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Department of Clinical Medicine, Faculty of Health Sciences

Multisite musculoskeletal pain in adolescence

The relationship with psychosocial problems, mental health and later welfare benefit receipt

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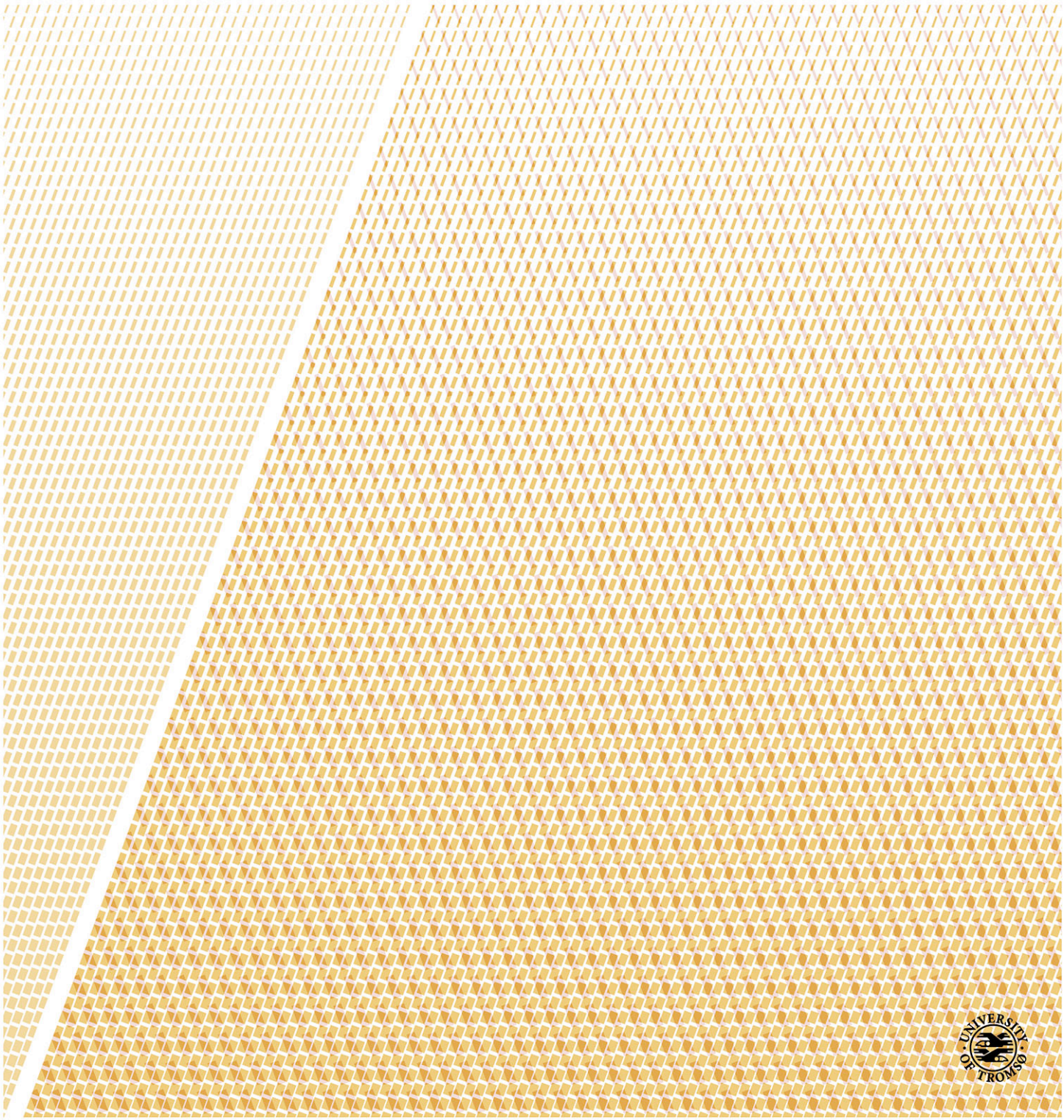
A dissertation for the degree of Philosophiae Doctor – May 2016



"As you ought not to attempt to cure the eyes without the head, or the head without the body, so neither ought you to attempt to cure the body without the soul. This is the reason why the cure of many diseases is unknown to the physicians of Greece, because they are ignorant of the whole, which ought to be studied also; for the part can never be well unless the whole is well. It is the great error of our day in the treatment of the human body, that physicians separate the soul from the body."

The Thracian King Zamolxis.
The Dialog of Charmides, Plato.

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NORSK POPULISTISK SAMMENDRAG (Norwegian summary)

Hvordan går det med smerteplaget ungdom?

En nordnorsk befolkningsundersøkelse.

Fysiske smerter er en utbredt plage blant unge. Ofte finner man ikke en klar fysisk årsak eller sykdom som kan forklare smertene, men vi vet at kroppslige smerter kan henge sammen med stress og psykiske vansker. Formålet med dette forskningsprosjektet var å undersøke sammenhengen mellom utbredte smerter og psykososiale vansker i ungdomstiden, og undersøke sammenhengen med senere psykiske lidelser og trygdeytelsesbruk fram til 25-års alderen ved kobling til nasjonale helseregistre.

Ungdomshelseundersøkelsen i Nord-Norge er en langsgående undersøkelse som følger ungdom fra hele Nord-Norge fra 10.klasse og 10 år fram i tid. En rekke forhold ved 10.klassingers liv ble undersøkt med spørreskjema i 2003–05. I 2014 koblet vi disse dataene til Norsk pasientregister og Trygderegisteret. Totalt svarte 4881 av 5877 (83 % av totalpopulasjonen) av ungdommene på spørreundersøkelsen og 3987 av dem (70 % av totalpopulasjonen) godtok kobling til helseregistre.

Utbredte smerter er en vanlig plage hos ungdom, 22,4% rapporterte å ha hatt mye smerter fra tre til fire ulike steder i kroppen det siste året. Jenter rapporterte betydelig mer smerter enn gutter og det var ingen forskjell i smerter mellom samisk og ikke-samisk ungdom. Vi fant en sterk sammenheng mellom utbredte smerter og psykososiale vansker i ungdomstiden hos begge kjønn, der angst/depresjon symptomer, negative livshendelser og skolerelatert stress var de viktigste faktorene.

Vi fant en tydelig sammenheng mellom utbredte smerter i ungdomstiden og en økende forekomsten av senere psykiske lidelser, arbeidsavklaringspenger, sykefravær og sosialstønad hos begge kjønn. Utbredte ungdomssmerter hadde sterkest sammenheng med senere angst og depressive lidelser, hos begge kjønn. Sammenhengen mellom ungdomssmertene og senere psykiske lidelser var i stor grad forklart av deltakernes psykososiale vansker i ungdomstiden.

Utbredte smerter hos unge bør tas på alvor hos begge kjønn. Helsepersonell som møter ungdom med slike plager bør undersøke hvorvidt ungdommen har psykososiale og psykiske vansker som kan tenkes å påvirke smertene. Det kan bidra til å redusere risikoen for vansker senere i livet.

ACKNOWLEDGEMENTS

The Norwegian Arctic Adolescent Health Study was a joint collaboration funded by UiT The Arctic University of Norway, The Centre for Sami Health Research and the Norwegian Institute of Public Health. The registry linkage with the Norwegian Patient Registry and the National Insurance Agency Registry was funded by the University Hospital of North Norway and Nordland Hospital. I would like to thank all the funders and all the adolescents who participated in this study.

First and foremost, I would like to thank my main supervisor Siv Kvernmo for introducing me to research and for sharing her knowledge with me. Her support, feedback, encouragement and drive has been of great importance to me.

I am also thankful to my co-supervisor Bjørn Straume for statistical advice and for interpretation and planning of paper II and III. I have appreciated our discussions of statistical issues and methods.

A personal interest in this field started when I worked at a psychiatric inpatient ward during my medical studies. I was struck by how the patients lives were influenced by their predicaments, this insight into public health has inspired my thesis. I would like to thank all my previous and current patients for having shown me how painful a troubled life can be.

I would like to thank the Department of Child and Adolescent Psychiatry, Division of Child and Adolescent Health, at the University Hospital of North Norway funding, facilities, flexibility and support and I would like to thank all of my clinical colleagues in the department for making my writing of the thesis less lonely than it could have been.

A warm thank you to my family and friends for encouragement and patience. A special thank you to Anna; our discussions and mutual support and encouragement has been vital. Thank you also to Anders for fruitful discussions and ideas and to my father for sharing his psychiatric knowledge with me. Last but not least thank you to my mother and sister for always being there, supporting me.

Tromsø, May 2016

Christian Eckhoff

LIST OF PAPERS

I. ECKHOFF C, KVERNMO S. Musculoskeletal pain in Arctic indigenous and non-indigenous adolescents, prevalence and associations with psychosocial factors: a population-based study. BMC Public Health 2014;**14**:617.

II. ECKHOFF C, STRAUME B, KVERNMO S. The relationship between multisite musculoskeletal pain in adolescence and mental health disorders in young adulthood – The NAAHS cohort study (Under review).

III. ECKHOFF C, STRAUME B, KVERNMO S. Multisite musculoskeletal pain in adolescence and later receipt of medical and social welfare benefits from adolescence into young adulthood – The NAAHS cohort study (Under review).

ABBREVIATIONS

AAP	Work assessment allowance
ANOVA	Analysis of variance
ADHD	Attention Deficit Hyperactivity Disorder
FD-trygd	The National Insurance Registry
HSCL-10	Hopkins Symptom Checklist, 10-item version
HUNT	The Nord-Trøndelag Health Study
IASP	The International Association for the Study of Pain
ICD-10	International Classification of Disease Version 10
ICPC-2	International Classification of Primary Care, Second edition
NAAHS	Norwegian Arctic Adolescent Health Study
NPR	Norwegian Patient Registry
SDQ	Strength and Difficulties Questionnaire

SUMMARY

Pain is common in otherwise healthy youth and is often associated with psychosocial problems. However, there is limited knowledge of how pain-troubled adolescents fare from adolescence into young adulthood.

To examine this, the Norwegian Arctic Adolescent Health Study, a 10th grade school-based survey (15–16-year-olds) conducted in North Norway, in 2003–2005, was linked to the Norwegian Patient Registry and the National Insurance Registry. In total, 4,881 out of 5,877 adolescents (83% of the total population) responded to the youth survey, and 3,987 (70% of the total population) consented to the registry linkage. Ten percent of the sample were indigenous Sami. Musculoskeletal pain was measured by the number of musculoskeletal pain sites (0–4). The aims of the thesis were to explore the relationship between multisite musculoskeletal pain and psychosocial problems in adolescence, and to determine whether or not adolescent musculoskeletal pain is associated with mental healthcare use and disorders in young adulthood (18–25 years of age). In addition, this thesis examines whether adolescent musculoskeletal pain is associated with later medical and social welfare benefit receipt from adolescence into young adulthood (16–24 years of age).

Similar to previous research, we found multisite musculoskeletal pain to be a common complaint in adolescence, associated with psychosocial and mental health factors in both genders. We found no major ethnic differences; indigenous Sami adolescents were not worse off. The most important adolescent factors associated with musculoskeletal pain were anxiety/depressive symptoms, negative life events, and school-related stress, which were found in both genders.

We found a significant relationship between the increasing number of adolescent musculoskeletal pain sites and an increasing proportion of later mental healthcare users, mental health disorders, sickness, medical rehabilitation and social welfare benefits, in both genders. Overall, adolescent musculoskeletal pain was not significantly associated with mental health problems in young adulthood when adjusted for adolescent psychosocial and mental health factors. However, adolescent musculoskeletal pain was significantly associated with anxiety disorders, and showing a strong trend toward mood disorders when adjusted for the adolescent factors. Adolescent musculoskeletal pain was a significant predictor of sickness benefits, in both genders, as well as social welfare benefits, in females, when adjusted for adolescent psychosocial and mental health problems.

Adolescents reporting frequent or recurrent pain may be troubled with psychosocial and mental health problems, and they are at risk of later mental health disorders, as well as health and social difficulties, from adolescence into young adulthood. Healthcare practitioners dealing with adolescents who are troubled by multiple physical symptoms should assess for psychosocial problems and mental health symptoms, offering interventions as necessary.

1 INTRODUCTION

1.1 About the thesis

This thesis explores the relationship between multisite musculoskeletal pain in adolescents and 1) psychosocial and mental health problems in adolescence, and 2) mental healthcare use and disorders in young adulthood and 3) medical and social welfare benefit receipt from adolescence into young adulthood.

The mind–body causality question has been a classical question throughout the history of philosophy and medicine. It can be traced as far back as to Plato's dialogs [1]. In the last decades, there has been growing attention to the mind–body causality concept and the underlying mechanisms in modern medicine.

Physical symptoms can be the primary presentation of emotional problems in primary healthcare settings and psychosocial problems are common among youth with unexplained medical symptoms [2]. Up until recent years, epidemiological research on pain focused on single-site pain in relationship with psychosocial problems, while epidemiological studies indicated that multisite pain is common [3, 4], showing a strong linear relationship with different health problems [4]. The lack of epidemiological studies from adolescence into young adulthood was evident concerning the relationship between physical pain and mental health problems [5]. What happens with pain troubled youth and their potential mental health problems in young adulthood? Is adolescent pain indicative of mental health problems over a longer time frame, and would adolescent psychosocial problems influence this relationship?

Adolescence and the early twenties can be a challenging developmental period and is often the time of mental illness debut [6, 7]. Chronic pain and mental health disorders are two major public health issues and research on these issues, especially in youth, can make an important contribution to public health knowledge.

The thesis is based on data from the Norwegian Arctic Adolescents Health Study [8], a cross-sectional population-based study of 15–16-year-olds in the three northernmost counties in Norway (2003–05). In order to examine the relationship between adolescent musculoskeletal pain and psychosocial and mental health problems into adulthood, the study was linked with the Norwegian Patient Registry [9] and the National Insurance Registry.

1.2 Understanding pain

Pain is a normal and common experience [3]. Pain is the body's alarm system that indicates that something is wrong. Fundamentally, it is a very useful and sensible system and is necessary for survival. Unfortunately, pain can become persistent, scary and complex, and the underlying cause can be unclear to the patient, their family and to health practitioners. Children and adolescents commonly express physical complaints without a clear physical cause [10]. For the most part it is solved by reassurance, but a high proportion of adolescents report chronic pain that disables them in their daily activities [11].

The International Association for the Study of Pain (IASP) defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" [12]. As the definition proclaims, pain is a subjective feeling and no objective test can verify or contradict the degree of the experience.

Acute pain, often due to injury, might be more straight forward with an obvious cause

compared to chronic pain. Chronic pain, however disabling, might not serve any protective function and can be present even in the absence of a clear physical cause or illness. Pain over time, which can be unclear or maladaptive, is often more associated with the central nervous system [13, 14]. Here, central processes, such as central sensitization, play the most important role in the reduction of inhibitory signals from the brain and amplification of sensory input [15–19]. As Latremoliere and Woolf state, "Pain is not then simply a reflection of peripheral inputs or pathology, but is also a dynamic reflection of central neuronal plasticity" [16].

Pain is a result of complex sensory mechanisms in the nervous system, primarily the brain. Pain and emotion share biological mechanisms [13, 14, 18, 20–22] and both, as most bodily functions, are a result of biopsychosocial processes [6, 13, 14, 18, 23]. It is well-established that psychosocial factors have an important role in chronic pain [14].

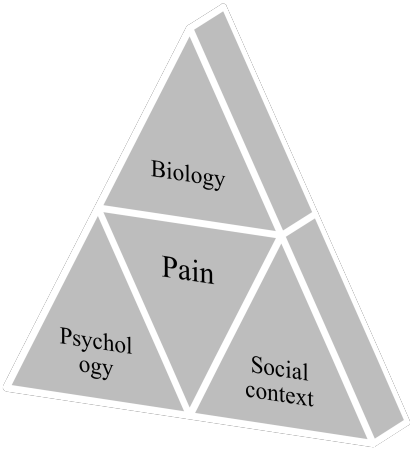
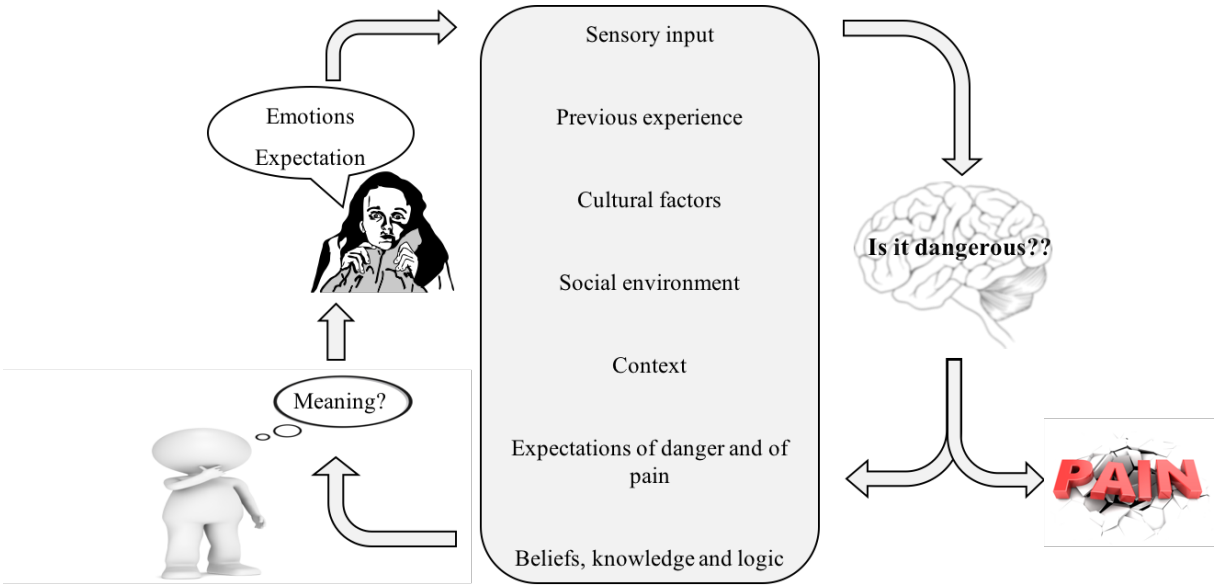


Fig 1 The aspects influencing pain and human processes in general (The biopsychosocial model).

Anxiety or fear, expectations and the social context are important factors in the modulation of pain [13, 14, 18]. All of these factors modulate the pain process (Fig. 2). Ultimately, the brain is responsible for making the final decision of whether the body is in danger and sounding the alarm in the way of pain [13, 14, 18].

Fig 2 An overview of the modern understanding of pain.



Note: Modified version of L. Moseley's original figure [14].

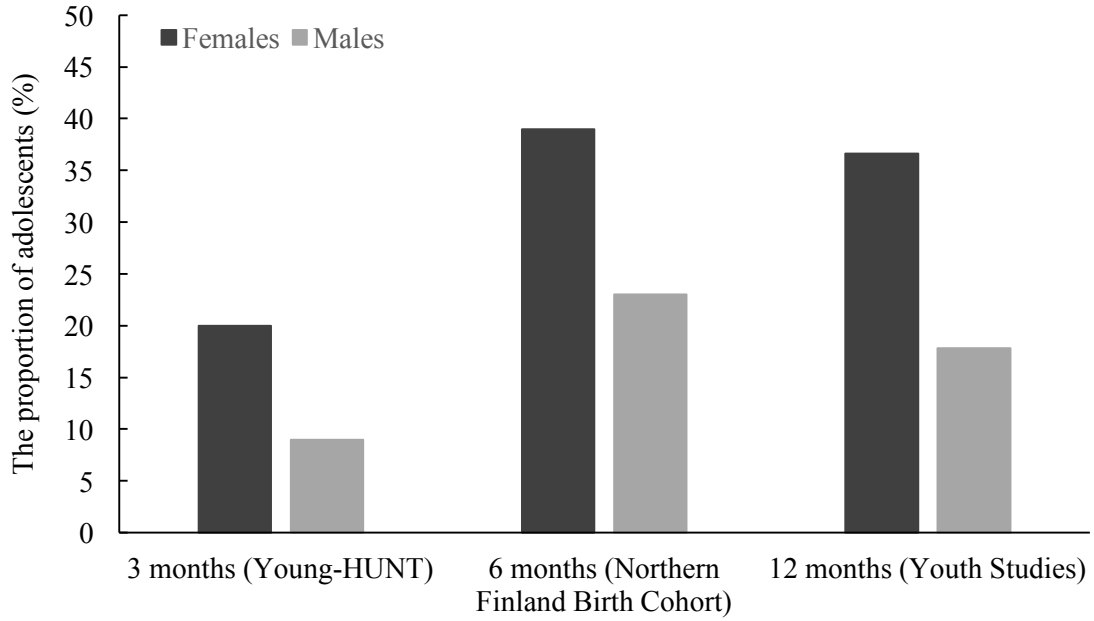
1.3 Epidemiological research on adolescent pain

1.3.1 Prevalence

Pain complaints are common in adolescents [3, 24] and tend to persist into adulthood [25–27]. Musculoskeletal pains are most prevalent in adolescents [3, 11, 28–30], showing an increasing trend in the last decades [31, 32]. Hoftun et al. found that 44.4% of the adolescents in the Young HUNT Study reported one or more pains at least once a week for at least three months, defined as chronic pain [11]. Musculoskeletal pain was most prevalent at 33.4%, followed by headache/migraine. Recurrent [3] and multiple pains [3, 11, 28–30, 33, 34] are also common in adolescence. In the Young HUNT Study 25.5% reported at least two pain sites and 8.5% reported three or more musculoskeletal pain sites [11], supported by high reports of multisite pain in the Norwegian Youth Studies [29] and in studies conducted in other European countries [30, 33, 34].

The self-reported proportions of pain are generally high, but the degree of pain-related functional disability is more unclear and difficult to examine in population studies that primarily rely on self-reports. Hoftun et al. found that 80% of the adolescents reporting chronic pain also described having one or more pain-related disabilities and there was an increased proportion of disability in those reporting multisite pain [11]. In adolescents reporting increasing mental health problems or disorders, chronic multisite pain with high disability is very prevalent [35, 36].

Fig 3 The proportion of multisite pain (three or more pain sites) in adolescents (%).



Note: Young-HUNT study: Pain at least once a week during the last 3 months [37]. Northern Finland Birth Cohort: Pain during the last 6 months [33]. Youth Studies: Often troubled by pain during the last 12 months [29].

1.3.2 Sociodemographic factors

Pain reports are generally higher in females than in males and increases with age [3, 11]. In the Young HUNT Study, 40.0% of females reported chronic musculoskeletal pain compared to 26.5% of the males [11]. The proportion of multiple chronic musculoskeletal pain was

10.9% in females and 6.1% in males, respectively [11]. Paananen et al. found that 39% of the females reported three to four musculoskeletal pain sites during a six month period compared to 23% of the males [33].

Research on the relationship between parental socioeconomic status and pain in youth has shown conflicting findings, but overall, King et al. concluded that low socioeconomic status was associated with increased pain complaints [3]. In some studies, lower parental education was associated with higher pain reports [38, 39], but other studies have found no such association [40, 41]. Low family income [38, 42] and parental unemployment are shown to be associated with increased pain reports [42].

Few studies have examined the ethno-cultural differences in physical pain and potential psychosocial differences [10, 24]. There have been no prior pain studies among the Sami, the indigenous population in Scandinavia, or in other indigenous adolescent groups.

1.3.3 Physical factors

Pain can be a result of muscular aches due to both vigorous activity and inactivity, and prior studies have shown conflicting results. There are reports of higher pain prevalence in adolescent groups reporting vigorous exercise [30, 33, 43–45], while others found no relationship with the level of physical activity [37, 46, 47]. An association between sedentary activity and pain reports has been found [33, 37, 44, 45], primarily in females [37, 44]. In addition, there is an indication of increased pain reports in adolescents with a higher BMI [30, 33, 40, 45].

1.3.4 Psychosocial factors

Adolescence may be a stressful period and several psychosocial difficulties are associated with adolescent physical complaints and pains. The high prevalence of physical complaints is considered to be a possible manifestation of psychosocial problems [2], or at least is potentially influenced by them. The minority of patients referred to pediatric outpatient clinics with medically unexplained chronic pain have somatic disorders that explain the pain [48].

Social support and positive relationships are important supportive factors. Physical complaints have been found to be associated with parental and peer problems [10, 49–53], poor resilience [35, 54] and low self-esteem [35, 50]. Parental support is important for the social functioning of adolescents with chronic pain [55], and parental chronic pain is associated with pain [56], psychosocial and mental health problems in their offspring [57, 58].

Stress, pressure and negative life events, known risk factors of mental health problems [6], are also associated with pain and other physical complaints [10, 46, 52, 53, 59–63]. Multiple somatic complaints impact daily life and function, and are associated with school difficulties and absence [49, 59].

In a clinical study, a model that included social difficulties, family structure, parental somatization and school problems predicted psychiatric morbidity in pediatric patients with medically unexplained chronic pain [48]. All the above mentioned findings emphasize the need for a dynamic understanding of pain in youth. Physical problems, such as chronic and/or recurrent pain, can have an impact on all social aspects of life and vice versa.

1.3.5 Mental health

The debut of most mental health disorders is during the 12–24 year age range [6]. Adolescence and young adulthood is the time when most people establish social relationships, academic careers and enter the job market. Mental health disorders can potentially have a negative impact on all of these areas [6]. Previous studies in youth have shown a strong relationship between pain, and other physical complaints, and mental health problems, and this relationship was found in both cross-sectional [30, 35–37, 41, 45, 46, 48, 59, 64–70] and in longitudinal studies [29, 33, 34, 43, 47, 71–79]. These findings are comparable to research in adults [80–84]. Overall, the longitudinal studies have shown a bidirectional relationship between pain and mental health problems in youth [29, 33, 34, 43, 47, 71–79]. Except for the recent findings Shanahan et al. [77] presented, most of the studies use a shorter timeframe [5] and do not examine this relationship beyond adolescence.

Up until recent years, pain studies focused on single-site pain in relationship with psychosocial and mental health problems. More recent research has shown that the association between pain and mental health problems is stronger for multisite pain compared to single-site pain [4, 30, 34, 35, 45, 75, 85]. As poor mental health is associated with several health concerns [6], an increased focus on multisite pain in relation to psychosocial and mental health problems is warranted [5].

Having multiple physical symptoms is strongly associated with mental health disorders, especially mood and anxiety disorders, influencing the clinical picture of these disorders [20, 36, 68, 82, 86–89]. Comorbid physical complaints are a common way of presenting mental health problems [10, 65, 86, 88, 89] and are important signs in the early detection of mental health problems [2, 68, 86]. Anxiety and mood disorders have been found in about 27% of patients with chronic pain complaints in primary healthcare [86]. Mental health problems are prevalent in patients referred to pediatric outpatient clinics with medically unexplained chronic pain [48, 74]. The majority of the patients continue to have pain and many struggle with mental health problems years later [74]. A matter of concern is the low recognition of mental health disorders, which are associated with high levels of physical symptoms, among adolescents in primary care [68].

Shanahan et. al.'s recent findings show that pain in children and adolescents is predictive of mood and anxiety disorders in young adulthood, and youth with persistent pain are at increased risk of later mental health problems [77]. This suggests that the relationship between pain and mental health problems in youth extends beyond adolescence. However, the influence of potential adolescent mediators needs to be examined further [77].

1.3.6 Medical and non-medical welfare benefit receipt

Mood and anxiety disorders are the most prevalent mental health disorders resulting in long-term medical benefits in Norway [90], and the mental health disorders with the strongest relationship with adolescent musculoskeletal pain [36]. Mental health problems in adolescence and young adulthood have been found to be associated with reduced workforce participation and increased medical welfare benefits in young adulthood [91–95]. Adolescent health complaints and single-site pains have been shown to be associated with long-term medical benefits in young adulthood [91, 96]. Studies in adults have shown that multisite pain predicts long-term medical benefits, both overall [97] and those due to mental health disorders

[98]. A potential relationship between adolescent pain and the later receipt of medical and non-medical benefits has only been sparsely examined.

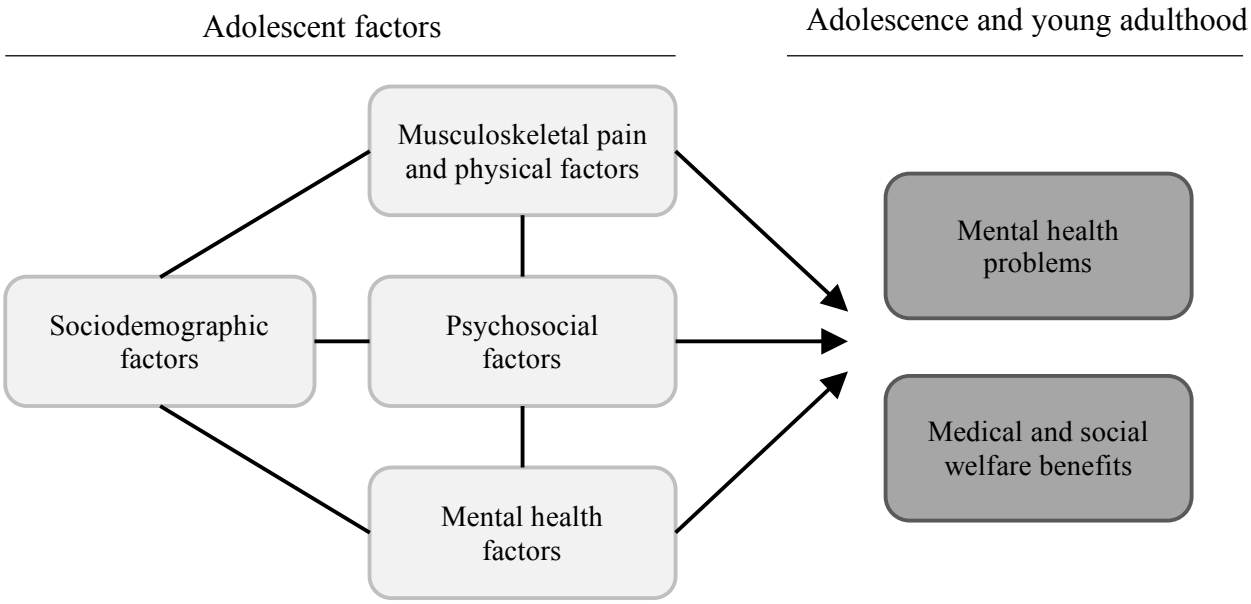
Young adulthood is an important period where major life struggles can lead to long-term benefit dependency [99, 100]. Continuous sickness benefits of more than eight weeks have been found to be predictive of later disability pension, especially due to mental health and musculoskeletal disorders, in Norwegians under 40 years of age [101]. Over the last decades, there has been an increase in long-term medical benefit recipients due to mental health disorders in 18–29-year-olds in Norway [90, 102]. Mental health disorders are the reason for medical rehabilitation benefits in two out of three cases in those under the age of 30, with a 30% increase from 1996–2008 primarily due to mood and anxiety disorders [90].

Chronic pain and mental health disorders, two major public health issues, are costly to the quality of life for young people [11, 103–105], to their families [103, 106] and to society [6, 97, 105, 107–109]. It is known that pain trajectories start early in life and the estimated economic healthcare costs of chronic pain in youth and adults are substantial [5, 109, 110]. Therefore, early detection and interventions are of major importance. Research on these issues, especially in youth, can make an important contribution to public health work.

2 AIMS OF THE THESIS

The overall aim was to explore the relationship between multisite musculoskeletal pain in adolescence and adolescent psychosocial and mental health problems, mental healthcare use and disorders in young adulthood and medical and social welfare benefit receipt from adolescence into young adulthood. To explore this, we linked the Norwegian Arctic Adolescents Health Study [8], a population-based study, with the Norwegian Patient Registry [9] section on specialized mental healthcare and with the National Insurance Registry.

Fig 4 Study design and hypothetical study relationships.



The specific aims of the research papers were as follows:

Paper I – Prevalence of multisite musculoskeletal pain in adolescence and the association with adolescent psychosocial and mental health problems

1 To examine the prevalence of multisite musculoskeletal pain in indigenous and non-indigenous Arctic adolescents.
2 To examine the association with physical, psychosocial and mental health problems in a hierarchical model and determine the importance of the factors.
3 To examine the importance of pain-related functional impairment on this association.

Paper II –The association between adolescent musculoskeletal pain and mental healthcare use and disorders in young adulthood

1 To examine if multisite musculoskeletal pain in adolescence was associated with mental healthcare use and disorders in young adulthood.
2 To determine the importance of adolescent musculoskeletal pain in relation to later mental healthcare use and mental health disorders, when adjusting for sociodemographic factors, as well as adolescent psychosocial and mental health problems.
3 To explore any potential difference in adolescent predictors of later mood, anxiety and developmental and behavioral disorders.

Paper III – The association between adolescent musculoskeletal pain and medical and social welfare benefits from adolescence into young adulthood

1 To examine if multisite musculoskeletal pain in adolescents was associated with an increase in medical and social welfare benefits receipt from adolescence into young adulthood.
2 To determine if adolescent musculoskeletal pain uniquely contributed to the prediction of later sickness and social welfare benefits when adjusting for sociodemographic, adolescent psychosocial and mental health problems.
3 To explore gender differences in adolescent predictors of later sickness and social welfare benefits.

3 MATERIAL AND METHODS

3.1 Study design and sample

The Norwegian Arctic Adolescent Health Study (NAAHS) [8] was linked to the Norwegian Patient Registry (NPR) and the National Insurance Registry in 2014. Paper I describes cross-sectional findings from the NAAHS, Paper II and III describes longitudinal findings from the registry linkage.

Fig 4 Study timeline.

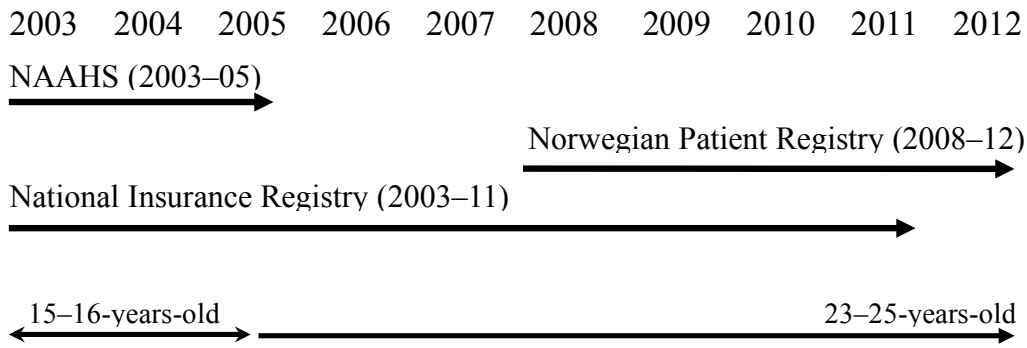
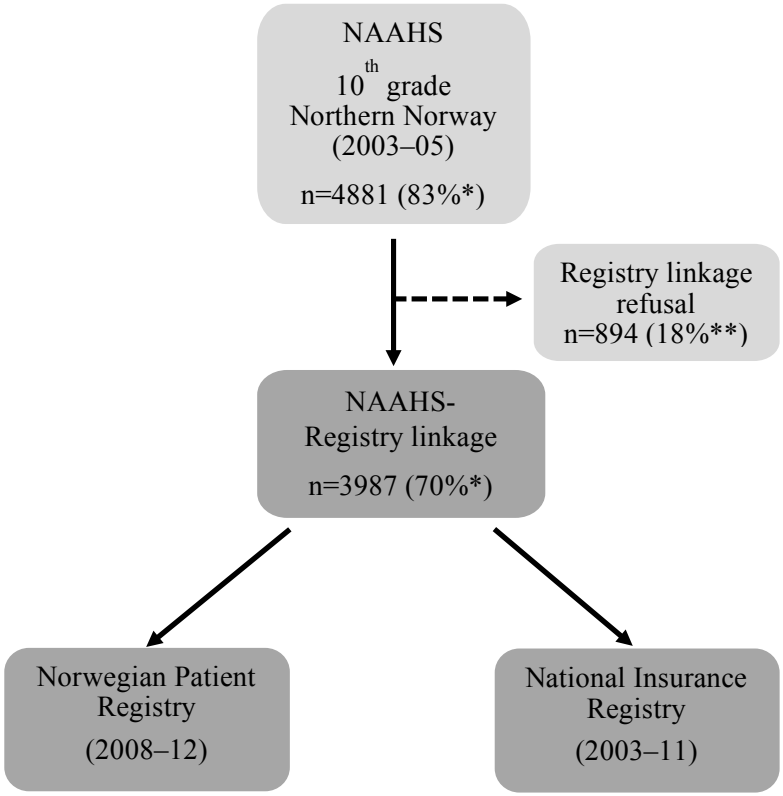


Fig 5 Study design and sample (*of the total population, **of NAAHS participants).



The Norwegian Arctic Adolescent Health Study

The NAAHS was conducted among 10th graders (15–16-year-olds) in nearly all junior high schools (292 out of 293) in the three northernmost counties in Norway, in 2003–05. The questionnaires were administered in classroom settings, monitored by project staff, and

completed during two school hours. Few students used more than 45–60 minutes. Students who were not present in class during the questionnaire administration completed the questionnaire at a later date. The students and their parents were given written information about the study, and the students provided written consent. There were no specific exclusion criteria in this study.

The Norwegian Patient Registry

The NPR [9], a detailed registry from 2008, includes personal identification of specialized healthcare utilization and diagnosis. We used available data from specialized mental healthcare from 2008 through 2012 when the participants were 18–20 to 23–25 years of age.

The National Insurance Registry

The National Insurance Registry (FD-trygd) keeps records of national medical and non-medical welfare benefits, and we used available data from 2003 through 2011. Follow-up time started at July 1st of the corresponding year the participants responded to the NAAHS, and had finished Norwegian junior high school. Resulting in a total follow-up time of 6.5–8.5 years (from 16 to 22–24 years of age).

In Norway, citizens can receive medical benefits for impairing illness resulting in reduced working ability. Medical benefits include sickness benefits (up to 52 weeks for employed citizens), medical and vocational rehabilitation, and temporary and permanent disability pension. Medical and vocational rehabilitation and temporary disability pension were organized into one single benefit in 2010, called AAP (work assessment allowance). Citizens have to be at least 18 years old to be eligible for AAP and disability pension, which requires 50% reduced work ability due to disease, injury or impairment. Social welfare benefits can be received by people who do not qualify for any other benefits and who are unable to financially support themselves.

Sample

In total, 4,881 of the 5,877 (83% of the total population) invited 10th grade students responded to the NAAHS, of whom 50.1% were females, and 10% were indigenous Sami. In the non-Sami group 64 adolescents reported having other nationalities, thus consisting mainly of majority Norwegians. The following response rates were 88% for Nordland, 82% for Troms and 71% for Finnmark. The lower response rates in Troms and Finnmark may be due to the fact that seven out of 74 schools in Troms and 12 out of 54 schools in Finnmark were not able to facilitate the health study at school, and the questionnaires were therefore mailed home to the students. All these schools had a low number of students. In Nordland one school refused to participate.

Of the NAAHS participants 3,987 (82%) consented to a future registry linkage, resulting in a 70% sample of all 15–16-year-olds in Northern Norway. The registry sample consisted of 49.9% females and 9.2% indigenous Sami.

In order to examine the representativeness of the proportion of mental healthcare users in our sample (30% nonresponders), the NPR calculated the total number of mental healthcare users in Northern Norway with the same age and registration period as the study sample. The total number of patients (n=850) was compared to total population data from the Statistics

Norway public database (n=5,715) to give and approximate cumulative prevalence of 14.9% mental health care users in the total population, which we compared our sample to.

3.2 Adolescent study measures

3.2.1 The Norwegian Arctic Adolescent Health Study and Statistics Norway

Adolescent musculoskeletal pain and physical factors

Musculoskeletal pain was measured by "yes/no" answers to the question: "*During the last 12 months have you often been troubled by pain in the head, neck/shoulder, arms/legs/knees, abdomen or back?*" Abdominal pain was excluded due to the potential confusion with menstrual pain. Headache was included based on its frequent co-existence with musculoskeletal pain and their shared mechanisms and risk factors [111]. Resulting in a variable ranging from zero to four pain sites.

Pain-related functional impairment was present if the participants reported reduced activity during leisure time due to pain (yes/no). Those reporting functional impairment due just to abdominal pain were excluded (n=23 in the registry sample).

Physical activity was measured by the question: *"How many hours per week do you spend on physical activity, to an extent that makes you sweat and/or out of breath?"* Possible answers: 0, 1–4, 5–7 and ≥8 hours per week [112].

Self-rated health was measured by the question: *"How is your health right now?"* with four possible options dichotomized into "not good/not so good" and "good/very good".

Physical injury during the last year was measured. Originally, the participants were asked if they had experienced a serious illness or injury during the last year, and were asked to describe their illness/injury. There were few reports of illness/injury of serious nature and the number of chronic illnesses reported was too low for statistical analysis. The number of physical injuries, mostly extremity injuries and some concussions, were 42.6% (n= 136) of the total responses.

Sociodemographic factors

Socioeconomic status: Information about the participants parent's occupation was obtained and classified according to the International Standard Classification of Occupation, ISCO-88 [113], and later reclassified into five categories based on the parent with the highest rated occupation. Parental work reported "unknown" was recoded into the missing group.

Parental education: Parents' highest education was obtained from Statistics Norway's education registry, registered when the participants were 15–16 years old. Parental education was categorized from "lower secondary" (≤10th grade), "upper secondary" (≤13th grade), "Lower university degree" (up to 5 years) to "higher university degree" (more than 4 years) [114].

Family income: Adolescents reported their family's economic situation compared to other families on a four-point scale from "not well off" to "very well off."

Sami ethnicity was measured by participants having one or more of the following factors: Sami parentage, Sami language competence in parents, grandparents and the participants, and Sami ethnic self-labeling [115].

Adolescent psychosocial factors

Resilience was measured by a five-item version (α=0.77) of the *General perceived self-efficacy scale* [116] with higher scores indicating higher resilience. In the five-item version questions one, two, four, seven and nine were used, and scored on a four-point Likert scale from "completely wrong" to "completely right."

Parental involvement was measured by a four-item version of the *Parental Involvement Scale* (α=0.78) [117]. Based on the questions: "My parents know where I am at and what I do in the weekend," "my parents know where I am and what I do on weekdays," "my parents know who I spend my leisure time with" and "my parents like the friends I spend time with."

Parental support (α=0.88) was measured by the following five statements: "I feel attached to my family," "my family takes me seriously," "my family values my opinions," "I mean a lot to my family" and "I can count on my family when I need help.".

Peer support (α=0.84) was measured by the following four statements: "I feel closely attached to my friends," "my friends value my opinions," "I can help/support my friends," and "I can count on my friends when I need help".

Parental involvement, *parental* and *peer support* were scored on a four-point Likert scale from "completely agree" to "completely disagree." Higher scores indicating more problems.

School-related stress (α=0.66) was measured by the following experiences: "Have you ever experienced any of the following:" "Heavy work pressure at school," "heavy pressure from others to succeed/do well at school," "find it very difficult to concentrate in class" and "find it very difficult to understand the teacher when he/she is teaching?" Responses were scored on a three-point Likert scale from "no" to "yes, often."

Negative life events (α=0.55) were measured by 12 dichotomized questions on different categories of difficult life experiences: "Have you in the last 12 months had anyone of the following problems," "conflict or fights with your parents," "parental mental health problems," "parental financial problems," "parental drug problems" or "peer problems?" Responses were measured on a four-point Likert scale from "no, never" (0), "yes, sometimes" (1), "several times" (2), to "very often" (3). Furthermore, respondents were asked, "have you in the last 12 months experienced trouble being bullied at school/ on the way to school?" with the following options: "never" (0), "sometimes" (1), "about once a week" (2), and "several times a week" (3). Also, "Have you in the last 12 months been exposed to violence?" with the following options of "never" (0), "yes, only by adolescents" (1), "yes, only by adults" (2), and "yes, by both adolescents and adults" (3). Lastly, respondents were asked, "have you in the last 12 months experienced the following:" "parental unemployment or social care," "serious illness or injury to yourself," "serious disease or injury to someone close to you," "death to someone close to you" or "sexual assault?"

For *peer problems* (α=0.52) we used the Strengths and Difficulties Questionnaire (SDQ) [118], that measures problems during the last six months.

Adolescent mental health factors

Mental health was examined by *anxiety/depression* symptoms measured by the Hopkins Symptom Checklist 10-item version (HSCL-10) [119]. The HSCL-10 (α=0.87) measures symptoms in the previous week. Psychometrics has been validated among subjects aged 16–

24, and for Sami and non-Sami [120, 121], with a cut-off of 1.85 indicating a presence of emotional distress.

For *hyperactivity* (α=0.64) and *conduct problems* (α=0.47) we used the Strengths and Difficulties Questionnaire (SDQ) subscales [118], that measures problems during the last six months. For paper III these two scales were summed into *externalizing problems* (α=0.69) [122].

Help seeking was measured by *mental health help seeking behavior* during the previous year (yes/no) and the *use of a psychiatrist/psychologist* during the previous year was dichotomized from the responses "no," "1–3 times", and "4 or more times".

3.3 Registry outcome measures

3.3.1 Mental health in young adulthood: The Norwegian Patient Registry

Mental healthcare users consisted of participants found in the specialized psychiatric patient registry, including use of *public psychiatric healthcare* and *private specialists*. We constructed an ordinal variable of "not a patient," "outpatient only" and "inpatient."

The number of *outpatient contacts* and *inpatient admissions*, and the sum of all *outpatient treatment hours* and *inpatient treatment days* was calculated.

Mental health disorders: Each participant's primary and secondary diagnoses were organized according to the main chapters in the ICD-10 [123]. We used a classical model for psychiatric diagnoses to achieve theoretically constructed groups of reasonable size. We recorded whether the participants had received a diagnosis from any of the five diagnostic groups: substance use disorders (F10–19), psychotic (F20–29), mood (F30–39), anxiety (F40–49), developmental and behavioral disorders (F50–98), and undiagnosed. We included both primary and secondary diagnoses due to an evident difference in diagnostic coding practice, making it difficult to pick out the primary disorder in patients with several diagnoses.

3.3.2 Welfare benefits from adolescence into young adulthood: The National Insurance Registry

Medical insurance benefits

Sickness benefits were measured as a continuous variable on total 100% sickness days during the registry period. Graded sick leave days were recalculated into 100% sickness days. Sickness benefits were also organized into the proportion of participants with <1, 1–3, 3–6 and 6–12 months of benefits in a 12-month period, not within a calendar year.

Sickness benefits due to mental health included disorders primarily from the ICPC-2 [124]. Primarily three diagnostic codes were used: P76 (Depressive disorder, 42.1%), P02 (Acute stress reaction, 26.2%), and P29 (Psychological symptom/complaint other, 12.0%).

Sickness benefits due to musculoskeletal problems from the ICPC-2 were dichotomized. Musculoskeletal problems due to injuries (L72-81) were excluded.

Medical rehabilitation benefits, overall and due to mental health problems, and *disability pension* were recorded.

Non-medical benefits

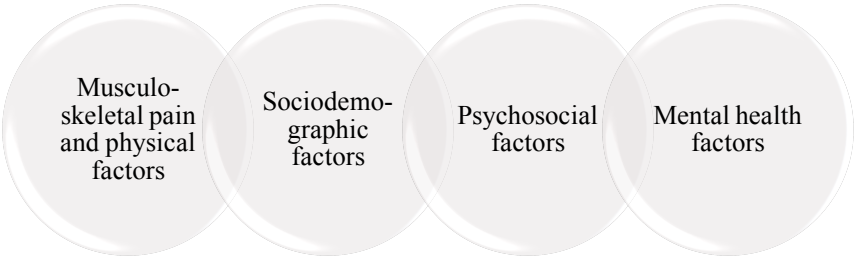
Social welfare benefits were measured as a continuous variable by the total number of months with social welfare benefits. The mean of total social welfare months was converted from

months into days in Figure 1 and Table 1 and 2 (Paper III) for comparison purposes with sickness days. Due to being recorded at a monthly basis social welfare benefits were organized into 1–3, 3–6 and 6–12 months of benefits in a 12-month period.

3.4 Statistical methods

The general thought for the methodology of this thesis was to examine the associations with the outcomes in more whole models controlling for relevant factors, while trying to minimize over-modeling. In general, the adjusting factors were controlled for in a hierarchical fashion following their respective characterized group.

Fig 6 The methodological groups of study factors.



We examined the adolescent factors to see whether the participants refusing the registry linkage differed from those who accepted. We found no significant difference between the registry sample and the missing sample except for slightly lower mean of negative life events in the missing sample. Overall, the missing sample was not worse off. Chi-square tests and one-way ANOVA were used for univariate analyses. Anxiety/depression (HSCL-10) was handled continuously in all multivariable analyses. All analyses were conducted with SPSS 21–23 (IBM software).

Paper I – Prevalence of multisite musculoskeletal pain in adolescence and the association with adolescent psychosocial and mental health problems:
Hierarchical, backward, linear multiple regression analysis was used for analysis of significant univariate predictors. Stratified analyses for gender, ethnic (Sami vs. non-Sami), and pain-related functional impairment were carried out. First, sociodemographic factors were analyzed, followed by physical, psychosocial, and mental health problems. The statistical significance level was set to .01 due to the large number of participants, except for the Sami group where .05 was chosen due to lower N.

Paper II – The association between adolescent musculoskeletal pain and mental healthcare use and disorders in young adulthood:
Initially we examined the prediction of later mental healthcare use by ordinal and multinomial regression. However, we found no linearity between the constructed ordinal groups (not a patient – outpatient only – inpatient). The main statistical difference was between the users and nonusers of mental healthcare, and not between the user groups (outpatient only vs. inpatients). We therefore present multivariable logistic regression results on mental healthcare users vs. no mental healthcare users.

Hierarchical logistic regression was used for the multivariable analysis for later mental health care use (Table 3). In Step 1 the sociodemographic (Model 1), physical factors (Model 2: musculoskeletal pain adjusted for sedentary and physical activity) and psychosocial factors (Model 3, 4 and 5) were analyzed grouped together in models based on their respective characteristic groups. Insignificant factors were not included in the next steps in order to simplify the models. In Step 2, the significant sociodemographic factors from Model 1 were added as adjustments for musculoskeletal pain alongside physical activity (Model 6). The significant psychosocial factors from Step 1 were analyzed together in Model 7. In the final model, the significant psychosocial factors from the second step (Model 7) were added to the adjustment of adolescent musculoskeletal pain.

Hierarchical logistic regression was used for the multivariable analyses on the diagnostic groups of mental health disorders (Table 4), following the same model building approach as described above for Table 3. However, only the significant factors from Step 1 in the mental healthcare use model were examined in order to simplify the models. In addition, musculoskeletal pain, physical activity and the sociodemographic factors were included in the final model regardless of if they were found insignificant in Step 1 and 2 (Model 1, 2 and 6), while insignificant psychosocial factors from Model 7 were excluded.

The statistical significance level was set at .05. Bonferroni-adjusted significance levels for multiple comparisons ($.05/n_{factors}$) are presented for the "final model" in the multivariable analysis tables (Tables 3 and 4) as a conservative comparison of significance.

Paper III – The association between adolescent musculoskeletal pain and medical and social welfare benefit receipt from adolescence into young adulthood:

Linear regression was used in the multivariable analyses on the total length of sickness and social welfare benefits (Tables 3 and 4). First, multivariable linear regression analyses with the sociodemographic, physical, psychosocial and mental health factors were analyzed in their characterized groups. The insignificant factors were excluded and the significant factors were used to adjust for adolescent musculoskeletal pain (Tables 3 and 4). Gender and parental education level were included in the models regardless due to adjustment reasons. In Tables 3 and 4 "Model 1" presents the adjustment for sociodemographic factors, "Model 2" with the addition of adolescent psychosocial factors, "Model 3" for adolescent mental health problems. To explore for gender differences "Model 3" was stratified by gender. Adjustments for follow-up time and counties did not alter the multivariable findings and are not presented in this paper.

The statistical significance level was set to .05. Bonferroni-adjusted significance levels for multiple comparisons ($.05/n_{factors}$) are presented for "Model 3" in the multivariable analysis tables as a conservative comparison of significance.

4 ETHICS

The Norwegian Data Inspectorate and the school authorities approved the NAAHS. The Regional Medical Ethical Committee approved the NAAHS and the registry linkage. The Norwegian Institute of Public Health and Statistics Norway carried out the registry linkage.

The students and their parents were given written information about the NAAHS, and the students provided written consent. The participants accepted future registry linkage at the time of the NAAHS. The participants had the opportunity to remove their consent at a later date.

Data from the NPR is used in this thesis. The interpretation and reporting of these data are the sole responsibility of the authors, and no endorsement by the NPR is intended nor should it be inferred.

5 RESULTS – SUMMARY OF RESEARCH PAPERS

5.1 Paper I – Prevalence of multisite musculoskeletal pain in adolescence and the association with adolescent psychosocial and mental health problems

The prevalence of musculoskeletal pain and mental health problems was significantly higher in females, except for arm/knee/leg pain, as was the number of musculoskeletal pain sites. In total, 29.1% of the female and 15.8% of the male adolescents reported three to four musculoskeletal pain sites. A total of 38.3% of the adolescents reported pain-related functional impairment. We found a strong association between musculoskeletal pain sites and adolescent psychosocial and mental health problems. Of the adolescents reporting zero or one musculoskeletal pain sites, 10% scored above the anxiety/depression measure cut-off (HSCL-10 $\geq$1.85), indicating emotional distress, compared to 36.5% for the adolescents reporting four pain sites. Anxiety/depression, negative life events, and school-related stress were the most important factors associated with musculoskeletal pain, especially in those reporting pain-related functional impairment. The gender difference in pain reports was due to increased reports of psychosocial problems in females. We found no major ethnic differences.

5.2 Paper II – The association between adolescent musculoskeletal pain and mental healthcare use and disorders in young adulthood

The proportion of mental healthcare users was 13.6% (59.5% were females). Multisite adolescent musculoskeletal pain was significantly associated with an increase in mental healthcare use and mental health disorders in young adulthood. The relationship was stronger for anxiety and mood disorders in both genders. Of the participants reporting zero or one musculoskeletal pain sites in adolescence, 10.3% were registered as mental healthcare users in young adulthood compared to 20.2% in those reporting three to four pain sites in adolescence. A higher proportion of mental healthcare users was found in the participants reporting pain-related functional impairment – 17.6% compared to 12.2% in the non-impaired. We found a three times increase in outpatient hours and a 3.7 times increase in the number of mental healthcare inpatients from zero to four adolescent pain sites. Overall, the association between adolescent musculoskeletal pain and later mental health problems was mediated by adolescent psychosocial and mental health problems, not by physical or sedentary activity. However, when we examined the different mental health disorders, we found musculoskeletal pain to be significantly associated with anxiety disorders, with a strong trend towards mood disorders, after adjusting for the adolescent factors.

5.3 Paper III – The association between adolescent musculoskeletal pain and medical and social welfare benefits from adolescence into young adulthood

The proportions of sickness benefit recipients, total number of sickness benefit days and sickness benefits due to mental health problems were higher in females. There was no gender difference for social welfare benefits. We found a linear relationship between adolescent musculoskeletal pain sites and the occurrence of sickness, medical rehabilitation and social welfare benefits in young adulthood. The participants reporting zero musculoskeletal pain sites in adolescence had received 17.1 sick days and 33.6 days of social welfare benefits on average, compared to 52.4 sick days and 93.9 days of social welfare benefits in those

reporting four pain sites in adolescence. The total amount of sickness and social welfare benefits was significantly higher in those reporting pain-related functional impairment compared to the non-impaired. Adolescent musculoskeletal pain was a significant predictor of sickness, in both genders, and social welfare benefits in females when adjusted for adolescent psychosocial and mental health problems. The most important adolescent psychosocial predictors were externalizing problems, less parental involvement and negative life events.

6 DISCUSSION

6.1 Methodological issues

6.1.1 Study design and sample

The main strength of this study is the linkage of a large population-based study to a patient registry. It is the first and only study inviting all 10th graders in Northern Norway to participate, including indigenous Sami adolescents. Only one high school refused to participate in the study. We had a high participation rate in the cross-sectional study and the registry linkage, and an equal gender distribution. Both aspects strengthened the validity and generalizability of the study. The 13% that refused the registry linkage did so at the age of 15–16 when they completed the questionnaire. This reduced the chance of bias in the registry outcomes as those that are seriously ill are more prone to be lost during the follow-up. Approval at a later date might have reduced the participation rate; however, all participants were informed that they could withdraw from the study at a later date if desirable. No participants have done this to date.

The registry sample was representative of the total sample and the participants refusing the registry linkage were not worse off. We had a representative sample of mental healthcare users in our sample, which was only 1.3% lower compared to the total population estimation (13.6% compared to 14.9%). A calculated estimation of mental healthcare users in our missing sample was 17.8%, supporting the notion that non-responders are more troubled. The higher proportion of mental healthcare users in the missing sample supports a mild selection bias, which is difficult to avoid in studies requiring consent. We compared the number of sickness benefit recipients in our sample to data from the statistical bank of Statistics Norway [125]. Sickness benefit recipients from the three northernmost counties in the first quarter of 2011, according to Statistics Norway, showed a 5.2% sickness absence compared to our 4.0%, indicating increased sickness benefits in the non-responders.

In light of these findings, the results of this study are representative of Norwegian adolescents. The relationship between adolescent musculoskeletal pain and mental health problems, and later medical and social welfare benefit receipt, is probably generalizable to other modern societies. Research from different nations has found a relationship between adolescent pain and later mental health problems, supporting this claim [3, 30, 33, 37]. Still, caution should be used as societal, cultural, socioeconomic and health service differences could influence these findings.

We only had one cross-sectional study linked to the registries, and regarding the timeframe of the study, there might be other factors influencing the associations found in this study. The lower explained variance of the regression models in Papers II and III can lead us to question the true impact of the significant adolescent factors. However, explained variance is a relative value, dependent on the nature of the true relationship examined. Repeated measures in adolescence may have singled out more troubled individuals compared to our single population study.

6.1.2 Statistical methods and precision

Epidemiological research depends on statistical regression models to explore associations in a population sample that hopefully resemble a true relationship found in the true population.

Psychosomatic problems are complex and the relationship between physical and mental health is truly a two-way street. The potentially influencing factors are many, while there is an upper limit to the complexity of regression models that can be derived with any acceptable degree of uncertainty [126]. Naturally, there are more important factors that are possible to highlight in a population sub-sample.

One goal of this thesis was to adjust for several relevant mediators found to be associated with pain and mental health problems. We had a large sample, with sufficient power to perform multiple comparisons. A hierarchical model was chosen as we wanted to show the dynamics of how each characteristic group of adjusting factors (sociodemographic, physical, psychosocial and mental health factors) influenced the relationship between adolescent musculoskeletal pain and the respective outcomes. Insignificant factors were generally excluded in the hierarchical steps up to the final models in order to reduce the complexity of the models and highlight the more important factors.

Bonferroni corrections were carried out to adjust for multiple comparisons in the multivariable regression models of Papers II and III. The Bonferroni correction is a conservative adjustment, adjusting the p-value at which the test is evaluated for significance based on the total number of tests being performed [127]. It targets Type 1 errors, reducing the number of incorrect rejections of the null hypotheses, at the expense of Type 2 errors and the power to detect a relationship. The Bonferroni adjustment was included to distinguish the more reliable associations from the more questionable. In Paper I, a significance level of 1% was chosen to reduce Type 1 errors.

6.1.3 The Norwegian Arctic Adolescent Health Study

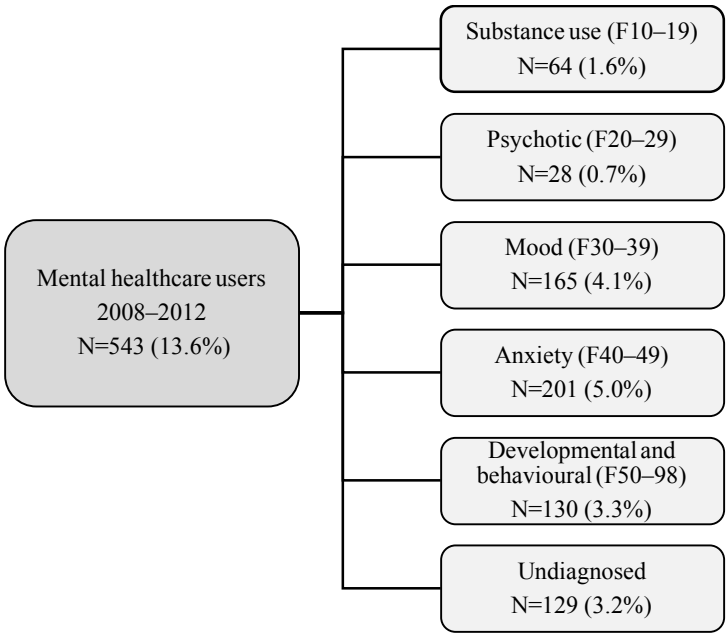
The population study relied on self-reports with the risk of information bias. The specification of a 12-month period for the pain questions may have increased the risk of recall bias compared to shorter time periods. The expression “several times” is objectively vague and is open for interpretation, but it indicates some regularity and seriousness of pain. The yes/no answers did not offer any further possibilities to differentiate the seriousness of the pain and a more stringent measure of pain, such as in the Young HUNT studies [11], might have resulted in stronger associations. However, by focusing on the number of adolescent pain sites the importance of multisite pain was still emphasized. Naturally, somatic illness could be the cause of multisite pain, but excluding a somatic cause for the pain was not possible due to the nature of the survey. In an attempt to adjust for somatic illness, we explored the descriptions of serious illness or injury during the previous year (n=366). We found a few reports of serious or chronic illness (for example, Juvenile Rheumatoid Arthritis and migraine), probably caused by underreporting, perhaps due to the subjective interpretation of the term “serious”. Most responses were normal physical injuries (extremity fractures and sprains).

The psychosocial and mental health factors in the population study included more commonly used and validated scales, such as the HSCL-10 [119, 120] and the SDQ-scales [118], and measures less frequently used outside of the Youth Studies [8]. The use of validated instruments reduces the chance of measurement error by increasing the validity and objectivity of the measure [128]. However, the HSCL-10 only measured anxiety/depression symptoms in the previous week. The less frequently used psychosocial measures make it harder to replicate the findings. Another weakness of these measures is the lack of a

timeframe for the psychosocial measures, with the exception of the SDQ-scales and the negative life events measure. Still, most scales had a high internal consistency.

6.1.4 The Norwegian Patient Registry

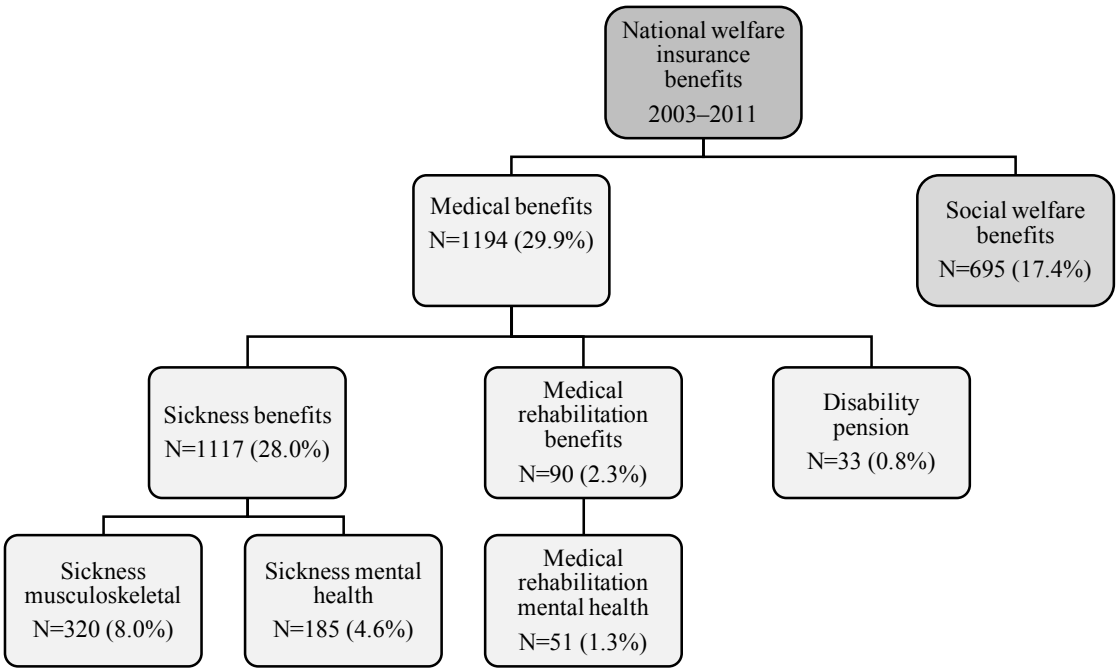
Fig 7 Mental healthcare users and disorders (percentage of the total population)



The NPR is a high quality national patient registry for specialist care; we found few errors. Ideally, it would have been preferable to differentiate between primary and secondary diagnoses, but from a close inspection of the NPR data, it was clear that attempting this would not be trustworthy due to the evident difference in the specialists' diagnostic coding practice. However, most of the primary and secondary diagnoses were within their respective main chapters of the ICD-10. A natural skepticism must be kept due to the specific diagnostic coding by health practitioners. Diagnostic coding can be a challenge, both in psychiatric and somatic care, and the practitioners' coding tradition can influence the choice of a specific diagnosis. As a result, there is a risk of misclassification in terms of specific diagnoses, a risk in all diagnostic psychiatric research. However, compared to a clinical study, we had no way to ensure that the clinicians were "on the same page".

6.1.5 The National Insurance Registry

Fig 8 Medical and social welfare benefits (percentage of the total population)



The National Insurance Registry had more errors compared to the NPR, primarily in the diagnostic coding, where 61% of disability pensions, 12% of medical rehabilitation and 21% of the sickness benefits recipients had no registered diagnosis. The diagnostic challenges were even greater for the medical insurance benefits compared to the NPR. Three diagnostic codes were primarily used by the general practitioners for sickness benefits due to mental health problems, and a few were due to anxiety disorders (5.5%), the most prevalent mental health disorder. Consequently, we did not differentiate between the ICPC-2 diagnoses for mental health problems. Most likely, the diagnoses for medical rehabilitation and disability pension were less prone to misdiagnosis due to the seriousness and the time aspect of the illness.

Contrary to previous studies where six months of sickness benefits were dichotomized with medical rehabilitation and disability pensions [91, 92, 96], we explored the outcomes on multiple levels. Since only shorter time periods, <1–3 months, of benefit reception was not significantly associated with adolescent musculoskeletal pain, we found it more reasonable to use the total amount of benefits received over the entire study period. We also recalculated graded sickness days into 100% sickness days, contrary to just counting 100% sickness days [96], increasing the validity of the measure. Some sick leave periods were missing a date for the completion of the benefit period. We used the last registered date for the benefit, a sick leave extension date, as the completion date in these cases. This made the sickness measure more reliable, but mildly underestimated.

Only 83 participants had received medical rehabilitation benefits or disability pension without prior sickness benefits. Almost half of the medical rehabilitation recipients had received sickness benefits. The exclusion of these 83 participants should not have influenced the sickness benefit findings to any great extent. Disability pension was neglected in this study due to the low number of recipients, the young age of our sample, and because it seemingly consisted of a different group of patients. We therefore found it more reasonable to explore sickness benefits as an outcome. In Norway, 34% of 19–24 year olds are students [129] and 60% working part-time [130]. Bachelor's degree students work 11 hours per week

on average [131]. Of the total population, there are only 14% of full time students that are not working, and therefore, potentially 86% (66% + 20%) of the 19–24-year-old population is entitled to sickness benefits if they work and get ill.

6.2 Discussion of results

6.2.1 Prevalence and impact of adolescent musculoskeletal pain

The prevalence rates for pain in youth vary and are influenced by the different time periods used for the pain measures [3]. In our sample, many adolescents were troubled by multisite musculoskeletal pain during a 12-month period, and females were significantly more troubled. Our prevalence rates were a bit lower, but fairly similar compared to other counties in Norway [29, 132] and the findings from the Northern Finland Birth Cohort Study [33].

The rate of pain-related functional impairment was lower than Hoftun et al.'s findings. Hoftun and colleagues examined pain that occurred at least once a week for three-months, defined as chronic pain [11]. However, we did find a similar increase in pain-related functional impairment with an increasing number of musculoskeletal pain sites [11]. Chronic multisite pain with high levels of disability is highly prevalent in adolescence in conjunction with mental health problems [35, 36], which our findings support. However, we found a relationship between the number of adolescent pain sites and mental health problems in adolescence and young adulthood regardless of pain-related functional impairment. The adolescents reporting pain-related functional impairment were at increased risk of mental health problems, sickness and receiving social welfare benefits in young adulthood. This is most likely due to the strong relationship between disabling pain and mental health problems [35, 36].

We found no difference in pain prevalence between Sami and non-Sami adolescents indicating that there is no Sami ethnicity influence on pain in our sample. These findings fit with the previous findings that demonstrated no difference in internalizing problems between Sami and non-Sami adolescents [133]. However, we did not examine for within-group differences in ethno-cultural factors such as ethnic identity and acculturation. One should be careful about drawing comparisons to other nations with more pronounced ethnic differences since the Sami are well-integrated into the Norwegian society and there are few differences in health status between Sami and non-Sami youth.

6.2.2 Gender differences in adolescent pain

Females were more troubled than males on nearly all measures – musculoskeletal pain, mental health problems in adolescence, later mental health disorders and medical benefits from adolescence into young adulthood. This supports previous findings and national data [3, 29, 35, 91, 92, 125, 134–137]. The exception was an equal gender distribution for social welfare benefits.

The gender difference for adolescent musculoskeletal pain was in large part explained by adolescent psychosocial and mental health factors. The gender difference in mental health disorders in young adulthood was explained by adolescent psychosocial and mental health factors.

The univariate relationship between musculoskeletal pain and mental health problems, and later medical and social welfare benefit receipt, was not gender specific, in spite of the increased reports of pain and mental health problems in females, supportive of previous findings [29, 33, 35, 96]. We found a clear linear relationship between these outcomes and the increasing number of musculoskeletal pain sites in both genders. Health practitioners seeing adolescents with multisite pain need to be attentive to psychosocial problems in both males and females.

The underlying biopsychosocial mechanisms responsible for the gender difference in pain and mental health problems is somewhat unclear [3, 138]. The harmful effects of stress might be negatively influenced by hormonal changes [24, 138], more social stressors, rumination and being more inclined to report problems, which might account for some of the underlying mechanisms of increased complaints in young females. There is some indication that hormonal changes in puberty lower the pain threshold in females [139]. However, female adolescents endure pain just as well as males, and the pain threshold is higher in 15–17-year-old females than in 9–11-year-olds [139], while the pain complaints increase from childhood to adolescence [3].

6.2.3 Adolescent musculoskeletal pain and psychosocial factors

We did not find any relationship between parental socioeconomic status and musculoskeletal pain in youth. However, lower family income (self-evaluated) was associated with pain in adolescence, supporting previous studies [38, 42]. Still, these measures are somewhat biased and the results are conflicting [38–41]. Family income was not associated with musculoskeletal pain when adjusted for adolescent psychosocial problems. It is more likely that low socioeconomic status and family income are risk markers associated with other factors that are themselves associated with pain [24].

Psychosocial factors have an influential role in physical complaints in youth [2], ranging from personal, parental and peer factors, to stress and adverse events [10, 35, 48–63]. Concerning supportive factors, we found that lower levels of resilience, parental involvement, and parental support, as well as increased peer problems, were associated with an increase in adolescent musculoskeletal pain. This is supportive of previous studies on adolescent physical complaints, including pain [10, 35, 49–55]. The two strongest psychosocial factors associated with adolescent musculoskeletal pain, in both genders, were school-related stress and negative life events, supporting previous findings [10, 52, 53, 59–63]. Daily stressors, pressure to succeed and adverse events are known risk factors of mental health problems [6, 140, 141] and are important factors associated with pain in adolescents. Altogether, these factors highlight the multifactorial aspect of adolescent pain.

Several of the psychosocial factors associated with adolescent pain were associated with later mental health disorders, as well as medical and social welfare benefit receipt. The most important predictors of later mental health problems were resilience, parental support, school-related stress and negative life events, in line with known knowledge [6]. Negative life events and lower levels of parental involvement were important predictors of social welfare benefits from adolescence into young adulthood. The important message is that adolescent psychosocial problems are associated with adverse outcomes and they should be taken

seriously. For many, these problems might be underlying and be presented through pain or other physical complaints [2].

6.2.4 Adolescent musculoskeletal pain and mental health problems

We found multisite musculoskeletal pain in adolescence to be associated with known psychosocial risk factors of mental health disorders. Accordingly, adolescent anxiety/depression symptoms and conduct problems were associated with multisite musculoskeletal pain in adolescence, supporting previous studies in youth [29, 30, 33–37, 41, 43, 45–48, 59, 64, 67, 69–72, 74–78]. Anxiety/depression symptoms were the strongest adolescent factor associated with adolescent musculoskeletal pain in both genders.

Approximately 50% of persons scoring above the anxiety/depression cut-off are likely to be diagnosed with a mental health disorder by a specialist [120, 142], corresponding to 9.0% of the males and 27.5% of the females that reported three or four musculoskeletal pain sites in our sample of adolescents. Conduct problems were associated with multisite musculoskeletal pain in both genders in the unadjusted analyses. However, conduct problems were significantly associated with musculoskeletal pain in males when we adjusted for other adolescent psychosocial and physical factors. This might be due to the higher rate of behavioral problems in males, which supports previous research indicating a male predominance in the relationship between behavioral problems and pain in adolescents [33, 66, 72].

Few longitudinal studies have explored the relationship between multisite pain and mental health problems in youth [29, 33, 34, 43, 47, 72] and we wanted to explore this relationship beyond adolescence. Comparable to Shanahan et al.'s [77] recent findings, we found multisite musculoskeletal pain in adolescence to be associated with mental health disorders in young adulthood in both genders. These findings are also supportive of previous longitudinal studies that have found an association between adolescent psychosomatic symptoms and mental health problems in young adulthood [73, 77, 79].

Shanahan et al. found pain in youth to be predictive of anxiety and mood disorders in young adulthood when adjusted for psychosocial factors [77]. In our results, this was the case just for anxiety disorders, but the relationship between adolescent musculoskeletal pain and mental health disorders was stronger for anxiety and mood disorders in both genders, supporting Shanahan et al.'s findings [77]. The differences in our findings may be due to the different methodology and adolescent mediators. In their study, the participants were assessed four to seven times between 9–16 years of age and the participants with pain that persisted across developmental periods were at increased risk of mental health problems in young adulthood [77]. We could not examine this in our study, but we did find a significant positive relationship between the number of adolescent pain sites and mental healthcare outpatient treatment and the proportion of inpatients in young adulthood. This indicates that adolescents with multisite pain and psychosocial problems may have an increased risk of being worse off and in need of more treatment. Zwaigenbaum et al. found an increased risk of major depression in highly somatizing adolescents, adjusted for baseline emotional disorders and gender [79]. They also found an increased risk for anxiety disorder and alcohol abuse; however, these increased relative risks were not significant [79]. Overall, these findings show that pain and other physical symptoms might be part of the clinical picture of struggling

youth. Our findings indicate that adolescents troubled with frequent or recurrent pain and psychosocial problems are at risk of mental health problems in young adulthood.

Modern science has greatly improved our understanding of pain and mental health disorders, but the daunting complexity of the central nervous system serves a challenging task in deciphering exactly how biological processes interact [23]. Even further, modern epigenetic research has expanded the boarders of complexity. Still, a relationship between mental health problems and pain is not to be doubted, though the exact mapping of the underlying multifactorial mechanisms is challenging.

Mental health problems in youth are predictive of mental health problems in adulthood [7], with the subsequent risk of social, academic and work-related difficulties [6, 94, 95, 143, 144]. A high proportion of adolescents were referred to specialized mental healthcare in young adulthood, comparable to national data [136]. We found that adolescent mental health problems were associated with later mental health disorders, as well as the receipt of medical and non-medical benefits, in line with known knowledge [7, 91–95, 143]. The main difference in our findings was that externalizing problems were a strong predictor of sickness benefits in males only, but a strong predictor of social welfare benefits in both genders. Externalizing problems can be an indication of attention deficit hyperactivity disorder, which is associated with poor school performance, comorbid disorders and several adult social and health impairments [143]. Most mental health disorders debut during the 12–24 year age range [6], and having the resources and the will to aid youth with their problems are most important to improve their outcomes.

6.2.5 Adolescent musculoskeletal pain and later medical and social welfare benefit receipt

Multisite adolescent musculoskeletal pain was associated with medical and social welfare benefits from adolescence into young adulthood in both genders. There is a lack of previous studies to compare with, but one study found single-site pains and other somatic health complaints in adolescence to be associated with welfare benefit occurrence in young adulthood [96]. Studies in adults have found multisite pain to be predictive of long-term medical benefits, both in general [97, 98, 145] and due to mental health disorders [98]. Our findings indicate that this is the case for adolescents as well.

It is natural to question the nature of the mechanisms behind the association between adolescent multisite pain and later medical and social welfare benefit receipt. The rate of chronic musculoskeletal disorders is much lower in 13–30-year-olds compared to those over 40 years of age [146]. We found a significant increase in the proportion of participants receiving sickness and medical rehabilitation benefits due to mental health problems and sickness benefits occurring as the result of musculoskeletal problems according to an increasing number of adolescent musculoskeletal pain sites. The univariate relationship was stronger for sickness benefits due to mental health problems compared to sickness benefits occurring as the result of musculoskeletal problems. This is in contrast to Øverland et al.'s findings, demonstrating that multisite pain was a stronger predictor of disability pension due to musculoskeletal disorders compared to mental health disorders in people over 40 years of age [98]. The above comparison between sickness and disability benefits should be

interpreted with some care as the measures are not equivalent. Collectively, these findings add to the evidence of a relationship between pain and mental health problems.

In spite of the relationship between musculoskeletal pain and mental health problems, adolescent musculoskeletal pain was a significant predictor of later sickness, in both genders, and social welfare benefits in females, when adjusted for adolescent psychosocial and mental health problems. The relationship between adolescent musculoskeletal pain and later social welfare benefits in females was more uncertain (p=.036), and would not be significant with a Bonferroni-adjusted significance level (p=.005). The significant prediction of sickness benefits is most likely due to a relationship between adolescent pain and physical illness or other mediating factors not included in the regression models.

The explained variances of the adolescent predictors for sickness and social welfare benefits were relatively low, probably due to the fact that there are additional present events resulting in welfare benefits other than the participants' adolescent health. This is in some part influenced by the study measures, the true nature of the associations and the fact that the associations were found in a low-risk general population sample.

Adolescence and young adulthood are important periods where most people get an education, start working and form relationships. Major life struggles in these periods can lead to long-term dependency [99, 100], a costly burden both for the individual and society. The considerable proportion of long-term sickness and social welfare benefit recipients is a concern because long-term sickness benefits are predictive of disability pensions in young adulthood [101]. The debut of these disabling disorders might start as early as adolescence; therefore, the will and resources to help struggling youth are of great importance.

7 CONCLUSION AND FUTURE PERSPECTIVES

⇒ In accordance with previous research, we found that multisite musculoskeletal pain in adolescents was common and was more likely to be associated with psychosocial and mental health problems compared to single-site pain is.

⇒ The most important adolescent factors associated with musculoskeletal pain were anxiety/depressive symptoms, negative life events and school-related stress in both genders.

⇒ We found no major ethnic differences in multisite pain in adolescence; indigenous Sami adolescents were not worse off.

⇒ We found a relationship between the number of increasing adolescent musculoskeletal pain sites and an increasing proportion of later mental healthcare use, mental health disorders, and medical and social welfare benefit receipt in both genders.

⇒ The relationship between adolescent musculoskeletal pain and later mental health disorders was stronger for anxiety and mood disorders in both genders.

⇒ Overall, the relationship between adolescent musculoskeletal pain and mental health problems in young adulthood was not significant when adjusted for adolescent psychosocial and mental health factors. However, examining the different mental health disorders, we found adolescent musculoskeletal pain to be significantly associated with later anxiety disorders when adjusted for the adolescent factors.

⇒ Adolescent musculoskeletal pain was a significant predictor of sickness, in both genders, and social welfare benefits in females when adjusted for adolescent psychosocial and mental health problems.

⇒ The most important adolescent psychosocial predictors of later sickness and social welfare benefits were externalizing problems, less parental involvement and negative life events.

⇒ The relationship between multisite pain and mental health problems was not gender specific, but females reported more problems overall.

7.1 Clinical implications

⇒ In line with current evidence, this thesis shows that frequent or recurrent pains might be part of the clinical picture of struggling youth in both genders.

⇒ Adolescents reporting frequent or recurrent pain may be troubled with psychosocial and mental health problems, and they are at risk of mental health disorders and increased medical and social welfare receipt.

⇒ Multiple pains might be a simpler clinical marker of mental health problems than the subjective degree of pain.

⇒ Healthcare practitioners dealing with adolescents troubled with multiple pains should explore and assess for psychosocial and mental health problems, offering appropriate interventions as necessary.

7.2 Research implications

⇒ This thesis supports the evidence that multisite pain in adolescence is more likely to be associated with psychosocial and mental health problems than single-site pain is. Future studies focusing on these aspects should take into account multisite pain.

⇒ This thesis shows that daily stress and negative life events are important factors associated with multisite pain, in addition to mental health problems. The temporal relationship between these factors and pain should be explored in longitudinal cohort studies.

⇒ Pain trajectories begin early in life and more high quality clinical and population-based prospective studies are needed, both from early childhood and from adolescence into adulthood. A focus on prevention targets and youth at risk for persisting symptoms is warranted.

⇒ Registry studies can be used to explore patient trajectories on a group level, in combination with population-based cohort studies or through cross-registry linkage.

9 REFERENCES

1. Plato: **The dialog of Charmides**. http://classics.mit.edu/Plato/charmides.html
2. Garralda ME: **The Interface Between Physical and Mental Health Problems and Medical Help Seeking in Children and Adolescents: A Research Perspective**. *Child Adolesc Ment Health* 2004, **9**:146–155.
3. King S, Chambers CT, Huguet A, MacNevin RC, McGrath PJ, Parker L, MacDonald AJ: **The epidemiology of chronic pain in children and adolescents revisited: A systematic review**. *Pain* 2011, **152**:2729–2738.
4. Kamaleri Y, Natvig B, Ihlebaek CM, Bruusgaard D: **Localized or widespread musculoskeletal pain: does it matter?** *Pain* 2008, **138**:41–46.
5. Jones GT: **Pain in children--a call for more longitudinal research**. *Pain* 2011, **152**:2202–2203.
6. Patel V, Flisher AJ, Hetrick S, McGorry P: **Mental health of young people: a global public-health challenge**. *Lancet* 2007, **369**:1302–1313.
7. Colman I, Wadsworth ME, Croudace TJ, Jones PB: **Forty-year psychiatric outcomes following assessment for internalizing disorder in adolescence**. *Am J Psychiatry* 2007, **164**:126–133.
8. The Norwegian Institute of Public Health. **Youth Studies** [http://www.fhi.no/artikler/?id=105586]
9. The Norwegian Directorate of Health. **The Norwegian Patient Registry** [https://helsedirektoratet.no/norsk-pasientregister-npr]
10. Campo J V, Fritsch SL: **Somatization in Children and Adolescents**. *J Am Acad Child Adolesc Psychiatry* 1994, **33**:1223–1235.
11. Hoftun GB, Romundstad PR, Zwart J-AA, Rygg M: **Chronic idiopathic pain in adolescence – high prevalence and disability: the young HUNT Study 2008**. *Pain* 2011, **152**:2259–2266.
12. The international Association for the Study of Pain. **IASP Taxonomy - Pain terms** [http://www.iasp-pain.org/Taxonomy]
13. Butler D, Moseley L: *Explain Pain*. First. Adelaide, Australia: Noigroup Publications; 2003.
14. Moseley GL: **Reconceptualising pain according to modern pain science**. *Phys Ther Rev* 2007, **12**:169–178.
15. Woolf CJ, Salter MW, Woolf CJ, Salter MW: **Neuronal Plasticity: Increasing the Gain in Pain**. *Science (80-)* 2000, **288**:1765–69.
16. Latremoliere A, Woolf CJ: **Central Sensitization: A Generator of Pain Hypersensitivity by Central Neural Plasticity**. *J Pain* 2010, **10**:895–926.
17. Ossipov MH, Dussor GO, Porreca F: **Central modulation of pain**. *J Clin Invest* 2010, **120**:3779–3787.
18. Garland EL: **Pain Processing in the Human Nervous System: A Selective Review of Nociceptive and Biobehavioral Pathways**. *Prim Care* 2012, **39**:561–571.
19. Woolf CJ: **What is this thing called pain?** *J Clin Invest* 2010, **120**:10–12.
20. Gambassi G: **Pain and depression: the egg and the chicken story revisited**. *Arch Gerontol Geriatr* 2009, **49 Suppl 1**:103–112.

21. Gatchel RJ, Peng YB, Peters ML, Fuchs PN, Turk DC: **The biopsychosocial approach to chronic pain: Scientific advances and future directions.** *Psychol Bull* 2007, **133**:581–624.
22. Blackburn-Munro G, Blackburn-Munro RE: **Chronic pain, chronic stress and depression: Coincidence or consequence?** *J Neuroendocrinol* 2001, **13**:1009–1023.
23. Brean A: **It's only mental**. *Tidsskr Nor Lægeforen* 2015, **135**:2127–28.
24. McBeth J, Jones K: **Epidemiology of chronic musculoskeletal pain**. *Best Pract Res Clin Rheumatol* 2007, **21**:403–425.
25. Brattberg G: **Do pain problems in young school children persist into early adulthood? A 13-year follow-up**. *Eur J Pain* 2004, **8**:187–199.
26. Hassett AL, Hilliard PE, Goesling J, Clauw DJ, Harte SE, Brummett CM: **Reports of chronic pain in childhood and adolescence among patients at a tertiary care pain clinic**. *J Pain* 2013, **14**:1390–1397.
27. Jones GT, Silman AJ, Power C, Macfarlane GJ: **Are common symptoms in childhood associated with chronic widespread body pain in adulthood? Results from the 1958 British Birth Cohort Study**. *Arthritis Rheum* 2007, **56**:1669–1675.
28. Perquin CW, Hazebroek-Kampschreur AA, Hunfeld JA, Bohnen AM, van Suijlekom-Smit LW, Passchier J, van der Wouden JC: **Pain in children and adolescents: a common experience**. *Pain* 2000, **87**:51–58.
29. Lien L, Green K, Thoresen M, Bjertness E: **Pain complaints as risk factor for mental distress: a three-year follow-up study**. *Eur Child Adolesc Psychiatry* 2011, **20**:509–516.
30. Rathleff MS, Roos EM, Olesen JL, Rasmussen S: **High prevalence of daily and multi-site pain--a cross-sectional population-based study among 3000 Danish adolescents.** *BMC Pediatr* 2013, **13**:191.
31. Hakala P, Rimpelä A, Salminen JJ, Virtanen SM, Rimpelä M: **Back, neck, and shoulder pain in Finnish adolescents: national cross sectional surveys**. *BMJ* 2002, **325**:743.
32. Ståhl MK, El-Metwally A, Rimpelä AH: **Time trends in single versus concomitant neck and back pain in finnish adolescents: results from national cross-sectional surveys from 1991 to 2011**. *BMC Musculoskelet Disord* 2014, **15**:1–7.
33. Paananen M V, Taimela SP, Auvinen JP, Tammelin TH, Kantomaa MT, Ebeling HE, Taanila AM, Zitting PJ, Karppinen JI: **Risk factors for persistence of multiple musculoskeletal pains in adolescence: A 2-year follow-up study**. *Eur J Pain* 2010, **14**:1026–1032.
34. Kröner-Herwig B, Gassmann J, Van Gessel H, Vath N: **Multiple pains in children and adolescents: A risk factor analysis in a longitudinal study**. *J Pediatr Psychol* 2011, **36**:420–432.
35. Skrove M, Romundstad P, Indredavik MS: **Chronic multisite pain in adolescent girls and boys with emotional and behavioral problems: the Young-HUNT study.** *Eur Child Adolesc Psychiatry* 2015, **24**:503–515.
36. Mangerud WL, Bjerkeset O, Lydersen S, Indredavik MS: **Chronic pain and pain-related disability across psychiatric disorders in a clinical adolescent sample**. *BMC Psychiatry* 2013, **13**:272.
37. Hoftun GB, Romundstad PR, Rygg M: **Factors Associated With Adolescent Chronic Non-Specific Pain, Chronic Multisite Pain, and Chronic Pain With High Disability: The Young–HUNT Study 2008**. *J Pain* 2012, **13**:874–883.

38. Grøholt E-K, Stigum H, Nordhagen R, Köhler L: **Recurrent pain in children, socio-economic factors and accumulation in families.** *Eur J Epidemiol* 2003, **18**:965–75.
39. Hoftun GB, Romundstad PR, Rygg M: **Association of parental chronic pain with chronic pain in the adolescent and young adult: family linkage data from the HUNT Study**. *JAMA Pediatr* 2013, **167**:61–69.
40. Deere KC, Clinch J, Holliday K, McBeth J, Crawley EM, Sayers A, Palmer S, Doerner R, Clark EM, Tobias JH: **Obesity is a risk factor for musculoskeletal pain in adolescents: Findings from a population-based cohort**. *Pain* 2012, **153**:1932–1938.
41. Hulsegge G, van Oostrom SH, Picavet HSJ, Twisk JWR, Postma DS, Kerkhof M, Smit H a HA, Wijga AH: **Musculoskeletal Complaints Among 11-Year-Old Children and Associated Factors**. *Am J Epidemiol* 2011, **174**:877–84.
42. Aslund C, Starrin B, Nilsson KW: **Social capital in relation to depression, musculoskeletal pain, and psychosomatic symptoms: a cross-sectional study of a large population-based cohort of Swedish adolescents**. *BMC Public Health* 2010, **10**:715.
43. Jones GT, Silman AJ, Macfarlane GJ: **Predicting the onset of widespread body pain among children**. *Arthritis Rheum* 2003, **48**:2615–2621.
44. Auvinen J, Tammelin T, Taimela S, Zitting P, Karppinen J: **Associations of physical activity and inactivity with low back pain in adolescents**. *Scand J Med Sci Sports* 2008, **18**:188–194.
45. Paananen M V, Auvinen JP, Taimela SP, Tammelin TH, Kantomaa MT, Ebeling HE, Taanila AM, Zitting PJ, Karppinen JI: **Psychosocial, mechanical, and metabolic factors in adolescents' musculoskeletal pain in multiple locations: A cross-sectional study**. *Eur J Pain* 2010, **14**:395–401.
46. Diepenmaat a CM, van der Wal MF, de Vet HCW, Hirasing R a: **Neck/shoulder, low back, and arm pain in relation to computer use, physical activity, stress, and depression among Dutch adolescents.** *Pediatrics* 2006, **117**:412–6.
47. Mikkelsson M, El-Metwally A, Kautiainen H, Auvinen A, Macfarlane GJ, Salminen JJ: **Onset, prognosis and risk factors for widespread pain in schoolchildren: a prospective 4-year follow-up study.** *Pain* 2008, **138**:681–7.
48. Konijnenberg AY, de Graeff-Meeder ER, van der Hoeven J, Kimpen JLL, Buitelaar JK, Uiterwaal CSPM, Group and the P of UO in CS: **Psychiatric Morbidity in Children With Medically Unexplained Chronic Pain: Diagnosis From the Pediatrician's Perspective**. *Pediatrics* 2006, **117**:889–897.
49. van Geelen SM, Rydelius P-A, Hagquist C: **Somatic symptoms and psychological concerns in a general adolescent population: Exploring the relevance of DSM-5 somatic symptom disorder**. *J Psychosom Res* 2015, **79**:251–8.
50. Rhee H, Holditch-Davis D, Miles MS: **Patterns of physical symptoms and relationships with psychosocial factors in adolescents**. *Psychosom Med* 2005, **67**:1006–1012.
51. Berntsson LT, Kohler L, Gustafsson JE: **Psychosomatic complaints in schoolchildren: a Nordic comparison**. *Scand J Public Health* 2001, **29**:44–54.
52. Gini G, Pozzoli T: **Bullied Children and Psychosomatic Problems: A Meta-analysis**. *Pediatrics* 2013, **132**:720–729.
53. Voerman JS, Vogel I, De Waart F, Westendorp T, Timman R, Busschbach JJ V, Van De

Looij-Jansen P, De Klerk C: **Bullying, abuse and family conflict as risk factors for chronic pain among Dutch adolescents**. *Eur J Pain* 2015, **19**:1544–1551.
54. Simonsson B, Nilsson KW, Leppert J, Diwan VK: **Psychosomatic complaints and sense of coherence among adolescents in a county in Sweden: a cross-sectional school survey**. *Biopsychosoc Med* 2008, **2**:4.
55. Gauntlett-Gilbert J, Eccleston C: **Disability in adolescents with chronic pain: Patterns and predictors across different domains of functioning**. *Pain* 2007, **131**:132–141.
56. Saunders K, Korff M Von, Leresche L, Mancl L: **Relationship of common pain conditions in mothers and children.** *Clin J Pain* 2007, **23**:204–13.
57. Kaasbøll J, Lydersen S, Indredavik MS: **Psychological symptoms in children of parents with chronic pain - the HUNT study**. *Pain* 2012, **153**:1054–1062.
58. Kaasbøll J, Ranøyen I, Nilsen W, Lydersen S, Indredavik MS: **Associations between parental chronic pain and self-esteem, social competence, and family cohesion in adolescent girls and boys - family linkage data from the HUNT study.** *BMC Public Health* 2015, **15**:817.
59. Hjern A, Alfven G, Ostberg V: **School stressors, psychological complaints and psychosomatic pain**. *Acta Paediatr* 2008, **97**:112–117.
60. Haavet OR, Straand J, Saugstad OD, Grunfeld B: **Illness and exposure to negative life experiences in adolescence: two sides of the same coin? A study of 15-year-olds in Oslo, Norway**. *Acta Paediatr* 2004, **93**:405–411.
61. Østerås B, Sigmundsson H, Haga M: **Perceived stress and musculoskeletal pain are prevalent and significantly associated in adolescents: an epidemiological cross-sectional study**. *BMC Public Health* 2015, **15**:1081.
62. Alfven G, Östberg V, Hjern A: **Stressor, perceived stress and recurrent pain in Swedish schoolchildren**. *J Psychosom Res* 2008, **65**:381–387.
63. Stensland SO, Dyb G, Thoresen S, Wentzel-Larsen T, Zwart JA: **Potentially traumatic interpersonal events, psychological distress and recurrent headache in a population-based cohort of adolescents: the HUNT study**. *BMJ Open* 2013, **3**.
64. Blaauw B a, Dyb G, Hagen K, Holmen TL, Linde M, Wentzel-Larsen T, Zwart J-A: **Anxiety, depression and behavioral problems among adolescents with recurrent headache: the Young-HUNT study.** *J Headache Pain* 2014, **15**:38.
65. Campo J V, Jansen-McWilliams L, Comer DM, Kelleher KJ: **Somatization in pediatric primary care: Association with psychopathology, functional impairment, and use of services**. *J Am Acad Child Adolesc Psychiatry* 1999, **38**:1093–1101.
66. Egger HL, Costello EJ, Erkanli A, Angold A: **Somatic Complaints and Psychopathology in Children and Adolescents: Stomach Aches, Musculoskeletal Pains, and Headaches**. *J Am Acad Child Adolesc Psychiatry* 1999, **38**:852–860.
67. Knook LME, Konijnenberg AY, van der Hoeven J, Kimpen JLL, Buitelaar JK, van Engeland H, de Graeff-Meeder ER: **Psychiatric disorders in children and adolescents presenting with unexplained chronic pain: what is the prevalence and clinical relevancy?** *Eur Child Adolesc Psychiatry* 2011, **20**:39–48.
68. Kramer T, Garralda ME: **Psychiatric disorders in adolescents in primary care**. *Br J Psychiatry* 1998, **173**:508–513.
69. Merlijn V, Hunfeld J: **Psychosocial factors associated with chronic pain in adolescents**.

Pain 2003, **101**:33–43.
70. Mikkelsson M, Salminen JJ, Kautiainen H: **Non-specific musculoskeletal pain in preadolescents. Prevalence and 1-year persistence.** *Pain* 1997, **73**:29–35.
71. Jones GT, Watson KD, Silman AJ, Symmons DPM, Macfarlane GJ: **Predictors of low back pain in British schoolchildren: a population-based prospective cohort study**. *Pediatrics* 2003, **111**:822–828.
72. Jussila L, Paananen M, Näyhä S, Taimela S, Tammelin T, Auvinen J, Karppinen J: **Psychosocial and lifestyle correlates of musculoskeletal pain patterns in adolescence: A 2-year follow-up study**. *Eur J Pain* 2014, **18**:139–146.
73. Kinnunen P, Laukkanen E, Kylmä J: **Associations between psychosomatic symptoms in adolescence and mental health symptoms in early adulthood**. *Int J Nurs Pract* 2010, **16**:43–50.
74. Knook LM, Lijmer JG, Konijnenberg AY, Taminiau B, van Engeland H: **The course of chronic pain with and without psychiatric disorders: a 6-year follow-up study from childhood to adolescence and young adulthood**. *J Clin Psychiatry* 2012, **73**:e134–9.
75. Larsson B, Sund AM: **Emotional/behavioural, social correlates and one-year predictors of frequent pains among early adolescents: influences of pain characteristics.** *Eur J Pain* 2007, **11**:57–65.
76. Lewandowski Holley a, Law EF, Zhou C, Murphy L, Clarke G, Palermo TM: **Reciprocal longitudinal associations between pain and depressive symptoms in adolescents.** *Eur J Pain* 2013, **17**:1058–67.
77. Shanahan L, Zucker N, Copeland WE, Bondy CL, Egger HL, Costello EJ: **Childhood somatic complaints predict generalized anxiety and depressive disorders during young adulthood in a community sample**. *Psychol Med* 2015, **45**:1721–1730.
78. Wilner JG, Vranceanu A-M, Blashill AJ: **Neuroticism prospectively predicts pain among adolescents: Results from a nationally representative sample.** *J Psychosom Res* 2014, **77**:474–6.
79. Zwaigenbaum L, Szatmari P, Boyle MH, Offord DR: **Highly somatizing young adolescents and the risk of depression**. *Pediatrics* 1999, **103**:1203–1209.
80. McBeth J, Macfarlane GJ, Silman AJ: **Does chronic pain predict future psychological distress?** *Pain* 2002, **96**:239–245.
81. Kroenke K, Wu J, Bair MJ, Krebs EE, Damush TM, Tu W: **Reciprocal Relationship Between Pain and Depression: A 12-Month Longitudinal Analysis in Primary Care**. *J Pain* 2011, **12**:964–973.
82. Katona C, Peveler R, Dowrick C, Wessely S, Feinmann C, Gask L, Lloyd H, de C Williams AC, Wager E: **Pain symptoms in depression: definition and clinical significance**. *Clin Med (Northfield Il)* 2005, **5**:390–395.
83. Gerrits MMJG, van Marwijk HWJ, van Oppen P, van der Horst H, Penninx BWJH: **Longitudinal association between pain, and depression and anxiety over four years**. *J Psychosom Res* 2014, **78**:64–70.
84. Gerrits MMJG, van Oppen P, van Marwijk HWJ, Penninx BWJH, van der Horst HE: **Pain and the onset of depressive and anxiety disorders**. *Pain* 2014, **155**:53–59.
85. Kamaleri Y, Natvig B, Ihlebaek CM, Benth JS, Bruusgaard D: **Number of pain sites is associated with demographic, lifestyle, and health-related factors in the general**

population. *Eur J Pain* 2008, **12**:742–748.
86. Bair MJ, Robinson RL, Katon W, Kroenke K: **Depression and pain comorbidity: a literature review**. *Arch Intern Mededicine* 2003, **163**:2433–2445.
87. Kroenke K, Spitzer R, Williams J: **Physical symptoms in primary care: predictors of psychiatric disorders and functional impairment**. *Arch Fam Med* 1994, **3**:774–779.
88. Kroenke K, Jackson JL, Chamberlin J: **Depressive and anxiety disorders in patients presenting with physical complaints: clinical predictors and outcome**. *Am J Med* 1997, **103**:339–347.
89. Simon GE, VonKorff M, Piccinelli M, Fullerton C, Ormel J: **An international study of the relation between somatic symptoms and depression.** *N Engl J Med* 1999, **341**:1329–1335.
90. Bragstad T, Brage S: **Unge på arbeids- og helserelaterte ordninger**. *Arb og velferd* 2011:36–47.
91. De Ridder KAA, Pape K, Krokstad S, Bjørngaard JH: **Health in adolescence and subsequent receipt of social insurance benefits - The HUNT Study**. *Tidsskr Nor Lægeforen* 2015, **135**:942–8.
92. Pape K, Bjørngaard JH, Holmen TL, Krokstad S: **The welfare burden of adolescent anxiety and depression: a prospective study of 7500 young Norwegians and their families: the HUNT study.** *BMJ Open* 2012, **2**:1–4.
93. Sagatun A, Heyerdahl S, Wentzel-Larsen T, Lien L: **Medical benefits in young adulthood: a population-based longitudinal study of health behaviour and mental health in adolescence and later receipt of medical benefits**. *BMJ Open* 2015, **5**:e007139–e007139.
94. Gibb SJ, Fergusson DM, Horwood LJ: **Burden of psychiatric disorder in young adulthood and life outcomes at age 30**. *Br J Psychiatry* 2010, **197**:122–127.
95. Fergusson DM, Boden JM, Horwood LJ: **Recurrence of major depression in adolescence and early adulthood, and later mental health, educational and economic outcomes**. *Br J Psychiatry* 2007, **191**:335–342.
96. Homlong L, Rosvold EO, Bruusgaard D, Lien L, Sagatun A, Haavet OR: **A prospective population-based study of health complaints in adolescence and use of social welfare benefits in young adulthood**. *Scand J Public Health* 2015, **43**:629–637.
97. Kamaleri Y, Natvig B, Ihlebaek CM, Bruusgaard D: **Does the number of musculoskeletal pain sites predict work disability? A 14-year prospective study**. *Eur J Pain* 2009, **13**:426–430.
98. Øverland S, Harvey SB, Knudsen AK, Mykletun A, Hotopf M: **Widespread pain and medically certified disability pension in the Hordaland Health Study**. *Eur J Pain* 2012, **16**:611–620.
99. OECD: *Jobs for Youth, Norway*. Paris; 2008.
100. OECD: *Off to a Good Start? Jobs for Youth*. Paris; 2010.
101. Gjesdal S, Haug K, Ringdal PR, Vollset SE, Mæland JG: **Risiko for uførepensjonering blant unge langtidssykmeldte**. *Tidsskr Nor Lægeforen* 2015, **125**:1801–15.
102. Brage S: **Ung uførhet og psykisk sykdom**. *Arb og velferd* 2015:37–49.
103. Hunfeld JA, Perquin CW, Duivenvoorden HJ, Hazebroek-Kampschreur AAJM, Passchier J, van Suijlekom-Smit LW, van der Wouden JC: **Chronic pain and its impact on quality of life in adolescents and their families.** *J Pediatr Psychol* 2001, **26**:145–53.

104. Konijnenberg AY, Uiterwaal CSPM, Kimpen JLL, van der Hoeven J, Buitelaar JK, de Graeff-Meeder ER: **Children with unexplained chronic pain: substantial impairment in everyday life.** *Arch Dis Child* 2005, **90**:680–6.
105. Goodman A, Joyce R, Smith JP: **The long shadow cast by childhood physical and mental problems on adult life**. *Proc Natl Acad Sci U S A* 2011, **108**:6032–6037.
106. Lewandowski AS, Palermo TM, Stinson J, Handley S, Chambers CT: **Systematic review of family functioning in families of children and adolescents with chronic pain**. *J Pain* 2010, **11**:1027–1038.
107. World Health Organization (WHO): *Caring for Children and Adolescents with Mental Disorders: Setting WHO Directions.* 2003.
108. Sleed M, Eccleston C, Beecham J, Knapp M, Jordan A: **The economic impact of chronic pain in adolescence: methodological considerations and a preliminary costs-of-illness study.** *Pain* 2005, **119**:183–90.
109. Groenewald CB, Palermo TM: **The price of pain: the economics of chronic adolescent pain**. *Pain Manag* 2015, **5**:61–64.
110. Pizzo PA, Clark NM, Carter Pokras O: *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research*. 2011(June).
111. Fumal A, Schoenen J: **Tension-type headache: current research and clinical management.** *Lancet Neurol* 2008, **7**:70–83.
112. Sagatun A, Søgaard AJ, Bjertness E, Selmer R, Heyerdahl S, Sogaard A: **The association between weekly hours of physical activity and mental health: A three-year follow-up study of 15-16-year-old students in the city of Oslo, Norway**. *BMC Public Health* 2007, **7**:155.
113. Elias P, Birch M: **Establishment of Community-Wide Occupational Statistics. ISCO-88 (COM). A guide for users.** *Volume 88*. University of Warwick, IER: Institute for Employment Research; 1994:1–35.
114. Statistics Norway **Norwegian Standard Classification of Education Revised 2000** [http://www.ssb.no/a/english/publikasjoner/pdf/nos_c751_en/nos_c751_en.pdf]
115. Kvernmo SE, Heyerdahl S: **Ethnic identity in aboriginal Sami adolescents: the impact of the family and the ethnic community context**. *J Adolesc* 1996, **19**:453–463.
116. Røysamb E, Schwarzer R, Jerusalem M: **Norwegian Version of the General Perceived Self-Efficacy Scale** [http://userpage.fu-berlin.de/~health/norway.htm]
117. Alsaker FD, Olweus D, Dundas I: **A growth curve approach to the study of parental relations and depression in adolescence**. *Paper presented at the Biannual Meetings of the Society for Research in Child Development, Seattle.* 1991.
118. Goodman R, Ford T, Simmons H, Gatward R, Meltzer H: **Using the Strengths and Difficulties Questionnaire (SDQ) to screen for child psychiatric disorders in a community sample**. *Br J Psychiatry* 2000, **177**:534–539.
119. Derogatis L, Rickels K, Uhlenhuth E, Covi L, Lipman RS: **The Hopkins Symptom Checklist (HSCL): a self-report symptom inventory**. *Behav Sci (Basel)* 1974, **19**:1–15.
120. Strand BH, Dalgard OS, Tambs K, Rognerud M: **Measuring the mental health status of the Norwegian population: a comparison of the instruments SCL-25, SCL-10, SCL-5 and MHI-5 (SF-36)**. *Nord J Psychiatry* 2003, **57**:113–118.
121. Bals M, Turi AL, Vittersø J, Skre I, Kvernmo S: **Self-reported internalization**

symptoms and family factors in indigenous Sami and non-Sami adolescents in North Norway. *J Adolesc* 2011, **34**:759–766.
122. Goodman A, Lamping DL, Ploubidis GB: **When to Use Broader Internalising and Externalising Subscales Instead of the Hypothesised Five Subscales on the Strengths and Difficulties Questionnaire (SDQ): Data from British Parents, Teachers and Children**. *J Abnorm Child Psychol* 2010, **38**:1179–1191.
123. World Health Organization (WHO). **The International Classification of Diseases version 10 (ICD-10)**. *Int Classif* 1994.
124. World Organization of Family Doctors (WONCA). **International Classification of Primary Care, Second edition (ICPC-2)**
[http://www.who.int/classifications/icd/adaptations/icpc2/en/]
125. Statistics Norway. **Sickness abcense, Statistics bank** [https://www.ssb.no/en/arbeid-og-lonn/statistikker/sykefratot/kvartal/2015-12-10]
126. Babyak M: **What You See May Not Be What You Get : A Brief , Nontechnical Introduction to Overfitting in Regression-Type Models**. *Psychosom Med* 2004, **66**:411–21.
127. Gelman A, Hill J, Yajima M: **Why We (Usually) Don't Have to Worry About Multiple Comparisons**. *J Res Educ Eff* 2012, **5**:189–211.
128. Szklo M, Nieto FJ: *Epidemiologi: Beyond the Basics*. 3rd edition. Burlington, MA: Jones & Bartlett Learning; 2012.
129. Statistics Norway. **Students in tertiary education in Norway and Norwegian students abroad, by sex and age** [https://www.ssb.no/en/utdanning/statistikker/utuvh/aar/2015-05-04]
130. Barstad A, Løwe T, Thorsen LR: **Studenters inntekt , økonomi og boutgifter**. *Stat Norw* 2012, **38**.
131. Einarsen KJ: **Norske studenter bruker minst tid på studiene (Norwegian)**. *Samfunnsspeilet* 2014, **4**:16–20.
132. Lien L, Claussen B, Hauff E, Thoresen M, Bjertness E: **Bodily pain and associated mental distress among immigrant adolescents**. *Eur Child Adolesc Psychiatry* 2005, **14**:371–375.
133. Bals M, Turi AL, Skre I, Kvernmo S: **Internalization symptoms, perceived discrimination, and ethnic identity in indigenous Sami and non-Sami youth in Arctic Norway**. *Ethn Health* 2010, **15**:165–179.
134. Whiteford HA, Degenhardt L, Rehm J, Baxter AJ, Ferrari AJ, Erskine HE, Charlson FJ, Norman RE, Flaxman AD, Johns N, Burstein R, Murray CJ, Vos T: **Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010**. *Lancet* 2013, **382**:1575–86.
135. Brage AS, Nossen JP, Cathrine I, Thune O: **Sykefravær med diagnose innen psykiske**. *Arb og velferd* 2012.
136. The Norwegian Directorate of Health: *Activity Data from Specialized Mental Health Care in Norway, 2012. Volume IS-2069*; 2013.
137. Mittendorfer-Rutz E, Hensing G, Westerlund H, Backheden M, Hammarström A: **Determinants in adolescence for adult sickness absence in women and men: a 26-year follow-up of a prospective population based cohort (Northern Swedish cohort).** *BMC Public Health* 2013, **13**:1–10.
138. Thapar A, Collishaw S, Pine DS, Thapar AK: **Depression in adolescence**. *Lancet* 2012,

379:1056–1067.
139. Schmitz AK, Vierhaus M, Lohaus A: **Pain tolerance in children and adolescents: Sex differences and psychosocial influences on pain threshold and endurance**. *Eur J Pain* 2013, **17**:124–131.
140. Edwards VJ, Holden GW, Felitti VJ, Anda RF: **Relationship between multiple forms of childhood maltreatment and adult mental health in community respondents: Results from the adverse childhood experiences study**. *Am J Psychiatry* 2003, **160**:1453–1460.
141. Green JG, Mclaughlin KA, Berglund PA, Gruber MJ, Sampson NA, Zaslavsky AM, Kessler RC: **Childhood Adversities and Adult Psychiatric Disorders in the National Comorbidity Survey Replication I**. *Arch Gen Psychiatry* 2010, **67**:113–123.
142. Veijola J, Jokelainen J, Läksy K, Kantojärvi L, Kokkonen P, Järvelin M-R, Joukamaa M: **The Hopkins Symptom Checklist-25 in screening DSM-III-R axis-I disorders.** *Nord J Psychiatry* 2003, **57**:119–123.
143. Colman I, Murray J, Abbott RA, Maughan B, Kuh D, Croudace TJ, Jones PB: **Outcomes of conduct problems in adolescence: 40 year follow-up of national cohort**. *BMJ* 2009, **338**:a2981.
144. Fergusson DM, Woodward LJ: **Mental health, educational, and social role outcomes of adolescents with depression.** *Arch Gen Psychiatry* 2002, **59**:225–231.
145. Haukka E, Kaila-Kangas L, Ojajärvi A, Saastamoinen P, Holtermann A, Jørgensen MB, Karppinen J, Heliövaara M, Leino-Arjas P: **Multisite musculoskeletal pain predicts medically certified disability retirement among Finns.** *Eur J pain* 2014, **19**:1119–1128.
146. Kinge JM, Knudsen AK, Skirbekk V, Vollset SE: **Musculoskeletal disorders in Norway: prevalence of chronicity and use of primary and specialist health care services**. *BMC Musculoskelet Disord* 2015, **16**:75.

Papers I-III