoid over-evaluation of the associations with pain symptoms and sleep problems, the item about health complaints in the emotional symptoms scale was omitted from the subscale score before statistical analysis. Pupils scoring among the highest 10% (in the prosocial scale the lowest 10%) were considered screen positive, as recommended in the Finnish study (Koskelainen 2008). In the present sample, the cut-off points for emotional difficulties, hyperkinetic problems, conduct problems, peer problems, and prosocial behavior were, in the respective order, ≥7, ≥7, ≥5, ≥5, and ≤4. An additional question that is included in the extended version of the SDQ (Goodman 1999), was also included: "Overall, do you think you have difficulties in any of the following areas: emotions, concentration, behavior or getting along with other people?" The answer categories were: 1. no, 2. minor, and 3. definite-severe.

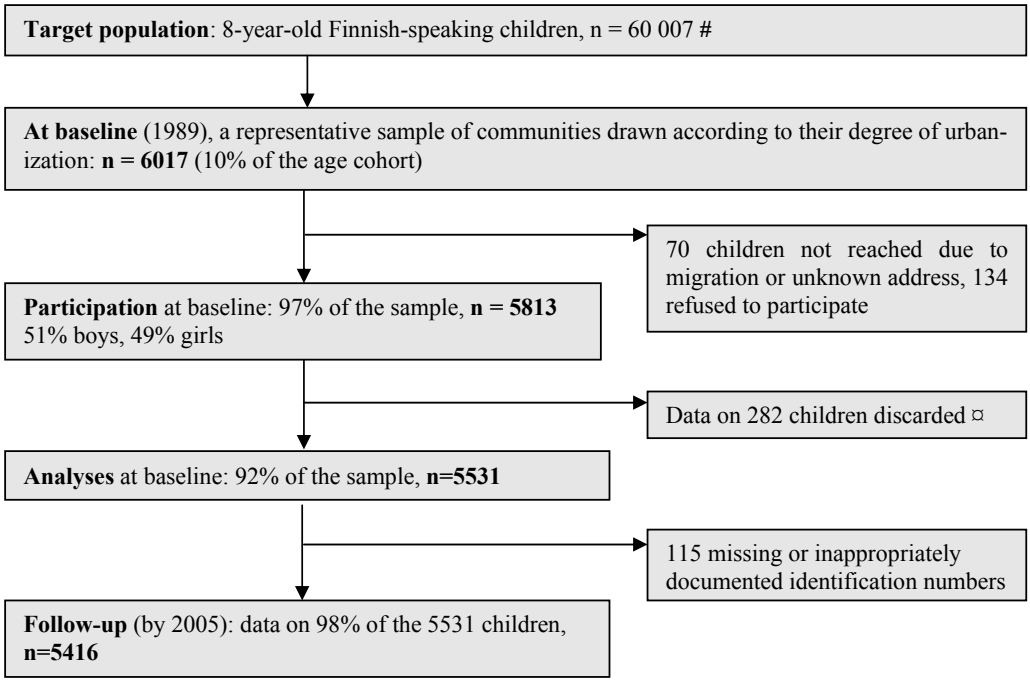
In addition to pain symptoms, sleep problems, and psychiatric difficulties, other psychosocial factors were also asked about. Some of the original answer alternatives (presented in the article, at the end of the thesis) were pooled together to create the following categories that were used in statistical analyses. ***1. Demographic variables*** included information about *school grade* (7^{th} versus 9^{th}), *family composition* (living with both biological parents versus other kind of family composition), and *ethnic background* (being of Finnish origin versus not). ***2. General health*** was determined with a question inquiring whether the adolescent had an illness, disability, or other health-related problem. Answer alternatives "no" and "yes" were proposed for five chronic illnesses: asthma, diabetes, epilepsy, atopic eczema, and allergy, and the answers were dichotomised into having versus not having one of the above-mentioned illnesses. ***3. Substance use***, i.e. *being drunk* and *smoking cigarettes* during the previous six months, were categorized as never, less frequently than weekly, and at least weekly. ***4. Bullying***, i.e. *victimization* and *bullying others* during the previous six months, was categorized as never, less frequently than weekly, and at least weekly. ***5. School environment***, i.e. *feeling safe at school* and *feeling that the teachers care* were categorized as almost never - sometimes versus often - almost always.

4.3 Prospective studies from childhood to adulthood (studies III-IV)

4.3.1 Participants and procedure

Studies III-IV are a part of the "Finnish 1981 nationwide birth cohort study" (Almqvist et al., 1999). In 1989, a representative sample of the communities was drawn according to their degree of urbanization (n = 6017, 10.0% of the age cohort). The questionnaires were distributed in October and November 1989 to eight-year-old children, their parents and teachers. The characteristics of the study sample and the study procedure at baseline are described in more detail in section 4.1.1.

The information collected at the age of eight was linked with register data on 1. antidepressant use (study III) and 2. severe suicidality (study IV) by the end of the year 2005 (age 24). A summary of the participants and response rates in studies III and IV is presented in Figure 3.



Note: # Severely disabled children, e.g. children who had severe mental retardation and did not attend school, were excluded from the study. ¤ Questionnaires not completed to an acceptable degree

Figure 3. A summary of the participants and response rates in studies III-IV

4.3.2 Measures

Measures at baseline assessment (age eight)

Children chose the alternative that best described their situation during the previous two weeks: I have headache / abdominal pain / other pains (only in study III): 1. seldom, 2. often, or 3. almost every day. The questions were designed especially for the study.

Parents reported the frequencies of the child's pain symptoms during the previous 12 months with two statements included in the Rutter's parent questionnaire (Rutter et al., 1970): Complains of headache / Has abdominal pain or vomiting 1. never, 2. sometimes, but less often than once per week, or 3. at least once per week. In study IV, due to the low number of subjects showing severe suicidal behavior, answer options 2. and 3. of the pain symptoms were pooled together to enable the statistical analyses.

The Child Depression Inventory Scale and ***the Rutter Questionnaires*** that were used in studies III-IV to assess psychiatric difficulties, are presented in section 4.1.2. The assessment of emotional difficulties was based on the CDI. To avoid over-evaluation of the associations with pain symptoms, the item "aches and pains" was omitted before statistical analysis. The assessment of hyperkinetic and conduct problems was based on the sum scores of the corresponding subscales from the parent and teacher Rutter questionnaires. In study III, emotional difficulties, hyperkinetic, and conduct problems were included in the analyses as categorical variables. In line with previous reports (Sourander et al., 2009), the cut-off points of 90% were calculated separately for both sexes, and children scoring among the highest 10% were considered screen positive. In study IV, emotional difficulties, hyperkinetic, and conduct problems were included in the analyses as continuous variables.

In addition to pain symptoms and psychiatric difficulties, some ***demographic factors*** in the parental questionnaire were included in the analyses: 1. family composition (living with two biological parents versus other kind of family composition), and 2. parents' educational level (father's or mother's completion of an upper secondary level education versus lower education level).

Measures during the follow-up (by age 24)

Follow-up information was collected from two nationwide registers including data about 1. antidepressant purchases (years 1994-2005) in study III, and 2. suicides (until the year 2005) and suicide attempts requiring hospital treatment (years 1994-2005) in study IV. The data from the registers were linked with other information by using the personal identification number, which has been assigned since 1971 to all residents in Finland.

Drug prescription register: The Social Insurance Institution of Finland reimburses prescription medications which are used in the treatment of an illness. The institution maintains a nationwide drug prescription register, which comprises data on 97%-98% of all reimbursed prescriptions within an outpatient setting. Drug purchases are coded according to the anatomic therapeutic chemical (ATC) classification system, 2000, whereby antidepressants have the ATC-code prefix N06A. To be reimbursed, the total drug cost had to be over 8.41 euros from 1994 to 2002, and over 10 euros from 2003. If a person only bought one small package of an inexpensive antidepressant, it is possible that the purchase was not included in the register.

The outcome primarily used in the present study was having at least one reimbursed antidepressant purchase, which is, for convenience, referred to as antidepressant use. As reported in an earlier report based on this study population, the mean number of antidepressant purchases during the follow-up was 7.9 (SD = 10.1, range = 1–72) among males, and 9.5 (SD = 11.6, range = 1–130) among females. Most of the subjects had purchased antidepressants more than once (males: 76.9%, females: 81.2%) (Gyllenberg et al., 2011).

The Statistics Finland's Cause of Death Register: The register (Statistics Finland 2011) produces data on causes of death based on information from death certificates. The death certificates are completed by pathologists, and include information about the manner and cause of death. Information about death causes and copies of death certificates can be obtained for research purposes prescribed by law. For the present study, all forensic medical documents of suicide and accidental death were reviewed by three specialists in psychiatry. There was disagreement only in one case, which was after a consensus discussion categorized as accidental death according to the forensic medical document classification.

The Finnish Hospital Discharge Register: This computerized discharge register includes, among other things, data on the dates of all hospital admissions and discharge diagnoses. The Register was established in 1967 and its good validity is documented in the field of epidemiological research (Sund 2012). Information about subjects who had been admitted to hospital with a diagnosis of a suicide attempt was collected for the present study. In Finland, only the patients who need treatment or observation for more than 12 hours in the emergency unit are admitted to a hospital ward. Thus, the register does not include patients who were discharged during a shorter time frame, meaning that only the most severe suicidal attempts needing hospital care were included in this study. The diagnostic codes for suicide attempts between 1994 and 1995 were International Classification of Diseases (ICD) 9 codes E950-E959, V156 or V658, and between 1996 and 2005, ICD-10 codes X60-X84, Z72.8 or Z91.5, including intoxication, deliberate traffic accident, hanging or suffocating, shooting, drowning, use of a sharp object, explosives, fire or smoke, jumping from a high place, and other or unspecified methods.

As reported in an earlier report on the same study population, altogether 13 males and two females had committed suicide, and 17 males and 25 females had been hospitalized as a result of a suicidal attempt during the follow-up period. Three males who had been hospitalized due to a suicidal attempt, later committed suicide. The most common methods of suicide and severe suicide attempt included running into traffic or jumping, drug overdose or poisoning, and hanging (Sourander et al., 2009). Because both suicides and suicide attempts requiring hospital treatment are rare phenomena, and have been shown to share similar characteristics (Beautrais, 2003), it was justified to pool them together. For convenience, in this thesis, "severe suicidality" refers to suicide or a suicide attempt which required hospital admission.

4.4 Ethical considerations

The research plans of the studies I-II were approved by the Ethics Committee of Turku University Hospital and the school authorities. The research plan of the baseline assessment in studies III-IV was approved by the Ethics Committees of all five university hospital units and clinics (Helsinki, Kuopio, Oulu, Tampere, and Turku), as well as the school authorities. Participation in all studies was voluntary. At follow-up in studies III-IV, the Ethics Committee of Turku University and Turku University Hospital approved the research plan. The Ministry of Social Affairs and Health approved the use of information obtained from the registers. The combined information from the questionnaires and the registers was analyzed in such a way that the subjects could not be identified.

4.5 Statistical methods

Prevalence changes in the frequencies of pain symptoms and sleep problems (study I): The differences in the frequencies of headache, abdominal pain, other pains, sleep problems, and tiredness in 1989, 1999 and 2005 were analyzed separately for boys and girls with a single predictor cumulative logistic regression analysis, which made it possible to analyze the symptoms as three-category variables (Agresti, 2002). The use of cumulative logistic models is recommended when the outcome variable includes more than two response categories that are ordered (e.g. having headache 1. seldom, 2. often, or 3. almost daily), as it results in potentially greater power than ordinary multicategory logit models, and simpler interpretation (i.e. one cumulative odds ratio instead of two odds ratios to illustrate the association between, e.g. study year and the three-category frequency of headache). The strength of the associations was quantified by calculating cumulative odds ratios (COR) with 95% confidence intervals (95% CI). In 1999, due to a technical error, some of the identification codes and thus information concerning sex were lost. Thus, 180 questionnaires could not be used in the analyses where boys and girls were analyzed separately.

Pair associations among pain symptoms and sleep problems (studies I-II): Pair associations between pain symptoms and sleep problems were analysed with a chi-square test.

Cross-sectional associations between psychosocial factors and pain symptoms and sleep problems (studies I-III): The analyses were carried out using cumulative logistic regression analysis (Agresti, 2002). The strength of the associations was quantified by calculating CORs with 95% CIs. In the first phase, the associations between psychosocial variables, and each pain symptom or sleep problem, were analyzed in a single-predictor model (associations between sex and each health complaint), or in a multi-predictor model (associations between each psychosocial variable and each health complaint, adjusted with sex (studies I-III) and year (study I)).

In the second phase, multi-predictor models including sex, year (only in study I), and all psychosocial variables, were created. In study II, to ensure that the psychosocial variables concerning different aspects of life would be equally considered in the statistical analyses, significant ($p < 0.05$) variables from the first phase were included in the age- and sex-adjusted multi-predictor analysis that was performed in two steps. In the first step psychosocial variables were divided into five subgroups: 1. Family composition and ethnic background, 2. General health and psychiatric difficulties, 3. Substance use, 4. Victimization and bullying, and 5. School environment. Multi-predictor analyses were carried out separately for each subgroup. In the second step, all variables from each subgroup that had a significance level of <0.1, were included in the final multi-predictor model.

Longitudinal associations between pain symptoms at age eight and antidepressant use and severe suicidality by age 24: In study III, associations between each pain symptom and antidepressant use (adjusted with 1. sex, and 2. all baseline psychosocial variables) were analyzed using Cox's proportional hazards regression analysis. The strength of the associations was quantified by hazard ratios (HR) and 95% CIs (Cox, 1972). The time from January 1st, 1994, to the first antidepressant purchase was considered as the event time. For those who died or moved abroad before any antidepressant purchase, the follow-up time was censored at that point. Additionally, the above-mentioned analyses were repeated by excluding antidepressants (amitriptyline, clomipramine, and duloxetine) that in Finland have an official indication for treating pain. In study IV, because of the small numbers of subjects showing severe suicidality, the exact conditional logistic regression technique was used in statistical analyses (Hirji et al., 1987). To reflect the strength of the associations, odds ratios (OR) and 95% CIs were calculated. As earlier studies have shown sex differences in the risk factors of suicidality (Achenbach et al., 1995, Sourander et al., 2009), the analyses were done separately for males and females. After conducting single-predictor regression analyses, multi-predictor models, including all baseline psychosocial variables, were conducted. Due to technical limitations, the exact conditional logistic regression technique could not be used in multi-predictor analyses.

To study ***agreement between the child's and parent's reports*** of the pain symptoms, the kappa coefficient (κ) with 95% CIs was calculated (Study III). The kappa coefficient can have values between -1 and 1, -1 referring to complete disagreement, and 1 to complete agreement. There are no unequivocal instructions on how to interpret the results. Landis and Koch (1977) characterized kappas 0–.20 indicating slight, .21–.40 fair, .41–.60 moderate, .61–.80 substantial, and .81–1 almost perfect agreement, whereas Fleiss considered kappas over .75 as excellent, .40 to .75 as fair to good, and below .40 as poor.

In all studies, p-values of <0.05 were considered statistically significant. For statistical analyses, SAS System for Windows, release 9.2/2008, was used in studies II, III, and IV, and SAS for Windows, release 9.1.3., in study I.

5 RESULTS

5.1 Prevalence of pain symptoms and sleep problems (studies I-III)

5.1.1 Prevalence of pain symptoms among eight-year-old children

According to parental reports, 52% of boys and 55% of girls suffered from occasional, and 2% of boys and 3% of girls from weekly headache (p=.011). Correspondingly, 44% of boys and 46% of girls suffered from occasional, and 1% of boys and 2% of girls from weekly abdominal pain (p=.005). According to child reports, 12% of boys and 13% of girls suffered from frequent, and 3% of both sexes from almost daily headache (p=.670); 8% of boys and 9% of girls from frequent, and 2% of boys and 3% of girls from almost daily abdominal pain (p=.162); and 10% of boys and 9% of girls from frequent, and 3% of boys and 2% of girls from almost daily other pains (p=.006). The level of agreement between child- and parental reports was low. κ-values and 95% CI:s for headache were 0.11 and 0.09-0.12, and for abdominal pain 0.08 and 0.06-0.10, respectively. The parents of 7% of the children who reported at least frequent pain answered that their child had not suffered from pain at all during the previous year.

5.1.2 Prevalence of pain symptoms and sleep problems among 13-18-year-old adolescents

Among middle adolescents (age range 13-18 years), 17% of boys and 26% of girls reported monthly, and 10% of boys and 15% of girls weekly headache (p≤.001); 9% of boys and 29% of girls monthly, and 4% of boys and 7% of girls weekly abdominal pain (p≤.001); and 27% of boys and 28% of girls monthly, and 23% of boys and 31% of girls weekly sleep problems (p≤.001). The prevalence of middle adolescents with none, one, two, or three of the symptoms at the same time, were 31%, 35%, 22%, and 12%, respectively. Of the adolescents suffering from one symptom, 32 % reported one co-occurring symptom, and 17% two co-occurring symptoms.

5.2 Prevalence changes of pain symptoms and sleep problems among eight-year-old children (study I)

Changes in the prevalence of pain symptoms and sleep problems among eight-year-old boys and girls from 1989 to 2005 are presented in Figures 4(a-e) and 5(a-b). A significant increase was found in the prevalence of all symptoms except for headache among boys and other pains among girls. With all three years' (1989, 1999, and 2005) data included, boys reported more other pains and sleep problems than girls. Other symptom frequencies were similar for both sexes.

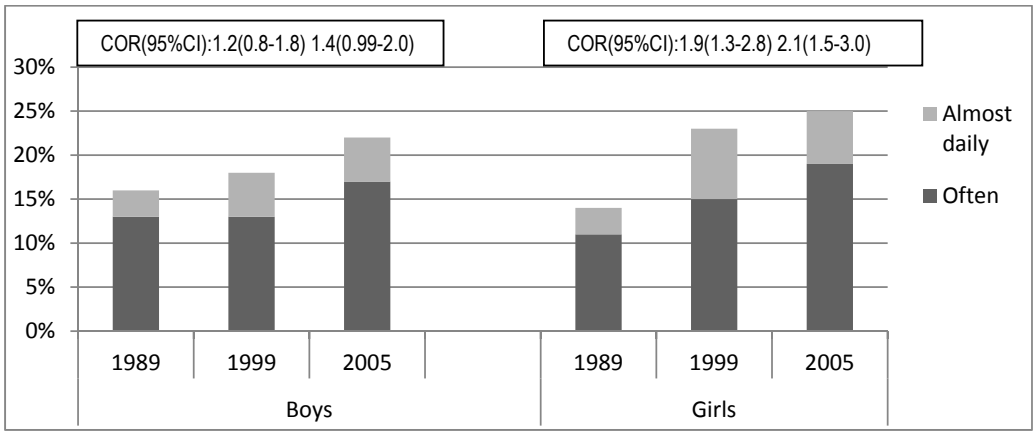


Figure 4a. Changes in the prevalence of headache

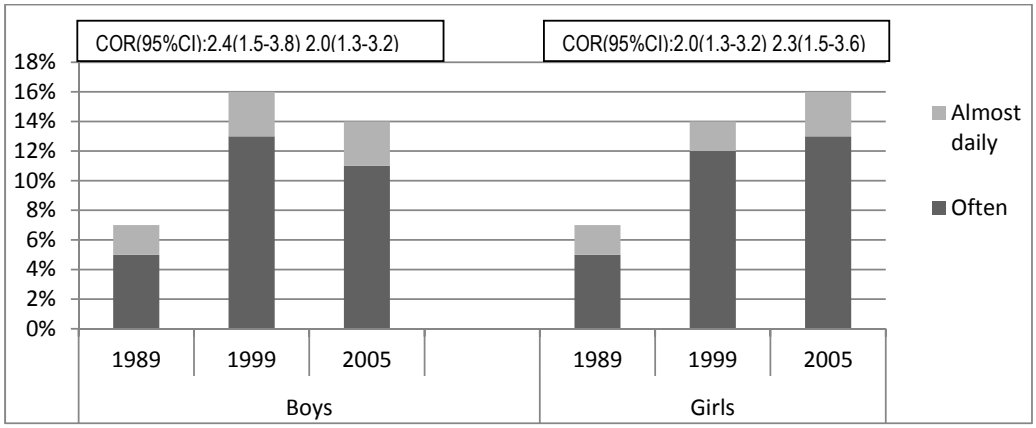


Figure 4b. Changes in the prevalence of abdominal pain

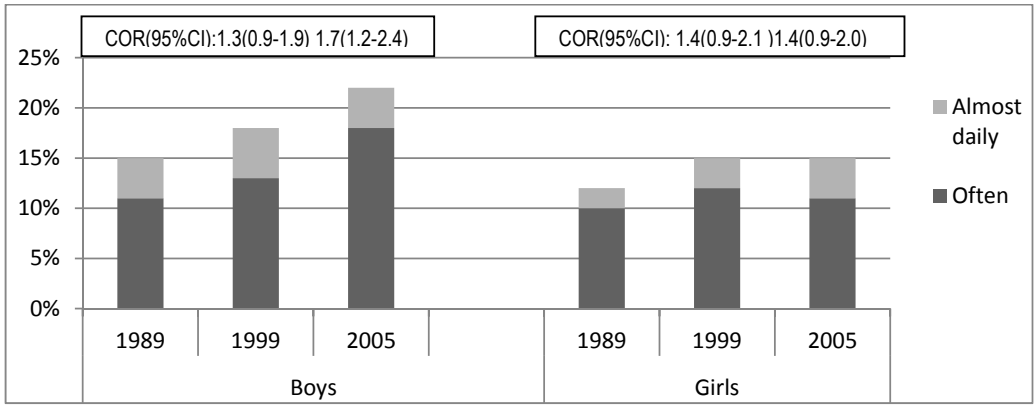


Figure 4c. Changes in the prevalence of other pains

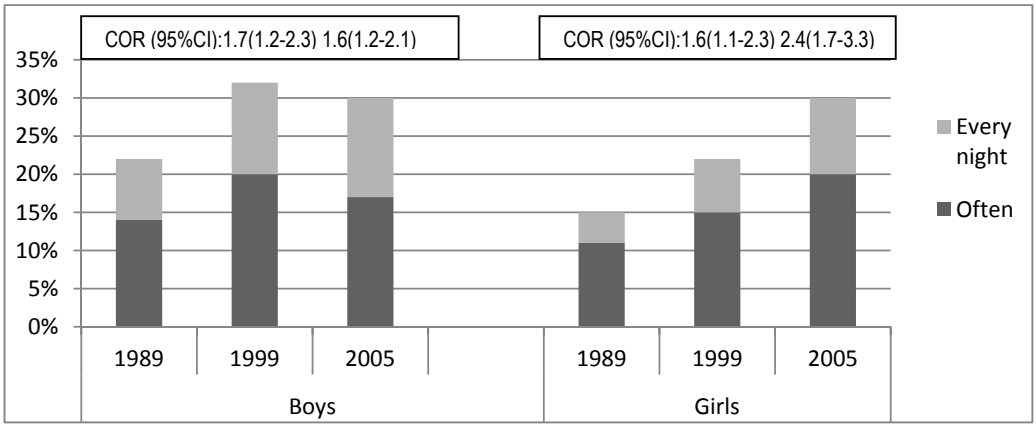


Figure 4d. Changes in the prevalence of sleep problems

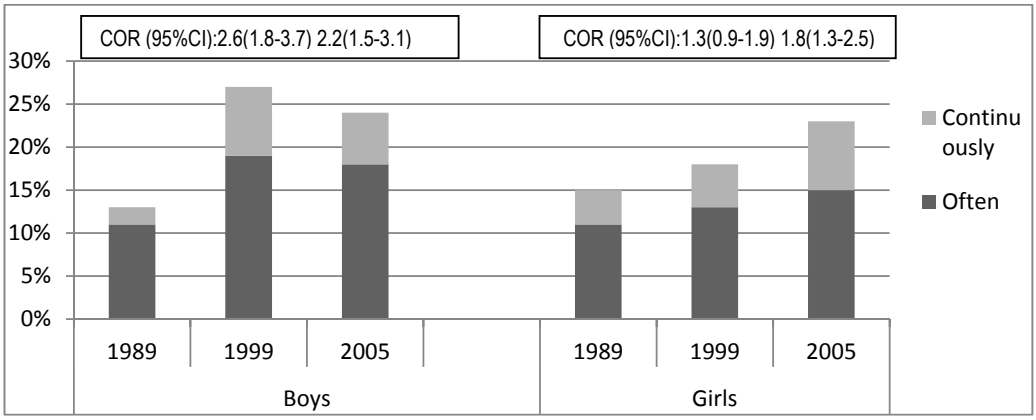
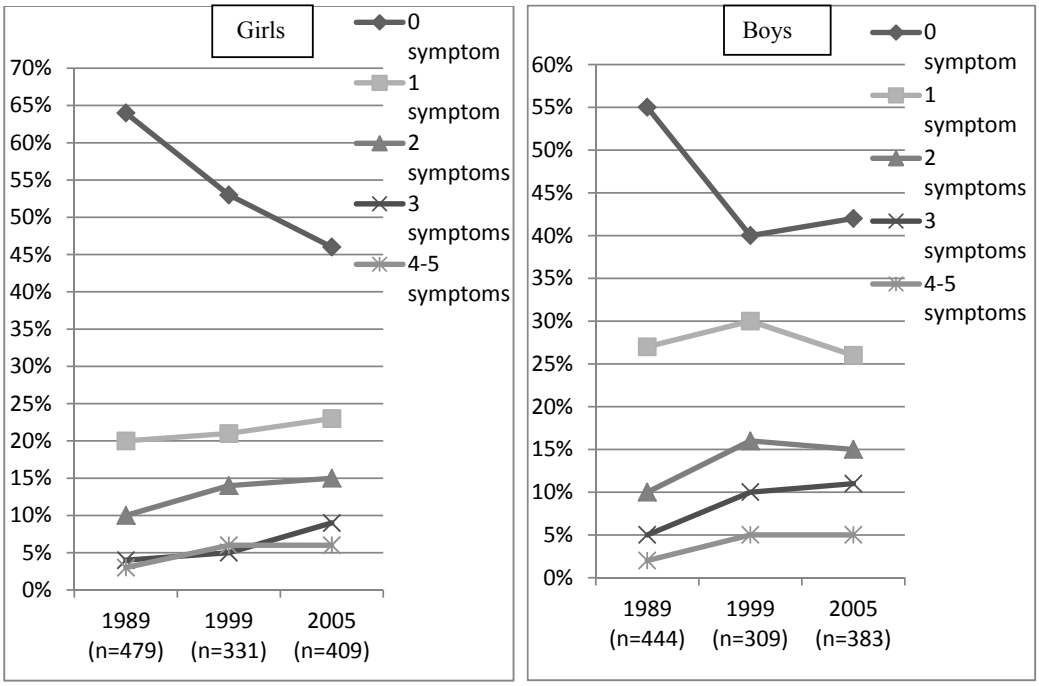


Figure 4e. Changes in the prevalence of tiredness

Note: CORs and 95% CIs reflect the increase in the prevalence from 1989 to 1999 (e.g. 2.6 (1.8-3.7) for tiredness among boys), and from 1989 to 2005 (e.g. 1.8 (1.3-2.5) for tiredness among girls)

Figure 4. Prevalence changes of pain symptoms and sleep problems based on eight-year-old children's own reports in 1989, 1999, and 2005 (study I, total n=2536)

The prevalence of children suffering from several symptoms at the same time, approximately doubled from 1989 to 2005. For example, the proportion of children who had at least two frequent symptoms, increased from 17% to 31%, and the proportion of children who had at least four frequent symptoms, from 2% to 6%. The results for both sexes are presented in Figure 5. CORs and 95% CIs reflecting the change were 1.9 (1.4-2.4) for boys, and 2.2 (1.7-2.8) for girls.



Note: Having a symptom refers to reporting at least frequent headache, abdominal pain, other pains, sleep problems, or tiredness

Figure 5. The number of self-reported symptoms among eight-year-old children in 1989, 1999 and 2005 (study I, total n=2536)

5.3 Pair-wise associations between pain symptoms and sleep problems (studies I-II)

Pair-wise associations between self-reported pain symptoms and sleep problems among eight-year-old children are presented in Table 5. All associations were statistically significant, with a p-value of <.001. For example, of the children suffering from frequent abdominal pain, 45% also reported frequent headaches, and 39% frequent sleep problems.

Table 5. Associations between self-reported headache, abdominal pain, other pains, sleep problems, and tiredness among eight-year-old children with 1989, 1999, and 2005 samples included (study I, total n=2536)

	Headache	Abdominal pain	Other pains	Sleep problems	Tiredness
Headache	X	27%#	40%	39%	35%
Abdominal pain	45%	X	48%	39%	38%
Other pains	49%	37%	X	44%	42%
Sleep problems	30%	23 %	28%	X	34%
Tiredness	35%	24%	34%	43%	X

Note: The percentages show the share of children with each symptom (at least often), who also have another symptom (at least often). # For example, 27% of the children with frequent / almost daily headache also suffer from frequent / almost daily abdominal pain.

Pair-wise associations between self-reported pain symptoms and sleep problems among middle adolescents are presented in Table 6. All associations were statistically significant, with a p-value of <.001. For example, of the adolescents who reported weekly abdominal pain, 56% also suffered from weekly headaches, and 56% from weekly sleep problems.

Table 6. Associations between self-reported headache, abdominal pain, and sleep problems among 13-18-year old adolescents in 2008 (study II, total n=2215)

	Headache	Abdominal pain	Sleep problems
Headache	X	25%#	49%
Abdominal pain	56%	X	56%
Sleep problems	23%	12%	X

Note: The percentages show the share of adolescents with each symptom (at least weekly), who also have another weekly symptom. # For example, 25% of the adolescents with weekly headache also suffer from weekly abdominal pain.

5.4 Cross-sectional associations between psychosocial factors and pain symptoms and sleep problems (studies I-III)

5.4.1 Associations between psychiatric difficulties and pain symptoms and sleep problems among eight-year-old children (studies I and III)

In study I, associations between the child's psychiatric difficulties (self-reported emotional difficulties, and parent- and teacher-reported overall psychiatric difficulties, used as continuous variables), and pain symptoms and sleep problems were analyzed among three eight-year-old children's samples (years 1989, 1999, and 2005 pooled together, total n=2536) of the Turku area. In the sex- adjusted model, all psychiatric symptom categories were significantly associated with headache, abdominal pain, other pains, sleep problems, and tiredness. The COR:s reflecting the associations with different pain symptoms and sleep problems varied between 1.8 and 2.5 for child-reported emotional difficulties, and between 1.2 and 1.4 for parent- and teacher-reported overall psychiatric difficulties. Associations according to the multi-predictor model are presented in Table 7.

Table 7. Associations between psychiatric difficulties and self-reported pain symptoms and sleep problems among eight-year-old children according to a multi-predictor model, with 1989, 1999, and 2005 samples of the Turku area pooled together (study I, total n=2536)

	Headache	Abdominal pain	Other pains	Sleep problems	Tiredness
CDI	1.7 (1.5-1.9)	1.9 (1.7-2.1)	1.9 (1.7-2.1)	2.6 (2.3-2.9)	2.1 (1.9-2.4)
Rutter Teacher	1.2 (1.1-1.3)	NS	NS	NS	1.1 (1.02-1.3)
Rutter Parent	NS	1.1 (1.000-1.3)	NS	NS	NS

Note: Emotional symptoms are measured by the Child Depression Inventory (CDI). Parents and teachers reported the child's overall psychiatric symptoms by Rutter Parent and Teacher questionnaires. The COR:s and 95% CI:s correspond to the change in SD. They are adjusted for study year, sex, family composition, maternal educational level, and self-, parent- and teacher-reported psychiatric symptoms, and are presented when overall p is <.05. NS=non-significant.

In study III, associations between the child's psychiatric difficulties (self-reported emotional problems, and parent- and teacher-reported hyperactivity and conduct problems, used as categorious variables) and self- and parent-reported pain symptoms were analyzed in the nationwide eight-year-old children's sample (n=5531). In the sex-adjusted model, all psychiatric symptom categories were significantly associated with all studied self- and parent-reported pain symptoms. The COR:s reflecting the associations with different pain symptoms varied between 1.5 and 5.4 for child-reported emotional difficulties, between 1.2 and 2.2 for parent- and teacher-reported hyperkinetic problems, and between 1.3 and 2.0 for parent- and teacher-reported conduct problems. Associations according to the multi-predictor model are presented in Table 8.

Table 8. Associations between psychiatric difficulties and self- and parent-reported pain symptoms, according to a multi-predictor model, in the nationwide birth cohort of eight-year-old children in 1989 (study III, total n=5531)

	Self-report			Parent-report	
	Headache	Abdominal pain	Other pains	Headache	Abdominal pain
Emotional	3.8 (3.1-4.7)	3.5 (2.7-4.4)	5.2 (4.1-6.4)	1.4 (1.2-1.8)	1.4 (1.2-1.7)
Hyperkinetic	1.4 (1.1-1.8)	NS	1.6 (1.2-2.1)	NS	NS
Conduct	NS	1.5 (1.1-1.9)	NS	NS	1.3 (1.1-1.6)

Note: Emotional symptoms are measured by the Child Depression Inventory. Hyperkinetic and conduct problems are measured by summing up the corresponding sub-scores from the Rutter Parent and Teacher Questionnaires. 90% cut-offs are used. CORs and 95% CIs are adjusted for sex, family composition, parental educational level, and the other two psychiatric symptom categories, and are presented when overall p is <.05. NS=non-significant.

In the multi-predictor model among three eight-year-old children's samples (years 1989, 1999, and 2005 pooled together, total n=2536) of the Turku area (see Table 7),

the COR:s of the variable "year" reflecting the increase in the prevalence of headache, abdominal pain, other pains, sleep problems, and tiredness from 1989 to 2005, remained practically the same when compared to the single-predictor model (see Figure 4). This indicates that the increase in the symptom levels cannot be explained by psychiatric difficulties, or any other variable (i.e. sex, family composition, or maternal educational level) that were included in the model.

5.4.2 Associations between psychosocial factors and pain symptoms and sleep problems among 13-18-year-old adolescents (study II)

Among 13-18-year-old adolescents, almost all the studied psychosocial factors were statistically significantly associated with headache, abdominal pain, sleep problems, and the increasing number of concurrent symptoms according to the sex-adjusted model. The strongest associations with all three symptoms and the number of concurrent symptoms were found for having psychological difficulties, i.e. difficulties with emotions, concentration, behavior, or getting along with other people. The prevalence of weekly symptoms among the participants who reported definite / severe difficulties, compared to the participants who reported no difficulties, were 37% and 8% (COR (95% CI): 5.2 (3.7-7.2)) for headache, 25% and 3% (COR: (95% CI): 4.4 (3.1-6.3)) for abdominal pain, and 63% and 16% (COR: (95% CI): 6.7 (4.7-9.6)) for sleep problems, respectively. Of the participants who reported definite / severe psychological difficulties, 91% had at least one symptom, while 34% suffered from all three symptoms. Corresponding figures among the participants who reported no difficulties, were 48% and 6%.

Associations between psychosocial factors and pain symptoms and sleep problems, according to the final multi-predictor model, are presented in Figure 6(a-d). Psychosocial factors that were associated with all three symptoms and the increasing number of concurrent symptoms, were female sex, psychological difficulties, emotional symptoms, smoking, victimization, and feeling not cared about by teachers.

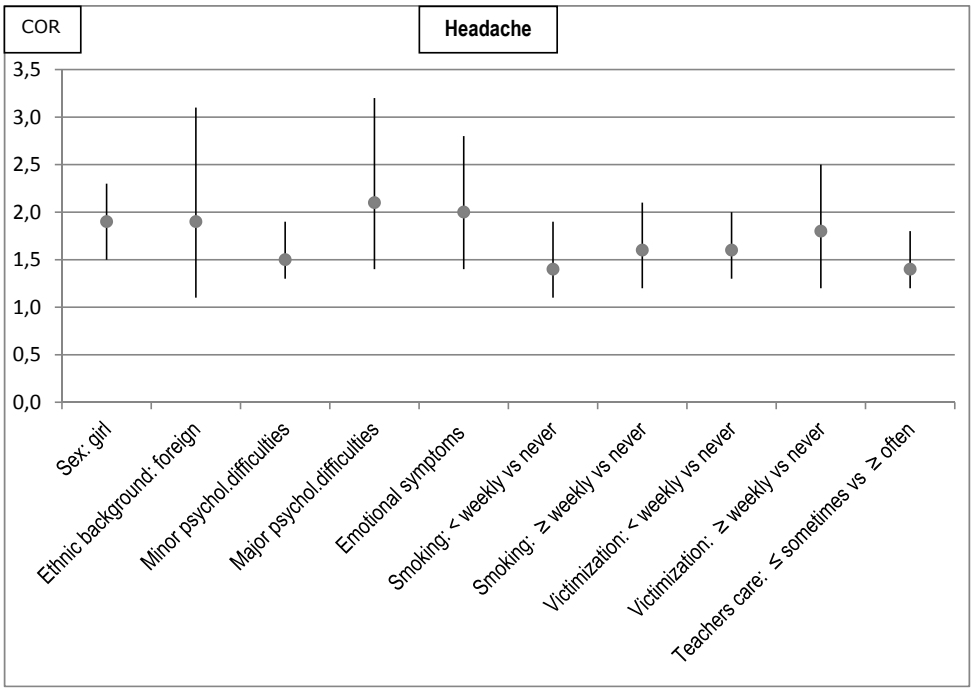


Figure 6a. Associations between psychosocial factors and headache

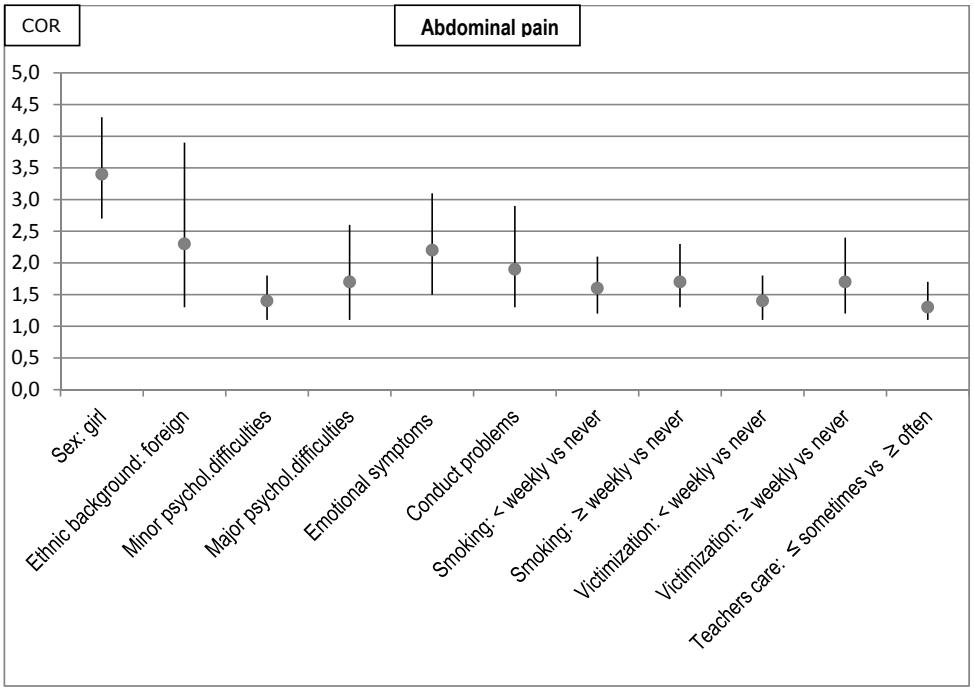


Figure 6b. Associations between psychosocial factors and abdominal pain

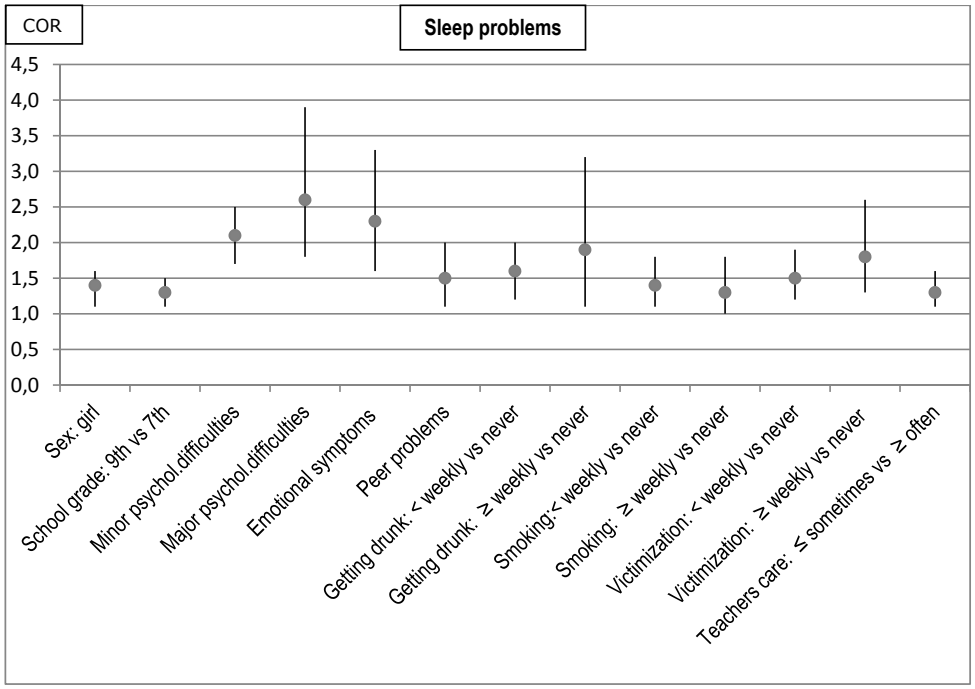


Figure 6c. Associations between psychosocial factors and sleep problems

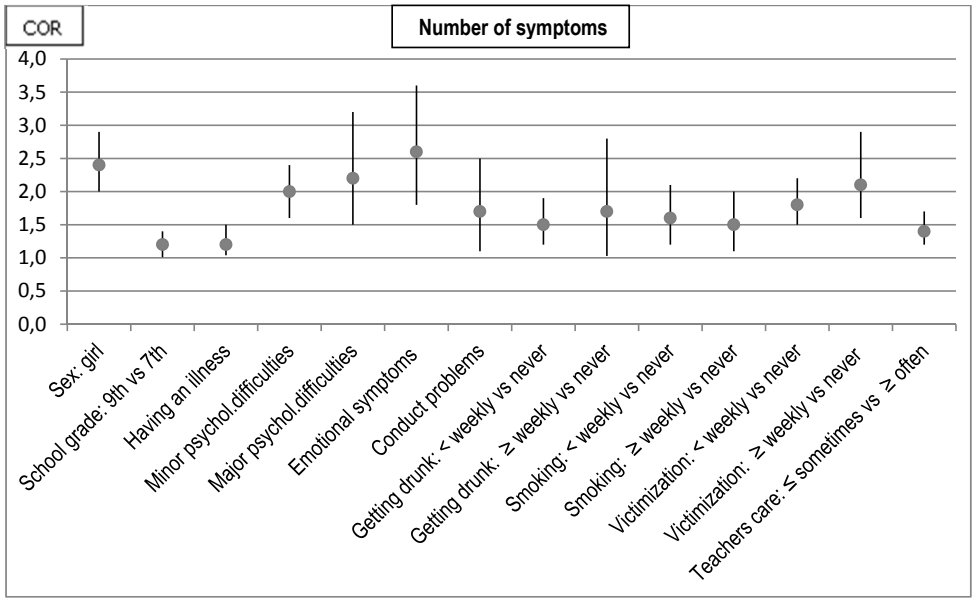


Figure 6d. Associations between psychosocial factors and the number of symptoms

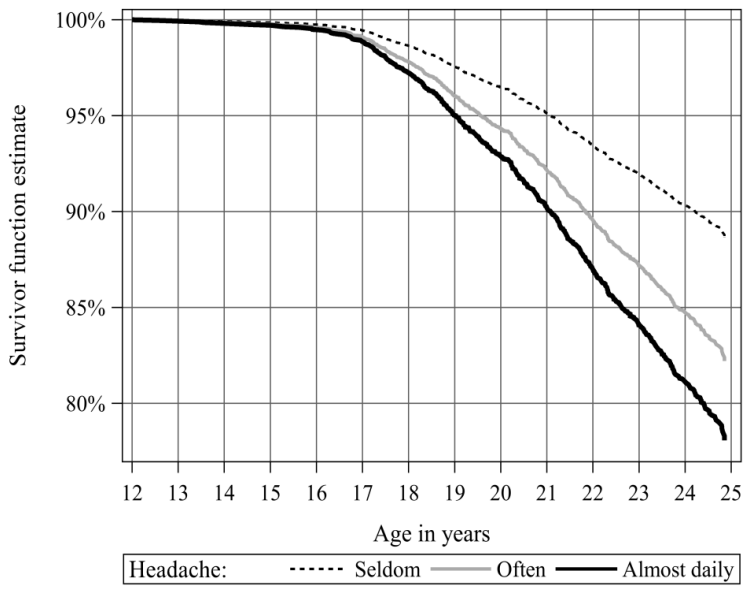
Note: The figure shows the associations in CORs and 95% CIs, adjusted with sex and all other psychosocial factors. Only the associations with a p-value of <.05 are presented. Emotional difficulties, conduct problems, and peer problems: scoring among the highest 10% in the corresponding subscale of the Strengths and Difficulties Questionnaire. Major = definite / severe.

Figure 6. Significant associations between psychosocial factors and self-reported pain symptoms and sleep problems among 13-18-year-old adolescents in 2008 (study II, total n=2215)

5.5 Longitudinal associations between pain symptoms in childhood and antidepressant use and severe suicidality in adolescence and early adulthood (studies III-IV)

The child's own report of headache and other pains, and the parents' report of the child's abdominal pain (overall p <.05) at age eight predicted antidepressant use in adolescence and early adulthood in the sex-adjusted model. The HRs with 95% CIs reflecting the likelihood of antidepressant use by age 24 were 1.6 (1.3-2.0) for self-reported frequent, and 2.1 (1.5-2.9) for self-reported almost daily headache; 1.4 (1.1-1.8) for self-reported frequent, and 1.5 (0.95-2.3) for self-reported almost daily other pains; and 1.3 (1.1-1.5) for parent-reported occasional, and 1.2 (0.7-2.2) for parent-reported weekly abdominal pain. No statistically significant differences between the sexes were found.

In the multi-predictor model, including sex, family composition, parental educational level, and childhood psychiatric difficulties (i.e. self-reported emotional difficulties, and parent- and teacher-reported hyperkinetic and conduct problems) as covariates, the child's own report of headache at age eight still predicted antidepressant use by age 24 with a dose-response relationship (p = <.001). HRs and 95% CIs for frequent and almost daily headache were 1.4 (1.2-1.8) and 1.7 (1.1-2.4). Headache predicted antidepressant use to a similar extent as female sex and childhood emotional difficulties, for which HRs and 95% CIs were 1.5 (1.3-1.8) and 1.5 (1.2-2.0), respectively. The result reflecting the association between self-reported headache and antidepressant use is presented in Figure 7.



Note: The figure represents the survival function estimates of time to the first antidepressant medication purchase, based on single-predictor Cox regression analysis. The curves show the estimates for the proportion of persons who have not purchased antidepressant medication.

Figure 7. Association between headache at age eight and antidepressant use by age 24 (study III, n=5416)

In addition, in the multi-predictor model, parent-reported child's abdominal pain predicted later antidepressant use (p = .03). HRs and 95% CIs for frequent and almost daily abdominal pain were 1.3 (1.1-1.5) and 1.1 (0.6-2.0), respectively. When antidepressants with an official indication for treating pain were excluded from the analyses, the results remained similar.

Longitudinal associations between pain symptoms at age eight and severe suicidality by age 24 are presented in Figure 8(a-b). Severe suicidality was predicted only by parent-reported abdominal pain among boys. In addition, boys' own report of headache as a predictor almost reached statistical significance (OR (95%CI): 2.3 (0.9-5.6), p = .09). No significant associations were found among females.

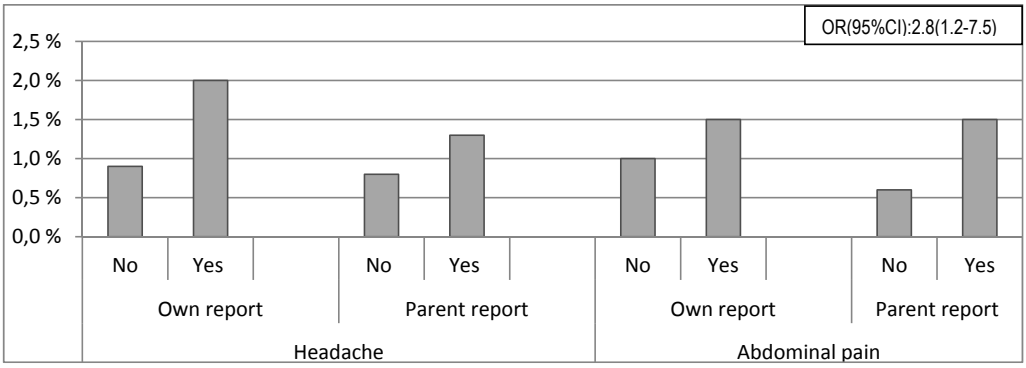


Figure 8a. Associations between pain symptoms at age eight and severe suicidality by age 24 among males

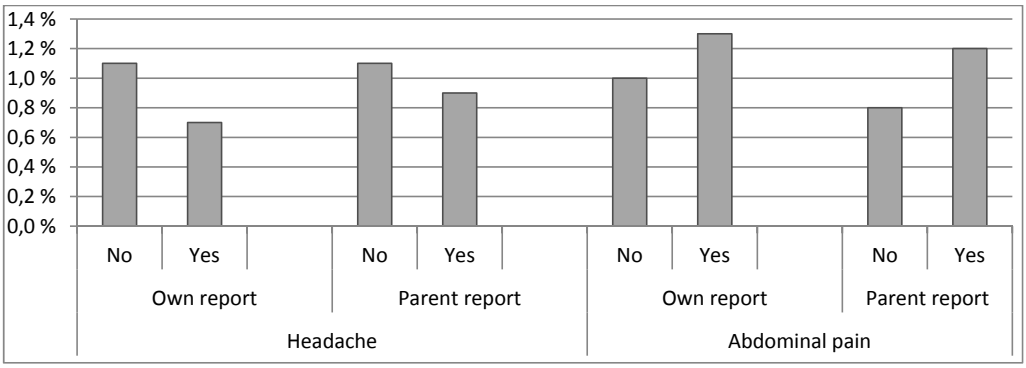


Figure 8b. Associations between pain symptoms at age eight and severe suicidality by age 24 among females

Note: Child report: no = seldom, yes = often / almost every day. Parent report: no = never, yes = sometimes, but less often than once per week / at least once per week. Vertical axis shows the percentage of the subject who committed or severely attempted suicide. The OR:s and 95% CI:s are presented when overall p is <.05

Figure 8. Associations between pain symptoms in childhood and suicides or severe suicide attempts in adolescence and early adulthood (study IV, n=5416)

When adjusted for family composition, parental educational level, and the child's psychiatric difficulties (i.e. self-reported emotional difficulties, and parent- and teacher-reported hyperkinetic and conduct problems) at age eight, boys' abdominal pain reported by the parents still predicted severe suicidality by age 24. OR and 95% CIs reflecting this association were 3.2 and 1.3 to 8.2, respectively.

6 DISCUSSION

6.1 Main results

The results of this thesis showed that pain symptoms and sleep problems are common among Finnish eight-year-old children and 13-18-year-old adolescents. The agreement between child-and parent-reported pain symptoms was found to be low, and a considerable amount of recurrent pain symptoms reported by the children remained unrecognized by their parents. Different pain symptoms, as well as pain symptoms and sleep problems, were associated with each other. Among eight-year-old children, the prevalence of pain symptoms (apart from headache among boys and other pains among girls) and sleep problems, as well as suffering from multiple simultaneous symptoms, approximately doubled from 1989 to 2005. Psychiatric difficulties or demographic factors did not explain the found increase. Psychiatric, and in particular emotional, difficulties were associated with pain symptoms and sleep problems. Among 13-18-year-old adolescents, pain symptoms, sleep problems, and having multiple symptoms associated with several psychosocial factors in a similar way. In longitudinal analyses, in particular the child's own report of headache, and to a lesser degree the parental report of the child's abdominal pain at age eight predicted antidepressant use by age 24. Parental report of the child's abdominal pain predicted severe suicidality among males. No associations were found for pain symptoms and severe suicidality among females.

6.2 Methodological considerations

6.2.1 Participants and procedure

The use of different study populations and study designs has both advantages and disadvantages. Information could be obtained from different age groups, and both cross-sectional and longitudinal associations could be investigated. On the other hand, the variations in collecting data and in the measures restricts direct comparison between different studies.

The strengths of ***the study populations*** include the use of general population samples in studies I, III, and IV. Eight-year-old children were selected as the study population, because due to the large number of study subjects, questionnaires were used as a self-report measure and reading skills were required. In Finland, where education is compulsory from the age of seven, children are taught to read during the first school year, so the age of eight was practically the first possible time when self-reports based on questionnaires could be used. In study II, two samples from two Finnish communities were used. In all

studies, the sample sizes were large, the response rates were high, and the characteristics of the study subjects were found to be representative of the target populations. In studies III and IV, the common problem of prospective studies, i.e. the loss of subjects during the follow-up period, was very low, especially as compared to earlier longitudinal studies (see Table 4), and due to random error (lost personal identification numbers). For these reasons, generalization of the findings to the study populations seems justified.

However, because in study II completely rural areas were not included in the study sample, these results have to be generalized to rural areas with caution. Additionally, in study I, the differences in response rates in 1989, 1999, and 2005 may have slightly biased the findings. Unfortunately, no information about the reasons for not participating, or about the characteristics of the non-participants, was available. It may be considered whether in the 1999 and 2005 samples, the extra step and work involved in the explicit requirement of parental written consent influenced the willingness to participate. However, the deterioration in response rates during recent decades also seems to be a more universal problem (Gerrits et al., 2001). Nonetheless, as the representativeness of the respondents, based on the comparison with national statistics, was good at each sampling point, this reduces the possibility of bias.

Regarding ***study procedures***, major strengths of study I were the long time period used for comparison purposes (from 1989 to 2005), the three identical sampling procedures implemented in the same geographical area, and the use of identical measures in each study year.

The use of register-based data in studies III and IV has both advantages and disadvantages. The registers cover the entire population and offer the possibility to continuously survey the occurrence of the selected outcome, instead of just at one or several distinct assessment points. In addition, both recall bias and under-reporting the use of psychiatric medication and severe suicide attempts could be avoided. Both of these factors are important strengths when compared to earlier longitudinal studies on the subject (see Table 4). On the other hand, only the information that is recorded in the registers can be used. For example, it was not possible to investigate the impact of pain or psychiatric symptoms immediately before the suicide attempts. In addition, the small number of suicides and severe suicide attempts, especially among females, decreased the statistical power to detect associations, and it was not possible even in this large sample to study suicides and severe suicide attempts separately.

6.2.2 Measures

The strength of all studies was inquiring about several symptoms (i.e. different pain symptoms and sleep problems) at the same time, and the use of the participants' own perception of these symptoms. In addition, the use of several reporters in studies I, III,

and IV was an advantage, as the correlation between children's self-reports and adults' reports, as well as the correlation between parents' and teachers' reports have been found to be moderately low (Achenbach et al., 1987, Haralstad et al., 2011, Puura et al., 1998, Sourander et al., 1999, Verhulst et al., 1997). For example, the majority of children who reported high scores on the CDI were screen-negative in both the parents' and teachers' reports of psychiatric symptoms (Sourander, et al., 2008). Compared to earlier longitudinal studies (see Table 4), the use of the child's own report of pain symptoms in studies III and IV can be seen as an important strength. In study II, asking about several psychosocial variables was an advantage, as it reduces the possible overestimation of the studied associations.

The limitations of all the studies include the facts that the questionnaires only inquired about certain subjectively evaluated symptoms during a limited time period, the frequency scales were rather crude, and no diagnostic classifications were used. Regarding sleep problems, only one general item was included in the questionnaire, and it was not possible to investigate different kinds of sleep problems, and possible variations in their associations with psychosocial factors. In addition, the item "other pains" was only inquired about from the children, and no information on the specified localization of the reported pain was available. A proportion of the reported pain symptoms and sleep problems were most probably also due to specific organic diseases, but unfortunately, possible diagnoses were not inquired about, and there was no possibility to carry out a medical examination in the children who reported high symptom levels. Earlier studies, however, have shown that specific organic diseases can be found only in a minority of cases, for example, among 5-10% of children with headache (Korinthenberg 1994), and among 20% of children with abdominal pain (Kokkonen et al., 2004). Correspondingly, 7% of adolescents' insomnia has been diagnosed as being related to a medical condition (Ohayon et al., 2000). Nor was diagnostic assessment regarding psychiatric disorders possible. Nevertheless, questionnaires enable the studying of large populations, and similar measures as were used in the present study have been widely applied in comparable population-based studies (van Gessel et al., 2011, Paavonen et al., 2003, Perquin et al., 2000, Petersen et al., 2006, Stanford et al., 2008). In addition, regardless of the etiology, pain symptoms and sleep problems restrict daily activities (Haraldstad et al., 2011, Roth-Isigkeit et al., 2005), decrease the quality of life (Kotagal 2003, Petersen et al., 2009), and can be seen as a potential risk factor for later well-being.

As children reported symptoms during the previous two weeks, and parents during the previous twelve months, and also the frequency classifications somewhat differed between child and parental questionnaires, their evaluations are not directly comparable (studies III and IV). The time frame in the eight-year-old children's questionnaire was two weeks, as it was assumed that a longer time window would not be appropriate due to the child's cognitive capacity to recall events in a classroom survey situation. Other

differences stem from the fact that the "Finnish 1981 nationwide birth cohort study" conducted in 1989 was not originally planned to be a baseline assessment for prospective studies. The parents' question about abdominal pain also included vomiting, which might have some effect on the findings. However, as recurrent vomiting is rare among children (Forbes and Fairbrother, 2008), it is unlikely that this would solely explain the found associations with antidepressant use and severe suicidality. In addition, the prevalence rates among eight-year-old children and among 13-18-year old adolescents could not be compared with each other, as the wordings of the items, the time frames that were used, and the frequency classifications differed from each other. The use of different scales assessing psychiatric symptoms also hinders direct comparison of the results between different age groups. Whereas in the study among eight-year-old children, first implemented in 1989, the evaluation of overall psychiatric difficulties was based on the Rutter Questionnaires, among middle adolescents, in 2008, the more modern Strengths and Difficulties Questionnaire was used. The study in mid-adolescence also included only self-reports of the pain symptoms, sleep problems, and psychosocial factors, which can be seen as a limitation because of possible recall bias or shared method variance. Furthermore, both the selection of covariates, as well as statistical methods, may have had an impact on the findings. And, finally, to avoid over-evaluation of the associations with psychiatric difficulties, the items concerning the studied somatic symptoms were omitted from the psychiatric problem scales; this may have changed the psychometric properties of the questionnaires that were used.

In study III, antidepressant medication purchases were used as a proxy for psychiatric, especially emotional, problems. Finnish studies have shown that the use of health care services and pharmaceutical treatment are predicted by the disorder's greater severity, longer duration, and higher perceived disability (Hämäläinen et al., 2004; Hämäläinen et al., 2009). As the public health care system in the Nordic countries is tax-supported, and offers the same services and reimbursements of purchased medication to all citizens, independent of socioeconomic status and insurance coverage, the register offers a reliable method for studying medication purchases. The information about prescriptions was available from January 1st, 1994, when the subjects were about 15 years old. As in Finland, the rate of antidepressant purchases has been shown to be very low (i.e. cumulative incidence of 0.2% by age 15) among young children (Gyllenberg and Sourander 2012), this does not have a major impact on the results. The prescription register data do not include the specific indications for the described medication. In addition to depressive and anxiety disorders, which are the most prevalent indications (Sihvo et al., 2008), antidepressant medication is used, for example, in eating disorders, bipolar disorder, post-traumatic stress disorder, and insomnia. Moreover, it is possible that the medication was used for pain symptoms. However, in the additional analyses, where the antidepressants that have an official indication for treating pain were excluded,

the results were very similar. In addition, even if the indication would have been, for example, pain, insomnia or fibromyalgia, the need for medication can still be seen as a negative long-term health outcome.

In studies III and IV, it would have been useful to have had further information about the development of pain symptoms as the children grew older. As pain symptoms tend to fluctuate (Ståhl et al., 2008, Virtanen et al., 2007), it is probable that by collecting information at only one time point, some children who were susceptible to suffer from pain, were not detected. However, an earlier study that investigated headache, abdominal pain and vomiting/bilious attacks in childhood, and widespread pain in adulthood, found that assessment at age seven (when compared to assessments at ages 11 and 16) was the strongest predictor of the outcome. In addition, the additional assessments during adolescence did not significantly improve the fit of the model (Jones et al., 2007).

In this thesis, the main focus was on pain symptoms, and no longitudinal associations were studied between sleep problems in childhood and later mental health. This area, however, will be of interest in future studies.

6.3 Discussion of the results

In this thesis, the ***prevalence of different pain symptoms and sleep problems*** were assessed both among eight-year-old children, and among 13-18-year-old adolescents. The comparison of the results with each other, as well as with earlier studies, is hampered by methodological differences, for example, in study populations (country, age group, clinical versus general population), reporters (parents, teachers, children) and questionnaires (symptoms examined, time intervals, frequency classifications). However, the prevalence rates that were found are within the range that has been reported in earlier population-based studies for similar age groups (Perquin et al., 2000, Petersen et al., 2003, Russo et al., 2007, Smedbråten et al., 1998, van Litsenburg et al., 2010). Regarding the findings among middle adolescents, the six-month prevalence rates of weekly pain symptoms (headache 13% and abdominal pain 6%) are among the lowest, and the prevalence of weekly sleep problems (27%) among the highest, when compared with international studies. Estimates of weekly headache have ranged from 13 to 38 % (Brun Sundblad et al., 2007, Petersen et al., 2003), of abdominal pain from 6 to 25% (Brun Sundblad et al., 2007, Petersen et al., 2003), and of sleep problems from 9 to 35 % (Brun Sundblad et al., 2007, Ostberg et al., 2006). Earlier research has also shown differences in prevalence rates between the countries. For example, in a Nordic comparison including children from Denmark, Finland, Iceland, Norway, and Sweden, the prevalences of sleeplessness and headache were higher in Finland than in the other four countries. The prevalence of abdominal pain was the second lowest in Finland

(Berntsson et al., 2001). In addition, in the present study, the definition of headache (i.e. disturbing activities) might have lowered the reported prevalence. Several studies have shown that headache causes impairment in everyday life (Hoftun et al., 2011, Roth-Isigkeit et al., 2005). Still, not all children who suffer from headache, report functional disability, as according to some reports, only about 20% of children with headache report moderate or severe disability (Kröner-Herwig et al. 2010).

Among eight-year-old children, the prevalences of headache, abdominal pain, and tiredness were equal among both sexes, whereas sleep problems and other pains were slightly more common among boys than among girls. In mid-adolescence, girls reported clearly more both pain symptoms and sleep problems than boys.

Before adolescence, earlier studies have, for the most part, found equal frequencies of headache, abdominal pain, sleep problems and tiredness among both sexes (Petersen et al., 2003, Russo et al., 2007, van Litsenburg et al., 2010). Previous findings with regard to sex differences in the prevalence of "other pains" are inconsistent (Egger et al., 1999, Groholt et al., 2003, Perquin et al., 2000, Petersen et al., 2003, Stanford et al., 2008). The present result of boys having more "other pains" than girls is supported, for example, by a large-scale population-based study by Perquin et al. (2000) who found a higher frequency of limb and "other" pain among boys. The present results are in line with the majority of earlier research apart from the slight male predominance that was found for sleep problems. This finding is also supported by some earlier research (Quine 2001). One possible explanation for boys having more sleep problems than girls could be the male predominance of neuropsychiatric disorders (Ullebø et al., 2012), which are often accompanied by sleep problems (Owens and Mindell 2011, Paavonen et al., 2008). In addition, it is possible that lifestyle factors, such as boys spending more time on computers (Kartovaara et al., 2007), or being more easily injured (Kohen et al., 2000), could explain the differences between the sexes.

Among adolescents, females tend to report more symptoms than males (El-Metwally et al. 2007, van Gessel et al., 2011, Kinnunen et al., 2010, Ostberg et al. 2006, Petersen et al., 2003), as was also shown in the present study. There are a number of possible explanations for why girls report more symptoms than boys. It could be due to hormonal factors, for example, due to menstruation, or as among adolescent girls, hormonal changes may delay the recovery from stress (Young 1998). However, differences in psychosocial factors must also be considered. One possible reason could be that adolescent females experience more interpersonal stress than adolescent males (Rudolph and Hammen 1999). In addition, females have been found to be more willing to report somatic experiences, such as pain, than males (Wise et al. 2002).

The ***level of agreement between self- and parental reports of the pain symptoms*** was low. This was not a surprising finding, as it is commonly reported both in the field

of child psychiatric research (Achenbach et al., 1987, Haralstad et al., 2011, Puura et al., 1998, Sourander et al., 1999, Verhulst et al., 1997), and in studies investigating children's pain symptoms and sleep problems (Garber et al., 1998, Haralstad et al., 2011, Paavonen et al. 2000, Santalahti et al., 2005, Sweeting and West 1998). In the present study, the differences in the frequency classifications in child- and parental questionnaires probably further lowered the agreement. However, the parents of 7% of the children who reported frequent or almost daily pain during the previous two weeks, reported that their child had not suffered from pain at all during the previous year. In addition to parents not being fully aware of their children's internal experiences, a number of factors, such as the parent's or the child's psychological or physical characteristics, may either decrease or increase the symptom rates reported by them (Fearon and Hotopf 2001, Garber et al., 1998).

In the present study, a significant ***increase in the prevalence of headache, abdominal pain, other pains, sleep problems, and tiredness*** from 1989 to 2005 was found among both sexes, apart from headache among boys and other pains among girls, for which a non-significant increase was found. The cumulative odds ratios reflecting the increase varied between 1.6 and 2.4. In addition, the prevalence of children who suffered from multiple symptoms at the same time, approximately doubled from 1989 to 2005.

The present results are in concordance with the few earlier studies that have been carried out among younger children (Anttila et al., 2006, Berntsson and Köhler 2001, Santalahti et al., 2005). Anttila et al. (2006) found the risk of headache in 2002 more than twice as high as in 1974. Previous results based partly on the same samples that were used in the present study (Santalahti et al., 2005), indicated an increase in the prevalence of headache and abdominal pain from 1989 to 1999. The present study confirms the earlier findings about the increase in the prevalence of headache and abdominal pain. In addition, novel information about the increase in the prevalence of other pain symptoms, sleep problems, tiredness, and multiple simultaneous symptoms, was found.

In a study using the same study population, it was shown that the prevalence of psychiatric difficulties among Finnish children has largely remained unchanged between the years 1989 and 2005 (Sourander et al., 2008). In addition, the present study shows that the increase in the prevalence of pain symptoms and sleep problems was not related to children's psychiatric difficulties, family composition, or maternal educational level. These findings indicate that possible causes for the rising symptom levels should be sought in other life areas.

One possible reason for the rising prevalence rates could be an increased willingness to report pain symptoms and sleep problems in 1999 and 2005. However, these symptoms are considered socially acceptable, and it seems unlikely that they would have been under-reported in 1989. Due to bidirectional associations between various pain symptoms and

sleep problems (Lautenbacher et al., 2006), it is also possible that when the prevalence of any of the symptoms increases, it leads to an increase in other symptom levels as well. During the same time period as the increase in the symptom levels was found, Finnish society has gone through several changes. Examples of these are cuts in the budgets of child welfare clinics and day care, increased number of children in a class (Committee for School Welfare 2005), and changes in the structure and demands in working places, possibly causing more stress among parents (Dufton et al., 2008) and decreasing the quality / quantity of the time spent with their children. Correspondingly, earlier research has associated high parental stress (van Tilburg et al., 2010), parents spending less time with their children (Bakoula et al., 2006, Sarioglu et al., 2003), the amount of support from teachers (Ghandour et al., 2004, Natvig et al., 1999), and high levels of noise in the classroom (Wålinder et al., 2007) with children's pain symptoms and sleep problems. Furthermore, a number of other factors that have been associated with pain symptoms and sleep problems, have changed. Examples would be the immense increase in the use of technology (Kröner-Herwig et al., 2008, Bakoula et al., 2006, Hoftun et al., 2012, Kartovaara et al., 2007, Mindell et al., 2009), changes in nutritional habits, such as the use of soft drinks (Hering-Hanit and Gadoth 2003, Kartovaara et al., 2007), and a growing prevalence of obesity (Hershey et al., 2009, Hoftun et al., 2012, Malaty et al., 2007) and allergic diseases (Anthracopoulos et al., 2011, Calhoun et al. 2011, Wilkinson et al. 1994). It can be speculated that these changes may at least partly be responsible for the rising symptom levels. However, the explanations for the increase found in the prevalence of children's pain symptoms and sleep problems remain unclear, since most studies have been cross-sectional and conclusions about causes and effects cannot be made.

In the present study, ***co-occurrence of pain symptoms and sleep problems*** was observed. Both among eight-year-old children and among 13-18-year-old adolescents, all the studied pain symptoms and sleep problems were pair-wise associated with each other. In addition, in both age groups, approximately one third suffered from at least two of the studied symptoms. The present results are similar to the findings of the earlier studies showing that pain symptoms and sleep problems often co-occur (Brun Sundblad et al., 2007, Perquin et al., 2000, Petersen et al., 2006). Earlier research has also demonstrated that one symptom often precedes the occurrence of another (Aromaa et al., 1998, El-metwally et al., 2007, Larsson and Sund, 2007)

There are a few possible mechanisms by which different pain symptoms can be associated with each other. It is possible than one pain symptom causes the other (Davidoff 1998), for example, when pain and tension in the neck lead to headache. However, it has been shown that the associations between different pain symptoms are not specific to the localization of pain (Groholt et al., 2003), and the findings showing that the most prevalent association is between headache and abdominal pain (Groholt et

al., 2003, Stanford et al., 2008), do not seem to support this kind of mechanism either. Another possible mechanism to be considered is the central sensitization (Coderre et al., 1993). The pain perception is a dynamic process including not only an analysis of afferent noxious input, but also the neuronal, cellular, and molecular effects of past pain experiences. These prior events may sensitize central neural systems involved in pain perception, and lead to enhanced responses to future pain stimulation. This kind of mechanism could at least partly explain the accumulation of pain symptoms from different anatomical localizations.

Regarding the associations between pain symptoms and sleep problems, some mechanisms have also been suggested. It is possible that pain experience disturbs sleep, for example, by inducing arousal (Haraldstad et al., 2011, Lautenbacher et al., 2006). Moreover, sleep problems can increase the perception of pain (Lautenbacher et al., 2006). It has been proposed that either pain or a sleep problem may launch an ongoing cycle in which each difficulty maintains the occurrence of the other (Lautenbacher et al., 2006).

Furthermore, it is possible that factors that have been associated with both pain symptoms and sleep problems, such as psychosocial difficulties, negative life events, cognitive mechanisms, insecure attachment style, life-style or even prenatal factors, as well as a shared genetic vulnerability (Aromaa et al., 1998, Berntsson et al., 2001, Boey and Yap, 1999, Brown 2004, Calhoun et al., 2011, Fabbri et al., 2012, Galli et al., 2007, Harvey 2002, Hershey et al., 2009, Malaty et al., 2007, Robinson et al., 1990, Sarioglu, et al., 2003, Smaldone et al., 2009, Smedje et al., 2001, Stone et al., 2010, Tremblay and Sullivan 2010, van Tilburg et al., 2010, Vaughn et al., 2011, Watson et al., 2003, Zhang et al., 2012), underlie the co-occurrence of these symptoms. Psychosocial factors have also been found to mediate the association between pain and sleep problems, as a study among children with sickle-cell disease showed that negative mood increased the effect of pain on sleep and vice versa, and positive affect decreased the negative impact of sleep problems on pain experience (Valrie et al., 2008). The co-occurrence of pain symptoms and sleep problems, when compared to having either symptom alone, has also been associated with more severe pain and sleep problems, as well as increased amounts of psychosocial stress and functional limitations (Siu et al., 2012).

The present study showed that ***the associations with psychosocial factors*** were similar for an increasing frequency of pain symptoms and sleep problems, as well as an increasing number of concurrent symptoms. The finding is comparable to the results of Larsson and Sund (2007). They showed that depression predicted the number of pain symptoms in a one-year follow-up, and concluded that the frequency and number of symptoms rather than the localization or duration of pain are associated with psychological problems.

Bullying, school-related factors, and substance use were assessed only in mid-adolescence. Both pain symptoms and sleep problems, as well as an increasing number of the symptoms were associated with victimization, feeling not cared about by teachers, and substance use.

The results showing an association with victimization are in line with the previous findings (Gini and Pozzoli 2009, Paavonen et al., 2002, Robinson et al., 1990, Smedje et al., 2001, Williams et al., 1996). In a recent meta-analysis of the associations between bullying and psychosomatic symptoms, it was stated that there is a lack of studies assessing the effects of potential confounders in several areas of life (Gini and Pozzoli 2009). In the present study, victimization was associated with a dose-response relationship with all studied symptoms, even after controlling for the covariates.

It is possible, that being bullied leads to having pain symptoms and sleep problems (Rigby 1999). However, it is also possible that children who suffer from these symptoms, and possibly at the same time from other, commonly co-occurring problems, such as obesity (Hershey et al., 2009, Knutson and Van Cauter 2008, Malaty et al., 2007) or psychiatric difficulties (Aromaa et al., 1998, Fearon and Hotopf, 2001, Kröner-Herwig et al., 2008, Galli et al., 2007, Guidetti et al., 1998, Paavonen et al., 2002 and 2003, Pine et al., 1996, Watson et al., 2003, Smedje et al., 2001), are more often bullied. Furthermore, due to possible co-occurring temperamental characteristics, such as negative ways of thinking among adolescents who report the symptoms (Moore et al., 2011, Walker et al., 2001), it is possible that their threshold to experience or to remember being bullied is lower than among those who do not suffer from recurrent pain symptoms or sleep problems.

The finding that pain symptoms and sleep problems were associated with feelings of not being cared about by teachers is also supported by earlier research (Ghandour et al., 2004, Hjern et al., 2008, Natvig et al., 1999). What is probably more alarming is, however, that 47% of the pupils experienced being mostly not cared about by their teachers. Also another Finnish study found that over half of the children felt that the teachers did not have time to listen to them (Arponen 2007). This result is important in the current economic situation as budgetary restraints may lead to larger class sizes, thus further reducing the time the teacher has to spend with each pupil.

The associations that were found between substance use and pain symptoms and sleep problems are in line with earlier research (Gromov and Gromov 2009, Hoftun et al., 2012, Kröner-Herwig et al., 2008, Levy et al., 1986, Patten et al., 2000, Waldie et al., 2008, Wong et al., 2004). The associations seem to be bidirectional. Both alcohol use and smoking can impair the quality of sleep (Gromov and Gromov 2009), and sleep problems in turn have been found to increase substance use (Wong et al., 2004). In addition, alcohol may be used in order to get to sleep (Gromov and Gromov 2009).

Similarly, it has been suggested that smoking may physiologically cause pain, serve as a coping strategy, or reflect co-occurring psychosocial difficulties (Hoftun et al., 2012). Furthermore, factors that have been associated with both substance use and pain symptoms and sleep problems, such as externalizing problems (Armstrong and Costello 2002, Campo et al., 2004, Paavonen et al., 2002), might at least in part explain the found associations.

In the present study, ***psychiatric, and in particular emotional difficulties***, were associated with pain symptoms and sleep problems. These results are in line with earlier research (Kröner-Herwig et al., 2008, Aromaa et al., 1998, Galli et al., 2007, Paavonen et al., 2002 and 2003, Smedje et al., 2001, Watson et al., 2003).

The child's own report of headache at age eight predicted antidepressant use between ages 15 and 24 with a dose-response relationship. In addition, parent-reported child's abdominal pain predicted later antidepressant use among children with frequent pain, but not among children with almost daily pain. No differences between the sexes were found. Regarding severe suicidality by age 24, no significant associations with pain symptoms at age eight were found among females. Among males, the parental report of the child's abdominal pain predicted later severe suicidality.

Previously, Hotopf et al. (1998) reported an association between parent-reported childhood abdominal pain and adulthood psychiatric disorders at age 36. In their study, the "caseness" of recurrent abdominal pain was strict compared to the present study, since it was defined as having abdominal pain on three different occasions: at the ages of seven, 11, and 15. In addition, organic reasons for the pain were excluded. Childhood psychiatric difficulties were also assessed, but not included in the final analysis. Fearon and Hotopf (2001) reported an association between parent-reported childhood headache as assessed at the ages of seven and 11, and psychiatric difficulties at age 33. This association remained significant even after adjusting for teacher-reported childhood depressive symptoms, childhood separation experiences, parents' chronic illnesses, and mental health problems in the family.

Earlier research has not investigated associations between pain and severe suicidality among children or adolescents. However, the finding that pain symptoms among males associated with severe suicide attempts and suicides, is supported by studies among adults (Breslau et al., 1991, Fishbain et al., 1991, Ilgen et al., 2008, Keefe et al., 2000).

A summary of the associated factors of pain symptoms and sleep problems presented in this thesis, is shown in Figure 9.

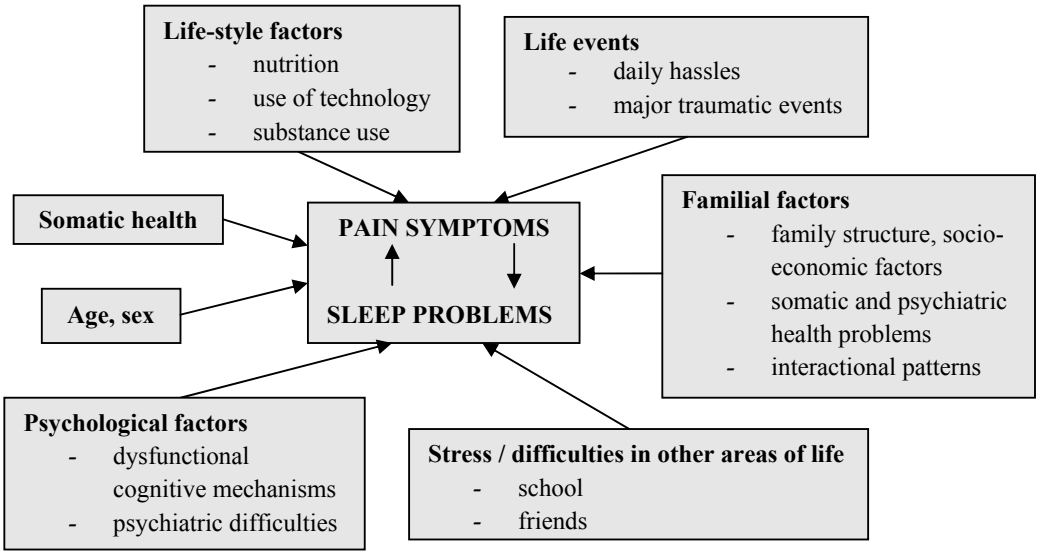


Figure 9. Summary of the associated factors of pain symptoms and sleep problems

There are several possible ***explanations for the associations between psychiatric difficulties and pain symptoms and sleep problems***. First, pain symptoms and sleep problems can be seen as causes of emotional problems. For example, as they build up difficulties in daily living, for example, regarding peer relations, school, and family (Haraldstad et al., 2011, Paavonen et al., 2002, Roth-Isigkeit et al., 2005, Schulte et al., 2010), these in turn may increase the risk for psychiatric symptomatology (Van Voorhees et al., 2008). Emotional distress could also be considered simply as a consequence of the stress of experiencing pain (Tunks et al., 2008). However, in the light of earlier studies, this does not seem to at least alone explain the association, as it has been shown that elevated levels of psychiatric symptoms do not correlate solely with the current pain state. Rather, adolescents who suffered from frequent pains, reported more psychological symptoms even in the absence of pain than adolescents who suffered from infrequent pain (Fichtel and Larsson 2002). Yet another possibility would be the mechanism of central sensitization caused by earlier pain experiences, which may lead not only to a lower threshold to perceive persistent pain, but also to affective dysregulation and behavioral disturbance (Rome and Rome 2000).

Second, psychiatric difficulties can be seen as a reason for experiencing pain or sleep problems (Larsson and Sund 2007, Powers et al., 2006, Rhee et al., 2005). For example, anxiousness commonly entails physiological hyper-arousal, which can make it more difficult to settle down to sleep (Kazarian et al., 1978), and it has been hypothesized that the decrease in coping skills associated with depression also can lead to sleep problems (Patten et al., 2000). Regarding pain symptoms, possible central and peripheral mechanisms have also been described: For example, anxiety and fear influence the

sympathetic nervous system, which may lead to changes in blood lipid and sugar levels, and to increased heart rate, respiration, and muscle tension, which in turn may intensify the pain experience (Nichoson et al., 2007). In addition, it has been suggested that the changes in the neurotransmitters (e.g. serotonin) that are associated with depression, increase attention and negative affect that is focused on the minor signals from the body, which may increase the reporting of pain (Bair et al., 2003).

Third, it is possible that the associations between pain symptoms, sleep problems and psychiatric difficulties are explained by shared risk factors, or by them being different dimensions of the same syndrome. It is notable that pain symptoms per se are included as a part of the diagnostic requirements for some of the anxiety disorders. Correspondingly, sleep problems are a diagnostic criterion for depression, and additionally, often associated with neuropsychiatric disorders (Owens and Mindell 2011, Paavonen et al., 2008). Some authors have suggested that there might be a syndrome-like association between anxiousness, pain symptoms, and depression in such a way that anxiety often precedes the onset of pain, which in turn is followed by the onset of depression (Merikangas et al., 1993). A similar pattern has been observed for insomnia, as when both depression and anxiety were taken into account, anxiousness predicted insomnia, but not vice versa, and insomnia predicted depression, but not vice versa (Johnson et al., 2006a). In addition, there are several factors that have been associated with pain symptoms, sleep problems, emotional difficulties, and suicidality. Examples of these are changes in the serotonine system (Adrien 2002, Stahl and Briley 2004, van Heeringen et al., 2003), negative life experiences (Juang et al., 2004, Pickles et al., 2010, Shanahan et al., 2008, Smaldone et al., 2009), and dysfunctional coping mechanisms (Bertelson and Monroe 1979, Brown 2004, Conrad et al., 2007, Garnefski et al., 2002, Garcia et al., 2012, Gregory et al., 2010, van Heeringen et al., 2003, Keefe et al., 2000), such as catastrophizing and rumination. The findings about dysfunctional coping mechanisms are also in concordance with a cognitive model (Brown 2004, Harvey 2002) stating that worrying about the symptom and its consequences leads to emotional arousal, and an increased amount of attention being paid to the symptom and the factors that might make it worse, which in turn leads to over-evaluation of the problem and to increased symptom levels and worrying, thus creating a vicious cycle.

There are some additional study results and viewpoints to be considered when discussing specifically the response to negative life events or stress among pain-suffering children. Children who suffer from pain symptoms, when compared to control children, seem to experience life events and daily stressors as more stressful, are less confident in their ability to change or adjust to them, show stronger associations between stress and physiological responses or somatic symptoms, and more easily direct attention to both painful and non-painful bodily sensations (Aromaa et al., 2000, Dorn et al., 2003, Hermann et al., 2008, Powers et al., 2006, Walker et al., 2001 and 2007). Furthermore, early adverse

life events and stress have been suggested to play a role, as they modulate the stress-response system, cause hyperalgesia, and increase the vulnerability of the individual to later suffer from stress-related somatic symptoms (Barad and Saps 2008, Charmandari et al., 2003, Dufton et al., 2008). When compared with emotional problems, it has also been shown that the increase in heart rate and blood pressure following a stressor among children with abdominal pain was similar to that among children with anxiety disorder, and higher than among healthy controls (Dorn et al., 2003). Psychological factors have also been suggested to have an effect on the relationship between stress and pain, as one study showed that the association between daily stressors and somatic symptoms was stronger among pain-suffering than among healthy children, and especially among those who also suffered from high levels of negative affectivity (Walker et al., 2001). As stress or psychiatric difficulties are found to precede or increase pain symptoms, and pain symptoms are associated with later emotional problems, it has been hypothesized that chronic stress-induced dysfunction of the hypothalamic-pituitary-adrenal axis, which reacts to both physical and psychological challenges, might be the link between chronic pain and depressive illness (Blackburn-Munro and Blackburn-Munro, 2001). It also has been proposed that common neuroanatomical structures are affected in emotional stress, depression, and persistent pain (Duric and McCarson 2006), that a malfunction of the serotonergic and noradrenergic neurons can lead to either pain or depression, or both (Stahl and Briley 2004), and that there is a broad vulnerability to depression, anxiety, and pain symptoms, rather than just to pain symptoms (Campo et al., 2007, Woodman et al., 1998).

Regarding ***sex differences*** that were found in the present study, it seems as if boys' pain symptoms predict both milder (antidepressant use) and the most severe (suicidality) adverse outcomes, whereas girls' pain symptoms only predicted antidepressant use, but not severe suicidality, by early adulthood.

Sex differences in the risk factors of suicidality have also been shown in other longitudinal studies (Achenbach et al., 1995, Sourander et al., 2009). For example, earlier findings from the present study population showed that childhood psychiatric difficulties, in particular co-morbid conduct and internalizing problems, predicted severe suicidality among boys, but not among girls (Sourander et al., 2009).

It is possible that the threshold for reporting pain is generally higher for boys (Pool et al., 2007, Wise et al. 2002), which would suggest that reported pain symptoms were more severe among boys than among girls. However, there are also several other factors that might explain the findings, such as differences associated with temperamental characteristics, hormones, social role expectations, childhood adverse events, or psychopathology. For example, both genders considered that males should tolerate more pain than females (Pool et al., 2007). Furthermore, females are more likely to visit health

care professionals, and thus more often get help for both their somatic and their psychiatric problems than their male counterparts (Beautrais 2002, Laukkanen et al., 2010). In fact, earlier studies have shown that help-seeking behavior is a protective factor for suicide (Taliaferro and Borowsky 2011), and that female suicide attempters more often suffer from severe psychiatric disorders and receive psychiatric treatment than male attempters (INSERM Collective Expertise Centre 2011). Health care professionals also seem to have a role in this respect, as they less often suggest getting help for emotional problems for adolescent males than females (Ozer et al., 2009). These factors together could possibly increase the risk for the most severe adverse outcomes among males.

The ***localization of pain*** also had an effect on adulthood outcomes. There are a number of possible explanations why headache in particular associated with antidepressant use, and abdominal pain in particular with severe suicidality.

As assessed in earlier research, both headache and abdominal pain have for the most part been associated similarly with several physiological, psychosocial, and environmental factors (Galli et al., 2007, Hershey et al., 2009, Hjern et al., 2008, Malaty et al., 2007). However, some differentiating findings have been shown. One reason that could explain the stronger association between headache and antidepressant use is the finding that headache and emotional symptoms to some degree share a genetical vulnerability (Anttila et al. 2010, Choudary et al., 2005). Regarding suicidal behavior, earlier research supports the idea that pain location is an important moderator, and abdominal pain has been cited as increasing the risk for suicidality more than other pain symptoms (Smith et al., 2004).

It is possible that abdominal pain, which in the present study could be considered as chronic, as the parental evaluation was based on the previous year, is a precursor for more severe, or different psychiatric problems than chronic headache. Of the pain symptoms that were assessed, only abdominal pain was associated with conduct problems in all analyses (i.e. eight-year-old children's self- and parent-reported pain symptoms, and 13-18-year-old adolescents' self-reported pain symptoms), whereas headache or "other" pain symptoms were not. Earlier, a four-year longitudinal study showed that self-reported conduct problems predicted the onset of abdominal pain, but only among males (El-Metwally et al. 2007). Childhood somatic symptoms have been associated with substance use in adulthood, especially among males (Fichter et al., 2009, Hofstra et al., 2002), while disruptive disorders, which are often associated with substance use (Armstrong and Costello 2002), have been linked with suicides more strongly among males than among females (Brent et al., 1999). These findings, put together, offer one possible explanation for the differences that were found between the sexes and pain localizations. Furthermore, it is possible that other factors associating with suicides, such as childhood traumatic experiences or poor coping abilities, are more prevalent

among subjects who suffer from chronic abdominal pain than among those who suffer from headache. For example, according to a recent review, functional gastrointestinal disorders, but not headache, were associated with sexual abuse (Paras et al., 2009).

In conclusion, a summary of the main results of the thesis, in the light of earlier studies, is presented in Table 9.

Table 9. Main aims and results of the thesis

Aim of the study: to examine	What was already known	Limitations of earlier studies	What this study adds
changes in the prevalence of PS and SP among 8-year-olds (years 1989, 1999, 2005)	The prevalence of HA, and possibly AP, has increased among young school children	Only HA has been studied using several identical samplings; no similar data on other PS or SP	HA, AP, OP, SP, T, and multiple simultaneous symptoms have increased from 1989 to 2005
associated psychosocial factors of PS and SP among 13-18-year-old adolescents	PS and SP, and several psychosocial factors are associated with each other	A lack of studies examining the similarities / differences in the associations with pain versus other kinds of somatic symptoms	Increasing frequency of HA, AP, SP, and the number of symptoms associated similarly with several psychosocial factors
associations between PS at age 8, and register-based antidepressant use by age 24	HA and AP in childhood/ adolescence are associated with psychiatric problems in adulthood	Few studies in general population; lack of studies on younger school children; mainly, no inclusion of childhood psychiatric difficulties; follow-up assessments based on one-time retrospective self-report only	Child-reported HA and parent-reported AP predicted antidepressant use in adolescence and early adulthood, after adjusting with demographic variables and childhood psychiatric difficulties
associations between PS at age 8, and register-based severe suicidality by age 24	Associations exist between various PS and suicidality	Only few (only one prospective) studies among children / adolescents; no studies on severe suicidality; all studies have used follow-up assessments based on one-time retrospective self-report only	Among males, parent-reported AP predicted severe suicidality, after adjusting with demographic variables and childhood psychiatric difficulties; no associations among females were found

Note: AP=abdominal pain, T=tiredness, HA=headache, OP=other pains, PS=pain symptoms, SP=sleep problems

7 CONCLUSIONS

The present study demonstrated several findings which are of significance when evaluating children or adolescents who suffer from pain symptoms or sleep problems. First, the strong associations between these symptoms indicate that if one of them is present, health care professionals should inquire about other symptoms as well. Acknowledging the possible co-occurrence is important, as suffering from multiple symptoms is increasingly associated with psychosocial problems. Second, even if the majority of the children who report these symptoms do not suffer from diagnosable mental health disorders, it is important to remember the possibility of co-occurring psychiatric difficulties. Psychiatric difficulties have been associated with a poorer prognosis for pain symptoms and sleep problems (Mulvaney et al., 2006, Patten et al., 2000), and individuals with subthreshold levels of depressive symptoms may not be different in terms of their risk for adult psychiatric difficulties from individuals who are diagnosed with major depression (Fergusson et al., 2005). Since the children who suffer from pain symptoms or sleep problems are often encountered in health care settings, this offers an opportunity to identify and refer to treatment children whose mental health problems have not been detected earlier. The other way around, health care professionals working with children who have psychiatric problems should inquire about possible co-occurring pain symptoms and sleep problems. Third, since there is an especially strong association between these health complaints and children's own report of emotional problems, questions about possible co-morbidities should be directed to the children themselves, not only to their parents, both in clinical work and in research. As the concordance between children and their parents was found to be low, and even daily symptoms may remain unnoticed by the parents, the same also applies to children's pain symptoms and sleep problems. Fourth, as pain symptoms and sleep problems were also found to be associated with substance use, victimization, and relations with teachers, inquiring about these possible risks or precipitating factors should be included in the assessment of children and adolescents who suffer from pain symptoms and sleep problems.

The present results showed a remarkable increase in the prevalence of children's pain symptoms, sleep problems, and multiple co-occurring symptoms during a relatively short time period. This may have a number of negative consequences. As the number of children suffering from pain symptoms and sleep problems increases, possibly the factors that are associated with these symptoms, such as stress in the families and school problems, also increase. Pain symptoms have also shown continuity into adulthood (Brna et al., 2005, Magni et al., 1987), and as the association between childhood pain symptoms and adulthood psychiatric difficulties was also confirmed in the present study,

it is possible that the increase in the symptom levels will be reflected in the prevalence of pain symptoms and psychiatric difficulties later in life.

In the light of present and earlier findings, it might be considered whether childhood functional pain symptoms could be seen as a marker of a higher vulnerability to react to stress, either with pain or with psychiatric problems, also in the long term. If this were the case, they might be regarded as an indication for closer monitoring and, when needed, also for preventive intervention to help the child to reduce the level of stress and manage it better. However, additional studies on the reasons that underlie the increased prevalence rates are needed in order to develop targeted preventive programs. In addition, studies providing information about factors that increase or decrease the risk for later mental health problems among pain-suffering children, are needed. However, it has already been shown that similar interventions that have been used in the treatment of emotional problems, such as relaxation and cognitive-behavioral methods, are also sufficient in the treatment of children's pain symptoms, at least in the short term (Palermo et al., 2010). Thus, it would be valuable to study whether such interventions could prevent the symptoms and impairment of these individuals during adolescence and adulthood as well.

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